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Editors' Choice
Perceived stigma by women with infertility accessing treatment in a tertiary health facility in Northern Ghana. Kyei et al., 2024. Pages 603-609
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About the cover portrait "PhD"
The stack of hefty books she carries symbolizes the extensive research and study she has undertaken to attain her PhD. The tea cup sitting on top of the books is a powerful symbol of the countless sleepless nights spent studying and researching.
Read more about the artist's perspective and the editor's view on Page 585

Summary Author Information

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The Logo is an *Adinkra* symbol rendered in the Akan language as ***Nea onnim no sua a, ohu***. It is loosely translated into English as "the one who does not know but learns, gets to know."

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Editorial

Welcome message from the Editor-in-chief

Professor Andrew Anthony Adjei
Email: hsijournal@ug.edu.gh

I welcome you to Volume 5, issue 1 of the Health Sciences Investigations (HSI) Journal. The field of biomedical sciences is experiencing an unprecedented era of innovations and discoveries. Thus, the HSI Journal continues to influence the biomedical and clinical communities worldwide with various research outcomes. Currently, the Journal is indexed in the African Journals OnLine (AJOL), the world's largest and preeminent platform for African-published scholarly journals, and Scopus, a worldwide abstract and citation database of peer-reviewed literature, including scientific journals, books, and conference proceedings. The Journal is working on indexing in other prominent online repositories. The HSI Journal's Editorial team works sedulously to maintain the quality of research articles published by the Editorial office. The current issue of the Journal has fourteen articles. Nine are original research articles, one review article, two short communications, one medical case report, and one clinical image. The medical case reports concern the comprehensive rehabilitation of a young individual with post-tuberculosis triple knee deformity and rehabilitation of a young individual with post-tuberculosis triple knee deformity. The original research articles featured in this issue cover areas such as practice awareness of some Ghanaian healthcare workers concerning pneumonia therapy in children, lactate dehydrogenase as a potential predictive index in breast cancer chemotherapy response, the impact of water, sanitation, hygiene, diarrhoea, and malnutrition on children in Chad, enhancing a conventional malaria therapy, risk factors for musculoskeletal complaints, dietary patterns and basal metabolic index among others. The commentaries in this issue are on emerging trends in surgical cases in Africa and the increasing burden of chronic diseases in Ghana, a call for behavioural interventions. The review article focuses on a medicinal plant for tropical diseases. I sincerely appreciate the assiduous Technical Team, Editorial Board Members and Reviewers for their effort in driving the vision of the Journal to be a driving force in the advancement of health sciences. I am also grateful to the Advisory Board, Authors and Publishers. I welcome suggestions, complaints, discussions and thoughts from Authors and Readers to help us improve and maintain high standards.

Thank you

Acknowledgements

The University of Ghana College of Health Sciences – the copyright owner, patron, and sponsor of the HSI Journal – has always shown a deep interest in the affairs of its constituent institutions. The Journal is indeed grateful to Professor Julius Fobil, the Provost of the College, for his immense support.

About the Editor-in-chief

Professor Andrew Anthony Adjei is a Professor of Immunology with over thirty years of biomedical and allied health sciences training and research experience. He is a Fellow of the following: Ghana Academy of Arts and Sciences (FGA), African Academy of Sciences (AAS), Ghana Association of Medical Laboratory Scientists (GAMLS) and African Sciences Institute (ASI). Professor Adjei has been Head of Department, University of Ghana (UG) School of Biomedical and Allied Health Sciences, Deputy Provost, College of Health Sciences (CHS), Director of Research, Innovation and Development (UG), Acting Director, Institutional Research and Planning Office (UG), Coordinator of Research, University of Ghana Medical School (UGMS), Editor-in-Chief, Ghana Journal of Allied Health Sciences, President of Ghana Association of Medical Laboratory Scientists, Project Coordinator, Transdisciplinary Training for Resource Efficiency and Climate Change Adaptation in Africa, Project Coordinator, Building Stronger Universities (Partnership between UG and Universities in Denmark), Project Coordinator, Fogarty Global Health Fellows Training Programme (Partnership between UGMS and University of Morehouse School of Medicine, Atlanta, Georgia, USA), and Project Coordinator, Minority in Health Research Training (Partnership between UGMS and University of Morehouse School of Medicine). Professor Adjei was the immediate past Coordinator of the Worldwide Universities Network and the Australia-Africa Universities Network. Currently, he is the Chairman of the following: Ethics and Protocol Review Committee, CHS Public Lecture Series and Scientific Conference Planning Committee, CHS Newsletter (In Focus), CHS Library Refurbishment Committee, Member of Korle Bu Teaching Hospital Institutional Review Board and the Coordinator, MPhil Programme in Immunology, at the Department of Pathology, UGMS. Professor Adjei is a reviewer of several clinical and biomedical Journals globally. He has served on various UGMS and UG committees and currently serves on both the UG and CHS Academic Boards.

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About the cover

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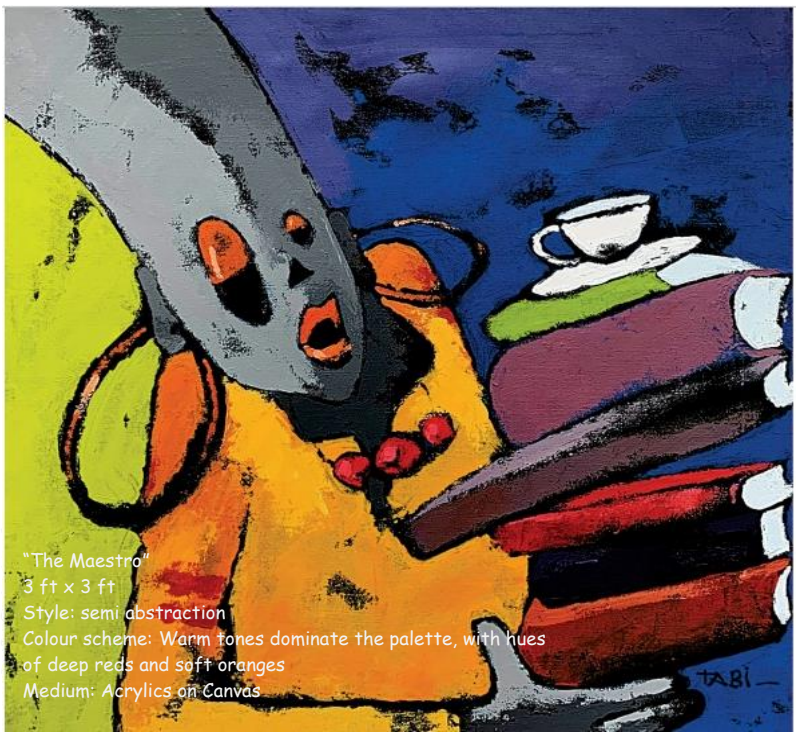

The painting is titled "PhD" and it is a striking and vibrant depiction of a female who has achieved the prestigious academic milestone of earning a doctorate. The painting showcases a female awash in a riot of vibrant colours. "PhD" is a visually arresting work. Does the artist portray the joy of achievement or the weight of knowledge?

This potrait serves as a reminder of the hard work, dedication, and sacrifice that is required to reach such a significant milestone in one's academic career.

Tabi Crentsil (2024). "*PhD*", a female who has reached the esteemed academic milestone of obtaining a PhD.

"PhD"

A painting that celebrates the pursuit of academic knowledge among women.

Artist's perspective

In appreciation, the stack of hefty books she carries symbolizes the extensive research and study she has undertaken to attain her PhD. Secondly, the teacup sitting on top of the books is a powerful symbol of the countless sleepless nights spent studying and researching. It represents the sacrifice and dedication that is required to achieve such a high level of academic success. The bright orange colours of the female's dress, the red necklace, and the lemon green background add a sense of vibrancy and energy to the painting, reflecting passion and determination. Overall, the painting "PhD" is a powerful and symbolic representation of the journey towards knowledge and academic achievement. The portrait celebrates the challenges, resilience, and triumphs of women in academia.

Take a journey through the painting and identify with the attributes. The rest of the story lies with the viewer.

A production from Tabi Crentsil, 2024

Editors' view

The artwork "PhD" encapsulates the odyssey of a doctoral student in health sciences. It also highlights the rigorous research process and the personal sacrifices made to pursue knowledge. A PhD programme typically involves a significant workload and demands long hours. This relentless pressure often leads to sleep deprivation, mirrored by the teacup in the painting. The intense focus on research productivity can exacerbate stress and contribute to burnout. The balance between demanding research projects and personal lives adds another layer of difficulty for PhD students. While these challenges affect all students, females in health sciences may face additional hurdles. The woman in the painting radiates determination, reflecting the resilience that many PhD students embody. Crucial aspects of navigating the PhD journey include excellent support from mentors and colleagues and prioritizing mental health. The artwork offers a powerful visual narrative of the demanding path towards a PhD. The HSI Journal recognizes the challenges faced by PhD students, particularly females, and advocates for research cultures that empower leaders and fuel breakthroughs.

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Commentary

HSI Journal (2024) Volume 5 (Issue 1):586-587. https://doi.org/10.46829/hsijournal.2024.6.5.1.586-587

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Progress and future directions in breast cancer research and treatment

Regina Appiah-Opong

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Keywords: Breast cancer, genomic profiling, immunotherapy, precision medicine, early detection

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Breast cancer remains a major prevalent and challenging disease worldwide including in the field of oncology [1]. Although significant progress has been made in diagnosis and treatment, the disease continues to pose substantial challenges in research and clinical fields. This commentary aims to highlight recent breakthroughs, current challenges, and future directions in breast cancer research and treatment.

The advent of genomic and molecular profiling has revolutionized our understanding of breast cancer [2]. The next-generation sequencing technique, for instance, allows for the detailed characterization of tumour genomes, leading to the identification of specific mutations and alterations that drive cancer progression. Such insights have made it possible to develop target therapies such as HER2 and PARP inhibitors, exhibiting significantly improved outcomes for some patients. Immunotherapy, particularly immune checkpoint inhibitors has shown promise in breast cancer treatment, especially triple-negative breast cancer [3]. The latter has traditionally been difficult to treat due to the absence of hormonal receptors and HER2 expression. Thus, introducing pembrolizumab and atezolizumab, both immune checkpoint inhibitors, has opened new avenues for treatment. Current research in this area is focused on identifying biomarkers and predicting responses to immunotherapy, thus, optimizing patient selection and efficacy of therapies. Also, Precision medicine is emerging as significant in breast cancer care. This treatment is based on the individual characteristics of patients and their tumours [4]. Multigene assays, including Oncotype DX and MammaPrint, may be used to assess the risk of recurrence and guide decisions about adjuvant therapy. Overtreatment is avoided when these tests are carried out and the side effects of unnecessary chemotherapy are reduced. In addition, Advances in imaging and surgical approaches have led to the adoption of minimally invasive procedures for breast cancer diagnosis and treatment [5]. Sentinel lymph node biopsy and oncoplastic surgery are some techniques that not only improve cosmetic outcomes but also reduce surgical morbidity. Moreover, techniques such as Magnetic Resonance Imaging and ultrasound have enhanced the accuracy of tumor localization and biopsy.

One of the commentaries in this issue of the Journal has stated that cancer is among non-communicable diseases (NCDs) of growing concern in Ghana [6]. According to the authors, the major underlying causes of the increasing prevalence of NCDs in Ghana are obesity and unhealthy diet. The continuing increase in NCD prevalence is anticipated, therefore, Ghana is at risk of overtaking several high-income countries. This issue also contains an original research article on a study that aimed to profile serum lactate dehydrogenase in breast cancer patients as a chemotherapy response index [7]. The researchers reported that serum LDHA mRNA levels and total LDH activity in breast cancer patients were reduced after the third cycle of chemotherapy. The serum mRNA level decreased significantly compared to the enzyme activity. The change in the LDHA mRNA level ratio identified serum LDHA mRNA as a good candidate for predicting chemotherapy response in patients.

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Resistance to therapy, whether intrinsic or acquired, remains a significant challenge in cancer therapy [1]. Notwithstanding the efficacy of targeted therapies and chemotherapies, several patients develop resistance, leading to disease progression. Understanding the mechanisms underlying resistance and developing strategies to overcome it are crucial areas of current research. Disparities in breast cancer outcomes also persist across different populations [8]. Socioeconomic status, race, and geographic location appreciably influence access to care, therapeutic options, and survival rates. Addressing these disparities through improved access to screening, education, and treatment is necessary to ensure equitable care for all patients. Another challenge to breast cancer treatment is the psychosocial impact of breast cancer diagnosis and treatment. Some patients face significant emotional, psychological, and social challenges, which can affect their quality of life and treatment adherence. Thus, integrating psychosocial support into cancer care is necessary to address the holistic needs of patients and improve their overall well-being.

For future directions, early detection remains a goal for successful breast cancer treatment. Research into novel biomarkers and imaging techniques which is ongoing is important to improve the sensitivity and specificity of early detection methods. Additionally, liquid biopsies, which detect circulating tumour DNA (ctDNA) in the blood, are promising for early diagnosis, monitoring treatment response, and detecting minimal residual disease. A combination of different therapeutic modalities, for example, targeted therapy, immunotherapy, and hormone therapy, could enhance treatment efficacy and overcome resistance. Currently, some clinical trials on such combination therapies are ongoing. Personalized cancer vaccines, designed to elicit an immune response against tumor-specific antigens, are also an emerging area of research. The needs of breast cancer survivors must be addressed by developing survivorship care plans and integrating them into routine care. Although the fight against breast cancer has seen significant progress, several challenges remain. Continued research and innovation are essential to overcome resistance to therapies, reduce disparities, and improve the quality of life for patients. Through collaboration among researchers, clinicians, patients, and policymakers, we can drive further advancements and move closer to a future where breast cancer is effectively managed and cured.

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Original Research Article

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Provider and district continuity and fragmentation of care during pregnancy and delivery in the Volta Region, Ghana

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Abstract

Background: Continuity of care (CoC) measures the extent to which a patient is attended to by a given provider over a specified period. It can be measured at the level of a patient to a provider or at the level of a provider to determine the average proportion of care provided by the provider.

Objective: The study aimed to determine the extent of provider and district continuity of care and the level of care fragmentation among districts during antenatal and delivery.

Methods: National Health Insurance claims data for 2013 in the Volta Region was used for the study, with 14,474 pregnant women meeting the inclusion criteria of delivery at a health facility and making at least two antenatal care visits. Provider continuity of care was calculated, and a social networking analysis approach was used to determine the level of care fragmentation across districts based on patient-sharing among districts. Network graphs were constructed to help visualise the fragmentation of care among districts during antenatal care and delivery.

Results: There were 196 providers from 26 districts involved in the study; 15% (n = 2,185) of the pregnant women had caesarean section (CS) delivery. The average provider and district continuity of care scores were 67% and 81%, respectively. About 12.70% (n = 1838) of all deliveries and 19.95% (n = 436) of all caesarean section deliveries were fragmented across districts. Among those with multiple providers, about 30.51% (n = 1,838) of all deliveries and 45.41% (n = 436) of CS were fragmented across districts. Eight districts that do not have hospitals located in them had more fragmentation during delivery (25% - 81%) compared to districts with hospitals.

Conclusion: Fragmentation of care during antenatal care and delivery was higher in districts without hospitals compared to districts with hospitals.

Keywords: Fragmentation of care, continuity of care, provider continuity, delivery, social network analysis, health insurance claims data

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INTRODUCTION

Continuity of care (CoC) measures the extent to which a patient is attended to by a health care provider in a logically coordinated and uninterrupted manner. [2]. Even though there is no single definition of continuity of care [3], there is agreement that it comprises interrelated dimensions, including informational continuity (availability of recorded information), longitudinal/ chronological continuity (having a regular site of care), and relational or interpersonal continuity (development of a trusting relationship between provider and patient over time) [3,4]. Continuity can be measured at the level of a patient to a single provider or a health facility [5]. It can also be measured at the level of a provider (or facility) to determine the average proportion of care provided by the provider for all the patients who visited the provider

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compared to other providers that those same patients also visited [6]. Continuity of care has been shown to be associated with improved quality of care [7].

In Ghana, the health services are organised in a five-tier functional structure consisting of the Community-based Health Planning and Services (CHPS) zone, sub-district, district, regional and national levels. The CHPS compound is the lowest level of service delivery point, undertaking both public health and basic clinical care activities at the community level [8]. The sub-district level is made up of health centres, health posts and clinics. The district level, through the district health administration, supervises and coordinates the activities of the sub-districts, with a district hospital acting as the first referral point for all the sub-districts. The district level includes both private, quasi-government and public health service providers. The district and sub-district levels mainly provide primary-level healthcare services of which maternal health (e.g. antenatal, delivery and postnatal care) is a key component. Healthcare service delivery in a district is expected to be coordinated and vertically integrated with the lower level facilities referring patients to higher levels [9].

Antenatal care, according to the World Health Organization recommendation, requires a minimum of 8 follow-up visits to a regular site of care (health facility) to aid prevention, early detection and treatment of complications that may arise in the course of the pregnancy [10]. Pregnant women are encouraged to have a regular site of care to facilitate the development of a mutual and trusting relationship between them and the provider. However, the extent to which facilities are able to retain pregnant women to repeatedly visit them and the extent to which a district as a whole is able to integrate and retain pregnant women within the district have not been estimated. The ability of facilities to retain women will enhance stronger patient-provider relationships, leading to better availability of information and a more coherent approach to managing the patient [2]. Knowledge of the extent of patient retention by facilities and the level to which the district as a whole is able to retain patients will help fashion policies to address care coordination at the district and regional levels.

MATERIALS AND METHODS

Study design and sites

This study used a retrospective cohort design approach. Using National Health Insurance claims data for January to December 2013 in the Volta Region. Fourteen thousand four hundred and seventy-four (14,474) pregnant women who met the inclusion criteria of delivery at a health facility and making at least two antenatal care visits were used with a total of 72,095 visits. For each pregnant woman, the health facilities visited, and the order in which they were visited (based on the visit date) was determined. Ethical approval was obtained from the institutional review board of the Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, before the commencement of the study (study ID: 052/15-16).

Provider continuity estimation

Provider continuity was measured from the angle of the health facility (provider) to determine the extent of repeat visits to providers during ANC and delivery [6]. First, the number of visits for a woman to each provider was counted by constructing a patient-provider matrix for each woman and provider. Second, the proportion of visits to a given provider out of the total number of visits made by a single woman was determined. The continuity of care score for each provider was calculated to represent an average of the proportion of visits that a provider got for all the women who visited the provider compared to other providers that those same women visited. Possible scores range from just greater than 0 (zero) to 1: a facility that was a woman's only provider was allocated a score of 1 for that woman. If a woman visited three facilities in equal proportions, each provider was allocated a score of 0.33 (as in row P2). Averages of all scores were calculated for each provider and then for all providers overall. The overall average score was used as the standard for comparison, and facilities that scored less than the standard were considered "below average", and those higher than the standard were deemed "above average" compared to other providers [6]. This same approach was applied to determine the district's continuity of care.

Fragmentation estimation

Fragmentation among districts was also identified based on the visit patterns of each pregnant woman using a social networking analysis approach. For each pregnant woman, the list of districts visited (the district where the facility visited is located) for care was identified in the order in which they were visited (based on the visit date). Two districts shared a pregnant woman if she visited facilities located in both districts in the course of her pregnancy and delivery. Patient sharing during delivery involves linking the most frequently visited district during ANC (source district) and the district of delivery (target district). A pregnant woman is said to have changed district during delivery if the district of delivery is different from the district where she sought most of her ANC. A matrix made up of two columns was created, with the columns representing the source district and destination district. For each pregnant woman, the source and the destination nodes were identified and appended to the matrix. The frequency of each pair of source and destination nodes was calculated. This count represents the weight of the connection between a pair of nodes. The data was subsequently converted into a graph data format using the Igraph package [11] in RStudio [12] and simplified by removing loops. The graph data was then exported to Gephi [13] using the rgexf package [14] for network visualisation and data analysis.

Network graphs were constructed to help visualise the fragmentation of care among districts during ANC and delivery using the Fruchterman-Reingold [15] and Force

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Atlas2 [16] algorithms as implemented in Gephi to optimally position facilities in the network based on their patient-sharing relations. Node colour indicates the community to which the district belongs (modularity), while the size of the node indicates the weighted degree of the node and edge weight indicates the number of pregnant women shared. Curved edges were used to indicate the direction of the edge by reading clockwise from a source node to a destination node. Network metrics (weighted in-degree and weighted out-degree) were used to determine the extent of care fragmentation and also the key districts contributing to the fragmentation. The weighted in-degree in this study was used to measure the number of pregnant women who moved in from other districts, while the weighted out-degree measured the number of pregnant women who moved out from the index district to other districts. An analysis of the extent of patient sharing among districts was undertaken to determine the number of pregnant women who had the most ANC from any given district ("potential deliveries") but had moved to other districts for delivery services. In other words, these women were expected to deliver to the districts that they had the most ANC. The proportion that moved for CS was also determined for each district. In addition, the proportion of clients who delivered in a district where they never received ANC services was also determined for each district.

RESULTS

Table 1 shows the number of visits, deliveries, district and average provider continuity of care for each of the 26 districts. There were 14,474 pregnant women included in the study, with 15% of the pregnant women having CS delivery. The average provider continuity of care score for all providers in the region was 66.5%. Hospitals had the highest score (72%) compared to CHPS (44.3%). The average district continuity of care score was 81.1% (± 28.7), with 14 districts having scores below the regional average. The district continuity of care score ranges from as low as 51.7% (± 24.3) to a maximum of 94.9% (± 16.9). Districts with higher continuity of care scores were able to retain pregnant women within the district compared to districts with low scores. As shown in Table 2, Christian Health Association of Ghana (CHAG) health facilities had an average continuity score of 67.7%, followed by Government health facilities with a score of 66.3%. The one-way analysis of variance revealed that there is no significant difference in the mean continuity of care score by facility ownership ($F = 2.13$, $p = 0.122$). However, there was a significant difference in the continuity of care score by the type of health facility ($F = 12.25$, $p < 0.001$). Pair differences were found between health centre and CHPS ($p = 0.001$), hospital and CHPS ($p < 0.001$), hospital and

Table 1. Number of deliveries, District and provider continuity of care, Volta Region, 2013. x̄ (± SD)

District	No. of Visits	Deliveries		District continuity of care score	Average Provider Continuity Score (%)			
		All	CS		Hospital	Health Centre	CHPS	All Facilities
Adaklu	217	35	-	59.0 (±26.7)	-	52.9 (±25.2)	-	52.9 (±25.2)
Afadjato South	1,147	119	-	59.3 (±27.6)	-	49.7 (±26.1)	23.9 (±09.9)	51.3 (±27.0)
Agortime Ziope	1,765	215	-	75.0 (±28.4)	-	59.0 (±31.3)	42.2 (±21.4)	58.7 (±31.2)
Akatsi North	98	7	-	51.7 (±24.3)	-	51.7 (±24.3)	-	51.7 (±24.3)
Akatsi South	754	180	22	83.2 (±26.7)	79.5 (±28.3)	45.0 (±24.0)	-	78.8 (±28.7)
Biakoye	1,832	425	74	63.6 (±32.6)	58.1 (±34.2)	53.5 (±24.3)	-	56.7 (±31.4)
Central Tongu	486	113	11	90.8 (±21.2)	62.0 (±33.4)	-	65.5 (±24.3)	63.5 (±29.7)
Ho	16,375	2,910	606	87.7 (±26.1)	74.3 (±33.0)	64.0 (±28.5)	36.2 (±22.0)	72.4 (±33.0)
Ho West	355	59	-	60.6 (±28.0)	-	60.4 (±27.5)	46.5 (±27.9)	59.3 (±28.1)
Hohoe	5,906	1,082	144	84.6 (±27.2)	74.7 (±32.6)	72.1 (±25.4)	51.5 (±32.2)	741 (±31.3)
Jasikan	2,379	549	93	75.6 (±32.1)	70.0 (±33.9)	63.6 (±30.1)	-	68.4 (±33.1)
Kadjebi	3,316	704	84	91.4 (±20.8)	62.9 (±30.2)	58.5 (±29.0)	-	60.8 (±29.7)
Keta	4,488	1,082	163	90.9 (±22.3)	73.9 (±31.1)	58.4 (±25.7)	-	69.2 (±30.5)
Ketu North	1,220	304	51	79.9 (±30.2)	79.7 (±30.7)	59.7 (±29.0)	-	76.2 (±31.3)
Ketu South	5,697	1,223	184	94.6 (±17.0)	90.1 (±22.8)	63.5 (±25.0)	-	87.3 (±24.7)
Kpando	6,890	1,407	360	76.6 (±32.4)	67.0 (±33.3)	46.4 (±29.7)	27.1 (±16.3)	61.5 (±33.7)
Krachi East	1,939	307	-	72.3 (±26.4)	-	57.4 (±28.8)	-	57.4 (±28.8)
Krachi Nchumuru	1,354	324	-	63.1 (±22.2)	-	52.5 (±24.6)	-	52.5 (±24.6)
Krachi West	3,390	641	134	70.8 (±32.2)	69.1 (±31.9)	35.5 (±16.9)	-	67.5 (±32.1)
Nkwanta North	1,748	352	-	83.3 (±21.9)	-	57.6 (±29.6)	54.3 (±22.9)	55.2 (±27.7)
Nkwanta South	3,335	769	100	73.3 (±33.6)	52.0 (±29.5)	33.7 (±16.0)	40.8 (±19.3)	49.9 (±28.3)
North Dayi	2,218	502	41	74.3 (±29.2)	68.9 (±29.2)	38.8 (±19.6)	35.6 (±19.8)	61.4 (±30.4)
North Tongu	1,889	436	61	94.9 (±16.9)	95.9 (±15.8)	78.5 (±25.9)	-	94.9 (±17.0)
South Dayi	2,843	604	43	87.5 (±24.5)	75.0 (±29.6)	53.2 (±29.7)	49.0 (±21.5)	65.5 (±31.2)
South Tongu	454	125	14	85.1 (±28.9)	60.0 (±35.9)	84.1 (±23.7)	-	72.1 (±32.6)
Grand Total	72,095	14,474	2,185	81.1 (±28.7)	72.0 (±32.4)	56.5 (±28.6)	44.3 (±23.5)	66.5 (±32.1)

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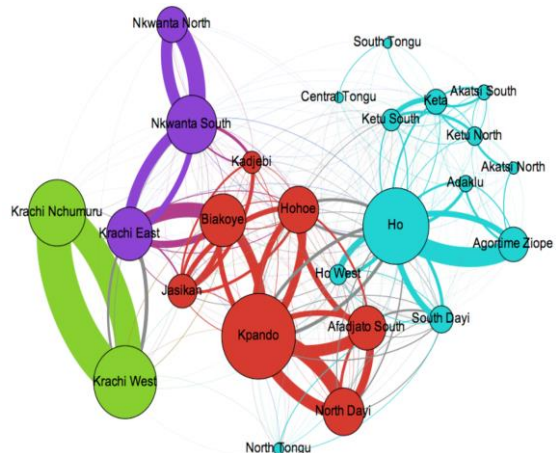

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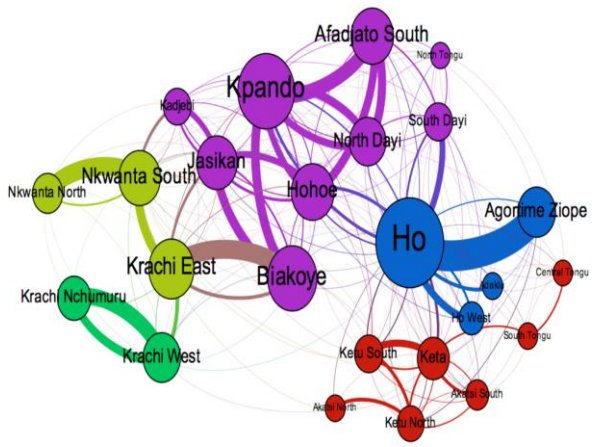

1b

Figure 1. Client sharing (a), and care fragmentation (b) among districts during ANC and delivery in the Volta Region, 2013

Figure 2. District map of Volta Region, Ghana

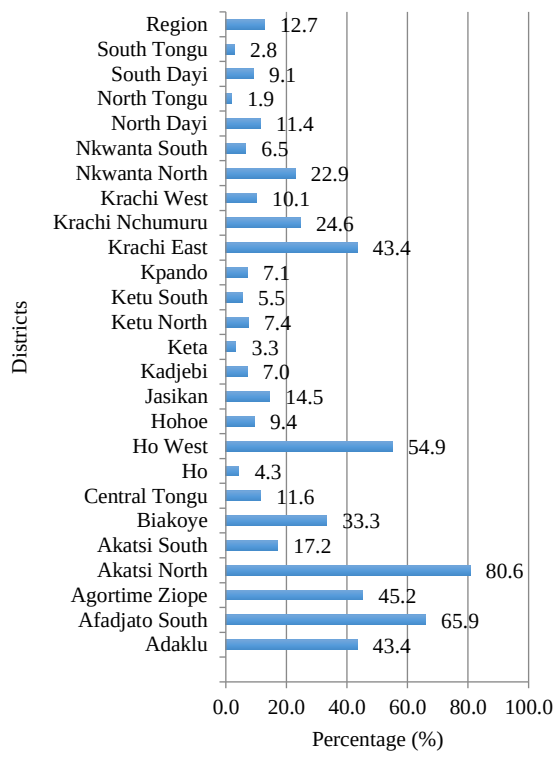

Figure 3. Extent of care fragmentation during delivery among the districts

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health centre ($p < 0.001$), and hospital and maternity home ($p < 0.001$)

Fragmentation

Figure 1(a) shows the extent of care fragmentation among districts during ANC and delivery visits by pregnant women in the Volta Region. This network diagram is based on 9% of the clients' movement (subsequent visits) across districts that were fragmented. Kpando Municipal shared more client visits than the rest of the districts. It had 621 incoming visits (weighted in-degree) from other districts and 487 outgoing visits (weighted out-degree) to 15 other districts, as shown in Table 3. Ho Municipal shared clients with 22 other districts as compared to 15 by Kpando (degree). There is a high sharing of clients between Krachi Nchumuru and Krachi West, with little sharing between these two districts and the rest of the districts in the region. Figure 1(b) shows the extent of care fragmentation during delivery. About 13% (n = 1,838) of participants delivered

Table 2. Provider continuity of care by provider type and ownership during ANC and delivery in the Volta Region of Ghana, 2013. x̄ (± SD)

Facility Type	No. of Visits	Ownership			
		CHAG	Government	Private	All
CHPS	1,146	-	44.3 (±23.5)	-	44.3 (±23.4)
Clinic	1,603	62.5 (±29.3)	32.5 (±18.7)	56.6 (±20.9)	61.1 (±29.2)
Health Centre	15,325	51.9 (±28.0)	56.9 (28.7)	-	56.5 (±28.6)
Hospital	52,853	69.7 (±32.2)	73.5 (±32.3)	68.6 (±34.3)	72.0 (±32.5)
Maternity Home	820	-	-	51.2 (25.9)	51.2 (±25.9)
Polyclinic	348	-	44.2 (±25.7)	-	44.2(±25.7)
All	72,095	67.7 (±32.0)	66.3 (±32.1)	63.4 (±32.8)	66.5 (±32.1)

Table 3. Characteristics of district-client sharing during ANC and delivery in the Volta Region, 2013

District	Visits				All Deliveries		C-Section		Extent of fragmentation				
	In-Degree	Out-Degree	Weighted in-degree	Weighted out-degree	Weighted in-degree	Weighted out-degree	Weighted in-degree	Weighted out-degree	% delivery on first visit	% of expected del – moving out	Prop moving out for CS (%)	Prop of CS from other facilities (%)	Prop of first visit CS (%)
Adaklu	6	5	61	60	5	23	0	5	2.9	43.4	21.7	-	-
Afadjato South	10	15	151	369	12	207	0	39	6.7	65.9	18.8	-	-
Agortime Ziope	8	10	91	290	8	171	0	49	3.3	45.2	28.7	-	-
Akatsi North	4	7	21	40	1	25	0	4	14.3	80.6	16.0	-	-
Akatsi South	9	7	49	54	16	34	2	9	6.7	17.2	26.5	9.1	4.5
Biakoye	12	13	324	318	129	148	26	32	23.5	33.3	21.6	35.1	21.6
Central Tongu	7	7	13	21	6	14	2	4	3.5	11.6	28.6	18.2	9.1
Ho	22	21	599	377	322	116	91	21	8.8	4.3	18.1	15.0	11.4
Ho West	8	6	68	106	18	50	0	5	11.9	54.9	10.0	-	-
Hohoe	12	16	300	258	123	99	30	34	7.7	9.4	34.3	20.8	17.4
Jasikan	11	10	206	164	132	71	39	17	18.4	14.5	23.9	41.9	36.6
Kadjebi	14	12	96	108	42	50	11	22	3.3	7.0	44.0	13.1	9.5
Keta	16	12	165	78	95	34	25	5	6.3	3.3	14.7	15.3	11.7
Ketu North	11	6	105	47	66	19	20	4	14.8	7.4	21.1	39.2	33.3
Ketu South	14	13	71	128	29	69	6	26	1.1	5.5	37.7	3.3	0.0
Kpando	15	15	621	487	255	88	94	10	10.2	7.1	11.4	26.1	14.2
Krachi East	11	14	225	423	29	213	0	48	3.6	43.4	22.5	-	-
Krachi Nchumuru	4	7	476	357	51	89		28	5.6	24.6	31.5	-	-
Krachi West	8	8	410	517	117	59	36	2	3.4	10.1	5.1	26.9	3.7
Nkwanta North	6	8	161	237	12	101	0	22	2.0	22.9	21.8	-	-
Nkwanta South	15	18	416	304	169	42	33	15	12.6	6.5	35.7	33.0	21.0
North Dayi	14	10	340	225	120	49	8	19	8.6	11.4	38.8	19.5	9.8
North Tongu	12	9	31	24	15	8	4	1	1.4	1.9	12.5	6.6	3.3
South Dayi	16	15	126	149	44	56	4	14	2.0	9.1	25.0	9.3	7.0
South Tongu	5	6	24	9	22	3	5	1	14.4	2.8	33.3	35.7	28.6
Total	270	270	5,150	5,150	1,838	1,838	436	436	7.7	12.7	23.8	20.0	12.8

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in a district other than the district where they had the most antenatal care (fragmented). Ho municipal and Kpando municipal had the highest number (322 and 255, respectively) of women coming from other districts to deliver in their municipalities. Generally, the structure of the network diagram during delivery is similar to the network structure during the entire ANC and delivery period. A comparison of Figures 1 and 2 shows that districts that are closer to each other share more pregnant women compared to distant districts. For example, the following districts share boundaries and shared more clients: Krachi Nchumuru and Krachi West; Nkwanta North, Nkwanta South, and Krachi East; Kpando, Hohoe, Biakoye, Jasikan, Afadjato, and North Dayi; Ho, Ho West, Adaklu and South Dayi. In all, about 42% (n = 6,025) of all the pregnant women visited more than one provider during ANC and delivery, with 15.9% (n = 960) delivering by CS and 84.1% (n = 5,065) having vaginal delivery (VD). About 9% (n = 8.9) of all subsequent visits during ANC and delivery, 13% (n = 12.7) of all deliveries, and 20% of all CS deliveries were fragmented across districts. Among those with multiple providers, 30.5% (45.4% CS and 27.7% VD) were fragmented across districts.

In addition, 2,147 of the pregnant women delivered at facilities that never received ANC services. Furthermore, 51.6% (n = 1,108) of all these deliveries were performed at facilities located in different districts. Table 3 shows the characteristics of the districts and the extent of care fragmentation during ANC and delivery. It shows the number of women that moved in or moved out (weighted in or out-degree) during ANC visits, delivery (all), and CS delivery. In addition, for each district, it describes the proportion of potential deliveries that moved out and the proportion that moved for CS or delivered in a district that did not receive any ANC services. In all, about 12.81% (n = 280) of CS and 7.66% (n = 1108) of all deliveries were performed in districts where the women never received ANC services. The proportion of "potential deliveries" that move out from a given district to deliver at other districts varies from district to district. For example, Akatsi North district had the highest proportion of 80.6% (n = 25) of women expected to deliver in Akatsi North district, moving out to deliver in other districts. Other districts with a high proportion of "potential deliveries" moving out for delivery services include Afadjato South (65.9%, n = 207) and Ho West (54.9%, n = 50), as shown in Figure 3. Most of these districts with a high proportion of fragmentation (women moving to other districts to deliver) are districts that do not have hospitals. These include Akatsi North, Afadjato South, Ho West, Agortime Ziope, Adaklu, Krachi East, and Krachi Nchumuru.

DISCUSSION

This study set out to determine the level of provider and district continuity of care and also the extent of care fragmentation among districts during pregnancy and delivery. To the best of our knowledge, this is the first study to extend the concept of provider continuity to a higher level by measuring district continuity, which gives an indication of the extent to which a district collectively facilitates repeat visits to healthcare facilities and vertical integration of care at the district level [6]. The average provider continuity of care was not very high (67%) for all providers in the region, giving an indication that providers are not able to retain pregnant women or vice versa. Hospitals had higher repeat visits by pregnant women compared to the other provider types. The study found that only 36% of the providers had a continuity score greater than 60%, and this is consistent with the study by Katz et al. [6] that found 43% of the providers had a continuity score greater than 60% and another study in Canada that found the average CoC index for health facilities (physician integrated network clinics) to be between 67% and 77% [17].

Frohlich et al. [18] also measured provider continuity for each physician in two regions in Canada and found provider CoC to be 70% (Winnipeg: 76% and Rural South: 71%), with rural physicians having lower scores compared to urban physicians. However, these studies in Canada were undertaken in a health system that encourages patients to have regular providers and, as such, are more likely to visit the providers repeatedly compared to Ghana, where the patient can choose to change providers regularly. It was also found that providers in the southern part of the Volta region had higher continuity scores than the rest of the region. This high score could be partly because facilities in that part of the region had a low proportion of submitted reports. For example, in the North Tongu District, only Battor Catholic Hospital consistently submitted reports for various months, while the rest of the facilities had a very low proportion of submitted reports. So, all the additional visits to other facilities by the women who visited Battor Catholic Hospital would not be included in the study since the other facilities did not submit the reports. This would seem as if the women who visited Battor Catholic Hospital did not visit any other facility, thus giving the hospital a high proportion of repeat visits. This situation applies to other hospitals like Ketu South and Akatsi South District Hospitals. As expected, districts' continuity of care scores were found to be consistently higher than the average provider continuity score for the facilities in the district. This is an indication that the districts as a whole were able to retain more pregnant women than the other facilities.

The study also found that geographically closer districts were more likely to share patients compared to distant districts. This is consistent with other work that shows geographically proximate providers are more likely to share patients [19]. According to the structure of the healthcare delivery, health services in the district are supposed to be integrated with the district health administration coordinating the care delivery while the district hospital acts as the first referral point for the health centres and CHPS Compounds in the district [8,20]. It would, therefore, be expected that the movements of pregnant women would

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be "vertical" along the hierarchy of the healthcare delivery system in a district. It was, however, found that even in districts that have hospitals, there were still high proportions of pregnant women moving from the districts where they had their most ANC to deliver in other districts and in some cases, even in districts where they never received ANC services. It may be understandable to find high proportions of women moving from districts that do not have hospitals to deliver in other districts with hospitals, given the high preference for hospital delivery as indicated in the study. According to Dako-Gyeke et al., providers' impatience, long waiting times, insufficient time with providers, and unfriendly attitude of staff are among some possible reasons why some pregnant women may move from one provider to the other [21].

However, further investigations are needed to understand the reasons for the high fragmentation of care among providers and districts. One limitation of the study was the low proportions of submitted reports by some of the health providers in the southern part of the region, making it difficult to compare the results of the providers and districts in the southern part of the region to the rest of the providers and districts. For example, Battor Catholic and Ketu South Municipal Hospitals and their respective districts had exceptionally good provider/district continuity. The low reporting by the other providers in these districts could give the facilities and the districts high continuity and, by extension, low fragmentation.

Conclusion

There is fragmentation of care during antenatal care and delivery. Most of the health facilities are not able to retain the pregnant women who visit their facilities during pregnancy, resulting in care fragmentation. This situation seems to be made worse by the fact that there is a high preference for hospital delivery. This preference has resulted in high levels of care fragmentation during delivery among the various health facilities and across districts in the region and is even more profound in districts that have no hospitals, with higher proportions of women moving from these districts to other districts with hospitals for delivery services.

DECLARATIONS

Ethical consideration

Ethical approval was obtained from the Institutional Review Board (IRB) of the Noguchi Memorial Institute for Medical Research, College of Health Sciences, University of Ghana, before the commencement of the study (study ID: 052/15-16).

Consent to publish

All authors agreed on the content of the final paper.

Funding

None

Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contribution

SKKD developed the concept for the study, study design, analysis and writing of the manuscript, and ETM and MA contributed to the study design and revision of the analysis and manuscript.

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Availability of data

The datasets generated and/or analysed during the current study are not publicly available due to the confidentiality agreement with the National Health Insurance Authority regarding sharing the data. However, the data can be requested from the National Health Insurance Authority.

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A survey of body-seat dimensions as physical risk factors of common musculoskeletal complaints among academics of a Ghanaian higher education institution

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Abstract

Background: Potential occupational stress, such as musculoskeletal complaints (MSCs), in relation to workstation arrangements in higher institutions requires population-based assessment. The potential mismatch in the body dimensions of academics and their workstation seats is grossly under-reported in Ghana.

Objective: This study aimed to assess physical risk factors such as body-chair mismatch as a correlate of the prevalence of MSCs among academics in a Ghanaian higher education institution.

Methods: Academics of one of the foremost health training institutions in Ghana participated in the study. Participants were enrolled using the convenience sampling method. The prevalence of MSCs was determined using the Standardised Nordic Body Map Questionnaire. The workplace physical risk factors were estimated using an ergonomic assessment checklist, while the body-seat dimensions were measured with an inelastic tape measure. The crude association of the variables was analysed with chi-square analysis at a $p < 0.05$ level of significance.

Results: Eighty-two academics, comprising 65.90% (n = 54) males and 34.10% (n = 28) females, participated in the study between October and December 2021. The point and period prevalence of MSC were 59.60% and 64.60%, respectively, and low back pain was the most reported MSC (73.60%). Over half (53.70%) of the staff reported high physical risks regarding their work activities. The body-chair mismatch and their self-reported workstation risk factors were also significantly associated with MSCs ($p < 0.001$).

Conclusion: A mismatch in the body dimensions of the participants relative to their seats seems to be partly responsible for the moderate prevalence of MSC, of which low back pain constituted the most reported complaint.

Keywords: Musculoskeletal complaints, Ergonomic risk factors, Academic Staff, Workstation seat

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INTRODUCTION

There have been rising concerns about workplace physical and ergonomic risk factors and their imminent health outcomes among different workforces. The rise in the reported work-related disorders lately seems to be linked to the increasing awareness among employers, including institutions of higher education. University staff comprises both academic and non-academic staff with complementary functions to attain the statutory goals of their institutions. In recent years, the number of prospective students has risen exponentially in developing countries, which seems to have increased the academic workload amid a low workforce. For instance, Balogun et al. [1] reported grossly inadequate faculty strength for physiotherapy training programs in the West African Sub-Region (Ghana in particular) compared to developed countries. This scenario is tantamount to disproportionate task assignments among the few available staff. Academics, in particular, spend long hours using computers for lecture presentations,

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e-learning activities, research proposals, publication writing, and, on a few occasions, administrative tasks, which can predispose them to biomechanical overload and subsequent musculoskeletal sequelae [2]. Thus, the scope and workload of academicians necessitate workstation assessment to ascertain possible association with work-related physical disorders such as musculoskeletal complaints (MSC). Aside from their exposure to cognitive pressure [3] and organisation issues [4], workstation seats and physical demands of their work constitute potential physical risk factors, which are insufficiently reported in Ghana's higher institutions of education. Previous studies on musculoskeletal disorders have alluded to the high prevalence of the disorders among various groups of workers in Ghana, including gold miners [5], nurses, and midwives [6], as well as workers in an informal electronic-waste recycling site [7]. There is, however, limited literature regarding similar studies on academics despite their crucial role in the Ghanaian workforce. Physical health-related complaints among workers are largely dependent on the nature of work (including the workstation arrangements), which justifies an adequate description of potential physical risk factors on a group or population basis [8]. In Ghana, previous efforts on a similar subject were conducted on physical assessment of classroom furniture among undergraduate students [9,10].

The present study sought to assess the mismatch in body-seat dimensions as a prelude to MSCs and exposure to physical risk factors at the workplace among academics in a higher education institution in Ghana. We hypothesised that body-seat dimensions and workplace physical risk factors would be associated with the prevalence of MSCs.

MATERIALS AND METHODS

Study design and sites

The study was conducted at selected academic constituents of the College of Health Sciences at the University of Ghana between October and December 2021. The college is an amalgamation of various schools that train healthcare professionals in Ghana.

Sample size and sampling technique

Academics in various constituent schools in the college were enrolled in this cross-sectional study using the convenience sampling method. The following criteria were set in advance for participation in the study: the eligible academics must have used their office chairs for at least six months before the conduct of this study and are actively involved in teaching and research activities. We excluded staff with any underlying physical impairments that can be aggravated during measuring procedures (Figure 1). The sample size for this study was calculated with the Taro Yamane formula [11] given as

$$n = \frac{N}{1 + N(e)^2}$$

Where N is given as 102 (eligible staff) out of the total study population of 134 from three out of the six schools in the College of Health Science, and e is the marginal error, given as 0.05. The three schools, which include the University of Ghana Medical School, University of Ghana Dental School and School of Biomedical and Allied Health Sciences, were selected based on their locations at the Korle Bu Teaching Hospital campus, as well as their similar modes of training. Thus, a sample population (n) of 82 staff was estimated to participate in the study. All the sampled population was measured.

Instruments and procedure for data collection

The Standardised Nordic Body Map Questionnaire (SNBMQ) (Kuorinka et al., 1987) was used to determine the MSC of participants at their workplaces using nine different body areas. A body map delineates the nine body segments to assist respondents in the completion of the form. We screened the physical risk factors with an ergonomics assessment checklist at each staff workplace [13]. The checklist consisted of 18 close-ended items, and each question required a 'yes' or 'no' response. The questionnaire was incorporated with various diagrams depicting occupational activities to help the participants identify ergonomic risk factors. A response with a 'yes' by the respondent was further explained in the separate space provided for justifications. The categorisation of respondents was based on the responses to 'yes' options. For instance, a respondent was classified under 'high ergonomic risk factor' if he or she checked 'yes' for item 1 and if it is affirmed that the institution has not made changes to correct the issue(s). A 'medium ergonomic risk factor' is defined if a 'yes' option is chosen for item 1 (of which the institution has made changes). Respondents who do not check 'yes' for items 1, 2, or 3 and have less than 3 'yes' responses in items 4 through 15 were classified in the 'low ergonomic risk factor' category.

Participants were briefed on the aim and their expected role in the study using an information sheet. The informed consent was obtained thereafter from those who agreed to participate. Permission was also sought from the school management of the selected schools and departments. Following approval, convenient dates and times were arranged via phone calls and personal contact with the staff regarding the data collection process. The socio-demographic information provided by the participants was recorded on a well-structured and self-designed data-capturing form. Copies of the SNBMQ and risk factors checklist were administered in succession by trained Research Assistants. Participants were asked to indicate any MSCs being experienced at the point of contact with the Research Assistants in the last seven days (point prevalence) or 12 months (period prevalence). Both the SNBMQ and the ergonomics assessment checklist took approximately 20 minutes to complete. The questionnaires were retrieved after the completion process.

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Body-chair dimension measurements

Anthropometric measures were taken on the dates arranged with each participant. Participants wore their usual attire and footwear and were required to adopt the generic seated posture with their torso upright, knees inclined at an angle of 90 degrees, and feet flat on the floor. An inelastic tape measure was used to measure the following dimensions: buttock-gluteal length, popliteal height, and hip height, as well as seat and desk dimensions (seat height, seat depth, and elbow height), in line with the procedure outlined by Parcells et al. [14] and was defined as body dimension and seat and workstation dimensions.

Body dimensions

Popliteal height (PH) was measured from the vertical distance from the popliteus at the apex of the underside of the knee to the floor while keeping the knee inclined at an angle of 90 degrees of flexion; gluteal popliteal length (GPL) was measured as the horizontal distance from the farthest point on the posterior surface of the buttock to the apex of the popliteal space with the knee inclined at an angle of 90 degrees; Knee height (KH), measured from the lateral knee condyle to the floor, with the knee inclined at 90 degrees and torso upright (90 degrees from horizontal).

Seat and workstation dimensions

Seat depth (SD) is the horizontal distance from the front of the backrest to the front of the seat surface; seat height (SH) is the vertical distance from the floor to the highest point on the front of the seat surface; seat width (SW), is the horizontal distance between the two front edges of the seat + 4 mm on either side (Figure 2).

Determination of body-chair mismatch

We determined whether the range of dimensions between the participants' body dimensions and that of the seats fell within (matched) the recommended ranges by Lee et al. [15] as follows: Mismatch for PH and SH: If SH is either greater than 95% or less than 88% of the PH. Mismatch for GPL and SD: if SD is either less than 80% or greater than 95% of GPL. Mismatch for KH/Table Height (TBH): if the (knee clearance) space between the seat surface and TBH is less than 2.50 cm or greater than 3 cm. Mismatch SH/TBH: if the SH is less than 64% or greater than 77% of TBH.

Data analysis

Data analysis was performed with IBM SPSS Statistics for Windows, Version 26.0, Armonk, NY: IBM Corp. Descriptive statistics involved percentage, frequency means, and standard deviation to summarise the body and seat dimensions as well as the workplace physical risk factors. The prevalence of MSC was determined by dividing the proportion of respondents who affirmed the presence of MSC in a body region by the total number of respondents, multiplied by 100. The crude association was performed between the prevalence of MSCs and body-seat dimensions as well as ergonomic risk factors using the Chi-square test at a level of significance set at $p < 0.05$.

RESULTS

Eighty-two (82) academics participated in the study with an age range of 34 - 68 years (mean age ± SD: 49.50 ± 8.30 years). They comprised 65.90% (n = 54) males and 34.10% (n = 28) females. The majority (96.30%, n = 79) of the participants were married. The mean (± SD) year of work experience was 13.00 (± 6.60) years, with a range of 5 - 30. Moreover, 41.50% (n = 34) of the staff had worked between 5 and 10 years at the institution. The point and period prevalence were 59.60% and 64.60%, respectively (Figure 3). The overall prevalence of low back pain was 73.60% of all the MSCs, followed by neck pain (66.00%), while elbow pain was the least 7.5%, as presented in Table 1. A larger proportion of staff was using mismatched seats, of which most (74.40%; n = 61/82) were observed for GPL and SD (Table 2). The self-reported ergonomic risk factors by the participants are presented in Fig 4. A moderate proportion of participants (53.70%, n = 44/82) were classified in the high-risk exposure category, compared to 46.30% (n = 38/82) under the low-exposure category. Crude association between the variables was determined with Chi-square analysis. There was a significant association ($p < 0.05$) between MSC prevalence and participants' body-seat dimension mismatches in the selected domains. Similarly, the association between the prevalence of MSC and categories of workplace physical risk factors was statistically significant ($p < 0.05$) (Table 3).

Table 1. Prevalence of MCS among participants across nine body regions

Body part	Frequency	Prevalence	95% CI
Neck	35	66.00	52.1-77.7
Shoulder	18	33.90	22.3-47.9
Elbow	4	7.50	2.7-18.8
Wrist	8	15.10	7.6-27.7
Upper back	19	36.50	24.4-50.7
Lower back	39	73.60	59.8-83.9
Hips/thighs	10	18.90	10.3-31.9
Knees	20	37.70	25.5-51.7
Ankle	11	20.70	11.7-34.1

Table 2. The proportions of matched and mismatched body and seat dimensions.

Body-chair	Frequency (N=82)	Percent
Popliteal height/ seat height		
Match	27	32.90
Mismatch	55	67.10
Buttock popliteal length/Seat depth		
Match	21	25.60
Mismatch	61	74.40
Knee height/ Table bottom height		
Match	23	28.100
Mismatch	59	71.9

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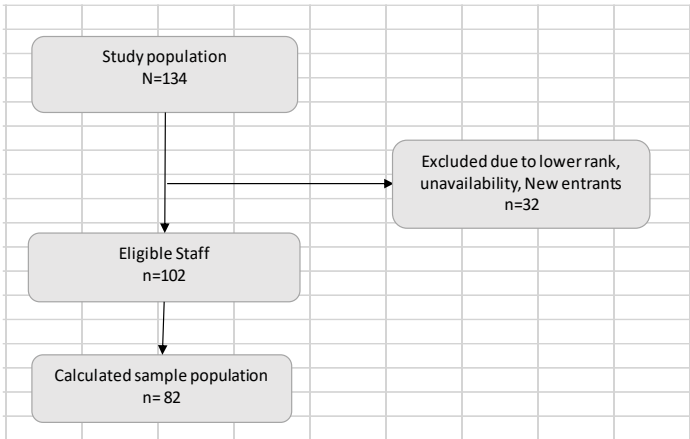

Figure 1. Flow chart for the recruitment of participants

Figure 2. Common swivel chair with adjustable seat height used by academic staff.

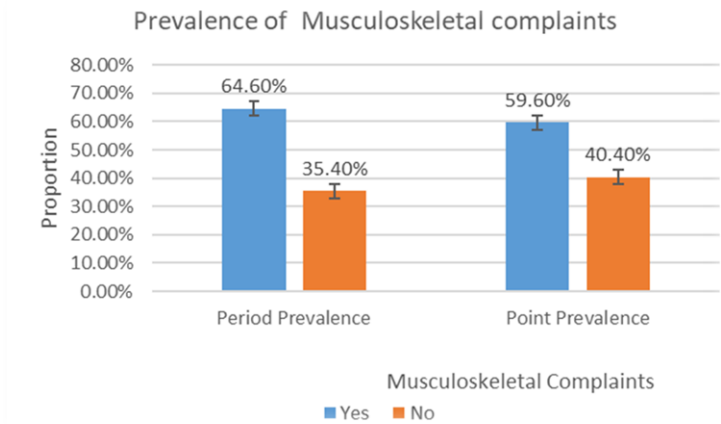

Figure 3. The period and point prevalence of musculoskeletal complaints among the staff

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Table 3. Chi-square analysis of the association between musculoskeletal complaints of participants and body-chair mismatch.

Body-chair dimension	Prevalence of MSC		χ^2	*p* value
Popliteal height/ seat height	No	Yes		
Match	10	17	8.24	0.04*
Mismatch	9	46		
Buttock popliteal height/Seat depth				
Match	9	12	18.40	0.003*
Mismatch	15	46		
Knee height/ Table bottom height				
Match	8	15	8.40	0.009*
Mismatch	11	48		
Physical risk factors				
Low	24	5	23.90	<0.001
High	14	39		

* - Significant, MCS - Musculoskeletal Complaints, χ^2 - Chi Square value, P - level of significance

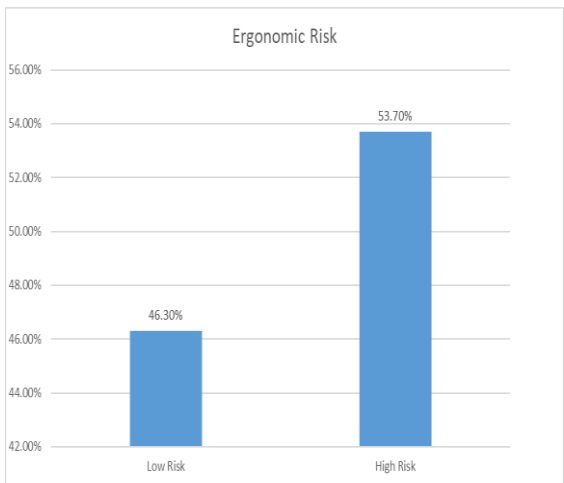

Figure 4. Physical risk factors among the academic staff as assessed independently with ergonomics assessment checklist at each workplace

DISCUSSION

The physical risk factors and body-seat dimensions in relation to the prevalence and patterns of MSC among academics in a Ghanaian health training institution were determined. The 12-month (period) and 7-day recall (point) prevalences of MSC were 64.60% and 59.60% respectively. Low back pain was the most prevalent, accounting for 73.60% of the overall MSC prevalence. More than half (53.70%) of the academics were captured in the high-risk exposure category, while the body-seat dimensions were disproportionate in more than half of the participants. The body-chair dimensions and the categories of physical risk factors were significantly associated with MSCs. Thus, we reject our initial hypothesis, which proposed no association between MSCs and the two variables.

Socio-demographic characteristics of the participants

More male than female faculty members participated in the present study, which concurs with earlier observations by Kumah et al. [16] and Sirajudeen et al. [17] in higher educational institutions. The dominance of males over their female peers may be hinged on many factors, including cultural discrimination against women, particularly in developing countries. Female individuals have often had to bear an unfair distribution of household responsibilities in comparison with their male counterparts and suffer in terms of their career prospects as well as a reduced ability to meet their occupational goals. In addition, most of the participants were within the age range of 34 - 68 years (mean = 49.50 ± 8.30 years). This suggests that the mainstream workforce in the university was within the middle-age range. Given the physical, organisational, and cognitive demands of academic tasks, a strong population of workers is required for such tasks. Most (41.50%) of the academics had worked between 5 and 10 years (mean = 13.00 ± 6.60 years) in the institution, which implicates the influence of their workstation on the reported MSCs. On the other hand, the inherent physiological adaptation of their body to the workstation seats might have also resulted in the moderate prevalence of MSCs.

Prevalence and pattern of musculoskeletal complaints among the participants

The most reported MSCs were low back pain and neck pain in more than half of the participants. These complaints were not surprising given the increasing need to use electronic and computer devices for academic tasks. Moreover, the use of such devices is often accompanied by prolonged sitting and awkward postures, thus culminating in low back and neck dysfunctions. These findings are consistent with the reports of previous studies on workstation risk factors in other populations by Velasco Garrido et al. [18] and Masilamani & Ganapathy [19], indicating pain at the waist, neck and several parts of the spine (particularly the lumbosacral region). The present study revealed a moderate prevalence of MSCs, which are speculated to be due to many factors, including workstation arrangements such as

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the types of seats and desks used, placement of the computer screen and keyboard, and workloads. The participants had no prior knowledge of the correct placement of the office items.

Body-chair dimensions and physical risk factors exposure among the academics

Mismatch in body-seat dimensions was found in more than half of the participants. The proportion of participants with mismatched seats was higher compared to those reported in previous studies [20,21] on similar populations. Indeed, most measured office seats and desks in this study were short of meeting the adaptability and adjustability features to accommodate varying body dimensions. However, it must also be noted that regardless of the high level of adjustability of the emerging workstation chairs in the market, the limited knowledge of the participants on the use of the chairs was worth noting. In reality, the provision of office chairs for workers is often plagued with high financial cost implications for any organisation. The high proportion of body-chair mismatches in the present study is consistent with the findings of Adu and Adu [10]. These findings thus strengthen the support for thorough ergonomic evaluations before the procurement of work seats to guarantee academic comfort. The inputs of professionals (such as Occupational Medical Practitioners, Physical Therapists, Occupational Therapists, Occupational Health Hygiene, and Industrial Nurses) are therefore imperative. Similarly, half of the participants (57.3%) reported high-risk factors in relation to their assigned task activities, which was significantly associated with MSC prevalence. As expected, academics perform most activities in prolonged sitting and for a long duration, thus potentiating a high prevalence of MSC [2]. Our findings agree with the previous report of Mohan et al. [22], which showed an appreciable number of participants who were exposed to high ergonomic risk. Likewise, Algani et al. presented similar findings in which the high prevalence of MSCs was associated with physical work components among academics. Indeed, there were significant associations between body-chair dimensions and the prevalence of MSCs in our study, which follows similar patterns to that of other populations, such as undergraduate students [9] and the IT industry [24]. The study was undermined by some limitations, including accessibility to the Faculty Members due to their time constraints, which prevented the researchers from exhausting all other requisite parameters, including sitting duration and ergonomic practices. In addition, the study could not differentiate other sources of MSC from those related to the seat of the academic workers.

Conclusion

The academic staff in this study presented a moderate prevalence of MSCs, which seems to be influenced by body-chair mismatches and high ergonomic risk factors. These findings underscore the requisite evaluation of workstations during the procurement processes. Thus, the engagement of relevant professionals within the university's existing incentive structure is necessary to provide expertise in the assessment of workstation seats prior to the procurements.

DECLARATIONS

Ethical consideration

Ethical approval for this study was obtained from the Ethics and Protocol Review Committee of the School of Biomedical and Allied Health Sciences, University of Ghana (Ref Number: SBAHS/AAPT/10628546/2020-2021). All the methods were performed in accordance with the Declaration of Helsinki. The participants also gave their informed consent, having been briefed thoroughly about the purpose of the study and their expected roles.

Consent to publish

All authors agreed on the content of the final paper.

Funding

None

Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

EEA was involved in the generation and editing of data for the article. AIB designed the study and drafted the manuscript. BM and AAA contributed to the editing and interpretation of data.

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The time made available by the participants is hereby acknowledged.

Availability of data

Data is available upon request to the corresponding author.

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Perceived stigma by women with infertility accessing treatment in a tertiary health facility in Northern Ghana

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Abstract

Background: Infertility is defined as the inability to achieve a clinical pregnancy following regular unprotected sexual intercourse for a period of 12 months or longer. One significant obstacle encountered by women dealing with infertility globally is the stigma attached to it.

Objective: The study aimed to explore the various ways by which women experiencing infertility are stigmatised in Ghana.

Methods: A cross-sectional survey was adopted, and participants were conveniently selected. A standardised Infertility Stigma Scale (ISS) was administered, and both univariate and multivariate analyses were performed. The alpha level was set at 0.5. Participants were recruited from a tertiary hospital in Northern Ghana between March 2020 and October 2021. A total of 302 women experiencing infertility and accessing fertility treatment participated in the study

Results: More than half of the participants (51.3 %, n = 155) self-reported perceived stigma. Age (r = 0.35, p = 0.01) and duration of infertility treatment (r = 0.33, p = 0.01) had a positive and significant relationship with infertility stigma, which is an indication that older married women and those with a longer treatment duration face the most stigma associated with infertility in their community. Further, married women with tertiary education were found to experience greater stigma from their families if they were unable to conceive after several years of marriage. Generally, participants perceived stigma from different social contacts, including family, friends, and the community at large.

Conclusion: Given the prevalence of infertility stigma in the study area, creating public awareness of the causes of infertility, as well as the consequences of stigma on the well-being of affected women, would be needed. It is also important that interventions that focus on enhancing the resilience of women with infertility to cope with public and enacted stigma are explored. These interventions, if designed with the views of the affected women and implemented in a culturally sensitive fashion, would help improve their quality of life.

Keywords: Stigmatisation, infertility, women, experiences, Ghana

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INTRODUCTION

Infertility occurs when there is a failure to achieve a clinical pregnancy after regular unprotected sexual intercourse for 12 months or more [1]. Recent evidence suggests a downward trajectory in the burden of infertility in high-income countries but an upward trend in other countries, including those in Africa [2]. What seems to be a major challenge facing women with infertility worldwide is stigmatisation [3,4,5,6]. There are numerous determinants of infertility-related stigma. These include the perception that women with infertility have been involved in multiple abortions, led a promiscuous lifestyle, or living under a generational curse of childlessness [3,4,7]. For example, a study conducted in Ghana examined the beliefs women hold regarding childbirth. It reported that women experiencing infertility were perceived to have had a series of abortions,

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leading to uterine abnormalities and, subsequently, miscarriages [3]. Others also believe that infertility is attributed to generational curses whereby the fulfilment of special demands, such as riches from a deity, could be exchanged for childlessness along that family lineage [4].

Infertility-related stigma manifests in various ways [3,5,7]. Studies across the globe indicate that women with infertility face discrimination by society [5,6] and are labelled as abnormal, useless, and deficient [8,9]. They are also insulted, despised, and considered as ominous [10]. Nonetheless, the experience of this stigma differs from one culture to another. For instance, in the United States (US), a study by Greil et al. on 'the Social Construction of Infertility' found that with a strong emphasis on every female becoming a biological mother across the culture of the United States, infertile women who participated in the study reported feeling marginalised and perceived as abnormal or deviant due to their unintended inability to become pregnant and bear children [11]. Further, a similar study in Northern Ghana indicated that women with infertility are often isolated from other society members, prevented from participating in ceremonies and particularly prohibited from having bodily contact with other people's children [12]. In Uganda, a survey by Cui [13] on the agony of infertility among females reported that women with infertility are faced with societal stigmatisation, ostracism, and discrimination. Some women are reportedly banned from appearing at social gatherings and regarded as "the cursed" [13].

This level of stigmatisation often intensifies the feeling of shame and guilt in these women. Infertility-related stigma has enormous consequences. It presents varied degrees of mental disorders in women [6,14,15,16], particularly in Africa [3]. These stressors are heightened among women above 35 years, those who have experienced 4 to 6 years duration of infertility and living in a cohabitation marriage [16,17]. Essentially, the challenges are mostly driven by beliefs about the causation of infertility [3,4] as well as the perceived benefit of children, including social and economic support, continuity of family lineage, and societal recognition [3]. For example, in the southern part of Nigeria, being able to conceive and bring forth a child are essential prerequisites for the initiation of females into motherhood, and women with infertility are maltreated and called "men" by their partners, relatives, and in-laws [18]. The stress that characterises infertility compels a number of affected women to adopt different treatment options, including the use of assisted reproductive technologies and herbal medicines [19,20]. Others also resort to prayer with the belief that God will intervene in their predicament [21], whereas some also opt for the adoption of a child [21].

In Ghana, quantitative assessment of infertility-related stigma appears to be missing despite the existence of stigma in the socio-cultural context. The only study that provides evidence regarding infertility was conducted in southern Ghana [8]. We believe that a quantitative assessment of infertility-related stigma, particularly in northern Ghana, would complement the findings in southern Ghana to inform stigma reduction intervention.

MATERIALS AND METHODS

Study design and sites

A cross-sectional survey was employed for this study. Women with infertility and accessing fertility treatment at the Tamale Teaching Hospital in the Northern Region of Ghana were recruited for this study. The region comprises a large geographical area but is sparsely populated. The hospital serves as a referral hospital for the five regions in the northern part of Ghana. It has various units, and it includes the Obstetrics and Gynaecology unit, which serves women with various reproductive health issues, including the treatment of infertility.

Sample size and sampling technique

A convenience sampling technique was employed to select women who were seeking infertility treatment. The Yamane formula for calculating sample size was used for sample size determination. A total of 302 women experiencing infertility and accessing fertility treatment were selected to participate in the study.

The Sample Size Determination of Yamane

$n = N/(1+N(e)2 = 682/(1+682(0.05)2 = 252$

Where:
n = Sample size
N = Population size
e = margin of error
The margin of error is permissible, e = 0.05.
The population size of women seeking fertility treatment at Tamale Teaching Hospital during the study period was N = 682.

However, 20% was added to the sample to take care of non-responses. The study's sample size was established at 302, following the above calculation. The purpose of the study was explained in detail to the participants in order to get their cooperation during the recruitment session. Informed consent was obtained from the study participants. Participants who agreed to take part in the study were provided with information regarding the study and were asked to sign a consent form. The Infertility Stigma Scale (ISS) questionnaire was used to measure both perceived stigma and self-stigma for women with infertility. The Infertility Stigma Scale contains 27 items divided into four factors, which include self-devaluation (7 items), social withdrawal (5 items), public stigma (9 items), and family stigma (6 items). The responses to each item were based on a 5-point Likert scale (1 = completely not agree, 2 = not agree, 3 = not sure, 4 = agree, 5 = completely agree). A research assistant aided the women in completing an interviewer-administered questionnaire. Data was collected between March 2020 and October 2021. The data was analysed using IBM SPSS Statistics for Windows, Version

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22.0, Armonk, NY: IBM Corp. The data was first entered in Excel and cleaned by running preliminary frequencies of all the variables to check for inaccuracies.

RESULTS

The study involved 302 women who were receiving fertility treatment. The average age of the women was 28.39 ± 3.14, with an age range of 22 to 40 years. The majority (70%, n = 211) of the women were between the ages of 26 and 30 years inclusive. All participants, but one woman, were married. The greatest proportion of the participants had no formal education (31.50%, n = 95), with secondary education being the least represented at 17.90% (n = 54). In relation to occupation, half of the participants were traders (49.70%, n = 150), with farming having the lowest representation (4.0%). The majority were Muslims (60.30%, n = 182). The average years of treatment was 3.78 ± 1.51. The demographic characteristics of participants are presented in Table 1. The overall stigma scores for infertility were found to be normally distributed, with skewness and kurtosis values within ±1. All the subscales, namely self-devaluation, social withdrawal, public stigma, and family stigma, had a normally distributed distribution and fell within the range of ±1. The result also shows that none of the participants had the lowest score of 27 and the highest score of 135. That indicated that none of the participants experienced extremely low or high infertility stigma (Table 2). Using the mean split procedure, it was seen that infertility stigma was prevalent across all four levels. Hence, more than half of the individuals reported having a high level of infertility stigma (Table 2). This demonstrates that most people held a negative view of infertility, which respondents were subjected to.

The descriptive statistics and Pearson correlation table show that at the 0.01 level of significance, age (r = 0.35, p = 0.01) and duration of infertility treatment (r = 0.33, p = 0.01) had a positive and significant relationship with infertility stigma. This suggests that, on average, older women and those with a longer treatment time faced the most stigma associated with infertility in their community. Additionally, two variables (age and duration of infertility treatment) were examined on the four dimensions of the infertility stigma construct. Age had a positive and significant association with self-devaluation (r = 0.25, p = 0.01), social withdrawal (r = 0.24, p = 0.01), and public stigma (r = 0.34, p = 0.01) at the 0.01 level of significance but had no significant relationship with family stigma. Infertility treatment duration had a positive and significant relationship with self-devaluation, social withdrawal, and public stigma but

Table 1. Sociodemographic characteristics of participants

Characteristics	n	%
Educational level		
No formal	95	31.50
Basic	75	24.80
Secondary	54	17.90
Tertiary	78	25.80
Occupation		
Farming	12	4.00
Trading	150	49.70
Civil servants	73	24.20
Healthcare worker	5	1.70
Unemployed	60	19.90
Other	2	0.50
Religion Affiliation		
Christian	120	39.70
Muslim	182	60.30

Table 2. Mean, standard deviation, skewness and kurtosis of the subscales of infertility stigma among women in the Northern part of Ghana

Measure	Scores			Dispersion			Normality	
	Min	*Max*	*Range*	*Mean*	*SD*	*Median*	*Skew*	*Kurtosis*
Self-Devaluation	9	32	23	19.23	4.51	19.00	.23	-.35
Social Withdrawal	5	22	17	12.59	3.22	12.00	.20	-.17
Public Stigma	11	42	31	22.73	4.76	22.50	.57	.78
Family Stigma	11	29	18	19.1	3.54	19.00	.08	-.46
Infertility Stigma	52	120	68	73.71	9.91	74.00	.51	.96

Table 3. Descriptive statistics and pearson correlations for study variables

Variables	M	SD	1	2	3	4	5	6	7
1. Age	28.39	3.14	-						
2. Infertility Treatment Duration (years)	3.78	1.51	.83**	-					
3. Self-Devaluation	19.23	4.51	.25**	.23**	-				
4. Social Withdrawal	12.59	3.22	.24**	.29**	.20**	-			
5. Public Stigma	22.73	4.76	.34**	.26**	.35**	.22**	-		
6. Family Stigma	19.16	3.54	-.02	.01	.03	.13*	.02	-	
7. Infertility Stigma	73.71	9.91	.35**	.33**	.70**	.57**	.72**	.42**	-

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not family stigma. It might be concluded that the age of married women and the duration of their infertility treatment influenced self, social withdrawal, and their anxiety about public stigma (stereotypes, prejudice, and prejudgment) (Table 3). Two demographic characteristics, which included religion and education, were used as independent variables, while self-devaluation, social withdrawal, public stigma, and family stigma were used as dependent variables. Significant multivariate effects were seen for both religion and education (Table 4), with religion and education accounting for 1.0 and 4.4% of the variance, respectively. Additionally, there is a substantial multivariate influence of the interaction between religion and education on infertility stigma, accounting for 2.4% of the variance in the four-infertility stigma experience. The participant's religious membership did not significantly predict self-devaluation, social withdrawal, or public stigma in univariate models. This demonstrates that a married woman's religion does not influence the stigmatisation of infertility. However, univariate analyses of education revealed that only family

Table 4. Significant multivariate effect for religion and education on infertility stigma ($p \leq 0.05$)

Factors	Pillai's Trace	F	df	Error df	p	Partial Eta Squared
Religion	.010	0.73[b]	4	291	.57	.010
Education	.131	3.347	12	879	.00	.044
Religion * Education	.071	1.778	1	879	.05	.024

Table 5. Univariate analysis of religion and education on infertility stigma subscales

Factors		Dependent variables	Descriptive		*F (1, 294)*	*p*
			M	*SD*		
Religion	Christianity	Self-Devaluation	18.51	4.45	1.98	.16
	Islam		19.70	4.50		
	Christianity	Social Withdrawal	12.30	3.29	.12	.73
	Islam		12.78	3.16		
	Christianity	Public Stigma	22.02	4.29	1.05	.31
	Islam		23.20	5.00		
	Christianity	Family Stigma	19.32	3.64	.80	.37
	Islam		19.06	3.48		
					(3, 294)	
Education	No Formal	Self-Devaluation	20.02	4.70	2.09	.10
	Basic		19.53	4.88		
	Secondary		18.65	3.81		
	Tertiary		18.35	4.21		
	No Formal	Social Withdrawal	13.12	3.16	2.29	.08
	Basic		12.81	3.05		
	Secondary		12.35	3.50		
	Tertiary		11.90	3.16		
	No Formal	Public Stigma	23.99	4.99	1.92	.13
	Basic		22.47	4.48		
	Secondary		22.20	4.27		
	Tertiary		21.82	4.84		
	No Formal	Family Stigma	18.20	3.21	8.09	.00
	Basic		19.35	3.27		
	Secondary		18.46	3.95		
	Tertiary		20.64	3.43		
Religion * Education		Self-Devaluation			2.82	.04
		Social Withdrawal			.66	.58
		Public Stigma			1.18	.32
		Family Stigma			1.15	.33

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stigma was relevant (p = 0.00), but not self-devaluation, social withdrawal, or public stigma. According to the mean scores, women with tertiary education in northern Ghana face greater stigma from their families if they are unable to conceive (Table 5). The interaction effect between religion and education was examined, and the result shows that there was a significant interaction effect on self-devaluation between religion and education (p = 0.04).

DISCUSSION

This study provides insight into the degree of perceived stigma among infertile women in the northern part of Ghana. The ISS questionnaire was used to assess stigma in the following forms: self-devaluation, social withdrawal, public stigma, family stigma, and the overall stigma of infertility. The findings show that women who were 35 years and above and have been seeking treatment for a longer period, usually after a year, face the most stigma associated with infertility in their community. It was found that the age of women and the number of years they had been seeking infertility treatment influenced self, social withdrawal, and their anxiety about public stigma. The findings in this current study are consistent with findings from a study that indicated that women faced pressure from the family and community [24]. In determining the relationship between age and duration of infertility treatment, the study found a significant positive relationship between age, duration of infertility treatment, and infertility stigma. Older women and those undergoing longer treatments experience more stigma in their communities. Age is significantly associated with self-devaluation, social withdrawal, and public stigma but not with family stigma. Similarly, the duration of infertility treatment is linked to self-devaluation, social withdrawal, and public stigma, but not family stigma. In conclusion, both age and treatment duration influence self-perception, social behaviour, and anxiety about public stigma among women facing infertility.

Similar findings were found in a study by Donkor and Sandall [8] on the impact of perceived stigma and mediating social factors on infertility-related stress among women seeking infertility treatment in Southern Ghana. Regarding social withdrawal stigma, the study found that respondents experienced the feeling of being embarrassed when asked questions about kids and were more sensitive to issues about pregnancy and children because they could not get pregnant. As a result, they avoided getting close to people who did not have fertility problems. Public stigma experienced by the participants in this current study indicated the most common form of the stigma the women experienced. These included being discriminated against during decision-making in society, people gossiping about them, and they felt people viewed them differently. Similar studies have also reported the negative attitude experienced by women experiencing infertility within their communities [6,26]. Family infertility stigma was found to come from different social agents, including the family members of the infertile women. The predominant form of the family stigma the women experienced was coming from their mothers-in-law, who had issues with them due to the problem of infertility. Other common forms of the family stigma they experienced included a negative relationship with their husbands, who thought the women were the cause of infertility. Again, some women also indicated that they were afraid their marriage would be affected as family members influenced their partners to divorce them. A study conducted by Feldman-Savelsberg [27] in Cameroun among women experiencing infertility also reported that the study participants experienced divorce due to family stigmatisation.

Earlier studies on infertility are limited to qualitative designs, but this study quantitatively assessed infertility-related stigma in northern Ghana. However, the application of a standardised scale for the measurement of stigma enhances the credibility and reliability of the study findings. The use of cross-sectional design in this study limits the establishment of a cause-and-effect relationship. The study sites were confined to the northern region of Ghana, and therefore, there is the possibility of variations that may not represent the views of individuals seeking treatment in the southern sector.

Conclusion

The study provides insight into the degree of perceived stigma among infertile women in Northern Ghana. We found that a woman's age and the number of years spent seeking infertility treatment influenced self, social withdrawal, and anxiety about public stigma. The predominant form of the family stigma the women experienced was traceable to mothers-in-laws. Generally, most people hold a negative view of infertility. Therefore, we recommend a public sensitisation programme on issues of infertility and its effect on the women experiencing it. Nurses at the forefront of health care should go through counselling training to be able to assist these women who are facing various forms of stigma relating to infertility. Again, knowledge about the psychological challenges women face will improve counselling sessions, as well as inform policy on how to address issues about the stigma associated with infertility.

DECLARATIONS

Ethical consideration

Ethical clearance was obtained from the Noguchi Memorial Institute (IRB NO: 049/19-20). Permission was sought from the management of the facility for data collection. Informed consent was obtained from the study participants.

Consent to publish

All authors agreed on the content of the final paper.

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Competing Interest
The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions
JMK conceptualised the study, SM and JMK designed it, MA, CAA, and JK analysed the data, and JMK, SM, and CAA critically reviewed the manuscript. All authors read and approved the manuscript.

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Availability of data
Data for this work is available upon reasonable request from the corresponding author.

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Assessing the impact of water, sanitation and hygiene (WaSH) on diarrhoeal disease and malnutrition among children under 5 in Chad

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Abstract

Background: Chad has the second highest under-5 mortality rate in the world, as well as the highest rate of under-5 mortality due to diarrhoea at the time of this study.

Objective: This study assessed the relationship between household WaSH sources, diarrhoeal disease prevalence, and malnutrition among children under 5 in Chad.

Methods: The samples used in this study consisted of 5,192 and 11,842 children under 5, respectively, from the 2004 and 2014 Chad Demographic and Health Surveys. Logistic regression analysis was employed to assess the relationship between improved versus unimproved household WaSH sources and diarrhoeal and malnutrition prevalence among children under the age of five in Chad.

Results: Analysis of the overall category of improved household WaSH sources versus the overall category of unimproved WaSH sources showed no evidence for the effects of using improved WaSH sources on the prevalence of diarrhoea. However, analysis of the individual WaSH sources within each category revealed that in 2014, specific types of water sources led to increased prevalence of diarrhoea, whereas specific sanitation facilities led to decreased prevalence of diarrhoea; also, having access to improved water sources and sanitation facilities significantly reduced malnutrition prevalence.

Conclusion: A better understanding of which household WaSH sources aid in decreasing the prevalence of the disease is consequential to global health professionals who operate developmental efforts so that funding can properly be allocated to making those resources available for intervention.

Keywords: WaSH, infectious disease, children under five, malnutrition, sub-Saharan Africa

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INTRODUCTION

A high proportion of preventable morbidity and mortality throughout developing countries are attributable to poor water, sanitation, and hygiene (WaSH) conditions, and research has shown that lack of clean water and proper sanitation are causal factors of disease transmission [1]. For instance, more than 25 diseases are caused by poor and inadequate WaSH conditions, killing more than two million people each year, including more children than acquired immune deficiency syndrome (AIDS), tuberculosis, and malaria combined [2,3]. Worldwide, poor WaSH conditions are the primary reason for diarrhoeal disease, which results in morbidity and mortality among children under 5 [4-10]. Across countries, 64.2 million disability-adjusted life years (DALYs) are attributed to unsafe water and poor sanitation and hygiene practices, of which 52.5 million DALYs (82%) are in low-income countries. The burden of disease resulting from these conditions lies heavily upon sub-Saharan Africa (46% of global DALYs) [1], where there is a dearth of clean or safe water sources in many communities. Over 25% of the population of many African countries lack portable drinking water, while more than 50% lack adequate sanitation and hygiene facilities, which gives rise to the

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spread of viruses and bacteria that cause diarrhoeal disease [11]. At the time of this study, Chad was the fifth largest country in Africa and the seventh poorest country in the world, according to the United Nations Human Development Index ranks [12,13]. In addition, Chad had the second highest under-5 mortality rate in the world at approximately 123.20 deaths per 1,000 live births [13]. A 2018 study reported that the highest rate of diarrhoea mortality among children under 5 occurred in Chad (499 deaths per 100,000) [12]. In 2002, two years after the Millennium Development Goals (MDGs) were developed and published, the World Health Organization (WHO) and United Nations International Children's Emergency Fund (UNICEF) categorised sources of WaSH as either being improved or unimproved.

Improved water sources are those that are protected from outside contamination, particularly from faeces, via active intervention or by the nature of how the source was constructed [14]. Improved water sources include technologies such as piped household water connections, public taps, standpipes, protected dug wells, and springs or rainwater collection [15]. Unimproved water sources do not protect from outside contamination; they include non-piped supplies such as unprotected wells and springs [15,16]. Improved sanitation facilities hygienically separate human waste from human contact; they include flush/pour toilets to a confined system, improved latrines (e.g., ventilated, with slab), or composting toilets [14,15]. Unimproved sanitation facilities do not assure hygienic separation of human excreta from human contact and include on-site sanitation: pit latrines without slabs, hanging latrines, and bucket latrines [16]. As of 2010, approximately 87% of the world's population had access to improved water sources; however, 39% of the world's population did not have access to improved sanitation facilities [14,15]. Studies have shown that globally, 780 million individuals do not have access to improved drinking water, and 2.5 billion individuals do not have improved sanitation [8,17]. Lack of proper WaSH resources mainly occurs in developing countries in which more than a billion people must resort to open defecation and where, on average, handwashing with soap is practised only after 19% of toilet use [14,15,18-20].

Few researchers and program implementers have considered WaSH in terms of WHO and UNICEF's categorisation, much less examined this categorisation at the household level. It is important to closely examine WaSH sources being utilised at home and understand if improved WaSH sources actually reduce the prevalence of diarrhoea and malnutrition among children. Therefore, the purpose of this study was to assess the relationship between household WaSH sources (improved versus unimproved), diarrhoeal disease prevalence, and malnutrition prevalence among children under 5 in Chad. The following research questions were examined in this study:

- How did the use of improved versus unimproved household WaSH sources affect the prevalence of diarrhoeal disease among children under 5 in Chad in 2004 and 2014?
- What was the relationship between each improved and unimproved household WaSH source and diarrhoeal disease prevalence among children under 5 in Chad in 2004 and 2014?
- What was the relationship between improved and unimproved household WaSH sources and the prevalence of malnutrition among children under 5 in Chad in 2004 and 2014?

MATERIALS AND METHODS

The data analysed in this study were derived from both the 2004 and 2014 Chad Demographic and Health Surveys (CDHS). This cross-sectional survey was designed to provide data on population and health indicators at the state and national levels. The sampling frame for the CDHS was a list of Enumeration Areas (EAs) developed from a recent population census. The primary sampling units (PSU), known as clusters, were selected from the list of EAs. The sample survey was selected using a stratified two-stage cluster design made up of approximately 300 to 500 clusters. Details about the sampling are available elsewhere [21]. Data analysis was limited to children who lived with their mother and whose mother was a member of the surveyed household. In all, 6,085 women and girls aged 15-49 participated in the 2014 CDHS for 2004 and 17,719 for the 2014 CDHS. The sample of children under 5 was 5,192 for the 2004 survey and 11,842 for 2014. The independent variables in this study were the source of drinking water and sanitation facilities.

Multiple response options for both variables were presented in the survey. Therefore, both variables were dichotomised into improved sources (1) and non-improved sources (0) based on WHO and UNICEF's categorisation [22]. Because this study was also interested in understanding the impact of each type of water source and sanitation facility, the full range of responses for both independent variables was examined. Improved water sources included piped water into dwelling, yard or plot, public tap or standpipe, tubewell or borehole, protected dug well, protected spring and rainwater receptacles, harvested rainwater, tanker truck or cart with a small tank, and bottled or sachet water. Unimproved water sources included unprotected dug wells, unprotected springs, and surface water sources (i.e., rivers, ponds, and streams). Improved sanitation facilities included flush toilets, septic tanks, pit latrines with slabs, ventilated improved pits (VIP), and compost toilets, while unimproved facilities comprised of flush toilets not connected to a sewer, pit latrines without a slab, hanging latrine or toilet, bucket latrines, and open defecation in bush or field or no facility.

The dependent variables in this study include diarrhoeal disease and malnutrition; diarrhoeal disease was dichotomised as one if a woman reported that their children had diarrhoea in the last two weeks and 0 if the child was

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reported as not having diarrhoea in the last two weeks. To measure malnutrition, every child's weight (kg) and height (cm) were recorded. Weight and height are two well-linked anthropometric indicators and are traditionally used to measure malnutrition status in children [23-29]. Thus, height-for-age (HAZ), weight-for-age (WAZ), and weight-for-height (WHZ) scores were used in this study. Children in this study were classified as stunted, underweight, and wasted if their z-scores were < 2 SD from the population [23-25,30]. HAZ, WAZ, and WHZ were converted into binary variables. HAZ was converted to stunted, which was one if HAZ < -200 and 0 otherwise (but considered missing if HAZ was 70 > 600). Similarly, underweight was coded as one if WAZ is 71 < -200 (or 0 if missing) and wasted was coded as one if WHZ is 72 < -200 (or 0 if missing). For both dependent and independent variables, "I don't know", and other responses were recoded as missing. Control variables included the respondent's current age, highest educational level, sex of child, type of place of residence, and wealth quintile. All data were analysed using IBM SPSS Statistics for Windows, Version 25.0 Armonk NY: IBM Corp.

RESULTS

The mean age of the respondents was 28 ± 6.9 years for both samples. Most respondents reported having no education in both the 2004 (n = 4,023; 74.30%) and 2014 (n = 13,058; 72.40%) datasets. The biological sex of the respondents' children was almost equally distributed between males and females in both datasets. In the 2004 sample, residence type was somewhat equally divided between urban and rural, while in the 2014 dataset, rural was more represented (n = 14,250; 79.00%). For the wealth index, all categories were somewhat equally represented, except for the category of 'richest' in 2004, which was slightly more present (n = 1,975; 36.50%) than in 2014 (n = 3,114; 17.30%) (Table 1). Descriptive statistics of the dependent and independent variables for the two time periods are presented in Table 2. For the first research question, the binary logistic regression model was statistically significant in 2004 and 2014; $\chi 2$ (12) = 43.162, $p < 0.000$ and $\chi 2(12) = 136.701$, $p < 0.000$, respectively (Table 3). The results showed that having access to an improved household source of drinking water did not significantly affect the odds of experiencing diarrhoeal disease in 2004 or 2014. Likewise, having access to an improved household sanitation facility did not influence the odds of experiencing diarrhoea in 2004 or 2014. As such, the improvement of household water sources and sanitation facilities had no statistically significant difference in terms of diarrhoea prevalence among children under five in Chad during both time periods.

However, some effects were found for the control variables. Mothers with primary and secondary education were significantly more likely to have a child who experienced diarrhoea compared to mothers with no education. Also, in 2014, living in a rural area decreased the odds of developing diarrhoea compared to living in an urban area. In 2004, having any level of wealth beyond the poorest significantly increased the prevalence of the diarrhoea effect, which reverted in 2014, where having any level of wealth beyond the poorest (except for the middle) significantly decreased the prevalence of diarrhoea. Finally, the odds of experiencing diarrhoea decreased with age, both in 2004 and 2014. For research question 2, the logistic regression model was statistically significant in 2004 and 2014; $\chi 2$ (15) = 40.290, $p < .000$ and $\chi 2(24) = 171.236$, $p < .000$ respectively (Table 5). The effects of the source of drinking water were systematically evaluated, where piped water was used as the reference category for comparison. In 2014, several sources of water led to a significantly higher prevalence of diarrhoea when compared to piped water, notably surface water, unprotected dug wells, protected springs, tubewells, and public taps.

For the comparisons of household sanitation facilities, the reference category was flush toilets. In 2014, several types of sanitation facilities led to reduced rates of diarrhoea when compared to flush toilets. Reduced rates of diarrhoea occurred when the sanitation facility was no facility, hanging toilet, pit latrine, and pit latrine with a slab. The control variables behaved much in the same manner as in the previous analysis. Educational level was statistically significant in 2014. As before, when compared to mothers with no education, mothers with primary and secondary education had children who were significantly more likely to have experienced diarrhoea. Also, in 2014, living in a rural area decreased the chances of developing diarrhoea compared to living in an urban area. Additionally, in 2004, having any level of wealth beyond the poorest (except for the rich) significantly increased the prevalence of diarrhoea,

Table I: Descriptive Statistics of the Control Variables

	2004		2014	
	Years	SD	Years	SD
Age of respondent M/SD	28	6.9	28	6.8
Highest educational level	N	%	N	%
No education	4,023	74.30%	13,058	72.40%
Primary	1,017	18.80%	3,507	19.40%
Secondary	345	6.40%	1,410	7.80%
Higher	29	0.50%	71	0.40%
Sex of child				
Male	2,734	50.50%	9,173	50.80%
Female	2,680	49.50%	8,873	49.20%
Type of place of residence				
Urban	2,375	43.90%	3,796	21.00%
Rural	3,039	56.10%	14,250	79.00%
Wealth index				
Poorest	892	16.50%	3,449	19.10%
Poorer	836	15.40%	3,684	20.40%
Middle	731	13.50%	3,814	21.10%
Richer	980	18.10%	3,985	22.10%
Richest	1,975	36.50%	3,114	17.30%

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an effect which was again reverted in 2014, where having any level of wealth beyond the poorest significantly decreased the prevalence of diarrhoea. Finally, as before, the risk of experiencing diarrhoea decreased with mothers' age, both in 2004 and 2014. For research question 3, the logistic regression model was statistically significant in 2004 $\chi2\ (12) = 45.1015$, $p < .000$ (stunted); $\chi2(12) = 59.426$, $p < 0.000$ (underweight); $\chi2(12) = 41.063$, $p < 0.000$ (wasted). The model was also statistically significant in 2014, $\chi2\ (12) = 101.048$, $p < 0.000$ (stunted); $\chi2(12) = 94.290$, $p < 0.000$ (underweight); $\chi2(12) = 93.100$, $p < 0.000$ (wasted). The results of the analysis are presented in Table 4 and Table 6. In 2014, when controlling for demographic characteristics, having access to an improved source of household drinking water significantly decreased the chances of a child being underweight, stunted, or wasted. Similarly, when controlling for demographic characteristics, having access to an improved household toilet facility significantly reduced the odds of being underweight, stunted, or wasted. Control variables behaved similarly to previous analyses with minor differences. In both samples, a mother with primary education (but not higher education) reduced the likelihood of a child being classified as wasted or underweight when compared to mothers with no education and when other variables were controlled. Being a female child significantly increased the odds of being underweight, stunted, and wasted compared to being a male child in both 2004 and 2014, although this effect was slightly less apparent in 2014.

Compared to living in an urban area, living in a rural area in 2004 significantly reduced the likelihood of being

Table 2. Weighted descriptive statistics for the dependent and independent variables

	2004		2014	
Independent Variables	N	%	N	%
Source of drinking water				
Unimproved	655	12.40%	8,113	45.00%
Improved	4,642	87.60%	9,915	55.00%
Type of toilet facility				
Unimproved	3,008	55.60%	15,899	88.50%
Improved	2,402	44.40%	2,066	11.50%
Source of drinking water				
Piped Water	1,237	26.60%	1,030	5.70%
Public tap, standpipe	0	0.00%	1,685	9.30%
Tubewell, borehole, dugwell, protected well	3,192	68.80%	7,020	38.90%
Protected spring	37	0.80%	52	0.30%
Rainwater	176	3.80%	5	0.00%
Tanker truck, cart with small tank	0	0.00%	112	0.60%
Bottled, sachet water	0	0.00%	11	0.10%
Unprotected dug well	0	0.00%	5,941	33.00%
Surface water, River, dam, lake, ponds, stream, canal, irrigation channel	0	0.00%	1,577	8.70%
Type of toilet facility				
Flush toilet, to pour, to piped sewer system, to septic tank, to pit latrine, to somewhere else	2,116	39.10%	224	1.20%
Pit latrine with slab	286	5.30%	1,842	10.30%
Composting toilet	0	0.00%	0	0.00%
Flush/pour flush not to sewer, septic tank, pit latrine	0	0.00%	0	0.00%
Pit latrine without slab, open pit	0	0.00%	2,871	16.00%
Bucket	0	0.00%	19	0.10%
Hanging toilet/hanging latrine	0	0.00%	151	0.80%
No facility/bush/field/open defecation	3,008	55.60%	12,858	71.60%
Dependent Variables				
Had diarrhoea recently				
No	3,455	74.90%	12,963	80.20%
Yes	1,156	25.10%	3,208	19.80%
Stunted				
No	851	17.50%	7,715	45.30%
Yes	4,013	82.50%	9,298	54.70%
Underweight				
No	723	14.90%	7435	43.70%
Yes	4,141	85.10%	9,578	56.30%
Wasted				
No	829	17.00%	7,561	44.40%
Yes	4,035	83.00%	9,452	55.60%

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Table 3. Logistic regression predicting incidence of diarrhoea by WASH sources and controls

Variable (2004)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	0.090	0.11	0.70	0.404	1.09	[0.89, 1.35]
Type of toilet facility (Improved)	0.018	0.12	0.02	0.878	1.02	[0.81, 1.28]
Highest education level (Higher)	0.288	0.65	0.20	0.658	1.33	[0.37, 4.77]
Highest education level (Secondary)	0.114	0.18	0.43	0.514	1.12	[0.80, 1.58]
Highest education level (Primary)	-0.020	0.09	0.06	0.812	0.98	[0.83, 1.16]
Sex of child (Female)	-0.057	0.07	0.76	0.383	0.95	[0.83, 1.07]
Type of place of residence (Rural)	0.248	0.13	3.73	0.053	1.28	[1.00, 1.65]
Wealth index (Richest)	0.540	0.19	8.49	0.004	1.72	[1.19, 2.47]
Wealth index (Richer)	0.362	0.13	7.92	0.005	1.44	[1.12, 1.85]
Wealth index (Middle)	0.434	0.12	13.03	0.000	1.54	[1.22, 1.96]
Wealth index (Poorer)	0.561	0.11	23.98	0.000	1.75	[1.40, 2.19]
Current age-Respondent	-0.010	0.00	4.18	0.041	0.99	[0.98, 1.00]
Variable (2014)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.021	0.04	0.26	0.609	0.98	[0.90,1.06]
Type of toilet facility (Improved)	-0.061	0.07	0.68	0.409	0.94	[0.81, 1.09]
Highest education level (Higher)	0.093	0.27	0.12	0.734	1.10	[0.64, 1.88]
Highest education level (Secondary)	0.349	0.07	27.14	0.000	1.42	[1.24, 1.62]
Highest education level (Primary)	0.385	0.04	76.52	0.000	1.47	[1.35, 1.60]
Sex of child (Female)	-0.04	0.04	1.10	0.294	0.96	[0.89, 1.04]
Type of place of residence (Rural)	-0.283	0.08	12.48	0.000	0.75	[0.64, 0.88]
Wealth index (Richest)	-0.413	0.10	17.18	0.000	0.66	[0.54, 0.80]
Wealth index (Richer)	-0.246	0.06	16.30	0.000	0.78	[0.69, 0.88]
Wealth index (Middle)	-0.114	0.06	3.72	0.054	0.89	[0.80, 1.00]
Wealth index (Poorer)	-0.149	0.06	6.60	0.010	0.86	[0.77, 0.97]
Current age-Respondent	-0.007	0.00	5.37	0.021	0.99	[0.99, 1.00]

Note: CI = confidence interval for odds ratio (OR). The weighted population was $N = 4{,}611$ in 2004; $N = 16{,}171$ in 2014.

Table 4. Logistic regression results of WASH sources and controls on malnutrition (stunted)

Variable (2004)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.221	0.12	3.37	0.067	0.80	[0.63, 1.02]
Type of toilet facility (Improved)	-0.175	0.12	2.01	0.157	0.84	[0.66, 1.07]
Highest education level (Higher)	-0.120	0.82	0.02	0.884	0.89	[0.18, 4.44]
Highest education level (Secondary)	0.261	0.22	1.44	0.230	1.30	[0.85, 1.99]
Highest education level (Primary)	-0.105	0.09	1.37	0.241	0.90	[0.76, 1.07]
Sex of child (Female)	0.208	0.07	8.40	0.004	1.23	[1.07, 1.42]
Type of place of residence (Rural)	-0.421	0.15	8.33	0.004	0.66	[0.49, 0.87]
Wealth index (Richest)	-0.217	0.20	1.17	0.280	0.81	[0.54, 1.19]
Wealth index (Richer)	-0.173	0.14	1.56	0.212	0.84	[0.64, 1.10]
Wealth index (Middle)	0.000	0.13	0.00	0.998	1.00	[0.77, 1.30]
Wealth index (Poorer)	-0.284	0.12	5.27	0.022	0.75	[0.59, 0.96]
Current age-Respondent	0.012	0.00	5.16	0.023	1.01	[1.00, 1.02]
Variable (2014)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.145	0.03	18.15	0.000	0.87	[0.81, 0.93]
Type of toilet facility (Improved)	-0.354	0.06	35.94	0.000	0.70	[0.63, 0.79]
Highest education level (Higher)	0.078	0.23	0.12	0.734	1.08	[0.69, 1.70]
Highest education level (Secondary)	-0.028	0.06	0.24	0.623	0.97	[0.87, 1.09]
Highest education level (Primary)	-0.039	0.04	1.12	0.291	0.96	[0.90, 1.03]
Sex of child (Female)	0.082	0.03	7.07	0.008	1.09	[1.02, 1.15]
Type of place of residence (Rural)	-0.085	0.07	1.61	0.205	0.92	[0.81, 1.05]
Wealth index (Richest)	0.070	0.08	0.75	0.387	1.07	[0.92, 1.26]
Wealth index (Richer)	0.139	0.05	7.76	0.005	1.15	[1.04, 1.27]
Wealth index (Middle)	-0.034	0.05	0.49	0.485	0.97	[0.88, 1.06]
Wealth index (Poorer)	-0.065	0.05	1.89	0.169	0.94	[0.85, 1.03]
Current age-Respondent	-0.008	0.00	13.21	0.000	0.99	[0.99, 1.00]

Note: The weighted population was $N = 4{,}864$ in 2004; $N = 17{,}013$ in 2014.

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Table 5. Logistic regression results of WASH source types and controls on diarrhoea incidence

Variable (2004)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Surface water)	-	-	-	-	-	-
Source of drinking water (Unprotected spring)	-	-	-	-	-	-
Source of drinking (Unprotected dug well)	-	-	-	-	-	-
Source of drinking water (Bottled, sachet water)	-	-	-	-	-	-
Source of drinking water (Tanker truck)	-	-	-	-	-	-
Source of drinking water (Rainwater)	-0.139	0.23	0.37	0.542	0.87	[0.56,1.36]
Source of drinking water (Protected spring)	-0.992	0.58	2.94	0.086	0.37	[0.12, 1.15]
Source of drinking water (Tubewell)	0.206	0.13	2.41	0.121	1.23	[0.95, 1.60]
Source of drinking water (Public tap)	-	-	-	-	-	-
Type of toilet facility (No facility)	-0.010	0.12	0.01	0.936	0.99	[0.78, 1.26]
Type of toilet facility (Hanging toilet)	-	-	-	-	-	-
Type of toilet facility (Bucket)	-	-	-	-	-	-
Type of toilet facility (Pit Latrine)	-	-	-	-	-	-
Type of toilet facility (Pit Latrine with slab)	-0.160	0.24	0.47	0.495	0.85	[0.54, 1.35]
Highest educational level (Higher)	0.398	0.66	0.36	0.546	1.49	[0.41, 5.43]
Highest educational level (Secondary)	0.120	0.18	0.42	0.497	1.13	[0.80, 1.59]
Highest educational level (Primary)	-0.050	0.09	0.32	0.570	0.95	[0.80, 1.13]
Wealth index (Richest)	0.508	0.20	6.56	0.010	1.66	[1.13, 2.45]
Wealth index (Richer)	0.276	0.15	3.57	0.059	1.32	[0.99, 1.75]
Wealth index (Middle)	0.356	0.14	6.56	0.010	1.43	[1.09, 1.87]
Wealth index (Poorer)	0.498	0.14	13.37	0.000	1.65	[1.26, 2.15]
Type of place of residence (Rural)	0.159	0.14	1.39	0.239	1.17	[0.90, 1.53]
Sex of child (Female)	-0.090	0.07	1.65	0.199	0.91	[0.80, 1.05]
Respondent's current age	-0.014	0.01	7.57	0.006	0.99	[0.98, 1.00]
Variable (2014)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Surface water)	0.270	0.13	4.22	0.040	1.31	[1.01, 1.69]
Source of drinking water (Unprotected spring)	0.104	0.16	0.43	0.514	1.11	[0.81, 1.52]
Source of drinking (Unprotected dug well)	0.369	0.12	10.25	0.001	1.45	[1.15, 1.81]
Source of drinking water (Bottled, sachet water)	0.897	0.75	1.44	0.231	2.45	[0.57, 10.65]
Source of drinking water (Tanker truck)	0.476	0.25	3.55	0.059	1.61	[0.98, 2.64]
Source of drinking water (Rainwater)	0.707	1.30	0.294	0.588	2.03	[0.16, 26.08]
Source of drinking water (Protected spring)	1.021	0.35	8.30	0.004	2.78	[1.39, 5.56]
Source of drinking water (Tubewell)	0.319	0.11	8.36	0.004	1.38	[1.11, 1.71]
Source of drinking water (Public tap)	0.276	0.12	5.67	0.017	1.32	[1.05, 1.66]
Type of toilet facility (No facility)	-0.623	0.17	12.95	0.000	0.54	[0.38, 0.75]
Type of toilet facility (Hanging toilet)	-0.533	0.26	4.31	0.038	0.59	[0.36, 0.97]
Type of toilet facility (Bucket)	-0.721	0.77	0.89	0.347	0.49	[0.11, 2.18]
Type of toilet facility (Pit Latrine)	-0.573	0.17	11.13	0.001	0.56	[0.40, 0.79]
Type of toilet facility (Pit Latrine with slab)	-0.683	0.17	16.11	0.000	0.51	[0.36, 0.71]
Highest educational level (Higher)	0.055	0.28	0.04	0.844	1.06	[0.61, 1.82]
Highest educational level (Secondary)	0.342	0.07	25.66	0.000	1.41	[1.23, 1.61]
Highest educational level (Primary)	0.372	0.04	70.20	0.000	1.45	[1.33, 1.58]
Wealth index (Richest)	-0.406	0.10	15.69	0.000	0.67	[0.55, 0.81]
Wealth index (Richer)	-0.261	0.06	17.86	0.000	0.77	[0.68, 0.87]
Wealth index (Middle)	-0.118	0.06	3.94	0.047	0.89	[0.79, 1.00]
Wealth index (Poorer)	-0.157	0.06	7.27	0.007	0.86	[0.76, 0.96]
Type of place of residence (Rural)	-0.295	0.08	13.09	0.000	0.75	[0.64, 0.87]
Sex of child (Female)	-0.039	0.04	1.04	0.308	0.96	[0.89, 1.04]
Respondent's current age	-0.007	0.00	5.68	0.017	0.99	[0.98, 1.00]

Note: "-" denotes response categories which were absent in the 2004 dataset. The weighted population was N = 4,611 in 2004; N = 16,171 in 2014.

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Table 6. Logistic regression results of WASH sources and controls on malnutrition (underweight and wasted)

Underweight						
Variable (2004)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.239	0.13	3.44	0.064	0.79	[0.61, 1.01]
Type of toilet facility (Improved)	-0.182	0.13	2.03	0.154	0.83	[0.65, 1.07]
Highest education level (Higher)	-0.366	0.82	0.20	0.657	0.69	[0.14, 3.48]
Highest education level (Secondary)	0.405	0.25	2.73	0.098	1.50	[0.927, 2.425]
Highest education level (Primary)	-0.170	0.09	3.28	0.070	0.84	[0.702, 1.014]
Sex of child (Female)	0.242	0.08	10.07	0.002	1.27	[1.097, 1.478]
Type of place of residence (Rural)	-0.496	0.15	10.31	0.001	0.61	[0.450, 0.824]
Wealth index (Richest)	-0.242	0.21	1.32	0.251	0.79	[0.519, 1.187]
Wealth index (Richer)	-0.297	0.15	4.13	0.042	0.74	[0.558, 0.990]
Wealth index (Middle)	0.028	0.14	0.04	0.847	1.03	[0.776, 1.362]
Wealth index (Poorer)	-0.255	0.13	3.68	0.055	0.78	[0.598, 1.006]
Current age-Respondent	0.013	0.01	5.15	0.023	1.01	[1.002, 1.024]
Variable (2014)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.142	0.03	17.44	0.000	0.87	[0.81, 0.93]
Type of toilet facility (Improved)	-0.312	0.06	27.84	0.000	0.73	[0.65, 0.82]
Highest education level (Higher)	-0.030	0.23	0.02	0.896	0.97	[0.62, 1.53]
Highest education level (Secondary)	-0.015	0.06	0.07	0.788	0.99	[0.88, 1.10]
Highest education level (Primary)	-0.075	0.04	4.14	0.042	0.93	[0.86, 1.00]
Sex of child (Female)	0.088	0.03	8.12	0.004	1.09	[0.82, 1.06]
Type of place of residence (Rural)	-0.071	0.07	1.11	0.292	0.93	[0.91, 1.26]
Wealth index (Richest)	0.069	0.08	0.71	0.400	1.07	[1.00, 1.22]
Wealth index (Richer)	0.098	0.05	3.86	0.050	1.10	[0.85, 1.03]
Wealth index (Middle)	-0.067	0.05	1.88	0.171	0.94	[0.84, 1.01]
Wealth index (Poorer)	-0.082	0.05	2.91	0.088	0.92	[1.03, 1.16]
Current age-Respondent	-0.009	0.00	17.09	0.000	0.99	[0.99, 1.00]
Wasted						
Variable (2004)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.064	0.12	0.29	0.587	0.94	[0.75, 1.18]
Type of toilet facility (Improved)	-0.140	0.12	1.30	0.254	0.87	[0.68, 1.11]
Highest education level (Higher)	-0.188	0.82	0.05	0.819	0.83	[0.17, 4.15]
Highest education level (Secondary)	0.275	0.22	1.52	0.218	1.32	[0.85, 2.04]
Highest education level (Primary)	-0.199	0.09	4.97	0.026	0.82	[0.69, 0.98]
Sex of child (Female)	0.189	0.07	6.87	0.009	1.21	[1.05, 1.39]
Type of place of residence (Rural)	-0.336	0.15	5.33	0.021	0.72	[0.54, 0.95]
Wealth index (Richest)	-0.139	0.20	0.48	0.490	0.87	[0.59, 1.29]
Wealth index (Richer)	-0.248	0.14	3.23	0.072	0.78	[0.60, 1.02]
Wealth index (Middle)	0.057	0.13	0.18	0.673	1.06	[0.81, 1.38]
Wealth index (Poorer)	-0.259	0.12	4.38	0.036	0.77	[0.61, 0.98]
Current age-Respondent	0.006	0.00	1.14	0.285	1.01	[1.00, 1.02]
Variable (2014)	β	SE	Wald	*p*	*OR*	95% CI
Source of drinking water (Improved)	-0.152	0.03	19.85	0.000	0.86	[0.80, 0.92]
Type of toilet facility (Improved)	-0.310	0.06	27.50	0.000	0.73	[0.65, 0.82]
Highest education level (Higher)	0.003	0.23	0.00	0.988	1.03	[0.64, 1.58]
Highest education level (Secondary)	-0.025	0.06	0.19	0.661	0.98	[0.87, 1.09]
Highest education level (Primary)	-0.073	0.04	3.97	0.046	0.93	[0.87, 1.00]
Sex of child (Female)	0.086	0.03	7.84	0.005	1.09	[1.01, 1.16]
Type of place of residence (Rural)	-0.105	0.07	2.47	0.117	0.90	[0.79, 1.03]
Wealth index (Richest)	0.054	0.08	0.45	0.504	1.06	[0.90, 1.24]
Wealth index (Richer)	0.097	0.05	3.77	0.052	1.10	[1.00, 1.22]
Wealth index (Middle)	-0.061	0.05	1.57	0.211	0.94	[0.86, 1.04]
Wealth index (Poorer)	-0.088	0.05	3.39	0.066	0.92	[0.83, 1.01]
Current age-Respondent	-0.009	0.00	14.59	0.000	0.99	[0.99, 1.00]

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underweight (β = -0.496, p < 0.001, OR = 0.609 [0.450, 0.824]), stunted (β = -0.421, p < 0.01, OR = 0.656 [0.493, 0.874]), and wasted (β = -0.336, p < 0.05, OR = 0.715 [0.538, 0.951]), with no corresponding effect in 2014. Wealth and age behaved in the same way as reported for the previous research questions, with age associated with increased malnutrition rates in 2004 and lower in 2014, whereas wealth was associated with lower malnutrition rates in 2004 and higher malnutrition rates in 2014.

DISCUSSION

This study found no evidence for the effects of the usage of improved household water sources and sanitation facilities on the prevalence of diarrhoea among children under 5 in Chad, both in 2004 and 2014. When examining the relationship between each type of improved and unimproved household WaSH sources and diarrhoea prevalence, this study also found no effects in 2004. However, it was determined that in 2014, specific types of water sources led to an increased prevalence of diarrhoea, whereas specific sanitation facility types led to a decreased prevalence of diarrhoea among children under 5 in Chad. Regarding the relationship between improved and unimproved household WaSH sources and the prevalence of malnutrition among children under 5 in Chad, no relationship was identified in the 2004 sample. However, in the 2014 sample, this study determined that having access to improved water sources and sanitation facilities significantly reduced the prevalence of malnutrition by reducing the odds of being classified as stunted, underweight, and wasted.

The results of this study indicate that in 2014, more Chadians reported improved rather than unimproved household drinking water sources compared to Chadians in 2004. This study also found that when controlling for demographic variables, having access to an improved household source of drinking water did not significantly affect the odds of a child experiencing diarrhoeal disease in 2004 or 2014. Likewise, when controlling for demographic variables, having access to an improved household sanitation facility did not decrease the odds of a child experiencing diarrhoea in 2004 or 2014. In addition, when controlling for demographic variables, having an improved household water source or an improved household sanitation facility did not solely contribute to a lower prevalence of diarrhoea or malnutrition in 2004 or 2014. Conversely, the types of reported household sanitation sources in Chadian homes worsened in 2014 compared to 2004. Given the increased number of rural households compared to urban households over the 10-year period, this finding was expected because unimproved types of WaSH structures are typically associated with rural areas. An unexpected finding from this study was that living in a rural area in 2014 decreased the chances of a child having diarrhoeal disease compared to living in an urban area in the same year. This is surprising because household WaSH conditions were demonstrated to be worse in rural areas than in urban areas. This finding may reflect the deteriorating infrastructure in Chad. This study also found that reported diarrhoeal disease and all three levels of malnutrition (stunted, underweight, and wasted) decreased from 2004 to 2014. Compared to flush toilets, reduced rates of diarrhoea occurred when the type of sanitation facility was no facility, hanging toilet, and pit latrine. This finding was surprising given that these facilities are unimproved. Additionally, having any level of wealth beyond the poorest significantly increased the prevalence of diarrhoea in 2004. Therefore, children from the poorest families had a lower prevalence of diarrhoea compared to children from wealthier families. These observations may be endogenous effects (i.e., higher rates of diarrhoea might not necessarily be due to flush toilets or wealthier households but to another common denominator shared by those who are wealthier or have a flush toilet). For instance, this finding may be linked to the increase in health education about sanitation in rural or poorer communities, which are the areas mainly targeted for WaSH interventions [31].

Unlike in 2004, in 2014, Chadians who had any level of wealth beyond the poorest (except for the middle) significantly decreased the prevalence of diarrhoea. This finding is expected given that children who have access to higher levels of wealth are more likely to have exposure to education, more likely to go to school and learn about sanitary practices, live in areas with improved water sources and toilet facilities, and reside in households where the mother is able to afford soap for hand washing. In 2014, several sources of water led to a significantly higher prevalence of diarrhoea, notably surface water, unprotected dug wells, protected springs, tubewells, and public taps. This finding was expected because these sources are unimproved. However, because these particular sources of water are more prevalent in rural areas than in urban areas, more people resided in rural areas in 2014, and MDG-related WaSH efforts, the increased prevalence of diarrhoeal disease among children living in urban areas in 2014 was unexpected. More unimproved water sources were expected in the rural areas, which are traditionally less modernised in their infrastructure compared to urban areas [31-33]. Well-designed and conducted randomised trials regarding WaSH and clinical treatments for diarrhoeal disease (e.g., oral rehydration salts [ORS] and zinc supplements) could shed light on the unexpected results. Unfortunately, due to the country's history of war and socio-political strife [35–40], conducting these trials is not always possible; therefore, researchers must rely on observational analyses to fill such gaps.

This study also revealed that the Chadian population experienced a major population shift from urban areas to rural areas over the ten years included in the study. This population shift may be attributed to the country's volatility, civil unrest, and misuse of funds by Chad's government. Despite a tumultuous history [35-40], Chad's recent leaders have seemingly supported national and international global policies and programs to improve

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WaSH conditions and the nutritional status of children. At the national level, Chadian leaders adopted a National Intersectoral Plan for Nutrition and Food (2017 - 2021), a National Policy for Nutrition and Food (2014 - 2025), and a national vision plan called Vision 2030, The Chad We Want [29,30]. Study findings should be interpreted in light of some limitations. This research used secondary data, so the researcher did not directly collect data that may have provided additional input for analyses. Additionally, the data was collected in a multi-stage sampling protocol with cross-sectional samples. The present study could have been strengthened with longitudinal data to examine how participants' household WaSH sources, health behaviours, and health outcomes may have changed over time. Another limitation is that DHS respondents were limited to women and girls aged 15 - 49 years; therefore, data collection regarding children under the care of women aged 50 years and older was not collected. Finally, research findings are not generalisable to all of sub-Saharan Africa.

Nevertheless, this study also had some strengths. Data was used from the same country within a 10-year time span during which the MDGs were being implemented. In comparison to the extant literature, this study is better equipped to support relationships between WaSH interventions and diarrhoeal disease and malnutrition among children under five. Moreover, this study makes a unique contribution to the body of knowledge as no other study has examined the relationship between the distinct household WaSH sources and health outcomes with DHS data. Finally, this study closely examined the widely accepted pre-existing categorisation of the purported improved and unimproved household WaSH sources to learn if improved sources actually result in better health outcomes. The findings from this study are useful for practice and policy because they support the need for a multi-pronged approach to improving WaSH. A multi-pronged approach calls for several actions, including designing water sources and sanitation facilities that are proven effective in mitigating disease spread, ensuring access to improved household WaSH sources and facilities, health education and promotion, provision of supplies (e.g., soap, water containers), and water treatment to support the use of improved sources, implementation of health behaviour change (e.g., regular handwashing, use of safe water, proper water storage, and safe disposal of faeces); and implementation of effective policies that prioritise the improvement of WaSH. Multi-pronged interventions should emphasise health education so that children and households also have the knowledge to understand the importance of key health behaviours like regular hand washing with soap, particularly before eating and after using toilet facilities.

Finally, unlike existing studies [4-7,9,15,20-23,27,33,34], this study delved beyond the mere classification of improved or unimproved and deliberately investigated access within the various types of improved and unimproved WaSH sources.

Conclusion

The results of this study indicate that the use of improved versus unimproved household WaSH sources did not affect diarrhoeal prevalence among children under 5 in Chad. Additionally, diarrhoea and malnutrition decreased over the 10-year period covered in this study. Prior studies have found that improved WaSH sources are effective but not the only factor in improving outcomes, and they do not work in isolation when it comes to diarrhoeal occurrences and malnutrition. Rather, other factors such as health education and effective policies work in tandem with all elements of WaSH, including the amount of clean water when used for washing, cooking, and drinking. Specific household sanitation facilities were found to decrease the prevalence of diarrhoeal disease among children under 5. The types of household sanitation facilities associated with decreased diarrhoeal disease included no facility, hanging toilet, pit latrine, and pit latrine with the slab.

While most of the household sanitation facilities associated with decreased diarrheal disease compared to 'flush toilet' were unimproved, it is important to underscore that the use of flush toilets allows people to properly dispose of waste, ultimately preventing contamination of their environment and diminishing risk to themselves and others. A better understanding of which household sanitation facilities aid in decreasing diarrhoeal disease prevalence is of particular importance to global health professionals who operate developmental efforts with strict budgets requiring prioritisation. With findings from this study, future global health policy and practice in Chad should focus on bridging gaps in the provision of sanitation facilities that are proven to contribute to decreasing the prevalence of diarrhoeal disease and malnutrition among children.

DECLARATIONS

Ethical consideration

The Institutional Review Board (IRB) on Human Subjects at Texas Woman's University, Denton, Texas, approved this research. Additionally, procedures and questionnaires for standard DHS surveys have been reviewed and approved by ICF IRB.

Consent to publish

Not applicable.

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Competing Interest

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Author contributions

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Availability of data

The data used in this study are publicly available on the DHS website (https://www.dhsprogram).

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Pneumonia, oxygen therapy, and amoxicillin dispersible tablets: a practice awareness study among Health Care Workers in three districts in the Eastern Region of Ghana

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Abstract

Background: The safe administration of Oxygen Therapy (OT) with appropriate monitoring is an integral component of the Health Care Workers' (HCWs) role. However, research suggests that HCWs lack adequate knowledge and practice on how to use oxygen delivery equipment appropriately.

Objective: To assess practice awareness (i.e., Knowledge, Attitude and Practice) of Health Care Workers (HCWs) regarding pneumonia, OT, and awareness of Amoxicillin Dispersible Tablets (Amox DT) in case management of children aged below five years

Methods: The study employed a cross-sectional study design involving 356 randomly selected HCWs in public and private (self-financing and faith-based) health facilities in three districts (i.e., New Juaben North, New Juaben South, and Lower Manya Krobo) in the Eastern Region of Ghana. The study adopted both univariate and multivariate data analysis involving Robust Ordinary Least Square and Logistic regression analysis for continuous and binary outcomes, respectively. All analyses were performed using Stata 16.1, and $p < 0.05$ was deemed statistically significant.

Results: The age of the participants ranged from 22 - 79 years, and the mean ± SD was 31.4 ± 1.7 years. There were more females (approximately 80% versus 17%) than males. The overall levels of practice awareness related to oxygen therapy were 45.8% (95% CI = 42.2 - 49.3), 41.4% (95% CI = 39.9 - 42.9), and 32.9% (95% CI = 30.2 - 35.7), respectively for knowledge, attitude and practice. Likewise, the overall practice awareness related to pneumonia was 69.2% (95% CI = 67.5 - 70.7), 89.2% (95% CI = 87.2 - 91.2) and 66.0% (95% CI = 63.7 - 68.3), respectively. Practice awareness regarding OT and pneumonia was significantly influenced by the level of the facility, category, and education level of the HCW. The Integrated Management of Neonatal and Childhood Illnesses (IMNCI) training workshop did not have a significant influence on the practice awareness regarding OT and pneumonia.

Conclusion: The level of practice awareness on the management of pneumonia in children was low (approximately one-third of HCW). In-service training on IMNCI increased the level of awareness of Amox DT but not on OT for the management of pneumonia.

Keywords: Oxygen therapy, pneumonia, amoxicillin dispersible tablets, knowledge, attitude, practice, awareness

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INTRODUCTION

Administration of oxygen therapy (OT) is an essential element of appropriate management for a wide range of clinical conditions, including pneumonia [1]. The use of OT has been established to improve patients' health outcomes when critically needed and used appropriately [2]. In view of this, oxygen has been classified as an essential medicine by the World Health Organization (WHO) and is one of the most effective and safe drugs used by Health Care Workers (HCWs) to treat

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respiratory illnesses like pneumonia in healthcare settings [3]. Pneumonia is a major cause of death in children under the age of five years, accounting for 18% of all deaths in this age group [4]. In every 39 seconds, a child dies of pneumonia globally, killing more children than any other infectious disease, claiming the lives of over 800,000 children under five every year (approximately 2,200 every day), including 153,000 newborns [5]. The United Nations Children's Fund (UNICEF) and WHO Global Action Plan for Pneumonia and Diarrhoea (GAPPD) by 2025 seek to reduce the incidence of severe pneumonia in children under five by 75%, and by 2030, ensure that 90% of cases receive proper antibiotic treatment such as Amoxicillin 250mg Dispersible Tablets (Amox DT) [6].

Unfortunately, access to these products is very challenging for many health systems, especially in Africa. Poor children and those who live in rural regions are less likely than their richer and urban counterparts to receive treatment for pneumonia [5]. Some older formulations of antibiotics (Amoxicillin OS) require manual mixing, measuring, and refrigeration, which may be compromised depending on the caregiver's ability to follow the instructions and whether or not they have a refrigerator. These difficulties may be more common in rural areas where health literacy and asset ownership are lower. Poor storage conditions resulting in exposure to light, heat, and humidity common to tropical areas can contribute to the loss of drug potency [7]. Additionally, if healthcare workers (HCWs) are not familiar with the use of oxygen delivery equipment, it may not be administered effectively to infants who need it, even if gas cylinders were available. A significantly high proportion of pneumonia deaths in young children is due to a lack of oxygen, thereby making oxygen administration a life-saving therapy among children [8]. In 2014, UNICEF recommended the replacement of generic Cotrimoxazole with Amox DT as a first-line treatment for pneumonia in children under five years due to ease of prescription and administration, no requirement for refrigeration, and lower costs because this was a different concept being introduced and was not necessarily linked to the storage conditions [9].

Reasons why Amox DT is preferred include not requiring refrigeration facilities, clear and easy instructions for prescribing and administering, cheaper compared to Amox OS, and logistic advantages in terms of weight and volume [10]. It has been recommended that community health workers should be trained to treat less severe pneumonia cases at the community level using Amox DT, depending on the child's age [9]. With this understanding, the SPRINT (Scaling Pneumonia Response InnovaTions) project was launched by UNICEF in 2019 and has since 2019 been applied by experts in Senegal and Ghana to make the recommended paediatric formulation of Amoxicillin dispersible tablets available at the community level and to scale up oxygen therapy which has been found to effectively avert pneumonia deaths in children [9]. The safe administration of OT with appropriate monitoring is an integral component of the HCWs' role. In Ghana, specifically at the Korle Bu Teaching Hospital, it is estimated that approximately 600 m^3 of cylinder oxygen is used per month among patients who require critical care [11]. However, research suggests that HCWs lack adequate knowledge and practice on how to appropriately use oxygen delivery equipment, as well as requisite training and competence in the practical administration of oxygen [8,12-16]. Further knowledge of pneumonia case management by HCWs has also been estimated to be very low in Western Turkey [17]. Therefore, it is crucial to study the practice awareness of HCWs related to pneumonia, oxygen therapy, and Amox DT to identify gaps in these treatment modalities, which would help improve the quality of care outcomes for children under five in Ghana.

MATERIALS AND METHODS

Study design and sites

The study was a cross-sectional study involving healthcare workers across three SPRINT-implementing districts in the Eastern region of Ghana. The study was conducted in three districts in the Eastern region, namely New Juaben North (NJN), New Juaben South (NJS), and Lower Manya Krobo (LMK). These districts were the sites for the pilot implementation of the SPRINT project in Ghana. The SPRINT project aims to strengthen health systems at all levels by scaling up Oxygen therapy and Amoxicillin Dispersible Tablets (Amox-DT) to manage pneumonia cases among children under five years. The study participants involved HCWs drawn from 99 public and private (i.e., self-financing and faith-based organisations) healthcare facilities in the three districts. The category of healthcare professions involved in this study were medical doctors, general and community nurses, and midwives, while the levels of health facilities involved were the regional hospital, district hospitals (which were mostly owned by the Christian Health Association of Ghana (CHAG), public and private clinics, health centres, and Community-based Health Planning and Services (CHPS) compounds (community clinics).

Sample size estimation

This study hypothesised that there would be a statistically significant difference in the outcome mean scores among the HCWs compared with an assumed mean of 50%. The study, therefore, employed a power sample size calculation for a one-sample mean test, as shown below [18]: $\left(\frac{Z_{1-\alpha/2}+Z_{1-\beta}}{\frac{|\mu_1-\mu_0|}{\delta}}\right)^2$ where $Z_{1-\alpha/2} = 1.96$ (alpha level z-score for a two-tailed test), $Z_{1-\beta} = 0.84$ (statistical power), $\mu1 - \mu0 = 0.015$ (assume the difference in mean scores) and $\delta = 0.1$ (assumed standard deviation). Additionally, a 2% non-response rate was added, and the estimated sample size was 356 HCWs stratified across the three districts.

Sampling and data collection procedure

The sample size was stratified by districts to estimate the sample size needed from each district. Within each district and in each health facility, the daily duty roster was accumulated, and a sampling frame was established. This enabled researchers to adopt a simple random sampling

strategy proportionate to the facility and subject to HCWs on duty. HCWs who were willing to participate in the study consented after the purpose of the study was thoroughly explained to their satisfaction. A questionnaire-based survey was conducted. A questionnaire comprising four sections (i.e. sections A - D) was self-administered. Researchers were available to provide clarity to the respondents as and when required; section A collected information on the socio-demographic characteristics of the participants. Sections B and C collected information on practice awareness about oxygen therapy and pneumonia, respectively, while section D collected information on the level of awareness about the use of Amox DT in the district.

Study variables

The study considered three main domains of outcomes (i.e., knowledge, attitude and practice) that correspond to the survey questionnaire. The three domains were compounded as practice awareness involving knowledge, attitude and practice (KAP). For the knowledge assessment on oxygen therapy, general questions were framed on six themes: oxygen administration treatment, normal range of oxygen saturation, oxygen therapy contraindication, movement of air through lungs, the passive process in respiratory physiology, and the normal breathing rate in adults. A mark was awarded to a correct answer, and scores ranging from 0 - 6 were estimated. A five-point Likert scale questionnaire (6 questions) with reversed scores ranging from 1 - 5 (1 = Strongly disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, and 5 = Strongly agree) was used for the attitude assessment. The overall oxygen therapy attitude score ranged from 6 - 35. For oxygen therapy practices, 11 questions were asked, and a mark was awarded to a correct answer, with the overall scores ranging from 0 – 11. Knowledge of pneumonia was assessed using three domains (pneumonia definition, signs, and symptoms). Participants were asked questions about the definition of pneumonia, some signs, and symptoms with a respective 6, 5, and 6 series of statements (multiple choice) with a correct answer corresponding to 1 mark. A total score ranging from 0 - 17 was generated to assess knowledge about pneumonia. Five positive series of questions were asked to assess the attitude of pneumonia with “Yes, No or Not Sure” responses. An overall score ranging from 0 - 5 was generated. For practice towards the management of pneumonia, five modalities of treatment of pneumonia in children were asked, and participants were to select the correct answer. A mark was awarded for a correct answer, and a score ranging from 0 - 5 was generated to assess the pneumonia practice level.

All practice awareness assessments were converted to percentages. For Amox DT awareness level, participants were asked; Have you heard of dispersible Amoxicillin? And is it used in treating pneumonia? Overall awareness was generated if participants answered Yes to both questions, which were coded as 1 and 0 if otherwise.

Demographic characteristics involved: sex (male versus female), age, marital status (never married, married, divorced), taking care of children under 5 (no or yes), category of the profession (Community Health Nurse, Gen. Nurse, Doctor, Physician Assistant, Midwife), religion (Christian, Islam, or Other), and educational level (Certificate, Diploma, Bachelor, or Master’s degree and above), and attended the training workshop (no or yes). Facility characteristics included the level of health facility (regional hospital, district hospital, CHAG, Health Centre, Clinic, CHPS, and private self-financing facility) and district where the facility is located (New Juaben North (NJN), New Juaben South (NJS), and Lower Manya Krobo (LMK)).

Data Analysis

Three approaches to data analysis were carried out which comprised: univariate descriptive, bivariate, and inferential. For continuous outcomes (practice awareness scores), bivariate data analysis involving a t-test or ANOVA was performed to assess the significant mean difference based on the response category. Before assessing mean equality, skewness and kurtosis test and Shapiro-Wilk test of normality were performed individually (p-value > 0.05 depicting not violating the normal distribution rule of thumb). For binary outcome (awareness), the chi-square test was adopted to assess the significant difference in proportion. The study adopted both univariate and multivariate data analysis involving Robust Ordinary Least Square regression and Logistic regression analysis for continuous and binary outcomes, respectively. Robust estimation was appropriate to control for heteroskedasticity. For multivariate data analysis, the study adopted a stepwise forward selection regression analysis model, setting a p-value ≤ 0.2 as the significance level in addition to the model. For all multiple regression analyses, a specification link test was performed to test for specification errors in all models. Analysis showed no specification error with a p-value > 0.050. All analyses were performed using Stata Statistical Software: Release 16.1 (February 2020), and $p < 0.05$ was deemed statistically significant.

RESULTS

The study achieved a 100% response rate. The proportion of HCWs involved in the study from the three districts was approximately 21%, 38%, and 40%, respectively, for NJN, NJS, and LMK. Ages ranged from 22 to 79 years, and the mean ± SD was 31.4 ± 1.7 years. The sample showed a higher percentage of females (approximately 80% versus 17%). A high proportion of respondents were from the district hospitals (that were owned by CHAG) (29.5%) and the CHPS (29.5%). Most participants were HCWs with two years of certificate educational level (47.2%) (Table 1). The overall level of practice awareness for OT among HCWs in NJN, NJS, and LMK was 45.8% (95% CI = 42.2 - 49.3), 41.4% (95% CI = 39.9 - 42.9), and 32.9 (95%CI = 30.2 - 35.7) respectively. In all three domains, mean differences were statistically significant between the outcome and the level of the facility, category of the profession, and educational level ($p < 0.050$). Meanwhile, the mean

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differences in knowledge and attitude were statistically significant between the sexes ($p < 0.050$). Knowledge scores for oxygen therapy were statistically associated with sex, level of facility, category of profession, and educational level ($p < 0.050$). Mean values for attitude and practice differed significantly between the sexes. The location (i.e., the district where the facility is located) of the facility was a significant contributing factor to the mean differences in HCWs' attitude towards oxygen therapy at NJN (41.9%) (Table 2). Table 3 demonstrates factors associated with practice awareness related to oxygen therapy among HCWs. Univariate analysis of knowledge assessment showed that the level of the facility, category of profession, educational level, and the district in which the facility is located significantly influenced knowledge scores. The analysis showed that knowledge scores on oxygen significantly decreased among HCWs practising in all other levels of the facility compared with those practising at the regional hospital.

Table 1. Demographic characteristics of health care workers involved in the study

Demographic characteristics	Frequency (356)	Percentage
Sex		
Male	60	16.9
Female	284	79.8
Missing	12	3.4
Age group		
≤29	153	43
30-39	144	40.4
40+	26	7.3
Missing	33	9.3
Mean±SD	31.45±7.10	
Level of the health facility		
Regional Hospital	34	9.6
District (CHAG Hospital)	105	29.5
Health Centre	75	21.1
Clinic	36	10.1
CHPS	105	29.5
Missing	1	0.3
Marital Status		
Never married	169	47.5
Married	183	0.6
Divorced	2	0.6
Missing	2	
Taking care of children under 5		
No	104	29.2
Yes	245	68.8
Missing	7	2
Category of profession		
Community Nurse	105	29.5
Gen. Nurse	108	30.3
Doctor	21	5.9
PA	22	6.2
Midwife	98	27.5
Missing	2	0.6
Religion		
Christian	339	95.2
Islam	12	3.4
Other	2	0.6
Missing	3	0.8
Educational level		
Certificate	168	47.2
Diploma	108	30.3
Bachelor	66	18.5
Master's and above	11	3.1
Missing	3	0.8
Attended the training workshop		
No	188	52.8
Yes	100	28.1
Missing	68	19.1
District		
NJN	76	21.3
NJS	136	38.2
LMK	144	40.4

NB: Abbreviation: SD = Standard deviation; CHAG = Christian Health Association of Ghana; PA = Physician Assistant; NJN=New Juaben North; NJS=New Juaben South; LMK=Lower Manya Krobo.

Multivariate analysis showed a significant increase in knowledge among HCWs at CHAG hospital (aβ = 9.60; 95% CI = 1.40 - 17.8). HCWs who were general nurses, doctors, physician assistants (PA), and midwives had a significantly increased knowledge score compared with their counterparts who were community HCWs ($p < 0.050$). There was an increased score in knowledge assessment as the level of education increased among the HCWs. Interestingly, HCWs who attended the training workshop had decreased knowledge scores in oxygen therapy by approximately 5 points compared with those who did not, and it was statistically insignificant (β = - 4.57; 95% CI = -11.55 - 2.39). HCWs in LMK had a significantly decreased knowledge coefficient score by over 5-fold compared with HCWs in NJS (β = -9.82; 95% CI = -16.80 - -2.85) (Table 3). Factors influencing the attitude of OT involved sex differential where the attitude score of males decreased significantly by over three points compared to attitude scores of females (aβ = -3.5; 95% CI = -6.3 - -0.70). HCWs in health centres and CHPS compounds had a significant increase in attitude scores compared with those in the regional hospital (β (95% CI) = 4.51 (0.56 - 8.47) and 5.07 (1.64 - 8.51), respectively).

Doctors had approximately a 6.6-point decrease in attitude scores compared with community health nurses (aβ = -6.56; 95% CI = -12.46 - -0.67). Regarding educational level, attitude scores in relation to oxygen therapy decreased among HCWs with higher education than those with certificates (Table 3). Multivariate analysis related to oxygen therapy showed a significant decrease in practice-related scores among HCWs aged 30 - 39 years compared with those aged ≤ 29 years (β (95% CI) = -7.13 (-13.32 - -0.96)]. It was worthy of note that there was a 9.6 times increase in the practice of oxygen therapy among HCWs in the district or CHAG hospitals compared to those in regional hospitals (aβ (95% CI) = 9.60 (1.39 - 17.89)). Contrariwise, univariate analysis showed a significant decrease in scores [β (95% CI) = -10.87 (-19.05 - -2.69)]. In addition, HCWs in health centres, clinics, and CHPS compounds also had significantly decreased scores related to the practice of oxygen therapy (CHAG hospitals) compared to those in the regional hospital (aβ (95% CI) = -

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Table 2. Level of practice awareness on oxygen therapy among health professionals involved in the study

Demographic characteristics	Category of response	Knowledge	Attitude	Practice
		Mean±SD	Mean±SD	Mean±SD
	Overall	45.83±23.92	41.39±9.73	32.98±18.32
Sex	Male	53.33±19.66	38.70±9.76	37.22±19.23
	Female	46.12±24.81	41.93±9.49	32.33±17.64
	P-value	0.049	0.024	0.154
Age group	≤29	49.44±23.76	41.65±9.47	34.28±18.50
	30-39	43.58±24.63	41.00±9.92	32.03±17.17
	40+	52.63±25.62	41.31±8.63	39.04±16.63
	P-value	0.115	0.865	0.304
Level of facility	Regional	66.00±17.66	38.82±8.38	37.37±13.55
	District (CHAG Hospital)	55.12±19.79	38.32±10.30	35.26±17.65
	Health center	41.53±25.75	43.33±10.47	37.56±20.72
	Clinic	42.75±23.47	40.28±7.70	30.91±19.07
	CHPS	40.53±23.85	43.89±7.72	26.09±14.47
	P-value	<0.001	<0.001	0.001
Marital status	Never married	47.07±22.69	41.57±9.23	33.41±19.15
	Currently married	48.02±25.43	41.08±9.66	31.86±16.35
	Divorced	33.33±23.57	34.28±20.20	45.45±00.00
	P-value	0.673	0.529	0.620
Taking care of under 5	No	51.02±24.47	41.49±8.88	35.31±19.00
	Yes	45.72±23.60	41.05±9.87	31.33±17.19
	P-value	0.096	0.719	0.122
Category of profession	Community Nurse	37.92±22.50	45.18±7.91	25.90±14.89
	General Nurse	53.58±23.37	38.19±9.15	34.33±17.82
	Doctor	62.50±16.99	39.68±9.64	48.25±10.08
	PA	64.58±20.06	40.86±12.02	37.37±17.86
	Midwife	43.84±23.65	41.18±9.43	34.16±19.34
	P-value	<0.001	<0.001	<0.001
Religion	Christian	47.44±24.24	40.85±9.46	32.55±17.77
	Islam	46.97±19.46	49.28±8.87	27.27±11.50
	Other	66.67±23.57	44.28±2.02	72.72±00.00
	P-value	0.53	0.009	0.059
Educational level	Certificate	38.89±22.99	44.17±8.49	28.24±15.95
	Diploma	52.92±22.78	37.85±9.46	34.55±19.94
	Bachelor	58.82±22.45	40.34±9.78	40.77±16.56
	Masters and above	50.00±17.57	38.70±11.16	41.56±7.15
	P-value	<0.001	<0.001	<0.001
Attended training workshop	No	48.29±23.51	41.38±9.54	32.86±18.99
	Yes	44.00±23.51	41.25±9.98	31.82±15.57
	P-value	0.195	0.916	0.712
district Facility is located in	New Juaben North	46.61±21.61	41.97±9.07	33.79±17.32
	New Juaben South	52.52±24.67	40.93±9.15	31.88±19.62
	Lower Manya Krobo	43.54±24.12	41.15±10.05	32.44±16.66
	P-value	0.53	0.009	0.059

Table 3. Robust and stepwise ordinary least square regression analysis showing factors associated with practice awareness of oxygen therapy among health professionals involved in the study

Variable	Knowledge		Attitude		Practice	
	Crude Point Estimate aβ[95%CI]	Adjusted Point Estimate aβ[95%CI]	Crude Point Estimate aβ[95%CI]	Adjusted Point Estimate aβ[95%CI]	Crude Point Estimate aβ[95%CI]	Adjusted Point Estimate aβ[95%CI]
Sex						
Female	ref		ref	ref	ref	
Male	7.49[-0.91-15.89]		-3.23[-6.07--0.38]*	-3.50[-6.30--0.70]*	7.21[-0.58-13.84]	
Age group						
≤29 years	ref	ref	ref		ref	ref
30-39 years	-6.27[-13.21-0.67]	-7.14[-13.32-0.96]*	-0.65[-3.03-1.74]		-5.85[-12.20-0.49]	-7.13[-13.32--0.96]*
40+ years	2.75[-10.16-15.66]		-0.34[-4.13-3.45]		3.20[-8.93-15.33]	
Level of facility						
Regional	ref	ref	ref		ref	ref
District (CHAG Hospital)	-10.80[-21.89-0.28]	9.60[1.40-17.81]*	-0.50[-4.19-3.21]		-10.87[-19.05--2.69]**	9.60[1.39-17.89]*
Health center	-26.68[-38.13--15.22]***		4.51[0.56-8.47]*		-24.47[-33.93--15.00]***	
Clinic	-22.32[-36.26--8.40]**		1.47[-2.62-5.56]		-23.25[-34-99--11.50]***	
CHPS	-26.91[-37.94--15.87]***		5.07[1.64-8.51]**		-25.46[-34.11--16.81]***	
Marital status						
Never married	ref		ref		ref	ref
Currently married	0.79[-5.52-7.11]		-0.49[-2.63-1.66]		0.95[-4.87-6.77]	
Divorced	-14.16[-50.87-22.55]		-7.29[-27.32-12.75]		-13.74[-37.40-9.92]	
Taking care of under-fives						
No	ref		ref		ref	ref
Yes	-6.65[-13.33-0.02]		-0.44[-2.74-1.86]		-5.29[-11.62-1.03]	
Category of profession						
Community Nurse	ref	ref	ref	ref	ref	ref
General Nurse	17.57[9.89-25.24]***	9.58[0.61-18.56]*	-6.99[-9.51--4.48]***		15.67[8.48-22.85]***	9.58[0.61-18.56]*
Doctor	25.09[12.99-37.18]***	17.76[8.10-27.41]***	-5.50[-10.19--0.80]*	-6.56[-12.46--0.67]*	24.58[15.70-33.46]***	17.76[8.10-27.41]**
PA	28.51[15.26-41.76]***	19.39[4.99-33.77]**	-4.32[-9.79-1.13]		26.67[15.81-37.52]***	19.39[4.99-33.77]**
Midwife	4.63[-3.21-12.46]		-4.00[-6.61--1.38]**		5.91[-1.47-13.30]	
Religion						
Christian	ref	ref	ref	ref	ref	ref
Islam	-1.20[-17.01-14.60]		8.43[3.45-13.41]***	9.00[4.45-13.55]***	-0.47[-11.95-11.01]	
Other	18.87[-17.57-55.32]	22.93[0.78-45.08]*	3.43[1.15-5.72]**	4.42[0.99-7.85]*	19.22[-4.30-42.75]	22.93[0.78-45.08]*
Educational level						
Certificate	ref	ref	ref	ref	ref	ref
Diploma	14.61[7.91-21.31]***		-6.32[-8.72--3.93]***		14.03[7.57-20.47]***	
Bachelor	21.72[13.94-29.50]***		-3.83[-6.72--0.94]**	-3.89[-6.85--0.93]**	19.93[12.55-27.32]***	
Masters and above	10.93[-4.47-26.33]	17.19[3.12-31.26]*	-5.47[-11.99-1.04]		11.11[-0.10-22.32]	-17.89[-31.26--3.11]**
Attended training workshop						
No	ref	ref	ref		ref	ref
Yes	-4.57[-11.55-2.39]		-0.14[-2.72-2.44]		-4.82[-10.82-2.25]	
Facility district						
New Juaben South	ref	ref	ref		ref	ref
New Juaben North	-6.64[-14.94-1.66]		1.03[-1.79-3.87]		-5.91[-13.29-1.45]	
Lower Manya Krobo	-9.82[-16.80--2.85]**	-5.73[-12.56-1.11]	0.23[-2.19-2.64]		-8.98[-15.63--2.33]**	-5.72[-12.56-1.11]

Note: ref denotes the reference category used for inference. β represents normalized coefficient estimate both crude and adjusted. CI present Confidence Interval

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9.96 (-16.15 - -3.81)). Furthermore, knowledge about pneumonia among doctors increased significantly compared to community health nurses. Also, HCWs with diplomas (aβ (95% CI) = 18.01 (11.18 - 24.84)) and bachelor's degrees (aβ (95% CI) = 18.86 (6.57 - 31.16)) had significantly increased knowledge scores in relation to pneumonia than those with certificates. HCWs in LMK had significantly increased knowledge scores in pneumonia compared to their colleagues in the NJS district (aβ (95% CI) = 6.17 (1.03 - 11.33)) (Table 5). Factors that significantly increased attitude scores in relation to pneumonia from the univariate analysis were respondents who were divorced, doctors and PAs, and those with higher educational levels ($p < 0.05$). Meanwhile, there was a significant decrease in attitude scores related to pneumonia among HCWs in LMK compared to those in NJS (aβ (95% CI) = -5.09 (-9.53 - -0.65)). The multivariate analysis showed a significant increase (nearly eight-fold) in attitude scores related to pneumonia among HCWs in health centres than those in the regional hospital (aβ (95% CI) = 7.78 (2.83 - 12.74)) (Table 5). The bivariate analysis showed a significant increase among the following factors: males, those aged 30+ years, divorced, all professions other than community health nurses, and increasing education level in practices relating to pneumonia ($p < 0.050$). From the multivariate analysis, males, HCWs aged 40+ years, doctors, and PAs had significant respective increases in their practice scores relating to pneumonia by over 7-fold, 9-fold, 12-fold, and 14-fold. In addition, as education level increased, the

Table 4: Level of practice awareness on pneumonia among health professionals involved in the study

Demographic characteristics	Demographic characteristics	Knowledge	Attitude	Practice
		Mean±SD	Mean±SD	Mean±SD
	Overall	69.12±14.17	89.18±18.07	66.03±20.53
Sex	Male	69.41±17.76	90.28±18.44	72.50±19.28
	Female	66.69±17.57	88.97±18.07	64.82±21.25
	P-value	0.278	0.631	0.013
Age group	≤29	64.90±18.79	87.32±20.76	61.88±23.16
	30-39	68.83±16.45	89.74±16.28	68.72±19.12
	40+	72.40±11.50	88.46±16.17	73.33±15.23
	P-value	0.043	0.559	0.006
Level of facility	Regional	76.99±20.29	92.97±19.30	77.24±16.67
	District (CHAG Hospital)	64.42±20.10	93.48±11.04	64.00±21.03
	Health center	66.90±14.69	88.38±18.34	66.30±21.31
	Clinic	69.77±18.61	86.03±17.61	68.00±21.25
	CHPS	65.60±14.49	85.97±21.56	63.30±20.35
	P-value	0.005	0.026	0.023
Marital status	Never married	66.59±15.78	87.42±20.42	64.41±21.11
	Currently married	67.31±19.33	90.88±15.31	67.22±20.53
	Divorced	79.41±4.15	100±0	80.00±0
	P-value	0.568	0.155	0.384
Taking care of under 5	No	66.68±19.22	89.74±16.51	65.00±19.47
	Yes	67.90±15.84	89.36±18.61	66.34±21.53
	P-value	0.54	0.866	0.6
Category of profession	Community Nurse	62.46±15.80	88.14±17.71	59.38±18.81
	General Nurse	66.12±18.14	91.41±16.15	63.67±21.17
	Doctor	77.03±24.81	97.50±7.69	83.53±16.18
	PA	86.90±6.27	94.05±10.91	85.71±14.34
	Midwife	66.56±15.17	85.87±21.71	67.78±19.36
	P-value	<0.001	0.029	<0.001
Religion	Christian	67.45±17.00	89.33±18.03	66.11±20.70
	Islam	61.76±14.64	95.00±10.54	56.00±22.71
	Other	67.65±12.47	62.50±17.68	80.00±28.28
	P-value	0.535	0.065	0.201
Educational level	Certificate	62.29±15.71	84.76±20.51	60.13±19.33
	Diploma	67.43±17.74	91.09±16.43	60.06±20.29
	Bachelor	75.85±18.05	93.55±11.92	76.67±19.54
	Master's and above	80.21±17.70	95.45±15.07	86.67±19.54
	P-value	<0.001	0.008	<0.001
Attended training workshop	No	65.77±19.49	88.37±18.41	64.12±21.42
	Yes	68.41±12.11	90.05±15.26	68.00±18.31
	P-value	0.218	0.453	0.138
Facility district	New Juaben North	67.18±16.43	89.44±16.72	65.35±20.55
	New Juaben South	67.13±20.14	91.93±16.73	69.33±19.74
	Lower Manya Krobo	66.83±15.69	86.84±19.36	63.13±21.50
	P-value	0.535	0.065	0.201

Table 5. Robust and stepwise ordinary least square regression analysis showing factors associated with practice awareness on pneumonia among health professionals involved in the study

Variable	Knowledge		Attitude		Practice	
	β[95%CI]	aβ[95%CI]	β[95%CI]	aβ[95%CI]	β[95%CI]	aβ[95%CI]
Sex						
Female	ref		ref		ref	ref
Male	2.71[-2.24-7.64]		1.30[-4.07-6.67]		7.67[1.99-13.25]**	7.25[0.62-13.89]*
Age group						
≤29	ref	ref	ref		ref	ref
30-39	3.93[-0.10-7.96]		2.42[-2.03-6.87]		6.83[1.76-11.92]**	
40+	7.50[2.20-12.79]**	5.19[0.43-9.96]*	1.14[-5.93-8.21]		11.44[4.28-18.62]**	9.50[1.75-17.25]*
Level of facility						
Regional	ref	ref	ref	ref	ref	ref
District (CHAG Hospital)	-12.56[-20.37--4.74]**	-9.98[-16.15--3.81]**	0.51[-6.52-7.54]		-13.24[-20.69--5.79]***	-9.24[-15.07--3.41]
Health center	-10.09[-17.65--2.52]**		-4.59[-12.50-3.33]	7.79[2.83-12.74]**	-10.94[-18.71--3.16]	
Clinic	-7.21[-16.31-1.88]		-6.94[-15.83-1.96]		-9.24[-18.50-0.01]	-10.14[-18.51--1.76]*
CHPS	-11.39[-18.73--4.05]**		-6.99[-14.92-0.92]		-13.94[-21.22--6.66]	
Marital status						
Never married	ref	ref	ref	ref	ref	
Currently married	0.72[-2.97-4.41]	-2.58[-6.37-1.20]	3.46[-0.51-7.43]		2.80[-1.77-7.37]	
Divorced	12.83[8.08-17.59]***		12.58[9.35-15.81]***	11.71[4.06-19.37]**	15.58[12.23-18.94]***	
Taking care of under 5						
No	ref		ref		ref	
Yes	1.21[-2.98-5.41]		-0.37[-4.49-3.74]		1.34[-3.49-6.16]	
Category of profession						
Community Nurse	ref	ref	ref		ref	ref
General Nurse	3.66[-0.93-8.24]	2.40[-2.99-7.80]	3.26[-1.55-8.07]		4.29[-1.36-9.95]	
Doctor	14.56[3.67-25.46]**	18.0111.18-24.84]***	9.35[4.49-14.27]***		24.15[15.71-32.58]***	12.00[0.55-23.45]*
PA	24.43[20.44-28.43]***	18.86[6.57-31.16]**	5.90[0.09-11.71]*		26.33[19.20-33.46]***	14.64[4.15-25.12]**
Midwife	4.11[-0.18-8.39]		-2.27[-7.97-3.42]		8.40[2.88-13.91]**	
Religion						
Christian						
Islam	-5.68[-19.26-7.89]		5.67[-0.89-12.23]	8.07[-1.69-17.82]	-10.11[-23.77-3.55]	
Other	0.20[-12.26-12.66]		-26.83[-44.41--9.25]**	-29.01[-44.03--14.00]***	13.89[-14.16-41.93]	
Educational level						
Certificate	ref	ref	ref	ref	ref	ref
Diploma	5.13[1.02-9.26]*	5.43[1.07-9.79]*	5.33[0.72-9.93]*		5.93[0.87-10.99]*	9.32[3.77-14.88]***
Bachelor	13.56[8.58-18.53]***	10.71[3.32-18.10]**	7.79[3.34-12.22]***	4.31[-1.06-9.68]	16.53[10.71-22.37]***	12.73[4.25-21.21]**
Master's and above	17.92[7.57-28.27]***		9.69[0.50-18.88]*		26.54[15.33-37.74]***	17.82[7.09-28.55]***
Attended training workshop						
No	ref		ref	ref	ref	
Yes	2.64[-1.03-6.31]		1.68[-2.48-5.84]	4.35[-0.15-8.86]	3.88[-1.02-8.79]	
Facility district						
New Juaben South	ref	ref	ref	ref	ref	
New Juaben North	0.05[-4.97-5.07]	4.80[-0.56-10.16]	-2.50[-7.39-2.39]		-3.98[-9.94-1.97]	
Lower Manya Krobo	-0.30[-4.56-3.96]	6.17[1.03-11.33]*	-5.09[-9.53--0.65]*	-4.98[-10.18-0.22]	-6.20[-11.29--1.10]*	

Note: ref denotes the reference category used for inference. β represent normalized coefficient estimate both crude and adjusted. CI present Confidence Interval

Table 6. Awareness of Amox DT by demographic characteristics and associated factors among health professionals involved in the study

Variable	Total	Awareness of Amox DT		Test	Logistic regression	
		No	Yes			
		%[95%CI]	%[95%CI]		OR[95%CI]	aOR[95%CI]
	356	68.5[63.5-73.2]	31.5[26.8-36.5]			
	n	%	%			
Sex						
Female	284	69.4	30.6		ref	
Male	60	71.7	28.3	7.26*	0.89[0.48-1.65]	
Missing	12	33.3	66.7			
Age group						
≤29	153	70.6	29.4	1.26		
30-39	144	68.8	31.3		1.09[0.66-1.79]	
40+	26	61.5	38.5		1.50[0.63-3.56]	
Missing	33	63.6	36.4			
Level of the health facility						
Regional Hospital	34	70.6	29.4	4.87	ref	ref
District (CHAG Hospital)	105	75.2	24.8		0.79[0.33-1.86]	0.63[0.33-1.20]
Health Centre	75	62.7	37.3		1.42[0.59-3.43]	
Clinic	36	61.1	38.9		1.53[0.56-4.14]	
CHPS	105	67.6	32.4		1.15[0.49-2.67]	
Missing	1	100	0.0			
Marital Status						
Never married	169	65.1	34.9	2.67	ref	ref
Married	183	72.1	27.9		0.72[0.46-1.13]	0.66[0.37-1.16]
Divorced	2	50	50.0		1.86[0.11-30.46]	
Missing	2	50	50.0			
Taking care of under 5						
No	104	67.3	32.7	0.58	ref	
Yes	245	69.4	30.6		0.91[0.56-1.49]	
Missing	7	57.1	42.9			
Category of profession						
Community Nurse	105	68.6	31.4	15.38**	ref	ref
Gen. Nurse	108	75	25.0		0.73[0.40-1.33]	
Doctor	21	81	19.0		0.51[0.16-1.65]	
PA	22	86.4	13.6		0.34[0.09-1.25]	0.33[0.07-1.47]
Midwife	98	55.1	44.9		1.78[1.00-3.15]*	1.61[0.86-2.99]
Missing	2	50	50.0			
Religion						
Christian	339	68.4	31.6	2.37	ref	
Islam	12	83.3	16.7		0.43[0.09-2.02]	
Other	2	50	50.0		2.17[0.13-35.13]	
Missing	3	33.3	66.7			
Educational level						
Certificate	168	64.9	35.1	8.88	ref	
Diploma	108	64.8	35.2		1.00[0.60-1.66]	
Bachelor	66	78.8	21.2		0.50[0.25-0.97]*	
Master's and above	11	90.9	9.1		0.18[0.02-1.48]]	
Missing	3	100	0.0			
Part of the training workshop						
No	188	72.9	27.1	10.24**	ref	
Yes	100	56	44.0		2.04[1.27-3.51]**	2.28[1.28-4.06]**
Missing	68	75	25.0			
District						
New Juaben South	136	71.3	28.7		ref	ref
New Juaben North	76	61.8	38.2	2.12	1.53[0.85-2.78]	2.08[1.10-3.92]*
Lower Manya Krobo	144	69.4	30.6		1.09[0.65-1.83]	

Note: ref denotes the reference category used for inference. OR represent Odd Ratio estimate both crude and adjusted. CI present Confidence Interval

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likelihood of practices relating to pneumonia increased significantly, and the reverse was also true. Furthermore, there was a significant decrease in coefficient scores related to pneumonia among HCWs in clinics and those in the LMK by over 10-folds and 6-folds, respectively, than those in the regional hospital and NJS district [aβ (95% CI) = -10.14 (-18.51 - -1.76) and -6.20 (-11.29 - -1.10) respectively) (Table 5). The pooled prevalence of awareness of Amox DT among HCWs in the three districts was 31.5 (95% CI = 26.8 - 36.5). The prevalence was, however, non-significantly higher among HCWs in NJN (38.2%) than in NJS (28.7%) and LMK (30.6%).

Differences in Amox DT awareness among participants showed a significant association with sex, category of profession, and those who attended the training workshop ($p < 0.050$) (Table 6). From the bivariate inferential analysis, the odds of Amox DT awareness among midwives was 1.78 (95% CI = 1.00 - 3.15), which was significant when compared with community health nurses. Additionally, there was a 50% chance of Amox DT awareness among HCWs with bachelor's degrees compared with those with a certificate [OR (95% CI) = 0.25 - 0.97)]. There was also an increased odds of Amox DT awareness among HCWs who worked in levels of health facilities other than in the regional hospital, though this was not statistically significant. Further, the level of Amox DT awareness among HCWs who attended the workshop was more than twice that of those who did not attend the workshop [aOR (95% CI) = 2.28 (1.28 - 4.06)). In addition, HCWs in NJN were more than twice as likely to be aware of Amox DT than those in NJS (aOR (95% CI) = 2.08 (1.10 - 3.92)).

DISCUSSION

The goal of the SPRINT project is to reduce pneumonia deaths in children under five years old by scaling up oxygen therapy and Amox DT through a health system-strengthening approach. This study focused on exploring the practice awareness of oxygen therapy, pneumonia, and Amox DT among 356 HCWs in 99 implementing healthcare facilities in three districts in the Eastern region of Ghana.

Oxygen therapy practices awareness and associated risk factors among Health Care Workers

Generally, practice awareness among HCWs on oxygen therapy (OT) was low. The overall average score was less than 50% in all domains. This poor knowledge can potentially have adverse outcomes on case management of pneumonia in children aged under five years. This knowledge gap requires urgent attention and action if the objectives of the SPRINT Project are to be realised. HCWs were less knowledgeable about the basic aspects of the domains assessed. For instance, half of them did not know that oxygen is administered to treat and prevent hypoxia and acute myocardial infarction. This finding could be explained by the fact that in the context of SPRINT and IMNCI, this was not covered. Similarly, a little more than half of HCWs did not know about contraindications in oxygen therapy and the process of ventilation. This worrying finding was similar to what Zeleke and Kefale reported at the Debre Tabor General Hospital in Ethiopia [1]. However, Aloushan and colleagues reported a higher finding (i.e., more than 80%) with respect to the levels of knowledge [12]. The study participants in the latter study were all working in emergency departments (ED), while our study participants were in other clinical areas of the hospital, including the ED, which might have accounted for the variation. About two-thirds of our respondents knew the normal oxygen saturation at rest among adults (i.e., ranges from 96% - 98%). Further, HCWs were also not trained on how to manage pneumonia among adults because all of these are situated within the context of SPRINT and IMNCI. Our findings were, however, comparatively higher than Kigali study of ED nurses whose knowledge level in oxygen therapy was described as "poor" [19]. However, HCWs need to maintain adequate knowledge of contraindications to oxygenation in order to help them assess patients' eligibility for oxygen therapy [20]. These measurement variables are indicative of how much knowledge HCWs have regarding the process of ventilation to facilitate their ability to identify any unusual movement of air in and out of the lungs of a patient [21].

Knowledge level about OT in our study was significantly influenced by the level of the healthcare facility, category of HCW, educational level, and the district in which the facility is located. These findings are similar to studies in Saudi Arabia and Uganda [12,19]. HCWs in the regional hospital were more knowledgeable than their colleagues in other facilities, likely due to the availability of oxygen equipment and the complexity of cases at that level of the facility. In addition, general nurses, doctors, PAs, and midwives had significantly higher OT knowledge scores than their counterparts, who were community HCWs. The quality of training received by these HCWs may have influenced this finding, as demonstrated by the level of education, which significantly increased the knowledge score on oxygen therapy. Doctors, PAs, and some general nurses have a minimum qualification of a bachelor's degree, while some community healthcare workers have a minimum qualification of a certificate. HCWs practising in LMK had significantly less knowledge of OT compared with HCWs in NJS. It is interesting to note how the practice and provision of healthcare services could significantly differ by location, and this affirms the need for policymakers to ensure that inequities in health systems are adequately addressed as part of efforts to attain the goals of Quality Universal Health Coverage (UHC). Further exploration of the causes of these variations among districts could be due to the sampling strategy. However, it could also serve as the basis for future research. There could also be a consideration of instituting a system of benchmarking and learning among districts and facilities. Additionally, attitudes towards OT varied among the sexes, with male

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HCWs having a significantly lower attitude score. In addition, a little more than half of the respondents agree that oral and nasal hygiene and administration of normal saline drops in the nostrils should be routinely performed when administering continuous oxygen in critically ill adult patients. It was encouraging to find that approximately four-fifths of the participants agreed that the administration of OT to patients serves as an indication of the severity of illness, and the process could both be therapeutic and dangerous depending on usage. This practical evidence contradicts what Aloushan and co-workers found in Saudi Arabia, where about 72% of HWCs in the emergency department of a tertiary hospital had a good knowledge of the administration of oxygen, being an indication of the severity of the illness. However, approximately 33% had a positive attitude toward the dangerous aspects of oxygen therapy [12].

The cadre of health professionals and level of education generally influence attitude towards oxygen therapy, but our study revealed a contrasting view where medical doctors demonstrated a decreased attitude towards OT as compared with community health nurses. This could be explained by the fact that the training organised by the implementing districts of the SPRINT project involved more nurses and fewer doctors. Most of the doctors interviewed were junior doctors (house officers) who were yet to complete their internship to obtain permanent licenses. This also indicates that increased knowledge of an HCW in any particular skill and competency may not necessarily translate into a change in attitude or behaviour. Practice scores regarding oxygen therapy were noticed to be generally low. The average score among our participants was approximately a third (i.e., 32%). It was quite surprising that only 14% of HCWs knew that the protocol for oxygen administration ought to be followed meticulously, including special monitoring of the patient.

Also, concerning the best practice on pulse oximetry, a little more than two-fifths knew that the waveform and/or signal strength of the patient must be optimal before an accurate reading could be obtained. In addition, only 32% of the participants knew that the high percentage of oxygen 95 - 100 % (Fi02) used for short-term treatment in trauma is achieved by using a non-rebreathing oxygen mask. This finding is significantly lower than what Zeleke et al. found in Ethiopia (82%) [1]. This could be because the majority of the HCWs worked in low-level healthcare facilities that did not have pulse oximeters. Furthermore, HCWs' age was found to be associated with increasing practice scores for oxygen therapy, where the practice of oxygen therapy was nearly seven times lower in those aged 30-39 years as compared with those aged ≤ 29 years. Zeleke et al. found that HCWs who are aged 30 - 39 years were more likely to demonstrate good practice, though statistically insignificant [1]. Research conducted by Kane and colleagues suggested that knowledge about oxygen therapy is key to a patient's survival [22].

Pneumonia practices awareness and associated risk factors among Health Care Workers

Treating pneumonia by HCWs with a high level of practice awareness would aid in optimal patient care, inspired by the ability to make sound judgments and prevent bad outcomes in the recovery of mechanically ventilated patients [17]. In this study, more participants (3/4) knew the signs and symptoms of pneumonia than in a similar study in Nigeria, where only a third (27.4%) did, and 19.4% could correctly identify fever and shortness of breath as a sign and symptom of pneumonia [23]. However, knowledge about pneumonia (both the definition, signs, and symptoms) among HCWs is generally poor in Ghana [24] and elsewhere [17,25]. In our study, the knowledge about pneumonia was associated with increasing age, level of healthcare facility, level of education, and category of health professional. A probable reason could be that those in the higher healthcare facilities, such as the regional hospital (the highest referral centre in the region), have higher levels of education and are more exposed to pneumonia cases than their counterparts at the lower levels. The differences in the attitude towards the management of pneumonia among HCWs were associated with the cadre of HCWs. A higher level of education, as embodied in doctors and PAs, contributed to a good attitude towards the management of pneumonia as compared with community health nurses. However, HCWs in the LMK district had a significantly poorer attitude towards the management of pneumonia compared with those in NJS. The practice of managing pneumonia revealed that less than half of the HCWs knew the use of oxygen therapy and parenteral antibiotics as examples of treatment options in the management of pneumonia in children. It was interesting to note that approximately 3% of the HCWs indicated that herbal medicines could also be used to treat pneumonia. However, these findings are not surprising as they translate into low average knowledge about oxygen therapy among participants, as found in this study. Pneumonia management practice scores were higher among male HCWs.

Similarly, HCWs at the regional hospital had the best attitude towards the management of pneumonia. This finding could result from the higher levels of knowledge the HCWs there might have about pneumonia, which is probably translating into good practice, as reported by other authors [26]. In addition, medical doctors and PAs were more likely to have good practices in pneumonia management than other categories of staff. However, this finding is not surprising as the aforementioned professionals commonly manage pneumonia cases compared to other health professionals. WHO recommends trained community health workers to treat children aged under five years with pneumonia at the community level [27]. However, the level of practice awareness of community health workers in this study was significantly low and will need to be improved if they are expected to perform the task required of them in treating children under

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five with pneumonia at the community level. There is no doubt that Community health workers play a significant role in the follow-up and referral of sick children during home visits. Since pneumonia is a major cause of morbidity and mortality in children, it is important that practice awareness gaps of all relevant HCWs be addressed as a priority. Further, HCWs who attended the SPRINT training workshop had a good attitude towards the management of pneumonia, though statistically insignificant compared with those who did not attend. Modules for such training activities have to be reviewed to achieve the desired goal of an overall increase in practice awareness towards the management of pneumonia in children under five years.

Amoxicillin dispersible therapy awareness and risk factors among Health Care Workers

The United Nations Commission on Life-saving Commodities for Women and Children has selected Amox DT as one of the 13 life-saving commodities [9]. It is a broad-spectrum antibiotic that is effective against bacterial pneumonia and can be used as the first-line treatment for pneumonia in countries with high cases [9]. The Amox DT model was implemented in Ghana in 2019. However, awareness among HCWs from the three implementing districts was very low, as found in this study. Approximately two-thirds of the participants in the three implementing districts (a higher proportion among those in the New Juaben North district), including those who had received training, were not aware of Amox DT. In this study, more female HCWs, community health nurses and HCWs with certificates and diplomas were more aware of Amox DT than others. This, however, raises the question of why there was low awareness of oxygen therapy and pneumonia practice among the same group. Additionally, HCWs with higher education (bachelor's or master's level) were relatively likely to have good practice awareness related to oxygen therapy and pneumonia but were less likely to be aware of Amox DT. Also, most HCWs at the regional and CHAG hospitals were unaware of Amox DT. This finding could be explained by the fact that Amox DT intervention is targeted at the community level, where HCWs at the clinics and the CHPS compounds or zones were to be trained to administer the drug [28].

Generally, the study found a very low level of practice awareness regarding oxygen therapy and pneumonia in addition to low Amox DT awareness prevalence among the participants. This could be a result of low technical knowledge on the job among HCWs regarding OT and exposure to pneumonia cases, unavailability of guidelines, and inadequate supplies of oxygen delivery devices, as was found elsewhere [29].

Strength and limitation

The main strength of the present study is that it provides useful information and direction for upscaling training to address practice awareness gaps across the country. The study included healthcare facilities at various levels of the healthcare system and clearly demonstrated the strengths at each level. This study provides useful information for training and supervision. It also provides additional information for program planners and implementers, including the Ghana Health Service, who are designing effective and impactful training programmes for their staff members. The overlapping similarities with some of the clinical features (e.g., pneumonia and oxygen therapy) of the ongoing COVID-19 pandemic make it even more urgent to address the findings of our study. The practice awareness design of the study permits mostly quantification of gaps. The addition of a qualitative component may have allowed further exploration of the reasons behind the gaps observed and might be useful in providing further information for training purposes and improving the delivery of healthcare. The findings were based on one region of the country as a pilot study; however, the application of probability-based sampling allows generalisation to the study population from which the sample was drawn. Further, healthcare worker knowledge assessment on oxygen therapy was based on their prior knowledge in the subject area other than from the workshop.

Conclusion

The practice awareness of oxygen therapy and pneumonia, as identified in this study, is low, and the gap established in this study can serve as a baseline to re-strategise and redesign a more effective execution of the SPRINT interventions in Ghana. Similarly, practice awareness among community health nurses regarding oxygen therapy and pneumonia was low, making it necessary to reconsider the WHO's recommendation for "community health nurses to treat children under five with pneumonia". The organisation of the training workshop only influenced Amox DT's awareness. However, it did not significantly impact practice awareness regarding either oxygen therapy or pneumonia. In order to achieve the WHO recommendation (i.e., that community health nurses treat children under five with pneumonia), it will be necessary to redesign training programmes for HCWs through improved content, facilitation and skill acquisition. The supply of oxygen delivery devices to health facilities should be accompanied by the appropriate guidelines and protocols. It is pertinent to include oxygen therapy in IMNCI training programmes for the management of pneumonia.

DECLARATIONS

Ethical consideration

Approval for the use of administrative and health facility data was provided by the Family Health Division (FHD) of the Ghana Health Service (GHS), the Eastern Regional Health Directorate, and the District Health Management Teams of the selected districts. Written informed consent was obtained from health workers and managers who provided administrative and health coverage information. Confidentiality was strictly observed, and no personal health worker information was included in this study.

Consent to publish
All authors agreed on the content of the final paper.

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Competing Interest
No potential conflict of interest was reported by the authors.

Author contributions
YAE, OEH, TJ AI, A-ME, and D-AD conceptualised the study. JT and YAE undertook the statistical analysis and data reporting. YAE, OEH, TJ, AI, A-ME, D-AD, YP, YE, QH, and YAO drafted the initial manuscript. SNAH, UEA, VL, AE, S-MI, AJ, BP, WP, and SM read and provided intellectual content revisions and suggestions for clarity and precision on the subject matter. All authors read and approved the final manuscript submitted for publication.

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Availability of data
Data is available upon request to the corresponding author.

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A combination of unsweetened natural cocoa powder and artemether/lumefantrine: A strategy to improve malaria treatment outcomes

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Abstract

Background: Reports suggest that unsweetened natural cocoa powder (UNCP) has antiplasmodial activity and contains enough fat content to enhance the absorption of artemether/lumefantrine (A/L).

Objective: This study assessed the pharmacokinetic and pharmacodynamic properties of UNCP co-administered with A/L

Methods: Male Sprague-Dawley (SD) rats were infected with A/L-sensitive *Plasmodium berghei*. Rane's curative model was used to assess the effect of the excipient UNCP (300 - 1500 mg/kg) formulated with A/L on parasite clearance. Additionally, healthy non-malarious male SD rats were co-administered orally with the fixed doses of A/L (recommended therapeutic dose of 2 mg/kg artemether and 12 mg/kg lumefantrine) with varying doses of UNCP (300, 600, 900, 1200 and 1500 mg/kg), to assess the effect of UNCP on the disposition of A/L. The number of mice in each group that were given each dose was five (n = 5). Plasma lumefantrine concentration was assayed using HPLC/UV-Vis.

Results: Co-administration of UNCP (1200 and 1500 mg/kg) with A/L caused a significant difference in parasite clearance compared to conventional A/L (Coartem®-only) or UNCP alone. Pharmacokinetic analysis showed that the peak serum concentration (Cmax) of lumefantrine for the A/L+UNCP (1200 mg/kg and 1500 mg/kg) was higher than the Coartem®-only group. Additionally, the area under the lumefantrine concentration-time curve (AUC0→24) post-drug administration was higher for the A/L+UNCP (1200 mg/kg and 1500 mg/kg) groups compared to the commercially obtained conventional A/L Coartem®-only group.

Conclusion: UNCP, co-administered with A/L, increased the in vivo antiplasmodial activity of A/L enhanced lumefantrine disposition (peak concentration and total drug exposure) in rats. Thus, it can be exploited as an excipient in the formulation of A/L for the management of uncomplicated malaria in humans.

Keywords: Artemether/lumefantrine, pharmacokinetics, cocoa powder, malaria, *plasmodium berghei*

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INTRODUCTION

The strategy of using pharmaceutical excipients that synergise the action of active pharmaceutical agents is recommended [1]. Some of these excipients exhibit the activity of the active ingredient, but the effects produced by their use alone are suboptimal. However, when used in combination with active pharmaceutical agents, they enhance the activity of the latter. In situations where enhanced activity is not desired, reduced quantities of the active ingredient can be used in combination with these

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excipients. Reducing the amounts of active ingredients leads to a reduction in the adverse (undesirable) effects caused by these active agents. Malaria still remains a major cause of morbidity and mortality worldwide [2,3]. The use of monotherapy for the management of infectious diseases has resulted in resistance to the agents used [3]. Thus, combination therapy has been adopted as a strategy to prevent multidrug resistance. The standard approach in the management of uncomplicated malaria is the use of Artemisinin-based Combination Therapy (ACT) [3,4].

In Ghana, the three commonly used ACTs for uncomplicated malaria include artemether/lumefantrine (A/L), artesunate/amodiaquine (A/A) and dihydroartemisinin/piperaquine (D/P), which are administered based on patient's body weight [2]. A/L is one of the first-line treatments for uncomplicated malaria in many jurisdictions. However, poor gastrointestinal (GI) absorption occasionally presents a major treatment challenge. This is because lumefantrine is highly dependent on dietary fat for GI absorption [5,6]. Studies have shown two-fold and sixteen-fold increases in systemic bioavailability of artemether and lumefantrine, respectively, when administered with fatty meals [7]. In order for patients to reap the full benefit of the use of A/L for the treatment of uncomplicated malaria, pharmacists usually advise patients to take the medication after a fatty meal. Appetite loss and vomiting are symptoms usually associated with malaria. Patients are unable to eat during this period; thus, poor gastrointestinal absorption is expected. It therefore comes as no surprise that drug resistance to A/L has been reported in some jurisdictions [3].

Unsweetened natural cocoa powder (UNCP) is a popular West African nutraceutical obtained from the beans of Theobroma cacao (cocoa). It is commonly consumed as a beverage in many African countries. UNCP possesses *in vitro* anti-plasmodial activity [8]. It has been reported to attenuate malaria-related liver damage in mice [9] and also mitigate high-dose A/L-induced hepatotoxicities, cardiotoxicities and nephrotoxicities in guinea pigs [10,11]. The chemical composition of Theobroma cacao has been widely studied and well documented to contain flavonoids and other phytochemicals [10]. There is also clear evidence of non-genotoxic and non-organ toxicity with the use of Theobroma cacao [12,13]. Although UNCP is prepared after the removal of the cocoa butter from powdered cocoa beans, there are indications to suggest that UNCP may contain enough fat to aid the absorption of some drugs when co-administered [14,15]. Co-administration of UNCP with A/L is envisaged to enhance the GI absorption of A/L. Additionally, a synergistic antiplasmodial effect is envisaged with the co-administration since UNCP is reported to possess antiplasmodial activity *in vitro* [8]. This study aimed to use an integrated approach to enhance the antiplasmodial effect of A/L by enhancing its absorption through co-administration with UNCP. Thus, plasma concentrations of lumefantrine after co-administration with UNCP and parasitemia clearance were evaluated in *Plasmodium berghei*-infected murine models.

MATERIALS AND METHODS

Materials

The test organism, *Plasmodium berghei* (NK65) malaria parasites, was obtained from the Immunology Department of the Noguchi Memorial Institute for Medical Research (NMIMR). UNCP was procured from Hords Company Ltd, Accra-Ghana (batch number 3010019SEP), under the brand name Brown Gold. The Lumefantrine reference standard was procured from Sigma Aldrich, USA, and the lumefantrine powder from IPCA Laboratories Limited, India. Ketamine injectable was obtained from the anaesthetic clinic of the Korle-Bu Teaching Hospital. Coartem was acquired from Korle Bu Hospital 24-Hour Pharmacy.

Animal Care and Housing

Eight-week-old male Sprague-Dawley (SD) rats with weights between 200 g and 250 g were used for this study. The rats were obtained from the Department of Animal Experimentation of the Center for Plant Medicine Research, Mampong, Ghana. The animals were kept in clean stainless-steel cages at the Animal House of the Department of Medical Microbiology, Korle-Bu, University of Ghana. The cages were kept in enclosed, well-ventilated rooms with proper lighting and under hygienic conditions. Each rat occupied a minimum space of 5.86 cubic meters (61 cm x 31 cm x 31 cm) with soft wood shavings as bedding for comfort. The animals were fed with a normal pellet diet (AGRIMAT, Kumasi), given water ad libitum, and maintained under standard laboratory conditions (temperature 25 ± 1°C, relative humidity 60 - 70%, and 12-hour light-dark cycle). All feeding and water troughs were regularly cleaned to prevent contamination. The animals were made to acclimatise for seven days under the aforementioned conditions before experimentation.

The study protocol was reviewed and approved by the Protocol Review Committee (PRC), College of Health Sciences, University of Ghana – Korle-Bu, Ghana (number: CHS-Et/M5-5.3/20190-2020). Clearance for animal experimentation was also obtained from the University of Ghana's Institutional Animal Care and Use Committee (UG-IACUC) (Number: 2016-02-2Q). All animal experiments were conducted in accordance with Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines [16] and the National Institute of Health guide for the care and use of laboratory animals [17] [18,19].

Preparation of various formulations of A/L with UNCP

The medications used for the study were administered by oral gavage. The medications being investigated were formulated as pharmaceutical suspensions. This is because the various components, artemether, lumefantrine, and UNCP, are not readily soluble in distilled water. The only excipient used was UNCP. This was to ascertain that any

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effect observed would be due solely to the UNCP. In order to administer the same volume of drug to each animal, six different formulations were prepared. The first formulation (A/L plus 300 mg/kg UNCP) was prepared by mixing by geometric dilution in a mortar and pestle the powdered ingredients (1.725 g of UNCP, 11.5 mg of artemether and 69 mg of lumefantrine).

A primary suspension was prepared using part of the vehicle (distilled water), which was further diluted with the remaining distilled water to obtain 50 mL suspension. Thus, each 2 mL dose administered contained 69 mg of UNCP, 0.46 mg artemether and 2.76 mg of lumefantrine [Ratio of artemether to lumefantrine in the marketed product for the treatment of malaria is 1:6, and the recommended therapeutic dose is 2 mg/kg artemether and 12 mg/kg lumefantrine]. Like the method just described, five other formulations were prepared. Since the goal was to determine the effect of UNCP on A/L, the amounts of artemether and lumefantrine were the same as in the previous formulation, but the amount of UNCP was varied. The amounts of UNCP in formulations 2, 3, 4, and 5 were 138 mg, 207 mg, 276 mg, and 345 mg, respectively. These were for animals in groups administered UNCP concentrations of 600, 900, 1200 and 1500 mg/kg respectively [10,11]. Thus, each animal received 2 mL of medication, but they contained the same amount of A/L but different amounts of UNCP.

Culture of *P. Berghei* and infection of SD rats with the parasite

The parasites, *Plasmodium berghei*, were cultured by initial inoculation of donor rats (non-experimental rats) with 0.2 mL of 107 *P. berghei* parasitised red blood cells (RBCs) per µL via the intraperitoneal route. A series of passages were performed until the infection was fully established. Parasite monitoring was performed by obtaining blood from the tail vein of the infected SD rats and placing the blood on a clean glass slide (All Pro Processed Microscope Slide, Cat # 7105, Surgifriend Medicals, Middlesex, England). This was taken through routine thick and thin film preparations for examination under a light microscope (Leica, Galen III, Cat# 317505; Leica Microsystems, Wetzlar, Germany) with immersion oil and ×100 objective lens [9]. After the target parasite density was achieved, the donor rats were anaesthetised with ketamine (5 mg/kg), blood was then drawn from donor animals into heparinised tubes and immediately diluted using normal saline (0.9% NaCl) to obtain a standard inoculum, which was used to infect the test animals. To infect test animals, a volume of 0.2 mL of blood equivalent to 107 *P. berghei* parasitised-infected erythrocytes was introduced into all the experimental animals via intraperitoneal injection. Parasite density was then monitored for three days, where the target parasite range (29% - 32%) was obtained before the administration of test samples commenced [20,21]. These values served as baseline parasitemia for each group prior to treatment. The thick film helped in the determination of parasite density, which was calculated according to the formula recommended by the WHO manual [22]. The number of parasites relative to the number of leucocytes is calculated and expressed as 'parasites per microlitre of blood' from the mathematical formula as follows [22]:

$$\text{Parasite Density/ µL of blood} = \frac{\text{Number of parasites}}{\text{200 white blood cells}} \text{ x } 800$$

The thin film was employed in calculating the percentage parasitemia as follows [22]:

$$\text{Percentage Parasitemia} = \frac{\text{Number of parasitised RBCs}}{\text{Total number of RBCs}} \text{ x } 100$$

Treatment of infected rats with various formulations

Prior to the administration of various treatments, it was ensured that all the SD rats in the various groups were infected with *P. berghei* (NK65) [23,24]. Rats were randomly divided into 12 groups (n = 5). Groups one to five received a combination of A/L and UNCP, groups six to ten received various concentrations of UNCP alone, and groups eleven and twelve were controls. Groups 1-5 were administered A/L (2/12 mg/kg) (at the recommended 1:6 artemether to lumefantrine ratios) in combination with different concentrations of UNCP. Group 1 received A/L (2/12) with 300 mg/kg of UNCP, Group 2 received the same concentration of A/L with 600 mg/kg of UNCP, Group 3 received A/L with 900 mg/kg of UNCP, Group 4, A/L with 1200 mg/kg of UNCP and finally, Group 5 received A/L with 1500 mg/kg of UNCP. Groups 6-10 were given varying doses of only UNCP: 300, 600, 900, 1200 and 1500 mg/kg respectively. Rats in Group 11 served as negative control and thus were administered (distilled water), whilst those in Group 12, the positive control, were administered coartem®- (2/12 mg/kg) (the innovator A/L brand). Treatments were administered per 2 mL oral gavage in fasted animals twice daily for three consecutive days. The animals that received 300 mg only, 600 mg only and vehicle only (negative control) were euthanised after the 24-hour samples were taken because they were in distress. After the third day, blood samples were drawn from the tail veins of rats at predetermined times (0,8,24,36,48 and 60 hours) to assess parasite clearance, which was done via microscopic examination. A two-hour gap of no feeding of the rats was maintained pre- and post-sample administration to ensure that the presence of food did not affect the absorption of various treatments. Additionally, rats were followed up to estimate survival times post-treatment. Animals were observed in compliance with all governing regulations involving humane care and the use of animals in research. Distressed rats were euthanised by placing them in a carbon dioxide (CO2) chamber [25,26]. Signs of distress included, but were not limited to, decreased mobility, scruffy coat, and hunched posture.

Pharmacokinetic estimation of UNCP and A/L formulations

This aspect of the study was performed in healthy non-malaria-infected animals. Thirty-five SD rats were randomly put into seven groups (n = 5). Groups 1-5 were

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administered A/L (at the recommended therapeutic doses of 2 mg/kg artemether and 12 mg/kg lumefantrine) formulated with varying concentrations of UNCP: 300, 600, 900, 1200 and 1500 mg/kg, respectively, via the oral route as done previously [10,11]. Rats in Group 6 were given coartem®-(2 mg/kg artemether and 12 mg/kg lumefantrine, the innovator A/L brand). Mice in each group received a single dose of the treatment assigned, after which blood samples were collected. The first blood sample was drawn 30 minutes after the last dose. This was done by taking 500 µL whole blood from the tail vein of the rats at times of 0.5,1, 2,4,8,12, and 24 hours into heparinised tubes. Samples were kept on ice packs immediately and centrifuged at 2,500 rpm for 15 minutes within one hour after collection. Plasma was collected into cryotubes, labelled, and stored at -20ºC for subsequent high-performance liquid chromatography (HPLC) analyses.

The peak plasma drug concentration (Cmax) and the time to achieve this peak (Tmax) of lumefantrine were extrapolated from concentration-time curves. The elimination rate constant (Ke) was determined by linear regression analysis of the terminal-linear part of the log plasma concentration-time curves. The elimination half-life (t1/2e) was calculated from 0.693K-1. The area under the concentration-time curve (AUC) was calculated using the linear trapezoidal rule. Pharmacokinetic analysis was conducted using GraphPad Prism version 7.0 for Windows, GraphPad Software, www.graphpad.com.

Plasma lumefantrine concentrations determined by high-performance liquid chromatography

The stored plasma samples were thawed at room temperature for about 1-2 hours. Samples were vortexed in seconds. Acetonitrile, 1.5 mL, was added to precipitate plasma proteins, vortexed for 1 minute, and then centrifuged for 5 minutes at 10,000 × g [34]. The supernatant was transferred into clean tubes and evaporated to dryness at 37°C under a steady stream of nitrogen gas. The residue was reconstituted with 500 µL acetonitrile, filtered using a 0.4 µm syringe filter and 20 µL injected into the HPLC column. HPLC analysis was performed on an LC-20AT (Shimadzu, Japan) liquid chromatograph equipped with an SPDM-20A UV detector (Shimadzu, Japan).

Separation was performed on a YMC-Pack Pro C18, 5 µm, 12 nm, length 150 mm and internal diameter 3.0 mm. The column temperature was set at 30 ºC, and the flow rate was 1.0 ml/minute. The detection conditions were as follows: UV set at 380 nm. A UV-visible spectrophotometer model-1700 (Shimadzu, Japan) was used to determine UV spectra. Analysis was carried out for lumefantrine alone due to the fact that artemether absorption is not known to be a challenge. The chromatographic analysis was carried out using the International Pharmacopoeia (IP) method [27,28]. A similar experiment using the same equipment has been performed in the same laboratory previously [29].

Liver function test

After the last time point, blood was also collected for liver function test (LFT). Whole blood (1 mL) was collected in clot activator gel tubes and allowed about 10 minutes to clot. This was followed by centrifugation at 1000 g for 10 minutes to obtain serum. Biochemical analysis was performed using an autoanalyser (URIT-8021AVet, China). Specific biochemical markers such as alanine aminotransferase (ALT), alkaline phosphatase (ALP), aspartate aminotransferase (AST) and albumin were determined.

Statistical Analyses

Results were reported as a Means. Error bars are indicative of the standard deviation of uncertainty. Statistical analysis was performed using one-way (ANOVA) followed by Bonferroni's multiple comparison test. Analysis was done using GraphPad Prism version 8.0.2 for Windows, GraphPad Software, and www.praphpad.com. Statistical significance was set at *p < 0.05, **p < 0.01 and ***p < 0.001.

RESULTS

Mean parasitemia levels after treatment with UNCP only

There was an initial increase in parasitemia 24 hours after UNCP administration across all the UNCP-only groups shown in Figure 1A. The animals that received 300 mg only, 600 mg only and vehicle only (negative control) were euthanised after the 24-hour samples were taken because they were in distress. There was a difference in parasitemia for the higher doses of the UNCP (1200 mg/kg and 1500 mg/kg) compared to the vehicle group at 24 hours (Figure 1B)

Mean parasitemia levels after treatment with UNCP and A/L

Varying UNCP doses, co-administered with a fixed dose of A/L, appeared to decrease parasitemia with increasing UNCP. Total parasitemia clearance was obtained for almost all the groups in 60 hours (Figure 2A).

For all the groups, there was a significant difference between the baseline parasitemia levels and the treated groups at predetermined time points. Twenty-four hours after treatment commenced, there was no observable difference between the treatment groups (Figure 2A). The drop in parasite levels of the positive control was comparable to that of the group treated with 900 mg UNCP + A/L. Groups that received 1200 mg and 1500 mg had much lower parasite levels than the positive control group (Figures 2B and 2C).

Pharmacokinetic estimation of UNCP and A/L formulations

A plasma concentration-time plot for lumefantrine in the A/L+UNCP groups showed a general increase in plasma occurring within 4 - 8 hours, followed by a general decrease within 24 hours post-dose administration (Figure 3).

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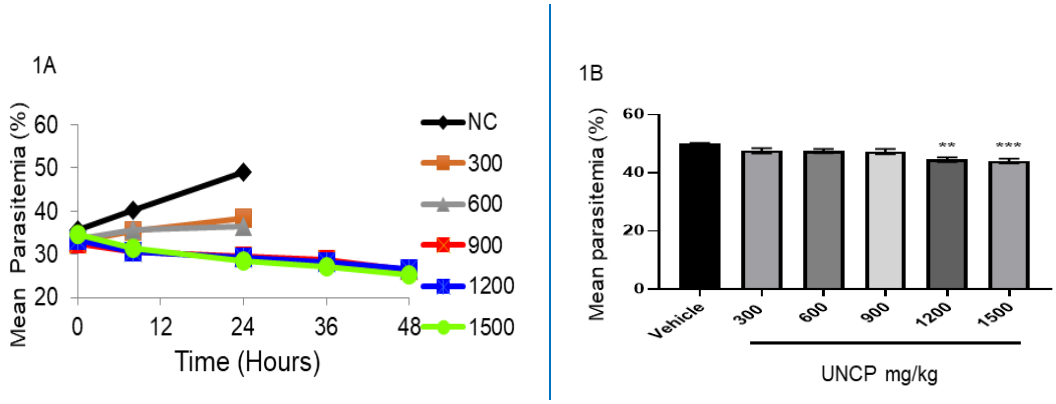

Figure 1. In vivo antiplasmodial activity of UNCP-only (300, 600, 900, 1200 and1500 mg/kg) on *Plasmodium berghei* (NK65) parasitemia; (A) Parasitemia trends from baseline till death of animals for UNCP-only formulations. (B) In vivo effect of higher doses of UNCP (1200 mg/kg and 1500 mg/kg) on parasitemia compared to the negative control group (no treatment) at 24 hours post exposure. (n = 5) and *p < 0.05, **p < 0.01 and ***p < 0.001 using two-way ANOVA followed by Bonferroni's multiple comparison post hoc analysis

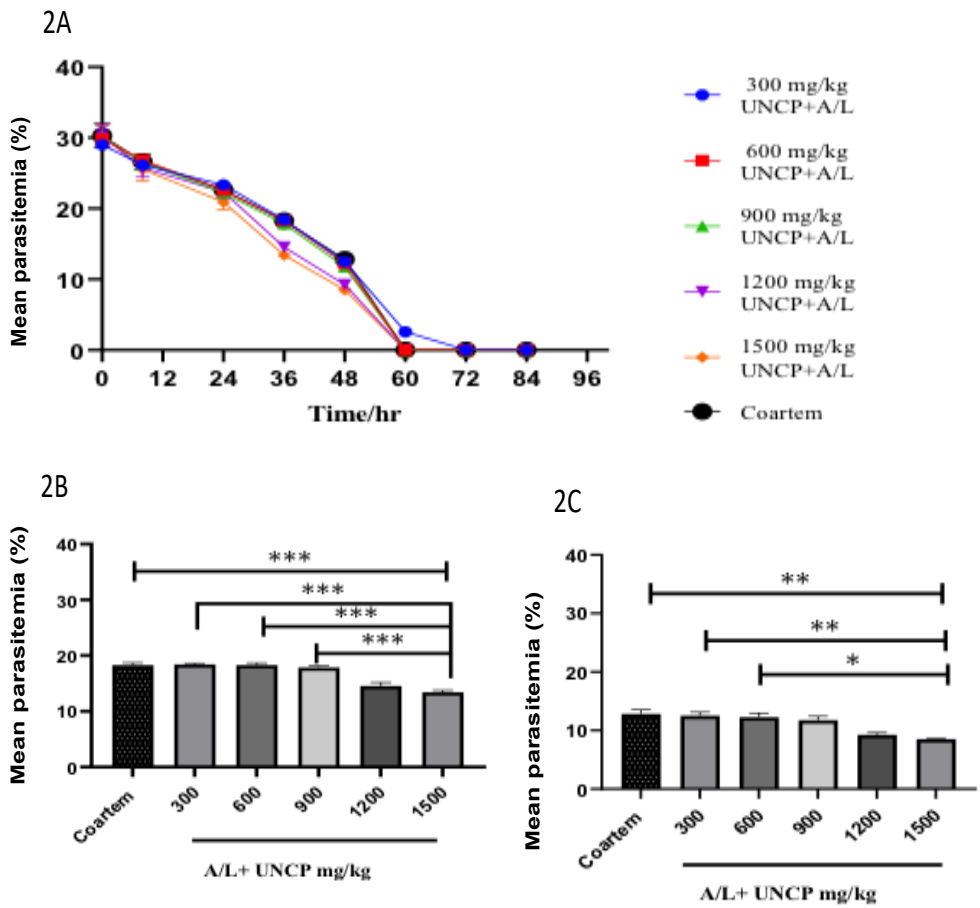

Figure 2A. *In vivo* antiplasmodial activity of A/L+UNCP (300, 600, 900, 1200 and 1500 mg/kg) in rats infected with *Plasmodium berghei* (NK65).

*The overall antimalarial trend over a 96-hour time course. Comparison of parasitemia clearance of A/L + UNCP (varying amounts) at time points 36 hours (Figure 2B) and 48 hours (Figure 2C) respectively. (n = 5). *P < 0.05, **P < 0.01 and ***P < 0.001 using Two-way ANOVA followed by Bonferroni's multiple comparison post hoc analysis).*

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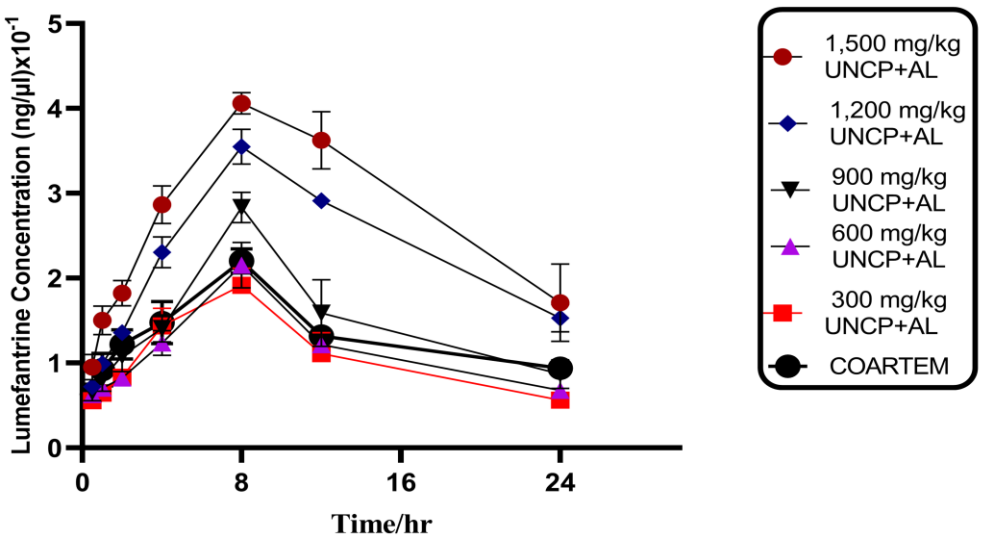

Figure 3. A 24-hour plasma concentration-time curve of lumefantrine in various treatment groups

Table 1. Pharmacokinetic Parameters of lumefantrine in the various treatment groups

PK Parameter	Treatment Group [Mean ± SEM]						Overall *p*-value
	A/L+300 mg/kg UNCP	A/L+600 mg/kg UNCP	A/L+900 mg/kg UNCP	A/L+1200 mg/kg UNCP	A/L+1500 mg/kg UNCP	COARTEM	
T_{max} (hr)	8.17±0.04^{B}	8.10±0.03^{B}	8.31±0.13^{B}	8.10±0.04^{B}	8.28±0.04^{B}	8.19±0.05	0.1667
C_{max} (ng/µl*10^{-1})	1.92±0.20^{B}	2.15±0.27^{B}	2.83±0.18^{B}	3.55±0.21^{A}	4.06±0.13^{A}	2.20±0.14	<0.000
$AUC_{0\rightarrow 24}$ (ng/µl*10^{-1}*hr)	26.11±3.01^{A}	28.04±1.59^{A}	35.89±4.79^{A}	56.57±2.13^{A}	68.21±6.11^{A}	32.12±1.85	<0.0001
K_e (hr^{-1})	0.05±0.02^{B}	0.05±0.00^{B}	0.05±0.01^{B}	0.06±0.01^{B}	0.07±0.02^{B}	0.03±0.01	0.3879
$t_{1/2}$ (hr)	17.75±0.20^{B}	14.27±0.27^{B}	14.65±0.18^{B}	13.26±0.21^{B}	11.86±0.13^{B}	26.23±0.14	0.2002

Table 2. Biochemical analysis of blood collected from rats in various groups

Liver function test	A/L +300 mg/kg UNCP	A/L +600 mg/kg UNCP	A/L +900 mg/kg UNCP	A/L +1,200 mg/kg UNCP	A/L +1,500 mg/kg UNCP	Coartem Only	Vehicle Only	p-value
AST U/L	478.20 ± 47.02	497.60 ± 39.90	624.32 ± 187.35	483.90 ± 33.38	564.52 ±194.41	774.16 ±198.61	863.01 ±117.6	0.3790
ALT U/L	99.02± 23.62	104.82± 20.41	204.42± 43.76	187.88 ±25.07	263.04± 92.58	278.48 ±44.51	204.90 ±23.78	0.1962
ALP U/L	119.14 ±32.22	131.04 ±35.33	188.72 ±25.46	118.04 ±24.07	204 ±49.94	305.80 ±13.47	225.34 ±15.20	0.0043
ALBUMIN g/L	67.58 ±20.34	70.12 ±23.29	159.40 ±53.88	56 ±18.65	200.48 ±110.74	200.48 ±46.25	60.8± 15.81	0.3495

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Liver function tests

Relative to the vehicle-only group (no treatment), ALT and AST levels did not appear elevated. Hence, it may be difficult to suggest liver damage after treatment.

DISCUSSION

In vitro, antiplasmodial activity of UNCP has been previously reported in mice [8]. However, *in vitro*, pharmacological activity does not always translate into in vivo activity due to pharmacokinetic factors such as drug absorption. This study sought to investigate the in vivo antiplasmodial activity of UNCP co-administered with A/L in SD rats. *Plasmodium berghei*-infected rodent models usually typify *P. falciparum* malaria in man and are commonly used for such studies. After establishing a baseline parasitemia of 29-32%, UNCP-only formulations (different concentrations) were administered to the animals. Twenty-four hours after treatment was initiated, there was no observed effect. Instead, the percentage of parasites in the blood continued to rise (Figure 1A). The groups that received lower doses (300, 600 mg/kg) were euthanised after the 24-hour time point. Even though UNCP showed parasite suppression activity at higher doses, it was observed that all the animals showed signs of distress between 24 and 48 hours.

The animals in the groups that received 900, 1200 and 1500 mg/kg of UNCP remained alive till the 48-hour time point and were also euthanised. The difference in survival time between these animals was not significant. The *in vitro* antiplasmodial property of UNCP has been attributed to the presence of flavonoids [9, 13,46] and other phytochemicals like alkaloids and tannins [8,15,27,30]. These same phytochemicals may be responsible for the observed in vivo activity. This can be postulated to mean that even though UNCP possesses some antiplasmodial activity, it is not efficient in clearing the parasites from the blood of the infected rats. Thus, UNCP alone may not be curative in cases of malaria. Trace minerals such as manganese, zinc, and copper found in UNCP have been reported to possess immunomodulatory properties [31,32] that may inhibit malaria parasite growth. This effect may have augmented the activity of the phytochemical constituents in UNCP in inhibiting parasite growth [15,33,34].

When higher doses of UNCP were co-administered with a fixed dose of A/L, a general dose-dependent decrease in parasitemia at various time points was observed (Figures 2B and 2C). This was, however, not coherent with the trend of activities of AST and ALT in Figure 2A. This observation may be due to the possible synergistic antiplasmodial activity of UNCP and A/L or an enhancement of the absorption of A/L by UNCP, which invariably would increase plasma concentration (bioavailability) of A/L. Other studies have shown the varying effects of AL in murine models [35,36,37]. Total parasite clearance was observed for almost all the groups within 60 hours (Figure 2A). From the results in Figures 2B and 2C, parasitemia clearance for A/L with UNCP 900 mg/kg and positive control (coartem®) were comparable. The conventional A/L (coartem®) used as positive control has been formulated with excipients to yield adequate absorption and bioavailability. However, the new formulations used contained just the active ingredients A/L and UNCP. This was done to ensure that any effect observed on the A/L was solely due to the UNCP. Combinations of UNCP (1200 and 1500 mg/kg) and A/L showed better parasite clearance than the positive control (Figures 2B and 2C). The findings of this research suggest that formulating A/L with 900 mg/kg of UNCP will produce results similar to the innovator brand (coartem®). Although the higher doses of UNCP (1200 and 1500 mg/kg) with A/L produced better results, the authors are not recommending its use in the formulation of a unit dosage form. This is due to the fact that the most convenient adult dosage forms are tablets or capsules.

From the formulation standpoint, tablets or capsules will not be appropriate in this instance as their sizes (due to the quantities of UNCP to be used) will pose swallowing challenges to patients. Authors are therefore proposing the formulation of individually divided granules (powders) that will contain A/L plus 900 mg of UNCP packaged in sachets to be reconstituted just before administration. Further studies need to be done on doses of UNCP between 600 mg/kg and 900 mg/kg in order to optimise the appropriate dose. Even though there was an observable difference in parasite clearance, this was only significant after 36 hours (Day 2), which corroborates the assertion of stimulation of an immune response by the UNCP [15], a process that requires time. Cocoa has been established to be rich in antioxidants and has immune modulatory properties [31,32]. Its immunomodulation has been linked with the presence of flavonoids with regulatory effects on acquired immune response in both *in vivo* and *in vitro* studies [38-40].

A/L, as an antimalarial agent used in the treatment of uncomplicated *falciparum* malaria, is fraught with the problem of poor GI absorption and this challenge is known to improve when the drug is administered with fatty food [5,41,42]. The observed increase in parasitemia clearance when A/L was co-administered with UNCP could be due to the fat constituent (28%) in UNCP (Figure 2). As absorption increases, there is a corresponding increase in systemic drug concentration [5,41]. The study focused on lumefantrine absorption and not artemether against the background of the aforementioned advantage that a fatty meal has on A/L absorption and/or bioavailability pertaining to lumefantrine and not artemether. It is worth mentioning that patients could benefit from the energy offered by the other components of UNCP as well.

The use of UNCP as an additive or excipient in the formulation of A/L powders may be an option worth employing to improve the therapeutic outcomes of A/L. West Africa produces about 70% of the world's cocoa, with

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Ghana and the Ivory Coast being the leading producers. Africa is one of the most malaria-endemic regions despite its rich medicinal plant sources [43,44]. Thus, employing UNCP as an excipient in the pharmaceutical formulation of antimalarial drugs may improve malaria treatment outcomes. From the observations made in this study, it is evident that administering A/L with UNCP translates to better systemic peak lumefantrine concentration, total lumefantrine exposure and parasite clearance. The strategy of incorporating UNCP into A/L malaria management in Africa is likely to be more cost-effective. The use of these nutraceuticals may be beneficial in malaria prophylaxis [43, 45, 46]. This can be recommended in addition to malaria treatment, especially in children below five years, a vulnerable group to malaria [45,47,48]. Paediatric dosage forms of A/L are sometimes presented as divided powders (individually packed) for reconstitution into suspensions before use, and UNCP could be used as an excipient. Data from the pharmacokinetic aspect of the study showed that AUC, a surrogate for total drug exposure, was found to be higher among rats administered UNCP with A/L. AUC can also be indicative of the extent of absorption of a drug or its bioavailability.

Overall, the amount of the A/L absorbed when co-administered with UNCP was greater than the conventional formulation in a fasted murine model. Additionally, the peak plasma concentrations (Cmax) of the AL+UNCP groups were higher than the coartem® group, which sometimes gives an indication of the overall absorption of the drug. Hence, we can postulate that absorption was better when UNCP was combined with A/L (Table 1). The LFT results showed a significant increase in ALP for only the AL+UNCP (300 mg/kg) group (Table 2). High serum ALP for this group could be from sources other than the liver, such as bone and kidney. Nevertheless, further investigations may be needed to explain this observation. This potential use of UNCP as an excipient in the formulation of A/L can be exploited in the management of uncomplicated malaria in humans in the form of nanoparticles. A limitation of this study might be the fact that liver enzymes were examined, but other toxicities (renal) were not assessed. Additionally, the animals that were given low-dose UNCP had to be euthanised between 24-48 hours. This posed a challenge in comparing the parasite levels with those of the other groups.

Conclusion

UNCP alone was not efficient in reducing parasitaemia in rats. A combination of UNCP with A/L was found to improve *P. berghei* parasite clearance in SD rats. A/L formulated with 900 mg/kg of UNCP produced results comparable with the innovator brand, Coartem. Co-formulation of A/L with UNCP, a nutraceutical, would ensure that adequate plasma concentrations of the antimalarial agent are achieved independent of the patient's ability to ingest a fatty meal.

DECLARATIONS

Ethical consideration

The study protocol was reviewed and approved by the Protocol Review Committee (PRC), College of Health Sciences, University of Ghana – Korle-Bu, Ghana (number: CHS-Et/M5-5.3/20190-2020). Clearance for animal experimentation was also obtained from the University of Ghana's Institutional Animal Care and Use Committee (UG-IACUC) (Number: 2016-02-2Q).

Consent to publish

All authors agreed on the content of the final paper.

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None

Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions

PD and IJAG conceived the study. PD, PA, SKA, IJAG and GLAB designed the methodology. PA performed the experiments under the supervision of PD, IJAG, SKA, JB and GLAB. PD, PA, SKA and AKN summarised the data. PD, PA, GLAB. BBN, PD, OAD, AKN, EOB, JES, SKA, MFA and IJAG were involved in the analysis of data and writing of the manuscript.

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Availability of data

Data for this work is available upon reasonable request from the corresponding author.

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Dietary patterns associated with body mass index in selected adult populations in Accra, Ghana

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Abstract

Background: Dietary pattern analysis is more appropriate for explaining diet-disease relationships instead of single nutrients in the treatment and prevention of diet and diseases.

Objective: The study aimed to identify dietary patterns and explore their association with body mass index among adults in selected areas in Accra.

Methods: This was a retrospective study comprising four (4) cross-sectional studies among healthy adults in the Greater Accra region of Ghana. Appropriately designed/pre-tested questionnaires submitted by 208 respondents were analysed for food patterns using principal component analysis to estimate pattern scores for each food item. Statistical significance was set at $p < 0.05$.

Results: Eight dietary patterns explaining 54.8% of the variation in the dietary intake of the study participants were identified. These were the traditional pattern, combined pattern, major protein pattern, modified pattern, white and red meat pattern, sweets and pastries pattern, rare dietary pattern and vegetables with moisture pattern. The mean BMI of the population was 23.1 ± 3.9 kg/m^2, with the prevalence of underweight, normal weight, overweight and obese observed to be 5.8%, 68.3%, 19.7%, and 6.2%, respectively. The traditional dietary pattern and the sweets and pastries patterns were significantly associated with BMI ($p < 0.05$ and $p < 0.001$, respectively).

Conclusion: Eight (8) dietary patterns were identified. The traditional sweets and pastries patterns were found to be related to weight gain.

Keywords: Dietary pattern, BMI, Adults, food frequency questionnaire

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INTRODUCTION

The traditional approach in nutritional epidemiology previously focused on using single nutrients to prevent and treat diseases such as scurvy, beriberi, pellagra, and nutritional anaemias [1]. To determine the association between diet and health, the focus is currently on the assessment of dietary patterns instead of single nutrients in disease treatment and prevention [2]. This is supported by the fact that nutrients are not eaten in isolation but rather as a diet, which is made up of a combination of foods that contain multiple nutrients [2]. Additionally, nutrients in foods may exert a synergistic or antagonistic effect in addition to bioactive compounds such as drugs. Hence, there is a need for a comprehensive understanding of how the pattern of consumption of nutrients and other bioactive compounds in foods influences health outcomes [3]. "Dietary pattern (DP) is defined as the quantity, variety, or combination of different foods and beverages in a diet and the frequency with which they are habitually consumed" [4]. It is a reflection of an individual's habitual exposure to a variety of foods [5]. Economic development and rapid urbanisation have resulted in changes in dietary patterns characterised by a shift in disease burden from undernutrition to overnutrition in both developed and developing countries [6]. Identifying and characterising

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dietary patterns will encourage healthy dietary practices and help create public health strategies [7].

Global reports have shown that dietary patterns with higher consumption of nutrient-dense foods such as fruits, cereals, vegetables, low-fat meat, and dairy products are associated with good health outcomes in adults, including a decline in the rate of weight gain over time and improved survival of malnutrition and quality of life [8,9]. On the other hand, nutrient-deficient and energy-dense dietary patterns with higher consumption of high-fat dairy products, desserts and sweets have been associated with increased rates of malnutrition in adults. The Centre for Disease Control [10] described BMI as one of the several modifiable indicators for the increased risk of non-communicable diseases (NCDs). The food frequency data was used as the theoretical basis for this study to explain latent factors underpinning patterns that correlate with other biological and clinical variables. The factor analysis offered the chance to decipher the underlying components of the diet that demonstrated a relationship with BMI. Values for BMI were used to determine the obesity and overweight status of the respondents. Whereas the individual nutrient of the diet influences the biochemical reactions within the body, it is the combined effect of these nutrients in the diet that ensures the adequacy and maximum utilisation of these nutrients [2]. Considering that diet is the main source of nutrients and energy for the body, it is generally considered that dietary patterns determine overall health outcomes rather than individual diet.

A significant association between Western dietary patterns and an increased risk of BMI and associated risk factors among adults in the Middle East and North Africa has been reported [9,11,12]. Increased adherence to the Mediterranean dietary pattern was associated with a decreased BMI and risk of coronary heart disease. Despite the link between dietary patterns and the BMI of adults [8,9,11], studies have not extensively examined such relationships among the Ghanaian population [13-15]. This study aimed to assess the dietary patterns and their association with BMI in an adult population in Greater Accra, Ghana.

MATERIALS AND METHODS

Study design and sites

This study was retrospective; it involved dietary data abstracted from a pool of data obtained from four (4) previous cross-sectional studies conducted in the Greater Accra region of Ghana. Two hundred and eighty-four questionnaires obtained from healthy adults were sampled from a pool of questionnaires on dietary studies from the databank of the Department of Dietetics, University of Ghana. A total of 76 questionnaires had incomplete demographic, dietary (food frequency), and anthropometric (weight and height) data and were excluded, resulting in a sample size of 208 for the present analysis. The data on the food frequency questionnaire covered different kinds of foods that were consumed over a month. The population included adults aged 18 to 60 years who were staff at the Korle Bu Teaching Hospital, the University of Ghana Health Services at Legon and the University of Ghana Korle-Bu campus. Participants in the previous studies were selected randomly by ballot.

Information on age and sex, marital status, educational background, religion, and tribe were extracted and pooled from the questionnaires. Data on height in meters (m) and weight in kilogram (Kg) was extracted to estimate the body mass index (BMI) (kg/m^2) (weight (kg)/height $(m)^2$). The BMI was classified based on the Centre for Disease Control BMI classification for adults; BMI less than 18.5 kg/m^2 was underweight, normal weight was 18.5 kg/m^2 < 25 kg/m^2, overweight 25 kg/m^2 < 30 kg/m^2 and obese ≥ 30 kg/m^2 [16,17]. Dietary intake was assessed using a quantitative food frequency questionnaire. Data on the frequency (daily, weekly, monthly, and never) of consumption of cereals and grains, root and tubers, fruits, vegetables, legumes, nuts, animal and animal products, processed food items, and fat and oil were extracted and pooled for analysis to identify the dietary patterns.

Data analysis

Data analysis was performed using SPSS version 25 (IBM Corp. Armonk NY). Descriptive statistics were summarised using frequencies for categorical variables and means and standard deviations for continuous variables. An independent sample T-test was used to test the differences in means between sex for weight, height, and BMI. The Chi-square test was used to compare the proportions of males and females among BMI categories. Dietary patterns were assessed using the Principal Component Analysis, which was calculated on the whole sample and not by age groups or gender. The criteria for the data to suit factor Principal Component Analysis (PCA) are the reliability, adequacy and sphericity of the data. The reliability, adequacy and sphericity tests for the data were done to determine the suitability of the data for the PCA, a form of the factor analysis procedure. For the reliability test, Cronbach's alpha was used, which gave a reliability value of 0.858. For the adequacy test, the Kaiser-Meyer-Olkin (KMO) measure was employed, which gave a value of 0.795, implying the adequacy of the data. For Sphericity, Bartlett's test gave a value of 5118.11 with $p < 0.001$, which implied that there was no evidence of correlation matrix identity. Fifty-one (51) food items from the food frequency questionnaire were used for the PCA analysis. The orthogonal rotation method, specifically varimax, was used to maximise variable loadings on the extracted factor components. To identify the number of principal components (PC) to retain, three commonly applied criteria were used: eigenvalue > 1, the interpretability of the components and Monte Carlos PCA for parallel analysis. The number of factors was determined by Kaiser's stopping rule; thus, eigenvalues > 1.0 yielded thirteen factors [18]. All these analysis steps are required to ensure a comprehensive identification of the most appropriate

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number of components for the factor analysis. This is required in order to relate the dietary pattern scores to the BMI. However, Monte Carlos PCA for parallel analysis was used to determine the statistical significance of the eigenvalues and the number of factor components to retain. The eigenvalues of the data were systematically compared with the eigenvalues from the parallel analysis. If the eigenvalue from the SPSS analysis eigenvalue was greater than the eigenvalue from the parallel analysis, then that factor component was retained. Therefore, only 8-factor components were retained. Scree plots were also used to confirm the adequacy of the eight components retained.

Significant contributing food items to the factor were those with an absolute factor loading of 0.40 or higher. A positive factor loading indicates that the original dietary variable was positively associated with the principal component in question, whereas a negative factor loading indicates the opposite. The food items had communality values considerably above 0.5, indicating that the number of components retained was appropriate. As a result, the data set was declared suitable for PCA. Dietary patterns produced from PCA were suitably labelled based on food items that substantially accounted for variation in the component. Based on the factors derived, specific factor scores were estimated for each food item. These factor scores for the food items were then correlated with the BMI and other demographic variables. The factor scores had a skewed distribution, so the Kruskal-Wallis test was used to test the association between dietary patterns and BMI with a level of statistical significance set at $p \leq 0.05$.

RESULTS

The demographic and physical characteristics of the participants are shown in Table 1. A greater proportion of participants, 123 (59%), were females. The median age of the sample was 59 years. The majority, 142 (68.3%) of the participants had normal BMI. More males (77.2%) had normal weights compared to females (55.3%). More females were overweight (28.2%) and obese (10.6%) compared to males (13.8% and 3.3% respectively). Thus, females were significantly more overweight and obese than males, p = 0.001. Fifty-one (51) food items used in the factor analysis yielded eight principal components. These were labelled as traditional patterns, combined patterns, major protein patterns, modified patterns, white and red meat patterns, sweets and pastries patterns, rare dietary patterns and vegetables with high moisture patterns. Table 3 shows the identified dietary patterns and their food

Table 1. Demographic characteristics of study participants

Parameter	Male (123) n (%)	Female (85) n (%)	Total (208) n (%)	P-Value
Median age (min, max)	25 (18,56)	25 (19, 58)	25 (18, 58)	
Educational level				
None	3 (2.4)	5 (5.9)	8 (3.8)	
Primary	13 (10.6)	14 (16.5)	27 (13.0)	
Junior High	20 (16.3)	13 (15.3)	33 (15.9)	0.464
Senior High	10 (8.1)	5 (5.9)	15 (7.2)	
Tertiary	77 (62.6)	48 (56.5)	125 (60.1)	
Marital Status				
Single	74 (60.2)	50 (58.8)	124 (59.6)	
Divorce	4 (3.3)	3 (3.5)	7 (3.4)	0.836
Married	44 (35.8)	30 (35.6)	74 (35.6)	

Table 2. Comparison of anthropometric variables between males and female

Variable	Male	Female	Total (208)	P-value
Weight (Kg)	65.3 ± 9.9	62.6 ± 12.4	64.2 ± 11.0	0.86
Height (m)	1.7 ± 0.1	1.6 ± 0.1	1.7 ± 0.1	<0.001
BMI (kg/m^2)	22.4 ± 3.0	24.1 ± 4.8	23.1 ± 3.9	0.001
BMI classification	n(%)	n(%)	n(%)	
Underweight	7 (5.7)	5 (5.9)	12 (5.8)	
Normal Weight	95 (77.2)	47 (55.3)	142 (68.3)	
Over Weight	17 (13.8)	24 (28.2)	41 (19.7)	0.004
Obese	4 (3.3)	9 (10.6)	13 (6.2)	

BMI (body mass index) = weight (kg)/height(m)^2, BMI (body mass index) classifications are based on (Center for Disease Control, 2021; World Health Organization,2021)

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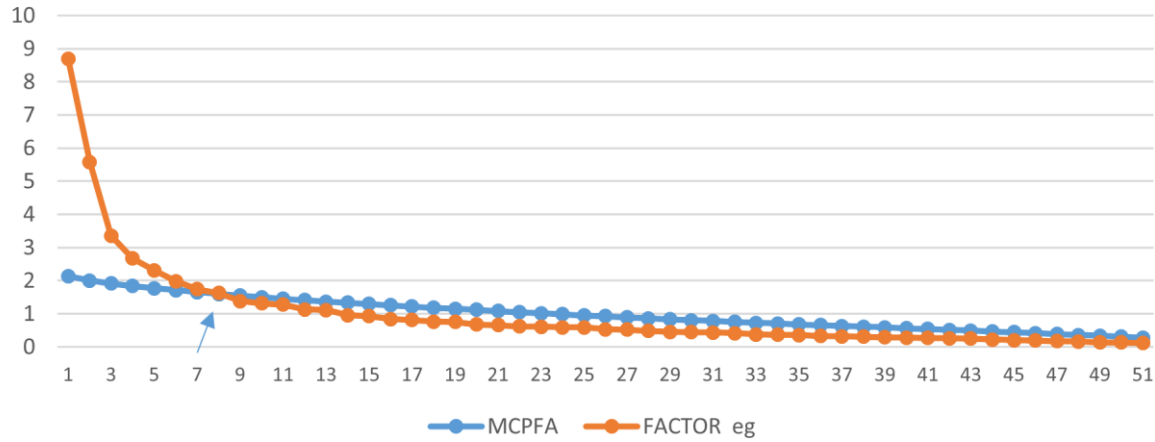

Figure 1. Scree plot of eigenvalues of data versus eigenvalues of Monte Carlos PCA for parallel analysis

Table 3. Identified dietary patterns and their food components

Dietary pattern	Food items
Traditional pattern (TDP)	cassava, sweet potato, yam, coconut oil, mango, sorghum, pawpaw, orange, garden eggs, plantain, okra and agushie
Combined pattern (CDP)	vegetables (carrot, cabbage, cucumber, and green leafy vegetables), fruits (apple, banana) and milk
Major protein pattern (MPDP)	game meat, crab, snail, shrimp, tigernut
Modified pattern (MDP)	gari, bread, millet, oats
White and red meat pattern (WRMDP)	poultry, meat, and fish
Sweets and pastries pattern (SPDP)	candies, chocolate, pastries
Rare dietary pattern (RDP)	Bambara beans, grape, soya, cheese
Vegetables with high moisture (VHMDP)	onion and tomatoes

Table 3a. Factor loadings by of dietary patterns

Food items	TDP	CDP	MPDP	MDP	WRMDP	SPDP	RDP	VHMDP
Cassava	0.699							
Sweet Potato	0.68							
Yam	0.65							
Coconut Oil	0.635							
Mango	0.586							
Watermelon	0.542	0.458						
Sorghum	0.528							
Pawpaw	0.522							
Pineapple	0.508	0.407						
Orange	0.505							
Garden Eggs	0.483							
Plantain	0.482							
Agushie	0.45							
Okro	0.437							
Coconut								
Carrot		0.756						
Cabbage		0.694						
Apple		0.663						
Cucumber		0.637						
Green Leafy Vegetables		0.629						
Milk		0.447						
Banana		0.422						

**Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization.*

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Table 3b. Factor loadings by dietary patterns continuation

Food items	TDP	CDP	MPDP	MDP	WRMDP	SPDP	RDP	VHMDP
Rice								
Game meat			0.848					
Crab			0.816					
Snails			0.802					
Shrimps			0.793					
Tiger nuts			0.57					
Corn			-0.428					
Beans								
Indomie								
Butter								
Gari				0.594				
Bread				0.567				
Millet				0.558				
Oats				0.471				
Wheat								
Groundnut								
Wean mix								

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.
a Rotation converged in 15 iterations

Table 3c. Factor loadings by dietary patterns continuation

Food items	TDP	CDP	MPDP	MDP	WRMDP	SPDP	RDP	VHMDP
Poultry					0.777			
Meat					0.759			
Fish					0.602			
Candies						0.828		
Chocolate						0.764		
Pastries						0.743		
Bambara beans							0.843	
Grape							0.65	
Soya beans							0.619	
Cheese							0.54	
Tomatoes								0.794
Onion								0.697

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.
a Rotation converged in 15 iterations.

components. The Monte Carlo's parallel analysis reduced the factor components from 13 to 8, which accounted for 54.8% of the variability in the dietary intake among participants. Tables 3a, 3b and 3c show the loadings of the food items on the extracted components. Food items with absolute values ≥ ± 0.4 significantly contributed to the components. Table 4 shows the correlation between dietary patterns factor scores and BMI. The traditional pattern and sweets and pastries pattern showed a significant correlation with BMI (p = 0.001 and 0.013, respectively). Further analyses to determine the association between the dietary patterns and BMI categories using the Kruskal-Wallis test revealed a significant association between the traditional dietary pattern (p = 0.032) and the Sweets and Pastries pattern (p < 0.001) with BMI categories. Obesity

Table 4. Association between dietary patterns and BMI

Dietary Pattern	Correlation coefficient (r)	P-value
Traditional pattern	.220**	0.001
Combined pattern	-0.112	0.109
Major protein pattern	-0.089	0.199
Modified pattern	0.07	0.313
White and red meat pattern	-0.067	0.337
Sweets and Pastries pattern	.172*	0.013
Rare dietary pattern	0.116	0.096
Vegetables with high moisture	0.043	0.539

Spearman correlation was used to assess association between the factor scores for each food pattern and the BMI

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Table 5. Association between dietary pattern and BMI categories

Dietary patterns	Weight category	N (208)	Mean Rank	P-value
Traditional pattern				
	Underweight	12	95.25	
	Normal Weight	142	100.85	
	Overweight	41	104.90	*0.032**
	Obese	13	151.69	
Combined pattern				
	Underweight	12	105.50	
	Normal Weight	142	109.15	
	Overweight	41	93.54	0.353
	Obese	13	87.38	
Major protein pattern				
	Underweight	12	95.08	
	Normal Weight	142	109.02	
	Overweight	41	85.10	0.076
	Obese	13	125.00	
Modified pattern				
	Underweight	12	114.17	
	Normal Weight	142	101.15	
	Overweight	41	116.17	0.459
	Obese	13	95.31	
White and red meat pattern				
	Underweight	12	102.08	
	Normal Weight	142	107.18	
	Overweight	41	93.00	0.552
	Obese	13	113.69	
Sweets and Pastries pattern				
	Underweight	12	96.50	
	Normal Weight	142	94.39	
	Overweight	41	139.83	*<0.001**
	Obese	13	110.92	
Rare Dietary pattern				
	Underweight	12	113.42	
	Normal Weight	142	102.64	
	Overweight	41	100.10	0.386
	Obese	13	130.46	
Vegetables with high moisture				
	Underweight	12	111.33	
	Normal Weight	142	102.02	
	Overweight	41	102.73	0.404
	Obese	13	130.85	

Kruskal-Wallis test was used for the analysis, N=total. This test was used to do the comparisons because the factor score values were ordinal and skewed.

was significantly higher with the Traditional dietary pattern, while overweight was significantly higher with the sweets and pastries pattern. Table 5 shows the association between dietary patterns and BMI categories.

DISCUSSION

This study assessed the dietary patterns of an adult population in Accra, the capital city of Ghana and determined their association with BMI. The mean BMI of participants in this study was 23.1 ± 3.9 kg/m^{2,} with females having significantly higher BMI than males. Previous studies on BMI have reported similar findings [19,20]. The World Health Organization [19] reported that the mean BMI in Africans was 23.1 kg/m^2, with the mean BMI of males and females being 22.4 kg/m^2 and 24.1 kg/m^{2,} respectively, which is consistent with the findings of this study. Overweight and obesity were predominant among the female participants in this present study, similar to findings in a systematic review and meta-analysis of the overweight and obesity epidemic in Ghana [6]. Other studies have also reported a higher rate of overweight and obesity in females than males [21-24]. These differences could be attributed to women having more body fat deposition than men [25,26]. Eight dietary patterns were identified in the study. By contrast, the Research on Obesity and Diabetes among African Migrants (RODAM) carried out among urban and rural Ghanaians in the Ashanti Region, and Europe identified three dietary patterns (mixed pattern: rice, pasta, meat and fish pattern; and the roots, tubers and plantain pattern) [27-29]. Even though the dietary patterns identified in this study did not map directly onto the dietary patterns in the RODAM study, elements of overlap exist. For instance, the mixed pattern identified in

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the RODAM study had characteristics similar to five (5) of the dietary patterns in this present study, i.e., the traditional DP, Combined DP, white and red meat DP, vegetables with high moisture DP, and sweets and pastries DP. The rice, pasta, meat, and fish patterns in the RODAM study had characteristics similar to the combined DP, modified DP, and sweets and pastries DP in this present study. Additionally, the root tubers and plantain pattern had characteristics comparable to the traditional pattern in this study. The present study, however, identified one new dietary pattern, the rare dietary pattern, which was not identified in the RODAM study. The rare dietary pattern consisted of these food items: Bambara beans, grapes, cheese, and soya beans.

In a similar study to determine the association between the risk of type 2 diabetes and dietary patterns among urban Ghanaians (Kumasi), two dietary patterns (purchase dietary pattern and traditional dietary pattern) were identified [30]. The component food items in the purchase dietary pattern were found in 4 separate dietary patterns in our study, namely sweets and pastries pattern, white and red meat pattern, combined pattern, and vegetables with high moisture content pattern. The traditional pattern identified in the Kumasi study also had elements of the traditional pattern and the combined pattern in our study with high loadings on plantains, fruits, garden eggs and green leafy vegetables. However, the modified pattern, major protein pattern and rare dietary pattern identified in the present study were not accounted for [30] in previous studies. The dietary patterns identified in this adult population in Accra corroborate other studies in different parts of the world. There is an overlap of the food items in some studies [31,32] despite slight variations in the naming of the patterns, likely due to differences in geographical locations, which influence the food environment. In Hangzhou, East China [32], four dietary patterns (animal food, traditional Chinese, western fast food and high-salt patterns), whose elements can be found in the major protein, traditional, combined vegetables with high moisture, rare, sweets and pastries dietary patterns were identified. Contrarily, this study identified the modified pattern whose elements cannot be found in any of the patterns reported in the Hangzhou study [32]. Some findings from other studies were not consistent with the results of our study [9,33,34]. For instance, a study in the Quebec City metropolitan area [9] identified two dietary patterns among adults: the western pattern with high loadings of refined grains, French fries, condiments, processed meats, regular soft drinks, pizza, snacks, and the prudent pattern with high loadings on non-hydrogenated fat, vegetables, eggs, fish and seafood, wine, coffee, regular dairy products as well as whole grain products. Despite a few similarities in the food items, there were more variations than in our study.

Similarly, three dietary patterns (cereals-savoury foods, fruit-veg-sweets-snacks and animal-food patterns) with elements different from those reported in our study were observed in India [33]. Two other dietary patterns (mixed and processed patterns) were reported in a study among four African populations [34]. These inconsistencies may reflect the differences in geographical location and culture and, hence, are not totally unexpected. Geographical location affects the availability, accessibility, and affordability of food items, whereas culture may influence the recipes for the food products as well as the type of food consumed. In line with this, a strong association was identified between geographical location and culture with variance in food intake among University students in the UK [35].

The traditional and the sweets and pastries patterns in the present study were significantly associated with BMI. Frequent consumption of the traditional pattern was seen among obese individuals, whereas the frequent consumption of the sweet and pastries pattern was observed among overweight participants. A plausible explanation for these observations could be the energy-dense nature of the foods identified under the two patterns. The sweets and pastries pattern was energy-dense with foods high in saturated fat and low in fibre coupled with high added sugars, whereas the traditional pattern was composed of some energy-dense food components such as cassava, sweet potato, yam, and coconut oil. A number of studies have also reported a strong association between energy-dense, high-saturated fat, low-fibre dietary patterns and overweight and obesity in adults [34,36,37]. These dietary patterns often contain carbohydrate foods that are high in glycaemic index and cause rapid changes in blood glucose and insulin levels. Frequent consumption of these diets leads to excess calories, which, when coupled with low physical activity, leads to overweight or obesity.

The results of our study are consistent with previous studies reporting that various dietary patterns of adults influence BMI [8,9,11]. In connection with this, a systematic review of studies evaluating the association between dietary patterns and BMI [38] found that the fatty, sweets or energy-dense patterns were positively associated with BMI, while fruits and vegetables DP were inversely associated with BMI. In addition, a significant association was found between the Processed Dietary Pattern and overweight and obesity in a study that assessed dietary patterns in Tanzania, South Africa, and peri-urban and rural Uganda [34]. This dietary pattern contained elements of the sweets and pastries dietary patterns identified among Ghanaian adults. No such association between overweight and obesity in the mixed dietary pattern was reported in the other African countries. The mixed dietary pattern contained elements of the combined white and red meat patterns seen in this present study.

Overall, the results of our study reveal that sweets and pastries and traditional dietary patterns play a significant role in obesity and overweight dispositions. The RODAM study [28] found that adherence to the ‘mixed’ and ‘rice, pasta, meat, and fish’ dietary patterns were significantly associated with a higher BMI ($p < 0.001$) and lower risk of

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type 2 diabetes and 10-year atherosclerotic cardiovascular disease risk (ASCVD) in Ghanaian adults in Ghana and Europe. The mixed, rice pasta, meat and fish dietary patterns had some elements of the sweets and pastries DP associated with high BMI in our study population. However, frequent consumption of 'roots, tubers, and plantain' dietary patterns in the RODAM study, which were similar to the traditional DP in the present study, were significantly associated with a lower BMI ($p = 0.003$) and reduced risk of type 2 diabetes. Contrary to this, the traditional dietary pattern in our study was associated with overweight and obesity. Portion sizes, as well as recipes for the foods, could be contributing factors to this difference.

The findings in our study did not show a significant association between the major protein pattern and BMI. This is not consistent with other studies conducted in sub-Saharan Africa and India, which found an association between protein patterns and BMI (overweight/obesity) [33,39]. An association between the protein dietary pattern and BMI among urban Ghanaian women, but not Malawi or Tanzania, was recently reported [39]. In contrast with some other studies, the results of our study did not also show an association between the red and white meat pattern and BMI (obesity) [33,40]. Varied recipes used in various countries may be a contributing factor to the inconsistencies. The results of this study show that it may be crucial for adults to receive nutrition guidance and education concerning dietary options, taking into consideration all the patterns identified with more emphasis on the traditional pattern and sweets and pastries pattern. The food frequency questionnaire used in this study is based on recall, which may be subject to bias. Dietary intake assessment using the food frequency questionnaires (FFQ), on the other hand, has been found to be appropriate in indicating usual intake, which is essential in this study. The results of this study may not be applicable to other populations.

Conclusion
Dietary patterns characterised by the intake of starchy root tubers, local vegetables, sweets and pastries may exert a negative effect on weight gain. Further studies assessing the food environment, availability, accessibility and preparatory methods would be useful in establishing causal relationships.

DECLARATIONS

Ethical consideration
The study was approved by the Protocol Review Committee of the University of Ghana, College of Health Sciences (CHS-Et/M.5 - 4.5/2020-2021).

Consent to publish
All authors agreed on the content of the final paper.

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None

Competing Interest
The authors declare that there is no conflict of interest regarding the publication of this article.

Author contributions
MA, TN, and JAQ participated in the conception and design of the study. BA and MA participated in the acquisition of data. Analysis and interpretation of data were done by BA, TN, MA, JAQ, AAM and RO. BA, RO, MA, TN, JAQ and AAM participated in the drafting of the manuscript.

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Availability of data
Data for this work is available upon reasonable request from the corresponding author.

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Serum Lactate Dehydrogenase as a potential predictive index of chemotherapy response in breast cancer patients

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Abstract

Background: Monitoring treatment during breast cancer management is crucial. Lactate dehydrogenase (LDH) expression and activity drive cancer progression through metabolic reprogramming.

Objective: The study aimed to profile serum lactate dehydrogenase in breast cancer patients as a chemotherapy response index.

Methods: A total of 65 breast cancer patients and 64 healthy controls were studied. Archival serum samples from the patients before initiation and after the third cycle of chemotherapy and controls were retrieved from -80 ºC freezer. Clinico-pathological data of study participants were retrieved. Total RNA was extracted from the serum using a commercial kit, and lactate dehydrogenase A mRNA was quantified by RT-qPCR. The serum total LDH activity was determined using a chemistry autoanalyser.

Results: The mean age difference between patients (49.55, SD 11.98) and controls (55.67, SD 13.99) years was statistically significant ($p < 0.01$). However, the BMI and waist-to-hip ratio of patients compared to the controls were not statistically significant ($p > 0.05$). Patients with tumour grade 3 (52.3%), HER 2 positive (30.8%) and stage 3 (46.2%) were over-presented. Serum total LDH activity was significantly elevated in the patients at baseline compared to the controls ($p < 0.01$) but not significant when the activity was compared with after the third cycle of chemotherapy ($p > 0.05$). The pattern remained unchanged when serum LDHA mRNA relative fold change was compared ($p > 0.05$). Nevertheless, the fold change ratio difference for mRNA (3.4) was higher than that of enzyme activity (0.24).

Conclusion: Serum total LDH activity and LDHA expression in breast cancer patients were reduced after the third cycle of chemotherapy. However, LHDA mRNA expression could be a better predictive index of chemotherapy response than enzyme activity.

Keywords: Lactate dehydrogenase, chemotherapy response, breast cancer, enzyme activity, mRNA levels

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INTRODUCTION

Breast cancer is the most common cancer and the fifth leading cause of cancer-related deaths globally [1]. Although the incident rate is higher in developed countries compared to developing countries, breast cancer mortality is higher in developing countries [2]. The high cancer-related mortality has been attributed to late presentation to health facilities, and the reasons include low health promotion for early detection, low education, superstition and sociocultural beliefs, and inadequate specialised health facilities [3].

Several medical approaches have been adopted in breast cancer management; however, treatment options largely

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depend on tumour characteristics such as type of cancer, tumour stage, grade, metastasis and biological subtyping of the cancer [4]. The overall health status of the patient, menopause status, and personal preferences are also considered in the choice of management plan [3,4]. The time of initiation of treatment is key in preventing the spread of the cancer cells, and the therapy could be given as an adjuvant or neo-adjuvant to surgery or to palliate the disease, especially in the metastatic stages [5]. Interventions are either local, such as surgery and radiation, or systemic therapies, where drugs are administered to kill cancer cells. The systemic therapy includes hormonal, targeted or biological therapies and chemotherapy [6]. Chemotherapeutic agents are designed to target cancer cell machinery that promotes active cell proliferation. The chemotherapeutic agents are categorised based on the cellular mechanisms. Alkylating agents and platinants, which include cisplatin and inhibitors of topoisomerase such as daunorubicin, doxorubicin, irinotecan, and etoposide induce DNA damage in proliferating cells [7].

Cytotoxic antibiotics function to prevent DNA and RNA synthesis, while antimetabolites such as gemcitabine interfere with intermediary metabolism [8]. Anti-microtubule agents, including paclitaxel and docetaxel, target microtubules and associated proteins to disrupt cell division [9]. Hormonal agents such as tamoxifen or enzalutamide are required to inhibit hormone synthesis or dysregulate the function of hormone receptors [10], while immunotherapy such as trastuzumab targets cancer cells that express a specific antigen or enhance the natural ability of T cells to fight cancer [9]. Despite several therapeutic attempts to suppress cancer cells' survival and proliferation, therapy resistance or tumour relapse remains a challenge. Several factors have been mentioned to underpin tumour resistance to chemotherapy in patients [11], warranting treatment monitoring to assess response. Currently, breast cancer treatment is based on molecular classification of receptor types, including estrogen receptor (ER) and progesterone receptor (PR) positive, human epidermal growth factor receptor 2 (HER2) positive and triple-negative non-receptor breast cancer [12].

Evaluation of treatment effectiveness is critical in breast cancer management, and predictive and prognostic markers identify patients who respond to treatment. Commercially available genomic assays are currently employed to establish possible recurrence and potential benefits of chemotherapy [13]. Search for new prognostic markers is on the increase and may be combined with histopathological evaluation to monitor therapy response. Serum CEA and CA 15 - 3 are promising biomarkers for evaluating therapy response in patients receiving systemic therapy, and new biomarkers such as circulating tumour cells and circulating tumour-derived DNA are being studied [14]. Breast cancer cells adopt metabolic reprogramming and avoid oxidative phosphorylation [15]. Derailed bioenergetic process characterised by low expression of the catalytic subunit of mitochondrial H+-ATP synthase and a drop in the ATPase activity is linked to a decreased oxidative phosphorylation [16]. Conversion of pyruvate to lactate in breast cancer cells is a very promising target for therapy evaluation. Lactate dehydrogenase A (LDHA) is a metabolic isoenzyme responsible for the conversion of pyruvate to lactate in the cytoplasm under anaerobic conditions [17]. The LDHA-mediated metabolic reprogramming promotes cancer cell proliferation and drug resistance by alleviating reactive oxygen species-associated apoptotic effects [18]. Data on LDHA isoenzyme expression and LDH activity as a predictive index for chemotherapy response in breast cancer patients is limited. The current study aimed to compare serum LDHA mRNA level and total LDH activity as potential predictive indices for chemotherapy response in breast cancer patients.

MATERIALS AND METHODS

Study design, participants and samples

A total of 129 archival serum samples kept at -80 ºC were retrieved for this study. The samples were collected from female breast cancer patients (65) visiting the Breast Cancer Suite, Korle-Bu Teaching Hospital, Accra, Ghana. The patients were compared with cancer-free healthy controls (64), recruited from the hospital environs in a longitudinal, case-control study. Breast cancer diagnosis was based on histopathology. Blood samples were taken from each patient before the commencement of chemotherapy as a baseline and after the third cycle of chemotherapy. The treatment plan for patients included intravenous (IV) cyclophosphamide 500 mg/BSA, IV adriamycin 50 mg/BSA, and IV 5-fluorouracil 500 mg/BSA, and the chemotherapeutic drugs were administered at three weekly intervals for six cycles. The control women were recruited from the hospital environs after written consent was obtained. Patients diagnosed with other chronic diseases were excluded from the study. Blood samples from the control group were collected at one-time point. Clinical data, including waist-to-hip ratio (WHR), body mass index (BMI) and pathological data, were retrieved from our previous study data files. Ethical clearance was obtained from the Ethical and Protocol Review Committee of the School of Biomedical and Allied Health Sciences, College of Health Sciences, University of Ghana, with ethics identification No. SBAHS/AA/MLAB/10710648/2021-2022.

Laboratory analyses

Serum total RNA extraction and LDHA mRNA quantification

Free total RNA was extracted from a 100 µL serum sample using a commercial kit (QIAamp Circulating Nucleic Acid Kit, USA) following the manufacturer's protocol. The purity and concentration of the eluted RNA were measured using Nanodrop (Thermo Fisher Scientific, USA). The mRNA expression levels of LADHA and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) genes in the serum samples were analysed by RT-qPCR using Luna Universal One-Step Reaction Mix (BioLabs, New England).

Parameters of the polymerase chain reaction (PCR) were as follows: reverse transcription at 55 ºC for 10 min and initial denaturation at 95°C for 1 min, 45 cycles of 95°C for 10 s and 60 °C for 30 s and final melting curve at 72 ºC for 5 min. The primer sequences for LDHA (forward: 5′-GGATCTCCAACATGGCAG CCTT-3′, reverse: 5-AGACGGCTTTCTCCCTCTTGCT-3′) and GAPDH (forward:5′-GTCTCCTCTGACTTCAAC AGCG-3′ and reverse:5′-ACCACCCTGTTGCTGAGCC AA-3′). Glyceraldehyde-3-phosphate dehydrogenase was used to normalise the data. Each sample was set in duplicate, and the average Ct value was used to calculate the expression fold change.

Serum total LDH activity

Serum LDH activity was measured using Anamol Laboratories PVT Ltd reagents (Kolgaon, India) and by UV kinetic method with Mindray BS 200 chemistry autoanalyser (Shenzhen, China) following standard protocols.

Statistical analysis

IBM SPSS for Windows, Version 24.0. Armonk, NY: IBM Corp. was used for statistical analyses. Categorical data was presented as proportion and continuous data was presented as mean and standard deviation (SD). Student T-test was used to determine the significance of the mean difference between continuous variables of patients and controls. ANOVA was used to compare the LDHA mRNA levels and total LDH activity among the baseline, after the second cycle and controls. The predictive index was determined as a ratio of mRNA or activity in patients to controls. $P < 0.05$ was considered significant for all statistical analyses.

RESULTS

Clinical parameters of study participants

A total of 129 female participants were recruited for the study: 50.38% (n = 65) were diagnosed as breast cancer patients, and 49.62% (n = 64) as the controls. The mean age (49.55, SD 11.98) of the patients compared to the control group and the age distribution was statistically significant (p = 0.009). The BMI and waist-to-hip ratio of patients and control were statistically insignificant (p > 0.05). About 52% (n = 34) of the diagnosed cancer cases occurred in the right breast, 45% (n = 29) in the left breast and about 3% (n = 2) in both breasts. (Table 1). The majority (60.0 %, n = 39) of the patients presented with grade 3. About 31% (n = 20) of the participants were human epidermal growth factor 2

Table 1. Clinical parameters of study participants

Characteristics	Case (N = 65)	Control (N =64)	95% CI of mean difference	p-value
Age (yrs)	49.55 ± 11.98	55.67 ± 13.99	-10.65 – (--1.58)	0.009*
BMI (kg/m^2)	29.35 ± 6.26	27.88 ± 4.55	-0.44 – (3.37)	0.131
W/H ratio	0.97 ± 0.98	0.85 ± .087	-0.12 – (0.36)	0.334
Affected breast	n (%)		-	-
Left	29 (44.6)		-	-
Right	34 (52.3)		-	-
Both	2 (3.1)		-	-

Table 2. Pathological characteristics of breast cancer patients

Characteristics	Frequency n (%)
Cancer Grade	
Grade 1	5 (7.7)
Grade 2	21 (32.3)
Grade 3	39 (60.0)
Molecular subtype	
Luminal A	1 (1.5)
Luminal B	4 (6.2)
Human Epidermal Growth Factor Receptor (HER 2)	20 (30.8)
Triple negative	18 (27.7)
Unknown	22 (33.8)
Stage of breast cancer	
Stage 1	5 (7.7)
Stage 2	21 (32.3)
Stage 3	30 (46.2)
Stage 4	9 (13.8)

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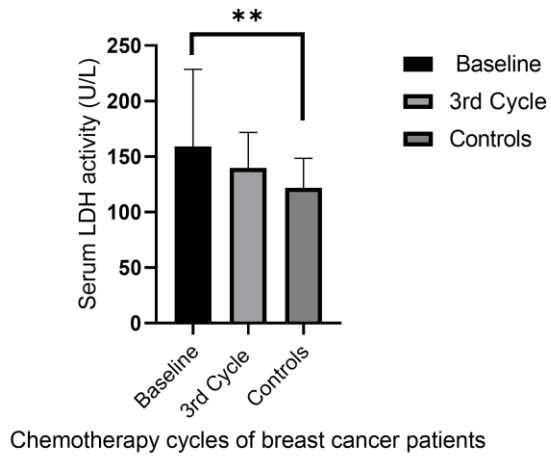

Figure 1. Serum LDH activity in breast cancer patients on chemotherapy. *p < 0.01

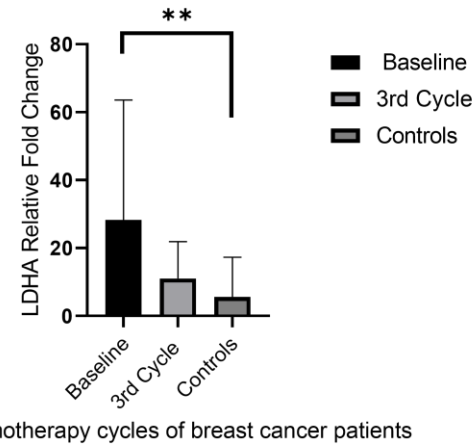

Figure 2. Serum LDHA mRNA expression levels in breast cancer patients on chemotherapy. *p < 0.01

Table 3. Predictive index of serum LDH in chemotherapy response in breast cancer patients

Biomarker	Ratio of mRNA levels and enzyme activity		Change in ratio
	Baseline	3rd Cycle	
LDHA mRNA levels	5.40	2.00	4.2
Total LDH Activity	1.28	1.04	0.24

Ratio was calculated by dividing mean LDH expression fold change or activity in patients by that of the controls.

(HER 2) positive, and 28% (n = 18) showed triple-negative subtypes (Table 2).

Serum total LDH activity

Figure 1 shows the serum LDH activity in breast cancer patients at baseline (chemotherapy-naïve patients) and the third cycle of chemotherapy compared with the apparently healthy controls. The controls showed a statistical significant reduced LDH levels compared to the baseline counterparts ($p < 0.01$). Among the cancer patients, there was a reduced LDH activity at the third cycle of chemotherapy compared to the baseline activity, although the level was not statistically significant ($p > 0.05$).

LDHA expression level

Serum LDHA mRNA expression levels in breast cancer patients at baseline and third cycle of chemotherapy compared with controls are shown in Figure 2. LDHA mRNA expression showed statistically significant increased levels in baseline breast cancer patients as compared to the control ($p < 0.05$). LDHA expression levels were seen to be reduced in third-cycle chemotherapy patients as compared to the baseline in breast cancer patients, even though the difference in levels was not statistically significant ($p > 0.05$). Table 3 shows the baseline and third cycle of the chemotherapy response predictive index in patients relative to the control. The difference between baseline and third cycle ratio for LDHA mRNA expression (4.2) is higher than that of the enzyme activity (0.24).

DISCUSSION

The current study reports a comparative analysis of chemotherapy response predictive indices of serum for the first time.

LDHA mRNA levels and total LDH enzyme activity in breast cancer patients

The serum mRNA level of the patients decreased significantly compared to the enzyme activity after the chemotherapy, and the change in the LDHA mRNA level ratio identifies serum LDHA mRNA as a good candidate for predicting chemotherapy response in patients. The current finding supports an earlier study that reported a decreased level of tumour suppressor gene mRNA in serum as a potential predictive biomarker for chemotherapy [19]. A low level of serum LDH in cancer patients after

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chemotherapy was associated with a longer overall survival [20,21]. Similarly, high lactate dehydrogenase mRNA levels and enzyme activity were associated with breast cancer, and the elevated level and increased activity after the first line of chemotherapy correlated with worse disease outcomes [22,23]. Also, the increased activity of LDH was implicated in several cancers, including nasopharyngeal and gastric cancers [24,25], and the activity has been linked to poor cancer prognosis through an accumulation of lactate [23]. LDH reversibly converts pyruvate in the glycolytic pathway to lactate, a pathway considered crucial in driving anaerobic metabolism to support tumour cell growth and survival [23,24]. A study correlated high levels of lactate with cancer metastasis, recurrence, and poor treatment outcome [27]. In similar studies, the degree of breast cancer progression was found to be dependent on lactate concentration, and the concentration was higher in triple-negative breast cancer tissues than in the blood [28,29]. Lactate is described as an oncometabolite since it creates tumour microenvironment acidosis to favour cancer metastasis, angiogenesis, and immunosuppression [30]. Increased acidosis triggers natural killer (NK) cells' inactivation and ineffective apoptosis, causing immune evasion by cancer cells [30].

Both LDH and lactate levels are considered novel targets for accessing cancer cells' survival and proliferation [31]. LDH isoform activity is tissue-specific, and altered expression and activity of the isoforms are indicative of changes in a tissue's metabolic function, especially in pathological conditions [32]. LDH level or activity as a diagnostic, prognostic or predictive biomarker in serum, pleural fluid, urine and tissues of various cancers has been extensively reviewed [32]. However, some reports have indicated that LDH is a non-specific diagnostic marker for cancers and is not routinely used in clinical laboratories [33]. Also, LDH was reported as non-specific for identifying a type of cancer, and an increase in the level or activity of LDH in cancer patients was attributed to necrosis within the tumour and possible haemolysis [33]. The current study did not establish a relationship between serum LDH profile and pathological outcomes and anthropometric measurements of the patients. A greater proportion of the patients presented with grade 3 and stage 3 advanced breast cancers. Further studies in a large study population to relate LDH profile with clinicopathological outcomes and other exposures, including diet and physical activity, will underscore the predictive value of LDH in Ghanaian breast cancer patients.

Conclusion

Serum LDHA mRNA levels and total LDH activity in breast cancer patients were reduced after the third-cycle chemotherapy. Reduction in the mRNA level was highly noticeable compared to the enzyme activity. Further study to establish the relationship between serum LDHA mRNA levels and clinic-pathological will strengthen the predictiveness of serum LDH for monitoring chemotherapy response in the patients.

DECLARATIONS

Ethical consideration

The study protocol was approved by the Ethical and Protocol Review Committee of the College of Health Sciences, University of Ghana. Protocol Identification CHS-Et/M:8-p4.12014-2015. Written informed consent was obtained from all study participants.

Consent to publish

All authors agreed on the content of the final paper.

Funding

None

Competing Interest

The authors declare no conflict of interest for this paper

Author contributions

EAT, BA-B, JN, and OQ conceptualised and designed the work. GKA, NE-BA and PMA conducted the experiments. EAT, DO, and OQ analysed data and interpreted the results. GKA, DO, JN, and SS wrote the manuscript. All authors reviewed the manuscript and approved the submitted version.

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Availability of data

Data is available upon request to the corresponding author

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Knowledge and practice of chronic wound management and associated factors among nurses at the Korle-Bu Teaching Hospital, Ghana

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Abstract

Background: Chronic wound management plays an important role in accelerating the recovery of patients. Reports show that nurses' poor performance in chronic wound management is often the result of poor knowledge of and skills in chronic wound care. It is significant for nurses to understand wound assessment and develop standard skills and practices to enable them to render quality wound management for patients' satisfaction.

Objective: This study investigated the knowledge and practice of chronic wound management and the factors associated with it among Ghanaian nurses. It also explored the association between the knowledge and practice of chronic wound management.

Methods: This is a cross-sectional study of 200 nurses from four Departments at the Korle-Bu Teaching Hospital Accra, Ghana. It was conducted from October 1st to December 31st, 2020. Knowledge and practice on chronic wound management among nurses were examined using a researcher-developed scale. Descriptive analysis, Chi-square tests, and multivariable logistic regressions were used for the analysis using SPSS 25.0.

Results: A total of 200 nurses from the Surgery, Medicine, Obstetrics and Gynaecology, and Paediatrics departments were recruited. About two-thirds (63.5%, n = 127) had adequate knowledge of chronic wound management, and 36.5% (n = 73) had poor knowledge. Factors significantly associated with good knowledge included years of working in the department and frequent attendance of workshops on wound care. Also, 52.0% (n = 104) of the participants had good practice in chronic wound management, and 48.0% (n = 96) had poor practice in chronic wound management. Nurses who had frequently attended workshops on wound management after school were 3.326 times more likely to report good practice in chronic wound management ($p < 0.001$, 95% CI: 1.788 - 6.189). Participants with good knowledge were 3.136 times more likely to have good practice ($p < 0.001$, 95% CI: 1.579 - 6.226).

Conclusion: Knowledge and practice of chronic wound management are required for effective wound management. Nurses' training in chronic wound management is associated with good knowledge and practice. Hence, there is a need to provide continuous professional training in wound management for nurses to improve quality care and outcomes.

Keywords: Nurses, chronic wound, management, knowledge, practice, associated factors, Ghana,

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INTRODUCTION

Chronic wound is a wound that fails to heal within the expected phases of healing due to the presence of intrinsic and extrinsic factors [1]. In general, chronic wounds are often caused by bacterial infection and underlying disease conditions [2]. Chronic wound management is very important to prevent infections. It facilitates wound healing and reduces complications [3,4,5]. Patient recovery from chronic wounds has accelerated as nurses have improved their chronic wound

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management skills. However, its management is often hindered by poor wound care knowledge and practices [6] due to a lack of access to evidence-based practices [7]. Chronic wound care is a challenge to nurses, and it consumes healthcare resources around the globe [14,15]. In addition, it imposes physical, psychological and financial stress on the nurses, the patients and the health facility [7]. A UK survey reported that 35% - 65% of community wound care nurses have caseloads, which gradually increase work overload [16]. Effective wound management will decrease the work overload of the nurses, reduce financial burden, stress, prolonged hospitalisation, morbidity, and mortality rate, as well as improve patient care satisfaction and quality of life [2,3,4,5,11]. This implies that continuous professional healthcare training in chronic wound management is necessary [4]. Study about the knowledge and practices of chronic wound healing will empower nurses to understand the factors that delay or facilitate wound healing [8]. Nurses across different healthcare settings frequently have inadequate knowledge or insight, which is significant in wound care [9,10]. Similarly, chronic wound management among Ghanaian nurses has not been adequately investigated. Studies have shown that there was poor access to evidence-based guidelines or poor knowledge and practice of chronic wound management and its associated factors among healthcare workers [11,12,13]. It has been reported that among nurses, chronic wound management and associated factors have not been adequately understood, and the effect on patient outcomes has not been studied [10].

A study reported that nurses with adequate knowledge of wound care are more likely to deliver evidence-based practice that satisfies their patients [17,18]. Another study in Brazil indicated that nurses' lack of knowledge of patients with wounds can affect their practice and influence other colleagues' nursing practices [19]. A survey done in Nigeria also revealed that only 6% had good knowledge of chronic wound management [20]. Additionally, a study done in Finland indicated that most of the respondents claimed that their wound care knowledge was either satisfactory (44%), fair (23%), or poor (3%) [21]. Nurses' knowledge of chronic wound management in a Finland study reported that wound management competencies were poor, as revealed by inexperienced graduated registered nurses [4]. Furthermore, a study done in New Jersey revealed that quality care for chronic wounds reinstated the function of daily life activities of the patients and avoided further wound complications [22]. A Sri Lankan study reported a positive impact of good knowledge, positive attitudes, and safe practices on chronic wound care among patients [23]. There are limited studies done in Ghana to address the gap in knowledge, practice and associated factors. Chronic wound management is a challenge in Ghana due to a shortage of specialty staff/experts, limited clinical settings, and inadequate standard logistics [17]. The benefit of good knowledge and practices of skilled wound care cannot be overemphasised. This study, therefore, assessed Ghanaian nurses' knowledge and practices of chronic wound management and their apprehension of the possible factors associated with poor chronic wound management.

MATERIALS AND METHODS

Study design and sites

This was a cross-sectional study carried out in four departments of the Korle Bu Teaching Hospital (KBTH), which were Surgery, Medicine, Obstetrics and Gynecology, and Paediatrics. These departments have units that provide wound management. In the surgery department, not less than 30 patients have their wounds dressed at the OPD daily. KBTH is the largest referral hospital with about 2000 bed capacity and located in Accra, the capital city of Ghana.

Sample size and sampling technique

The study was carried out during the COVID-19 pandemic, and all nurses who consented to the study during the data collection were recruited. This was a consecutive recruitment of all participants present at the time of the study. They were then stratified into their ranks to ensure proportional representation of all levels of the nurses. A total of 50 eligible nurses in each department were consecutively selected from October 1st to December 31st, 2020. Respondents were 18 years and above working in the selected departments. In total, 200 nurses were recruited. The sample size was calculated by using event per variable (EPV) for logistic regression analysis. In general, the sample size should be 5-10 times the number of variables. There were 23 variables in the Likert scale by eight events (23 * 8), which gave us a sample size of 184, which was rounded up to 200 to allow for possible missing data. Equal numbers were chosen to ensure balance across the departments since nurses are rotated across the departments.

Research Instrument

A 43-item questionnaire was developed and pretested for data collection. Information collected included demographic characteristics, educational background, knowledge and practices of chronic wound management and its associated factors. The structured questionnaire had input from experts/consultants in chronic wound care from Reconstruction Plastic Surgery/Burns Center Ghana, senior nurses with experience in wound care from Surgery, Medicine, Paediatrics, and Obstetrics and Gynecology in Ghana, and seven international research professors with specialists in chronic wound management. All of them had over ten years of working experience in clinical nursing and research. The general information included departments, job titles, years of working experience, years of working in the current department, the highest level of education, work status (full-time, part-time, or casual) and religion. The following five questions assessed the training background on chronic wound management: Have you ever had any theoretical or practical instruction on wound management during your studies? Have you had any hands-on

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opportunities in wound management during internships? Were you given extra training opportunities on wound management before working in the current department? Have you frequently attended workshops on wound care after schooling?

There were eight questions to assess the knowledge of chronic wounds among nurses at KBTH. The correct response for each question was scored 1 point. The highest score for the eight questions was eight. The mean score was used as the cut-off for the scale [24]. Participants who had a total score equal to or higher than the mean were rated as having "good knowledge"; otherwise, they were regarded as having "poor knowledge". The internal reliability (Kuder-Richardson-20) of this questionnaire was 0.634. Participants were asked to rate how often they practised chronic wound management on a 23-item with a four-point Likert scale ranging from "Never, Sometimes, Most times, and Always.". The scale-level content validity index (S-CVI) scores were 0.87. Cronbach's α was found to be 0.80. Each item was scored from 1 (never) to 4 (always). The mean score was used as the cut-off for the scale [24]. Participants who scored equal to or higher than the mean score were considered to have good practice in chronic wound management. Those having less than the mean score were rated as having poor practice.

Data collection

Data collection started after consent was obtained from the respondents. The survey was conducted separately in undisturbed rooms for each department to protect participants' privacy. It took approximately 20 minutes to complete the self-administered questionnaire. Approval for the study was given by the KBTH Institutional Review Board (IRB) with the approval ID KBTH-IRB/000139/2020. Permission was granted by all the heads of the four participating departments

Data analysis

Each questionnaire was immediately checked for errors after collection, and any missing items were immediately verified with participants. The data were entered and analysed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. A descriptive summary was conducted for all variables. Continuous variables were summarised as means and standard deviation, while categorical variables were presented as frequencies and percentages. The chi-square test was used to identify the factors associated with knowledge and practice on chronic wound management. Independent variables found to have statistical significance by the chi-square tests were entered into the final multivariate regression models. Statistical tests were two-sided, and a p-value less than 0.05 was considered significant.

RESULTS

A total of 200 participant nurses were recruited from four departments in KBTH: Surgical, Medical, Paediatric, and Obstetrics and Gynecology. More than half (56%, n = 113) of the participants were of senior rank. Less than half (45%, n = 90) had only 1 - 3 years of working experience. The participants have worked in multiple departments, but nearly half of them (49.5%, n = 99) had worked in their current department for one to three years. Ninety-six (48%) nurses had Bachelor's degrees, 12% (n = 24) had Masters degrees, and the remaining were below Bachelor's degrees. Part-time workers formed 2.5% (n = 5), while the majority of the participants (96.5%, n = 193) were full-time nurses. The number of years of working experience (p = 0.030), the number of years of working in the current department (p = 0.002), and the highest level of education (p = 0.019) of the respondents were seen to be significantly associated with the level of knowledge of chronic wound management (Table 1). Those working in the current department for 4 - 6 years had a higher likelihood of good knowledge with an odds ratio of 4.282 (95% CI = 1.369 - 13.393, p = 0.029). A total of 98.0% of participants (n = 196) had received theoretical instruction, while 97.5% (n = 195) received practical instruction in wound management. During their internships, 97% (n = 194) of participants had hands-on opportunities to practice. However, 60.5% (n = 121) have had extra training before working in the current department, and 57.0% (n = 114) have had frequent workshops after school (Table 2). Binary logistic regression was used to investigate the mode of training and its association with knowledge of chronic wound management. The dependent variable was knowledge of chronic wound management, categorised by the mean score as poor knowledge (mean score < 5.75, coded 0) and good knowledge (mean score ≥ 5.75, coded 1). Attendance of frequent workshops on wound care after school was significantly associated with good knowledge (p < 0.001). The other covariates, such as the number of years of work experience, the number of years of work in their current department and the highest level of education, were not significantly associated with the level of knowledge (Table 2). Those with frequent workshop attendance on wound care after school were 2.867 more likely to have good knowledge of wound management (95%, CI = 1.383 - 5.942, p = 0.005).

The knowledge in chronic wound management scores ranged from zero to eight. The mean score of the eight items was 5.75 ± 0.14 (95% CI: (5.47 - 6.02) median = 6.0, IQR = (4.50 - 7.31). Then, the knowledge scores were categorised into two groups: those below the mean score and those equal to or above the mean score. A total of 63.5% (n = 127) participants scored 5.57 and above and were considered to have good knowledge, and 36.5% (n = 73) nurses were considered to have poor knowledge of chronic wound management. The practice score ranged from 59 to 92 points for this 23-item, four-point Likert Scale. The mean score for this scale was 79.56 ± 0.454 (95% CI: 78.66 - 80.45, median = 60, IQR = 74.84 - 84.30). The practice of the nurses was categorised using the mean score of the scale as the criteria. In total, 52.0% (n = 104) of participants scored 79.56 and above. These were

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considered to have good practice, and 96 participants (48.0%) were considered to have poor practice in chronic wound management (Figure 1). There was a significant association between knowledge and practice of chronic wound management, p = 0.025. Almost all the participants, 99.5% (n = 199), believed that it is beneficial to assess the wound before dressing, and 95.5% (n = 195) thought that they understood the concept of chronic wound management, while 53.1% (n = 106) of the respondents actually stated the precise concept of chronic wound management. Likewise, 60.5% (n = 121) of the participants were aware that there are seven key steps for wound assessment in chronic wound management. In addition, 82% of the respondents understood the knowledge of specific concepts of wound techniques, and 69.5% of the nurses were familiar with the idea of chronic wound management. Oxygenation and stress were the least

Table 1. Demographic characteristics of the participants and association with their level of knowledge of chronic wound management

Characteristics	N (%)	Level of knowledge		
Department		Poor	Good	p-value
Surgery	50 (25.0)	30 (60.0)	20 (40.0)	0.181
Medicine	50(25.0)	11 (22.0)	39 (78.0)	
Paediatric	50 (25.0)	12 (24.0)	38 (76.0)	
Obstetrics/Gynaecology	50(25.5)	16 (32.0)	34 (68.0)	
Category of job title				
Staff Nurse	61 (30.5)	24(39.3)	37(60.7)	0.176
Senior Staff Nurse	26 (13.0)	9(34.6)	17(65.4)	
Nursing Officer	66 (33.0)	17(25.8)	49(74.2)	
Senior Nursing Officer	27 (13.5)	6(22.2)	21(77.8)	
Principal Nursing Officer	20 (10.0)	3(15.0)	17(85.0)	
Years of working experience				
1 – 3	90(45.0)	36(40.0)	54(60.0)	0.030*
4 – 6	31(15.5)	7(22.6)	24(77.4)	
7 – 9	39(19.5)	7(17.9)	31(82.1)	
≥10	40(20.0)	9(22.5)	31(77.5)	
Years of working in the current department				
1 – 3	99(49.5)	41(41.4)	58(58.6)	0.002*
4 – 6	31(15.5)	6(19.4)	25(80.6)	
7 – 9	36(18.0)	4(11.1)	32(88.9)	
≥10	34(17.0)	8(23.5)	26(76.5)	
The highest level of education				
Masters	24(12.0)	2(8.3)	22(91.7)	0.019*
Bachelor's degree	96(48.0)	25(26.0)	71(74.0)	
Diploma	72(36.0)	29(40.3)	43(59.7)	
Certificate	8(4.0)	3(37.5)	5(62,5)	
Work status				
Full-time	193(96.5)	58(30.1)	135(69.9)	0.686
Part-time	5(2.5)	0(0)	5(100.0)	
Casual	147(73.5)	1(50.0)	1(50.0)	
Religion				
Christian	32(16.0)	47(32.0)	100(68.0)	0.083
Muslim	16(8.0)	10(31.3)	22(68.8)	
Traditionalist	5(2.5)	1(6.3)	16(93.8)	
Others	5(2,5)	1(20.0)	4(80.0)	

Significance at 0.05

Table 2. Training received on chronic wound management and adequacy of knowledge on wound management. (n=200).

Training received in wound management	N (%)	Poor knowledge	Good knowledge	p-value
Theoretical instruction on wound management during studies	196 (98.0)	57 (29.1)	139 (70.9)	0.723
Practical instruction on wound management during studies	195 (97.5)	7 (29.2)	138 (70.8)	0.98
Hands-on opportunities on wound management during internships	194 (97.0)	55 (28.5)	138 (71.5)	0.266
Extra training opportunities on wound management before working in the current department	121 (60.5)	18 (22.8)	61 (77.2)	0.092
Attendance for frequent workshops on wound care after school	114 (57.0)	4 (16.3)	72 (83.7)	<0.001*

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Table 3. Knowledge on concepts and assessment of wound management

Concepts of wound management	Yes N (%)	No N (%)
Being familiar with the concept of chronic wound management	139 (69.5)	61 (30.5)
Understanding the concept of chronic wound management	195 (95.5)	5 (2.5)
The specific concept of chronic wound management	106 (53.1)	94 (46.9)
Awareness of seven key steps for wound assessment in chronic wound management	121 (60.5)	79 (39.5)
Recognizing the benefit of assessing the wound before dressing	199 (99.5)	1 (0.5)
Understanding the concept of wound techniques	164 (82.0)	36 (18.0)
Main factors that delay wound healing		
Infection	132 (66.0)	68 (34.0)
Chronic disease	47(23.5)	153 (76.5)
Oxygenation	1 (0.5)	199 (99.5)
Lifestyle	20 (10.0)	180 (90.0)
Stress	0 (0)	200 (100)
	Good knowledge	Poor Knowledge
Knowledge of specific concept of wound techniques	146 (73.0)	54 (27.0)
	Adequate (score ≥ 5.75)	Inadequate (score < 5.75)
Adequacy of knowledge on wound management	127 (63.5)	73 (36.5)

Table 4: Association between demographics and level of practice of chronic wound management

Characteristics	Practice on chronic wound management		P-value
	Poor practice n (%) 96 (48.0)	Good practice n (%) 104 (52.0)	
Department			0.181
Surgery	32 (64.0)	18 (36.0)	
Medicine	23 (46.0)	27 (54.0)	
Paediatric	18 (36.0)	32 (64.0)	
OB/GYN	23 (46.0)	27 (54.0)	
Category of job title			0.111
Staff Nurse	32 (52.5)	29 (47.5)	
Senior Staff Nurse	16 (61.5)	10 (38.5)	
Nursing Officer	33 (50.0)	33 (50.0)	
Senior Nursing Officer	8 (29.6)	10 (70.4)	
Principal Nursing Officer	7 (35.0)	13 (65.0)	
Years of working experience			0.061
1 – 3	49 (54.4)	41 (45.6)	
4 – 6	18 (58.1)	13 (41.9)	
7 – 9	16 (41.0)	23 (59.0)	
≥10	13 (32.5)	27 (67.5)	
Years working in the current department			0.073
1 – 3	55 (55.6)	44 (44.4)	
4 – 6	16 (51.6)	15 (48.4)	
7 – 9	14 (38.9)	22 (18.7)	
≥10	11 (32.4)	23 (67.6)	
The highest level of education			0.037*
Masters	5 (20.8)	19 (79.2)	
Bachelor's degree	49 (51.0)	47 (49.0)	
Diploma	37 (51.4)	35 (48.6)	
Certificate	5 (62.5)	3 (37.5)	
Work status			0.037*
Full-time	94 (48.7)	99 (51.3)	
Part-time	1 (20.0)	4 (80.0)	
Casual	1 (50.0)	1 (50.0)	
Religion			0.276
Christian	65 (44.2)	82 (55.8)	
Muslim	20 (62.5)	12(37.5)	
Traditionalist	8 (50.0)	8 (50.0)	
Others	3 (60.0)	2 (40.0)	

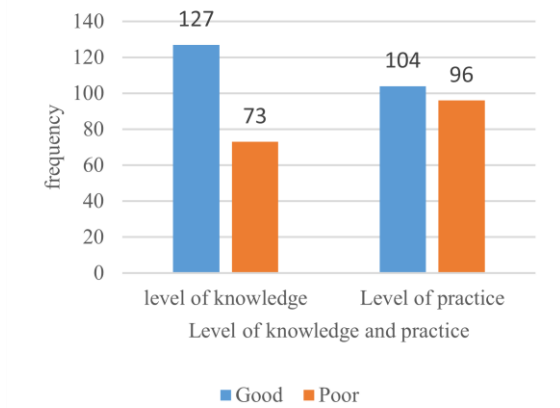

Figure 1. Association between levels of knowledge and practice of chronic wound management, p = 0.025

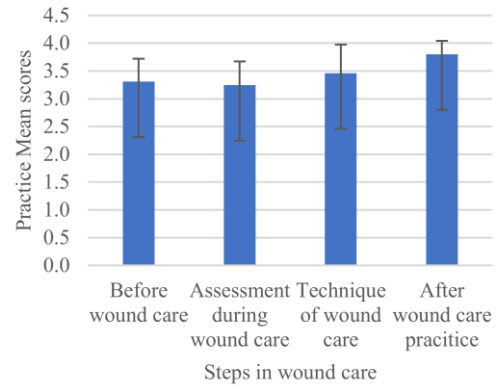

Figure 2. Wound care assessment and practice among the participants

Table 5. Association between type of training and level of practice on chronic wound management

Characteristics	Practice on chronic wound management Poor (n = 96) n (%)	 Good (n = 104) n (%)	p-value
Theoretical instruction on wound management during studies			0.558
No	3 (75.0)	1 (25.0)	
Yes	93 (47.4)	103 (52.6)	
Practical instruction on wound management during studies			0.928
No	3 (60.0)	2 (40.0)	
Yes	93 (47.7)	102 (52.3)	
Hands-on opportunities on wound management during internships			0.099
No	6 (85.7)	1 (14.3)	
Yes	90 (46.6)	103 (53.4)	
Extra training opportunities on wound management before working in the current department			0.022*
No	66 (54.5)	55 (45.5)	
Yes	30 (38.0)	49 (62.0)	
Attendance for frequent workshops on wound care after school			<0.001*
No	71 (62.3)	43 (37.7)	
Yes	25 (29.1)	61 (70.9)	
Knowledge on chronic wound management			<0.001*
Poor knowledge	42 (71.2)	17 (28.8)	
Good knowledge	54 (38.3)	87 (61.7)	

** p < 0.05*

Table 6. Significant factors that predict practice of chronic wound management. (n = 200)

Variable	Category	OR (95% CI)	p - value
Attendance for frequent workshops on wound care after school	No	Ref.	
	Yes	3.326(1.788-6.189)	<0.001
Knowledge on chronic wound management	Poor knowledge	Ref.	
	Good knowledge	3.136 (1.579-6.226)	0.001

Ref., reference; OR, odds ratio; CI, confidence interval.

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identified factors that delay wound healing (Table 3). The mean scores of wound care assessment and practice among the participants are as follows: before wound care (3.3 ± 0.4), during wound care (3.2 ± 0.4), the technique of wound care (3.5 ± 0.5) and after wound care practice (3.8 ± 0.2). On a scale of 1 - 4, all the mean scores were higher than 3.0. This indicated adequate wound care assessment and practice, Figure 2. The association between demographics and level of practice on chronic wound management showed that the highest educational level ($p = 0.037$) and work status ($p = 0.037$) were significantly associated with the level of practice on chronic wound management (Table 4). Factors that were significantly associated with the level of practice of chronic management included extra training opportunities on wound management before working in the current department ($p = 0.022$), attendance of frequent workshops on wound care after school ($p < 0.001$), and knowledge of chronic wound management ($p < 0.001$) (Table 5).

Multivariable logistic regression was used to investigate the significant predictors of the level of practice on chronic wound management. The dependent variable of practice on chronic wound management was categorised by the mean score as poor practice (mean score < 79.56 = 0) and good practice (mean score ≥ 79.56 = 1). Independent variables were the highest level of education, extra training opportunities on wound management before working in the current department, attendance of frequent workshops on wound care after school and knowledge of chronic wound management. Only two variables were significant independent predictors of good practice in chronic wound management. Nurses who had attended frequent workshops on wound care after school were 3.326 times more likely to report good practice on chronic wound management ($p < 0.001$, 95% CI: 1.788 - 6.189). Participants with good knowledge were 3.136 times more likely to perform good practice ($p = 0.001$, 95% CI: 1.579 - 6.226) (Table 6).

DISCUSSION

The goal of this study was to investigate the level of knowledge and practice and other associated factors on chronic wound management among nurses at KBTH, Ghana. A total of 200 nurses from the departments of surgery, medicine, obstetrics, gynaecology, and paediatrics were recruited for the study. The findings suggested that, in general, the nurses' competencies in knowledge and practice of wound management were inadequate. The study also showed that factors such as socio-demographic characteristics and educational background in wound management affected the knowledge and practice of chronic wound management.

The majority of the nurses in the departments, apart from those in surgery, indicated good knowledge and practice in the management of chronic wounds. Overall, 63.5% (n = 127) were considered to have good knowledge, and 52% (n = 104) had good practice. Significantly, those with good knowledge also had good practice. In this study, nurses in the surgery department had the lowest knowledge of wound care, contrary to a study by Lynn, who reported that nurses in the surgical department rather had a better knowledge of chronic wound care [25]. Another study also showed that nurses across different healthcare settings often have insufficient time and a lack of knowledge or insight, which are important in wound management [9]. It is crucial for nurses to improve their competence to achieve patient satisfaction and also assist in implementing educational programs to help patients develop self-care behaviours to improve wound care.

Some factors, such as the number of years of work experience, number of years of working in their current department, the highest level of education, and frequent attendance at workshops on wound care after school, were significantly associated with good knowledge of chronic wound management. This implies that nurses who have good knowledge of chronic wound management are most likely to provide evidence-based practice to satisfy their patients as compared to those with inadequate knowledge but with an optimistic approach [14,26]. Other studies also show that nurses who had post-basic training or specific wound management courses had adequate knowledge of wound care [27,28]. This is an indication of the need for nurses to learn and be engaged in educational activities that build on their knowledge and practice in the field of wound management. A previous study done in Ghana confirmed that there was poor knowledge about field practices of chronic wound management in connection with the application of the basic principles in wound care [25]. Almost all nurses, 98% (n = 196), received theoretical instruction on wound management during training. This skill needs to be upgraded and applied in a clinical setting. The majority of participants' (95.5%, n = 191) responses to awareness of concepts of wound management indicated having some understanding of the concept of chronic wound management, and about half (53.1%, n = 107) correctly indicated the right answer for specific concepts. Kielo et al. reported that most of the respondents claimed that their wound care knowledge of concepts on wound management was either satisfactory (44%, n = 88), fair (23%, n = 46) or poor (3%, n = 6). By contrast, another study on registered nurses stated that 35% (n = 70) of those working on acute cases reported that their wound care knowledge was either good or excellent [4]. Our study showed that about two-thirds (69.5%, n = 139) of the nurses were familiar with the concept of chronic wound management.

The participant's responses on the knowledge of the associated factors of chronic wound management included infection as an associated factor that delayed wound healing, which was indicated by 66% (n = 132) of the nurses. However, other factors like chronic diseases, oxygenation, lifestyle, and stress seem not to be much understood by the nurses as factors influencing chronic wound management. Other studies showed that chronic

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wound management and associated factors have not been adequately taught to nurses [20,29]. In addition, they lack knowledge of the effect of stress and lifestyle as systemic factors that have a negative influence on wound healing [29,30]. Oxygenation as a local factor also influences wound healing negatively when it is lacking in the tissues, as in hypoxia, but most of the nurses did not have this insight. [31,32]. The majority of nurses (82%, n = 164) had a good understanding of the concepts of chronic wound management techniques, while those who had good knowledge of specific concepts of chronic wound techniques (73%, n = 146). However, those with poor knowledge of the concepts of chronic wound management techniques were only 18% (n = 36).

A study done to explore the effect of wound cleansing solutions and techniques on pressure ulcer healing [33] showed that proper assessment was very vital before dressing. Almost all of the participants in our study were of the view that adequate wound assessment before dressing is beneficial. The results of this study also showed that participants with good knowledge were 3.14 times more likely to perform good practice. Similarly, nurses who had attended frequent workshops on wound care after school were 3.33 times more likely to report good practice on chronic wound management. Granick et al. also reported that quality management and wound dressing with the practices of the 7-Key-Steps for wound assessment was common knowledge among nurses [34]. Thus, 60.5% (n = 121) of the nurses were aware of the 7-Key-Steps for wound assessment. However, another study was done to investigate the District Nurses' level of knowledge regarding wound care, and it was found that there were weaknesses in both theoretical and clinical knowledge concerning wound assessment [35]. Our study showed that the majority of the nurses in the paediatric department (64%, n = 128) followed good practice of wound management, whereas the same proportion (64%, n = 128) of nurses in the surgical department rather showed poor practice of wound management. Reports from other studies showed a contrary result, with the surgical nurses having better knowledge and practice [23]. Studies done in Denmark and the United Kingdom supported that knowledge varies as the role of nurses varies [16]. The study revealed that higher educational levels were associated with better wound management practices than those with lower educational levels. Thus, 79.2% (n = 159) of the nurses with master's degrees had good practice. The results indicated that an adequate educational level in chronic wound care confirmed a link with good practice.

A study done in Canada revealed that the healing of wounds was enhanced when delivered by nurse practitioners with progressive wound management training in the health care institution [25]. According to the study, nursing officers account for 33% (n = 66) of all the respondents who have had contact with chronic wounds, while principal nursing officers account for just 10% (n = 20). Critical attention should be given to nurses with certificates, as 62.5% (n = 125) of them have poor practice [17]. A report by Kielo et al. indicated that extra practice on wound management and training could boost nurses' confidence, which will facilitate their competence [4]. Nurses who received extra training and hands-on practice before and during internship and those who attended frequent workshops mostly had good practice in chronic wound management. Another report about fundamental quality management of wounds from the UK stated that not all settings have provided adequate advanced education for nurses. [25]. A similar argument is also made for the "Years in the department" and the "Highest level of education". It was also observed that the level of good practice declined with increasing years of working in a particular department, which needs to be addressed [36,37]. Another report from Finland also indicated poor access to evidence-based guidelines and inadequate understanding of techniques for quality wound management and its associated factors [18,38].

According to the results of this study, there was an increase in knowledge level on wound assessment and its associated factors that delay wound healing. It is crucial for nurses to understand those factors in order to improve their competencies by assisting in implementing educational programs to help patients improve their behaviour towards the healing of wounds. It is also important to have the right understanding of the concept of chronic wound management. Moreover, the management of chronic wounds facilitates healing in order to prevent complications and reduce work overload, long hospitalisation, and financial restrain. Therefore, frequent workshops and regular seminars on wound management must be consistent and mandatory. The findings also show that about half of those nurses received and added to the knowledge they obtained during their training. In addition, not all steps regarding the protocol for wound assessment results after the opening of the wound are always followed by the majority of the nurses, and this is an indication that much awareness needs to be created. This suggests the need for nurses to learn and be engaged in educational activities that build on their ability to practice in the field. Also, there must be a protocol for proper assessment of wound characteristics and the decision of the available dressing product suitable for that particular wound. In addition, appropriate standard wound techniques for a particular wound must be provided since every wound is unique and needs to be treated as such. Moreover, the practice of chronic wound management from our study indicates the need for nurses to implement proper wound management.

It is important for nurses to understand and improve their knowledge, techniques, and practice to enhance the quality of wound care. Furthermore, critical attention must be given to nurses who hold certificates since they had a high percentage of not practising wound techniques properly, which then calls for additional training seminars on good practice of management of chronic wounds. The analysis revealed that the majority of the nurses in the surgical department recorded the greatest number of nurses who did

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not practice all the steps in wound management. This is crucial since the department admits a greater number of patients with chronic wounds. This needs further investigation to examine the reasons and to explain if workload may be responsible.

Conclusion

The majority of the nurses in the surgical department recorded the highest number of nurses who do not practice 7-Key Steps in wound assessment before dressing is done. More than half (53.1%, n = 107) of the nurses do not have the right understanding of chronic wound management, and 39.5% (n = 79) of them were not aware of the 7-Key Steps in wound assessment. Nurses who classified wounds before assessing and dressing the wounds possessed good knowledge. Similarly, nurses who apply the right wound techniques have good practice. Nurses' competency can facilitate chronic wound healing, which will reduce long hospitalisation, work overload, stress, and financial burden on both the patient and institution, as well as mortality if complications set in.

DECLARATIONS

Ethical consideration

This study was approved by the ethics committee of Xiangya School of Nursing at Central South University with approval ID 12020001 and the Korle Bu Teaching Hospital Institutional Review Board with clearance approval ID KBTH-IRB/000139/2020.

Consent to publish

All authors agreed on the content of the final paper.

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Competing Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

Author contribution

DOB acknowledges instructors at the Central South University School of Nursing, all the participants from Korle Bu Teaching Hospital, and those who supported the collection of the data. DOB is grateful to the Chinese government and the Ghana government through the Ministry of Health for their sponsorship.

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Availability of data

Data for this work is available upon request from the corresponding author.

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Medicinal uses, pharmacological activities, and bioactive compounds of *Nauclea latifolia* and implications in the treatment of tropical diseases

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Abstract

Nauclea latifolia Sm. is a medicinal plant from the family Rubiaceae which is widely distributed in the tropical regions of Africa and Asia. Different parts of the plant are known to have many ethnomedicinal uses. The aim of this review is to compile knowledge available on the ethnomedicinal uses, pharmacological activities, and bioactive compounds present in different parts of the plant and identify their relevance in the treatment of tropical diseases. This review will preserve traditional knowledge, promote responsible use, and advance scientific and medical research on this plant. *N. latifolia* is used for the treatment of malaria, skin conditions, pain, hypertension, diabetes, fever, stomach problems, female infertility, gastric ulcer, jaundice, respiratory tract ailments, eye conditions, menstrual disorders, yellow fever, gonorrhoea, haemorrhoids, urine retention, male sexual dysfunction, dysentery, diarrhoea, HIV/ AIDS, measles, typhoid fever, leprosy, oral diseases, hernia, cancer, filariasis (helminthiasis) and central nervous system injuries. This plant has been investigated for its antidepressant, anticonvulsant, antimicrobial, antiplasmodial, antioxidant, antidiabetic, anti-ulcer, antipyretic, antinociceptive, hepatoprotective, larvicidal, ovicidal, antidiarrheal, antihypertensive, hypocholesterolemic, hypoglycaemic, anti-inflammatory, anxiolytic, myorelaxant and sedative activities. Scientific justification for its usage in the treatment of viral infections, hypertension, helminthiasis, stomachache, diabetes, backache, fever, cancer, malaria, diarrhoea, measles, conjunctivitis, and gastric ulcer has been established. However, further studies are needed to justify its use in the treatment of urine retention, male sexual dysfunction, HIV/ AIDS, hernia, female infertility, as well as Parkinson's and Alzheimer's disease. The phytoconstituents documented include proanthocyanins, alkaloids, tannins, flavonoids, glycosides, phenols, steroids, saponins, and terpenoids, with many compounds having been isolated.

Keywords: Nauclea latifolia, ethnomedicinal uses, phytochemistry, bioactive compounds, pharmacological properties, traditional uses

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INTRODUCTION

In Africa, medicinal plants have been used therapeutically since ancient times by early empirical observations and generational transmission via oral tradition. [Sofowora, A. (1996). Research on Medicinal Plants and Traditional Medicine in Africa. The Journal of Alternative and Complementary Medicine, 2(3), 365–372. doi:10.1089/acm.1996.2.365] are extensively used due to their long history of use in the African culture, but also in certain remote areas, even more appreciated due to limited access to modern healthcare services or as an augmentation to modern healthcare [1]. The use of medicinal plants is believed to be a fundamental component of the African traditional healthcare system and is perhaps the oldest and the most assorted of all the therapeutic systems [2]. The World Health Organization reports that 70% to 95% of the human population in most developing countries, including Africa, use medicinal plants for daily health improvement [3]. Africa is a tropical continent plagued with tropical diseases. The term tropical disease refers to a number of

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infectious diseases that commonly occur in the tropics due to the warm and moist environmental conditions, and these are often quite challenging to manage and control. These diseases include leishmaniasis, schistosomiasis, onchocerciasis, lymphatic filariasis, Chagas disease, African trypanosomiasis, dengue fever, and even malaria, diarrhoeal diseases and tuberculosis etc. [4]. Currently, the World Health Organization (WHO) recognizes 17 neglected tropical diseases (NTDs): Buruli ulcer, Chagas disease, cysticercosis, dengue fever, dracunculiasis, echinococcosis, endemic treponematoses, foodborne trematode infections, human African trypanosomiasis, leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, rabies, schistosomiasis, soil-transmitted helminthiases, and trachoma [5].

The treatment of neglected tropical diseases, in particular, has been challenging, resulting in millions of blind, maimed and disfigured individuals in the poorest parts of the world [5]. Medicinal plants have long been used in the management and treatment of various NTDs [6]. Most of these treatments are part of the traditional and alternative medicine systems, and some have gained recognition for their potential efficacy even in modern medical research, as is the case of the treatment of malaria with *Artemisia annua* [7]. In this respect, we review information available on *N. latifolia* Sm. from the family Rubiaceae. This is a medicinal plant widely used in West Africa for the treatment of several diseases [8]. *N. latifolia* is traditionally important in Ghana and Sub-Saharan Africa for both medicinal and non-medical purposes [8,9].

In Ghana, the plant is used non-medically as a roofing material and for firewood, while the fruits are consumed by some as food. The leaves, stem, and bark of *N. latifolia* are prepared as decoction in water and used traditionally against malaria [10] and other infections [11-14]. Also, decoctions of roots, bark, stem or leaves of the plant are taken as dewormers [15] and used for treating toothache, dental caries, septic mouth, diarrhoea and dysentery [16]. The citizens of Mali and Cote d'Ivoire use the aqueous extracts of *N. latifolia* to treat fever and malaria [17]. In addition to the numerous benefits of the plant to humans, it is also reported for use in the treatment of diseases that affect animals, such as diarrhoea [18-20] and helminthiasis [21]. Recently, researchers have developed an interest in the isolation of compounds present in different parts of *N. latifolia* in order to determine their bioactivity and toxicity. The investigation was occasioned following the isolation of the synthetic analgesic tramadol at a considerable at a considerable concentration from the root bark [22]. Such findings are rare in nature. The medicinal potentials of *N. latifolia* necessitate this review of its ethnomedicinal uses, pharmacological activities, and bioactive compounds.

MATERIALS AND METHODS

Study design and sites

From November 2020 to July 2021, relevant articles were accessed from Google Scholar, Science Direct, Web of Science, and African Journals Online. Key terms that were used in the search included phytochemistry, bioactive compounds, pharmacological properties, pharmacological activity, pharmacological model, *Nauclea latifolia*, *Sarcocephalus latifolius*, African Peach, Pin Cushion tree, traditional uses, ethnomedicinal uses, herbal medicine, indigenous, preparation and route of administration. The publications obtained were first screened using their abstracts, and subsequently, their full texts were reviewed. A total of 137 articles, books and book chapters were accessed. Information on the various ethnomedicinal uses, pharmacological activities, and bioactive compounds obtained from the literature sources is examined below.

RESULTS

N. latifolia belongs to the family Rubiaceae. The family Rubiaceae has about 611 Genera, with 13,100 species in the Wet Tropics [23]. The genus Nauclea has various species. *N. latifolia, N. diderrichii (De Wild. & Th.Dur.) Merrill, N. gilleti (De Wild.) Merr, N. vanderguchtii (De Wild) Petit, N. pobeguinii (Pobég. ex Pellegr.) Merr. ex E.M.A. Petit and N. xanthoxylon* (A.Chev.) Aubrév. are those commonly found in Africa [24]. N. latifolia is known in English as an

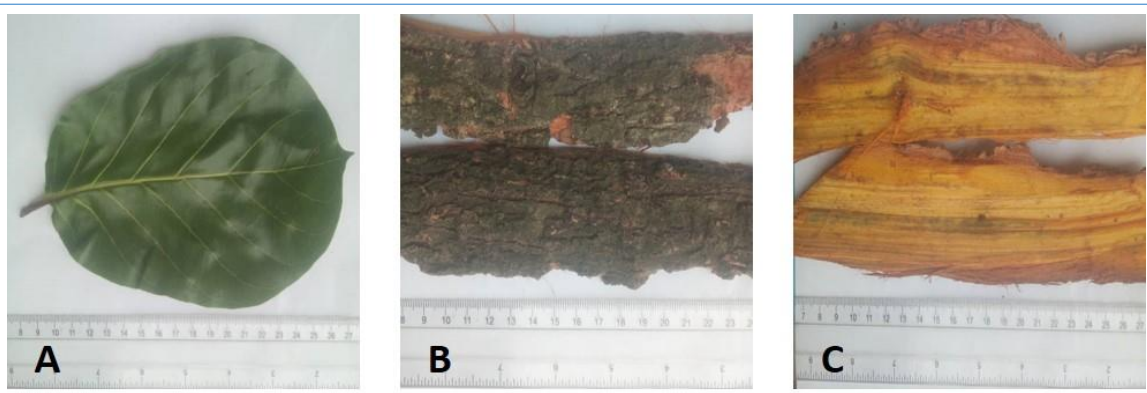

Figure 1. Leaf (A), Outer bark (B), Inner bark (C) of N. *latifolia*

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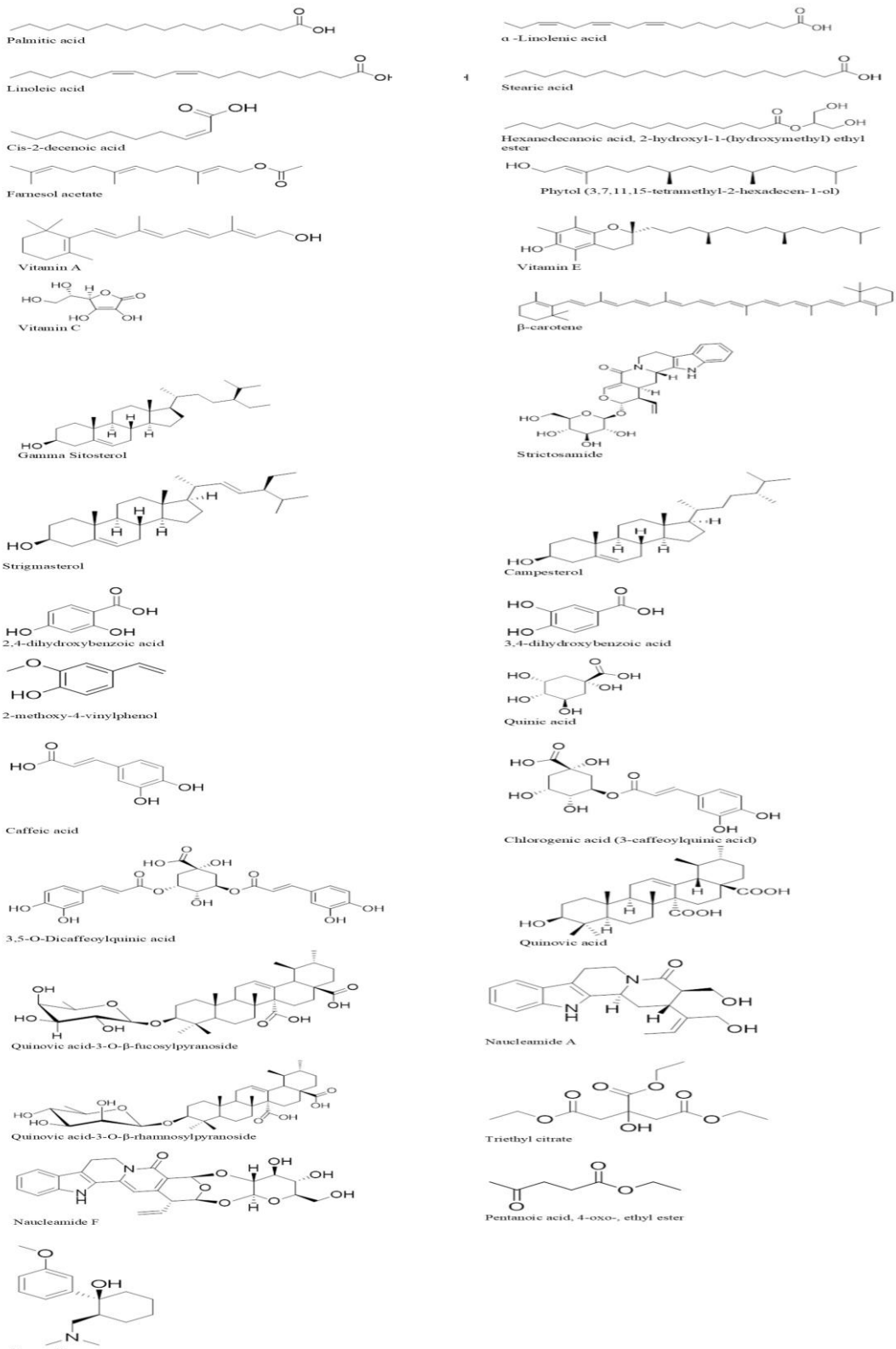

Figure 2. Bioactive molecules of N. latifolia

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Table 1. Treatment of Malaria using *N. latifolia*

Plant Part	Preparation	Administration	Country/ Region	Reference
Roots	Decoction	Oral	Benin/ Plateau of Allada	[34]
Roots, Leaves	Decoction (Root) Maceration (Leaves)	*N/A*	Burkina Faso/ Baskoure, Kourritenga Province	[31]
Stem bark, Roots	Decoction	Oral	Cameroon / Yaoundé and Mbalmayo	56
Stem	Maceration	Oral	Ghana/ Eastern, Central, Greater Accra and Ashanti regions	[42]
Roots Root bark	Decoction Infusion	Oral	Ghana/ Dangme West District/ Northern	[10, 41]
Leaves, Roots, Stem bark, Root bark	Decoction	Oral, Steam bath	Guinea/ All regions	[55], [54]
Leaves, Bark	Maceration (Bark) Decoction (Leaves)	Oral	Mali/ All regions	[14]
Leaves	Decoction	Oral, Bath	Mali/ Sélingué subdistrict	[53]
Bark, Roots	Decoction (Root)	Co-administered orally with other plant species.	Nigeria/ Ogun state	[49]
Bark, Roots	Decoction (Root)	Co-administered orally with other plant species.	Nigeria/ Ogun state	[49]
Leaves Co-administered orally with other plant species	Decoction	Oral	Nigeria/ Ogun state/ Okigwe Imo state	[45, 47]
Leaves	Infusion	Oral	Nigeria/ Ekiti state	[44]
Leaves, Roots, Stem bark	Maceration (Leaves)	Co-administered orally with other plant species	Nigeria/ Southern region	[48]
Leaves	Decoction	Oral	Nigeria/ South West	[133]
Leaves, Stem bark, Roots	Tincture (Root), Decoction (Root)	*N/A*	Nigeria/ Southern	[134]
Stem, Roots	Decoction	Oral	Ghana	[135]
Roots	Maceration, Decoction, Infusion	Oral	Nigeria/ Akwa Ibom state	[136]
Leaves	Maceration	Co-administered orally with other plant species	Sierra Leone	[57], [56]
Roots	Decoction, Maceration	Oral	Togo/ Plateau and Maritime region	[50], [51]
Stem, Bark	Aqueous infusion	Oral	Ghana/ Accra	[9]
Roots, Leaves	Maceration (Root)	Oral	Togo	[52]

Table 2. Treatment of Skin Conditions using *N. latifolia*

Disease	Plant Part	Preparation	Administration	Country/ Region	Reference
Boils	Roots	Decoction	Oral	Nigeria / Rivers state	[59]
Itching	Roots, Stem	Decoction	Bath	Nigeria / Benue and Ekiti states	[30], [60]
Burns	Leaves	Infusion	Bath	Senegal / Kédougou	[65]
Wounds and Infantile dermatosis	Inner bark, Stem, Sap, Fruit, Roots, Root bark	Decoction	Oral	Nigeria / Odeda and Lagos state	[63], [62]

Table 3. Treatment of Pain using *N. latifolia*

Disease	Plant Part	Preparation	Administration	Country/ Region	Reference
Backache	Roots, Leaves	Decoction (Root, Leaves)	Oral	Nigeria / Kainji Lake National Park	[66]
Headache	Leaves	Decoction	Oral, Bath	Mali/ All regions	[14]
Abdominal ache	Leaves, Roots	Infusion (Roots)	*N/A*	Senegal/ Kédougou	[65]
	Leaves, Roots, Bark	Decoction	Oral	Nigeria/ Abia and Bauchi State	[83], [35]
	Bark, Roots	Decoction (Bark, Roots), Maceration (Bark, Roots)	Oral	Mali/ All regions	[14]
	Roots, Leaves	Decoction	Oral	Burkina Faso/ Baskoure, Kourittenga Province	[31], [137]

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Table 4. Summary of Pharmacological Activities of *N. latifolia* Crude Extracts

Activity Tested	Plant Part	Extract	Methodology	Effect	Reference
Anticonvulsant	Root bark	Aqueous	Fisher's Exact Test	Extract at 160 mg/kg dose provided 75% and 71% protection of mice ($p < 0.01$) against strychnine-induced seizures and pentylenetetrazol-induced seizures, respectively.	[91]
Antidepressant	Root bark	Aqueous	Forced Swimming Test	Extract significantly shortened immobility time of mice.	[92]
Antidiarrheal	Root bark	Ethanol	Inhibition of Castor Oil- Induced Diarrhea	Extract showed a 77.42% protection against diarrhea.	[93]
			Small Intestinal Motility Model	Extract produced 50% dec rease in the propulsive movement of the charcoal meal through the small intestine.	
			Isolated Rat Ileum Model	Extract caused a significant dose-dependent relaxation on the acetylcholine-induced contraction.	
Antihypertensive	Root bark, Stem bark	Ethanol	Change in Body and Organ Weight in Wistar Rats.	Extract significantly reduced the body, heart, kidney, and liver weights.	[94]
	Roots	Ethanol	Change in Systolic Blood Pressure in Rats.	Extract at dose of 2.5 – 20 mg/kg and 2.5 – 10 mg/kg effectively lowered blood pressure in normotensive rats and in hypertensive rats, respectively.	[138]
Anti-inflammatory	Root bark	Aqueous	Egg-Albumin-Induced Inflammation in Rats.	Extract significantly reduced inflammatory responses in test rats.	[95]
Antimicrobial	Leaf	Ethanol	Agar Plate Method	Extract exhibited significant inhibitory activity against moulds, *Staphylococcus spp* and *Candida albicans.*	[98]
		Methanol		Extract exhibited significant inhibitory activity on *Candida albicans*, *Aspergillus spp* and moulds.	
	Stem bark	Chloroform	Agar Diffusion Method	Extract demonstrated activity against *E. coli, S. aereus, S. dysentariae, B. subtilis, C. albicans* and *P. aeruginosa* with percentage susceptibility of 64%, 64%, 82%, 64%, 58% and 70%, respectively.	[29]
	Root	N-hexane, Ethyl acetate, Methanol	Agar Diffusion Method	All three isolated compounds exhibited potent activity against eleven human pathogenic bacteria and fungi in the order 3,4 - dihydroxybenzoic acid > quinovic acid > strictosamide. The most susceptible were *E. aerogenes, P. vulgaris, S. aureus and C. albicans.*	[103]
	Stem bark, Leaves, Roots	Methanol	Agar Diffusion Method	Extracts actively inhibited *S.* dysenteriae, *E. coli, S. aureus* and *S. pneumonia* with zones of inhibitions of 10 -25 mm.	[74]
	Leaf	Methanol	Agar-Well-Diffusion Method	Extract exhibited activity against *S. typhi, S. enterica, E. coli* and *lactobacillus spp* with MIC of 0.782 mg/*mL*, 3.125 mg/*mL*, 1.563 mg/*mL*, and 1.563 mg/*mL*, respectively.	[100]
	Stem bark			Extract exhibited activity against *S. typhi*, *E. coli* and *lactobacillus spp* with MIC of 1.56 mg/mL, and against *S. enterica* with MIC of 3.125 mg/mL.	
	Leaves, Bark, Roots.	Aqueous	Agar-Well-Diffusion Method, Broth Dilution Method	All extracts exhibited activity against *K. pneumoniae, E. coli, P. aeruginosa, S. aureus* and *S. dysenteriae.*	[101]
		Ethanol		Ethanol extract exhibited higher activity against all the above micro- organisms as compared to the aqueous extracts.	
	Stem bark	Chloroform	Agar-Well-Diffusion Method	Extract was active against *S. aureus, B. subtilis, S. viridans, E. coli, K. pneumonia* and *A. niger* with MICs of 2.5, 10, 5, 5, 5 and 15 mg/*mL*, respectively.	[96]
		Methanol		Extract demonstrated activity against only *P. aeruginosa and S. aureus* with MICs of 20 mg/*mL* and 10 mg/*mL*, respectively.	
	Leaves	Methanol	Agar Cup- Plate Method	*B. subtilis, Cl. sporogens E. coli, K. pneumonia, P. fluorescence, P. aeruginosa, S. aureus* were susceptible to five isolated compounds: caffeic acid, quercitin, quercetin-3-O-*β*-glycopyranoside, chlorogenic acid and 3,5-O-dicaffeoylquinic acid with MIC ranges of 0.625- 5 mg/*mL*, 0.156- 2.5 mg/*mL*, 1 mg/*mL*, 1-10 mg/*mL* and 1.25- 5 mg/*mL* respectively.	[97]

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Table 4. cont.

Activity Tested	Plant Part	Extract	Methodology	Effect	Reference
	Root bark	Dichloromethane-methanol mixture	Plaque and Viral Yield Reduction Assays	Extract, with an IC_{50} value of 1.46 µg/*mL* (95% CI:1.07 - 1.91), reduced the yield of the acyclovir-sensitive *Herpes simplex* virus-2.	[102]
	Leaves	Ethanol (hot)	Agar-Well-Diffusion Method	Extract exhibited activity against *E. coli, S. aureus and P. aeruginosa* with MICs of 3.24, 3.28 and 4.82 mg/*mL*, respectively.	[99]
	Stem bark	Ethanol	Agar-Well-Diffusion Method	Extract demonstrated activity against *S. aureus, E. coli, S. typhi* and *B. subtilis* with MIC of 2.5 mg/*mL*.	[104]
Antioxidant	Leaves	Ethanol	2,2- Diphenyl-1-Picrylhydrazyl (DPPH) Radical Scavenging Assay, Ferric Reducing Antioxidant Power (FRAP) Assay, Total Antioxidant Capacity (TAC) Assay	Extract showed significant activity against DPPH with an IC_{50} of 2.58±0.08 mg/*mL*, dose-dependent increase in FRAP with the highest power being 1314.45±197.64 mg AAE/g, and a dose- dependent increase in TAC with the highest capacity being 73.81± 2.27 mg AAE/g.	[105]
	Leaves	Methanol	DPPH Radical Scavenging Assay, FRAP Assay, TAC Assay, Nitric Oxide Inhibition Assay, Metal Chelating Ability (MCA) Assay	The isolated compounds (caffeic acid, quercetin, quercetin-3-O- *β*-glycopyranoside, chlorogenic acid and 3,5-O-dicaffeoylquinic acid) exhibited significant DPPH scavenging ability with IC_{50} range of 2.71 ± 0.09 to 21.3 ± 1.01 *µg/mL*. The isolated compounds) had good FRAP values ranging from 0.28 ± 0.01 to 1.21 ± 0.05 mg AAE/g. Also, all the isolated compounds demonstrated good TAC ranging from 2.57 ± 0.01 to 4.23 ± 0.23 mg AAE/g, and exhibited better inhibition of NO radical activities (IC_{50} ranged from 5.17 ± 2.59 to 55.17 ± 0.66 µg/mL). All the isolated compounds exhibited good MCA with the IC_{50} ranging from 104.55 ± 2.73 to 229.18 ± 7.76 *µg/mL*.	[97]
	Leaves, Fruits	Aqueous	DPPH Radical Scavenging Assay, FRAP Assay, Trolox Equivalence Antioxidant Capacity (TEAC), Oxygen Radical Absorbance Capacity (ORAC)	Leaf extract demonstrated better DPPH activity than fruit extract with IC_{50} values of 20.64 mg/*mL* and 120.33 mg/*mL* respectively, and showed higher FRAP (86.10 ± 3.46 *µ*mol AAE/g sample) than fruit extract (12.23 ± 0.40 *µ*mol AAE/g sample). Also, higher TEAC was demonstrated by the leaves extract than the fruits extract with values of 94.83 ± 3.57 *µ*mol TE/g sample and 12.48±0.21 *µ*mol TE/g sample, respectively, and the mean value of ORAC for leaves extract was 196.55 ± 0.073 *µ*mol TE/g sample while that of the fruits extract was 55.88 ± 0.073 *µ*mol TE/g sample.	[106]
	Root	Aqueous	Lipid Peroxidation and Oxidative Stress.	Extract reduced the activity of catalase, superoxide dismutase (SOD) and malondialdehyde (MDA) and restored the level of glutathione (GSH).	[107]
Antiplasmodial	Leaves	Aqueous	Curative Test	Extract caused significant decrease in organism parasitaemia in mice when compared to the negative control group.	[113]
	Leaves	Aqueous	Antioxidant Enzyme and Histopathological Changes	Extract eliminated *P. berghei* in the brain and liver tissues and improved antioxidant defense by restoring the levels of superoxide dismutase, catalase, and glutathione.	[114]
	Leaves	Aqueous	*In-Vitro* and *In-Vivo* Inhibitory Effect on haemozoin concentration	Extract exerted appreciable decrease on the haemozoin concentration at 24-hour intervals.	[111]
	Leaves	Methanol	Rane's Test	Extract caused a statistically significant dose-dependent decrease in organism parasitaemia, and a dose-dependent increase in the chemosuppressive effect on parasitaemia.	[110]

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Table 4. cont.

Activity Tested	Plant Part	Extract	Methodology	Effect	Reference
	Stem bark	Methanol	Rane's Test	Extract caused a dose-dependent reduction in parasitaemia.	[109]
		Ethanol		The groups treated with extract showed a significant dose-dependent decrease in parasitaemia.	[112]
	Roots	Ethanol	Suppressive and Curative Tests in Albino Mice	Extract at 150 mg/ kg caused 96.2% and 33.3% growth inhibition of *P. berghi* in suppressive and curative tests, respectively.	[108]
Antipyretic and Antinocicep tic	Root	Aqueous	Antipyretic Test	Extract caused a significant and dose- dependent hypothermia. Fever was reduced by 0.5 degrees Celsius one hour after administering 160mg/kg of extract.	[115], [95]
			Acetic Acid- Induced Abdominal Constriction	Extract caused inhibition of acetic acid- induced abdominal constriction in a dose- dependent manner.	
			Formalin- Induced Nociception	Extract caused a significant and dose-dependent inhibition of formalin-induced biphasic pain responses in mice.	
			Hot Plate Model	Extract produced a dose- dependent protection against heat- induced pain.	
			Tail Immersion Model	Extract produced a dose- dependent increase in tail withdrawal latency.	
		Ethyl acetate, n- butanol	Von Frey Test	The alkaloids fraction demonstrated dose- dependent inhibition of hyperalgesia with an ED_{50} value of 35.94 (24.25–51.39) mg/kg.	[116]
Anti- ulcer	Leaves	Aqueous	Gastro Mucosal Protection	Extract caused significant and dose- dependent anti-ulcer activity against indomethacin-induced ulcers in the rats-highest dose of 510 mg/kg produced 90.57% protection.	[77]
		Methanol		Extract at a dosage of 150 mg/kg body weight produced an ulcer index of one (1) in aspirin- induced rats and caused a reduction in free acidity, pH, and total acidity content.	[117]
	Stem bark	Aqueous	Gastric Mucus Production	Extract caused a significant and dose dependent elevation in gastric mucous production. At 200 mg/kg, extract produced curative ratios of 73.63% and 77.62% in ethanolic acid and indomethacin-induced ulcers, respectively.	[118]
	Stem bark	50% Methanol	Cytoprotective Assay	Extract significantly inhibited gastric lesions in aspirin and histamine-induced ulcer in rats.	[78]
			Cyto- Healing Assay	Extract dose of 100 mg/kg caused 60.35% healing in ulcerated gastric mucosal cell walls.	
			Anti-*Helicobacter Pylori* Assay	Extract demonstrated activity against *helicobacter pylori* with an MIC of 25 mg/*mL*.	
Anxiolytic	Root bark	Aqueous	Hole- Board Test	Extract reduced anxiety resulting in significant and dose- dependent increase in the number and duration of head- dips.	[92]
			Elevated Plus Maze Test	Extract reduced anxiety resulting in decreased percentage of time spent in closed arms, increased number of entries into, percentage of entries into, and time spent in open arms.	[91]
Hepatoprot ective	Root	Methanol	Biochemical and Histopathological Changes in Wistar Rats	Extract reduced serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels and attenuated deleterious histopathologic changes in liver caused by paracetamol and CCl_4.	[119]
	Root bark	Aqueous	Change in Serum Biochemical Markers	Extract at 300 mg/kg caused 44.3%, 8.1%, 37% and 47. 6% protection for aspartate transaminase, alanine transferase, total bilirubin, and conjugated bilirubin respectively in CCl_4 induced hepatotoxicity in rats.	[120]
Hypocholes terolemic	Leaves	Ethanol	Lipid Profile Analysis	Extracts caused reduction in the levels of triglycerides (TG), low density lipoproteins (LDL), very low-density lipoproteins (VLDL) and total cholesterol in alloxan- induced diabetic rats.	[125]
	Fruit	Methanol	Lipid Profile Change	Extract reduced plasma cholesterol in a dose-dependent order in albino rats.	[124]

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Table 4. cont.

Activity Tested	Plant Part	Extract	Methodology	Effect	
				Extracts caused a dose- dependent decrease in the levels of triglycerides (TG), low density lipoproteins (LDL) and very low-density lipoproteins (VLDL) in alloxan-induced rats.	[123]
Hypoglycaemic	Root	Ethanol	Body Weight and Blood Glucose Level	Extract caused a dose-dependent decrease in blood glucose level and a significant weight gain in alloxan-induced diabetic rats.	[128]
	Leaves	Aqueous	Blood Glucose Level	Extract lowered the blood glucose level in alloxan-induced rats by 79.9% after administration for three days.	[127]
				Extract lowered the blood glucose level in alloxan-induced rats by 45% four hours after administration.	[27]
	Leaves	Ethanol	Glucose Tolerance Test	Extract at dose 200 mg/kg significantly inhibited the increase in glucose level in Wistar rats after glucose load.	[129]
			Blood Glucose Level	Extract at 200 mg/kg dose lowered blood glucose level by 60.77% in streptozotocin-induced diabetic rats after 45 days of administration.	[126]
Larvicidal	Stem bark	Aqueous, Ethanol	Larval Mortality of *Heligmosomoides bakeri*	Extracts destroyed *H. bakeri* with median lethal dose (LC_{50}) of 243, 2246 and 713 µg/*mL* for hot, cold water and ethanolic extracts, respectively.	[122]
		Methylene Chloride: Methanol (1:1)	Larval Mortality of *H. Bakeri*	Extract at concentration of 5000 µg/*mL* caused 54.76% and 51. 44% mortality rates in the first and second larval stages respectively, 24 hours after administration.	[121]
	Leaves	Aqueous, Ethanol	Larval Development Assay	Extracts exhibited activity with median lethal dose (LC_{50}) of 0.704 mg/*mL* and 0.650 mg/*mL* for aqueous and ethanolic extract respectively with a statistically significant difference.	[32]
Myorelaxant	Root bark	Aqueous	Horizontal Wire Test	Extract produced a dose- dependent increase in the number of impaired mice. These impaired mice experienced significant muscle relaxation at concentration of 80 mg/kg, similar to that induced by diazepam.	[92]
Ovicidal	Stem bark	Aqueous, Ethanol	Egg Assays of *H. Bakeri*	Extracts exhibited activity with median Inhibitory Concentration (IC_{50}) of 1082, 4554 and 0.10 µg/*m* for hot, cold and ethanolic extract respectively.	[122]
	Stem bark	Methylene Chloride: Methanol (1:1)	Egg Assays of *H. Bakeri*	Extract inhibited embryonation in a dose-dependent manner. At maximal concentration of 5000 µg/*mL*, there was 38.15% inhibition of embryonation.	[121]
	Leaves	Aqueous, Ethanol	Nematode Egg Recovery Technique	Extract caused a reduction in the nematode egg count.	[32]
Sedative	Root bark	Aqueous	Diazepam-Induced Sleep Model	Extract at dose of 80 mg/kg increased the sleep time from 12 minutes in control group to 64 minutes in test group.	[91]

African peach or Pin cushion tree [25]. In Ghana, it is commonly called "kusia" among most Akans, "oyefa-owenfa" among the Gas, "nyimo" among the Ewes, and hwene hwenti" among the Bonos [26]. *N. latifolia* is a shrub with green leaves and multiple stems that is found in tropical Africa and Asia [27]. *N. latifolia* is distributed in the Savannah woodlands and the tropical rainforest of the Western and Central parts of Africa [8]. In Ghana, it is widely distributed in the Togo Plateau Forest Reserve in the Volta Region [28]. The plant measures about 20 ft tall in the Savanna woodland and about 100 ft tall in the forest zone. It has dark upper surface leaves which are acuminate, short, glabrous, opposite, and glossy green. The plant bears white, sweet-scented flowers and has a dark grey to brown cracked stem with a fibrous reddish slash [8,29]. Figure 1 shows images of various parts of *N. latifolia*.

N. latifolia is used for a wide range of therapeutic purposes among the indigenes of West Africa. The plant is used for treating infectious ailments, including yellow fever, gonorrhoea, diarrhoea, measles, HIV/AIDS, typhoid fever, helminthiasis, and malaria. Of the many NTDs, *N. latifolia* is reported to be used in the treatment of leprosy and filariasis (helminthiasis) [5,15,30,31]. The plant is also used

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Table 5. Pharmacological Activities of Bioactive Compounds in N. latefolia

Pharmacological Activity	Compound(s) responsible	Plant Part/ Extract	Reference
Antiplasmodial Activity	Strictosamide	Leaves/ Aqueous	[111]
Anti- inflammatory Activity	Quercetin	Leaves/ Methanol	[97]
	Gamma-sitosterol; 2- Methoxy-4 –vinylphenol; Phytol (3,7,11,15-tetramethyl-2-hexadecen-1-ol); Palmitic Acid (Hexadecanoic acid); α-linolenic acid (9,12,15-octadecatrienoic acid); Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester	Leaves/ Ethanol	[131]
Anticancer Activity	Quercetin	Leaves/ Methanol	[97]
	Stigmasterol	Leaves/ Ethanol	[131]
	β-carotene; Lycopene	Leaves/ Ethanol	[105]
Antibacterial Activity	Isoquercitrin (quercetin-3-O-β-glucopyranoside); 3,5-O-dicaffeoylquinic acid	Leaves/ Methanol	[97]
	2,4-Dihydroxybenzoic acid; Farnesol acetate Cis-2-decenoic acid; Phytol (3,7,11,15-tetramethyl-2-hexadecen-1-ol)	(Leaf, stem bark)/ methanol	[100]
	Quinovic acid; Strictosamide.	Roots/ Ethyl acetate	[103]
	3,4-dihydroxybenzoic acid	Roots/ Methanol	
Antioxidant Activity	Isoquercitrin (quercetin-3-O-β-glucopyranoside); 3,5-O-dicaffeoylquinic acid; Quercetin; Chlorogenic acid (3-caffeoylquinic acid); Caffeic acid (trans-3,4-dihydroxycinnamic acid)	Leaves/ Methanol	[97]
	Palmitic Acid (Hexadecanoic acid), 2-hydroxy-1-(hydroxymethyl) ethyl ester; linoleic acid (9,12-octadecadienoic acid); Campesterol; 2- Methoxy-4–vinylphenol; Stigmasterol; Triethyl citrate	Leaves/ Ethanol	[131]
	Vitamin A; Vitamin C; Vitamin E	(Stem bark, Root bark)/ Ethanol	[139]
Antifungal Activity	Strictosamide; Quinovic acid	Roots/ Ethyl acetate	[103]
	3,4-dihydroxybenzoic acid	Roots/ Methanol	
	Strictosamide; Naucleamide A; Naucleamide F; Quinovic acid-3-*O*-β-rhamnosylpyranoside; Quinovic acid 3-*O*-β-fucosylpyranoside	Roots/ Ethanol	[140]
Hepatoprotective Activity	Pentanoic acid, 4-oxo-, ethyl ester; Stigmasterol; α-linolenic acid (9,12,15-octadecatrienoic acid); linoleic acid (9,12-octadecadienoic acid)	Leaves/ Ethanol	[131]
Antidiabetic Activity	Quinic acid; Phytol; Stigmasterol; Gamma-sitosterol; Phytol (3,7,11,15-tetramethyl-2-hexadecen-1-ol); Stearic acid (Octadecanoic acid);	Leaves/ Ethanol	[131]
Antiarthritic Activity	Phytol (3,7,11,15-tetramethyl-2-hexadecen-1-ol); α- linolenic acid (9,12,15-octadecatrienoic acid)	Leaves/ Ethanol	[131]
Hypocholesterolemic Activity	Palmitic acid (Hexadecanoic acid); Campesterol; Stigmasterol; Linoleic acid (9,12-octadecadienoic acid); α-linolenic acid (9,12,15-octadecatrienoic acid);	Leaves/ Ethanol	[131]
Antiandrogenic Activity	Palmitic Acid (Hexadecanoic acid); linoleic acid (9,12-octadecadienoic acid)	Leaves/ Ethanol	[131]
Anti- Glutathione S-transferase Activity	Strictosamide; Naucleamide F	Roots/ Ethanol	[140]
Analgesic Activity	Tramadol	Roots/ Methanol	[132]

in the treatment of non-infectious ailments, digestive disorders, disorders of cardiovascular and metabolic functioning, reproductive disorders, skin disorders, pain, respiratory disorders, and eye conditions [30,32-40]. Tables 1-3 provide detailed uses of *N. latifolia* in the treatment of various diseases. *N. latifolia* is indicated for the treatment of malaria among the indigenes of Ghana [9,10,41,42], Nigeria [43-49], Togo [50-52], Mali [14,17,53], Guinea [54,55], Sierra Leone [56,57], Benin [34], Burkina Faso [31], Cameroon [58] and Cote d'Ivoire [17]. The stem, leaves, roots, stem bark, and root bark are commonly used. These parts are used either alone or in combination with other plants in the preparation of decoctions, macerations, infusions, or tinctures [48]. The preparation is administered orally throughout all these countries. Details of the use of *N. latifolia* in the treatment of malaria are provided in Table 1. The plant is used as a remedy for dermatological disorders [59,60], itching [30,61], wounds [62], infantile dermatosis

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[63], scalp infection [64] and burns [65]. Detailed uses of *N. latifolia* in the treatment of these skin conditions are provided in Table 2. Different parts of *N. latifolia* are used for the treatment of abdominal pains [14,31,35,65], headache [14] and backache [66]. Detailed uses of the plant in the treatment of these conditions are provided in Table 3. Preparations made from the roots, stem, leaves, and bark are used for treating helminthiasis in Nigeria [21,32,67], Ghana [15], Togo [68] and Sierra Leone [56], and specifically for treating filariasis in Nigeria [30]. In Ogbomoso and Edo states of Nigeria, preparations from the roots, leaves, stem, and bark of the plant are used to treat high blood pressure [43,46,69]. In the Ouémé region of Benin, root decoction is also administered orally to treat hypertension [70]. Also, *N. latifolia* is known as a remedy for hypertension in Accra, Ghana [71]. Decoction prepared from the stem bark of *N. latifolia* is administered as a cure for diabetes in Cote d'Ivoire [72] and Guinea [37]. The roots are reportedly used for the treatment of diabetes in Nigeria [43] and Benin [73].

Different parts of the plant are used as a remedy for fever in Ghana [9] and in various states of Nigeria [43,62,74], in particular the people of Tivland who rank it as the first choice of remedy for fever management [40]. The stem, bark, root, and fruit are used to treat stomach ailments in Cameroon [75], Nigeria [62,74] and Togo [52]. Infusion and decoction of the roots of *N. latifolia* are used to treat female infertility in Togo [52], Nigeria [76] and Burkina Faso [31]. The root, bark, and stem of *N. latifolia* are used to cure gastric ulcers in Nigeria [77-79]. The preparations from the stem and bark are used in the treatment of jaundice among the indigenes of the Accra metropolis, Ghana [9] and in parts of Nigeria [62,80,81]. Maceration of the roots of the plant is administered orally as a remedy for asthma [82]. Decoctions of the inner bark, stem, leaves, sap, fruit, root, and root bark are administered orally for the treatment of cough in Nigeria [36,62,83]. Sap from the stem and leaves of *N. latifolia* are reported to be used in Sierra Leone [56] and Cote d'Ivoire [39] for the treatment of eye conditions such as conjunctivitis, respectively. The root and bark of *N. latifolia* are used to remediate menstrual disorders in Nigeria [62,84] and Benin [85]. In Nigeria, decoctions and macerations of parts of *N. latifolia* are taken to treat yellow fever [30,49]. Decoction of the roots of *N. latifolia* is used as a cure for gonorrhoea in Nigeria [47,86]. Preparations of the roots, leaves, stem, and bark are either taken orally or used as enemas for the treatment of haemorrhoids by indigenes of the Tem tribe in Togo [52] and in parts of Nigeria [62]. The roots, leaves, and bark of *N. latifolia* are used as a remedy against urine retention in Burkina Faso [31] and Nigeria [32]. Male sexual dysfunction is treated in Nigeria using an alcohol infusion of the root bark [38] and in Mali using the root decoction [14].

The leaves of *N. latifolia* are known for the treatment of dysentery in Sierra Leone [56] and diarrhoea among the indigenes of Abidjan in Cote d'Ivoire [33]. The leaves of *N. latifolia* are claimed to be used for the treatment of HIV/AIDS in Nigeria [87]. The inner bark, stem, sap, roots, root bark and fruit of *N. latifolia* are reported among the inhabitants of Lagos in Nigeria for the treatment of measles [62]. The bark and roots of *N. latifolia* are prepared into decoctions and used for the treatment of typhoid fever in Nigeria [49] and in the Accra metropolis of Ghana [9]. The roots and leaves are reportedly used for the treatment of leprosy among the indigenes of the Baskoure, Kourittenga Province of Burkina Faso [31]. The stem, fruits and bark are used for the treatment of oral thrush [62]. In Nigeria, the stem of *N. latifolia* is chewed as a remedy for oral disorders [88]. The leaves and roots have been reported for use in the treatment of hernia in Burkina Faso [31]. A decoction prepared from the leaves is administered orally to cure cancer in Nigeria [89]. Indigenes of Togo administer root decoctions orally to treat Alzheimer's disease and Parkinson's disease [90].

In-vivo and in-vitro studies have been performed using extracts from parts of *N. latifolia* to investigate its pharmacological potential. The extracts of the various parts of the plant have been shown to exert anticonvulsant [91], antidepressant [92], antidiarrhoeal [93], antihypertensive [94], anti-inflammatory [95], antimicrobial [29,74, 96-104], antioxidant [97,105-107], antiplasmodial [108-114], antipyretic and antinociceptic [115,116], anti-ulcer [77,78,117,118], anxiolytic [91,92], hepatoprotective [119, 120], larvicidal and ovicidal [32,121,122], hypercholesterolaemic [123-125], hypoglycaemic [27,126-129], myorelaxant [92] and sedative [91] activities. Many of these pharmacological studies have been performed to scientifically prove the efficacy in ethnomedicinal uses of the various parts of the plant. Bioactive compounds are the specific compounds present in parts of plants that are responsible for particular biological or pharmacological activities. Table 5 indicates the active compounds present in specific parts of *N. latifolia*, the pharmacological activities they account for, and the extraction media used.

DISCUSSION

N. latifolia Smith has numerous ethnomedicinal uses in many West African countries, including Ghana, Togo, Mali, Sierra Leone, Burkina Faso, Cote d' Ivoire, Benin, Cameroon, Guinea, Cote d'Ivoire, and Nigeria [8-10,14,17,31,34,41-58,130]. Extracts of the roots, stem, bark, and leaves have demonstrated pharmacological activities that confirm some of the ethnomedicinal uses. Additionally, bioactive compounds, which account for a number of proven activities, have been isolated and characterized. The use of this plant as an antimalarial [31,53] is justified by tests performed by Anowi FC, Chibueze I [113] and Udobre AS, Udobang JA [110] using aqueous and methanolic leaf extracts, respectively. The extracts demonstrated a significant reduction in parasitaemia in laboratory mice. Strictosamide, a bioactive compound isolated from aqueous leaf extract, accounts for the anti-plasmodial activity [111]. Also, decoctions prepared from the leaves are administered as a cure for diabetes in Cote d'Ivoire [72] and Guinea [37]. This is justified by tests performed by Ezekwesili and

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Ogbunugafor [127] and Gidado and Danladi [126] using aqueous and ethanolic leaf extracts, respectively. The extracts caused a significant reduction in blood glucose levels in diabetic rats. Quinic acid, phytol, and stigmasterol are bioactive compounds isolated from ethanolic leaf extract that have been proven to be responsible for hypoglycemic activity [131]. Oral thrush is a fungal disease remediated in Nigeria using stem, root, and bark preparations of *N. latifolia* [62]. The antifungal activity of the plant is proven by tests performed by Ezem and Akpuaka [103] using ethyl acetate and methanolic extracts of the roots. Quinovic acid, Naucleamide A and Naucleamide F are components isolated from ethanolic and ethyl acetate root extracts and are responsible for the antifungal activity [103]. Tramadol, a widely known synthetic analgesic, was recently isolated from the methanolic root extract of the plant [132] and may possibly account for the ethnomedicinal use of the plant for the treatment of headaches in Mali [14] and backache in Nigeria [66]. Bacterial infections such as gonorrhoea and typhoid fever are treated in Nigeria using root and leaf decoctions [47,49]. Methanolic and ethanolic extracts of the leaves have demonstrated potent antibacterial activity using the agar-well-diffusion method [97,99]. Bioactive compounds responsible for the antibacterial activity include isoquercitrin, farnesol acetate, and cis-2- decanoic acid [97,100]. Quercitin, gamma-sitosterol, palmitic acid, and alpha-linolenic acid are anti-inflammatory compounds isolated from ethanolic and methanolic leaf extracts [97, 131] and whose potency has been proven using the egg-albumin-induced inflammation model in rats [95]. These tests justify the ethnomedicinal use of the plant in treating conjunctivitis [39].

Although pharmacological test models have been developed to demonstrate the antidepressant, anxiolytic, anticonvulsant, antihypertensive, anti-ulcer, antipyretic, and myorelaxant activities of the plant, specific bioactive compounds that account for these activities have not been identified and isolated. Furthermore, ethnomedicinal uses of the plant as a treatment for female infertility, male sexual dysfunction, urine retention, HIV/AIDS, hernia, Parkinson's, and Alzheimer's disease await scientific validation and, therefore, remain anecdotal. Of the many NTDs, *N. latifolia* is reported to be used in the treatment of leprosy and filariasis (helminthiasis) [5,15,30,31]. In the ethnomedicinal uses of this plant in the treatment of leprosy [5,15,30,31] and helminthiasis across several West African countries [15,21,32,56,67,68], and its use in the treatment of filariasis, in particular in Nigeria [30], few studies exist on its efficacy. Further pharmacological studies must be performed to validate its ethnomedicinal use as a remedy for a number of ailments, including female infertility, male sexual dysfunction, urine retention, HIV/AIDS, hernia, Parkinson's, and Alzheimer's disease. Secondly, the specific bioactive compounds that account for the antidepressant, anxiolytic, anticonvulsant, anthelminthic, antihypertensive, anti-ulcer, antipyretic and myorelaxant activities of the plant remain to be isolated. Finally, there is a need for further clinical evaluation of the toxicity of parts of *N. latifolia* as a medicinal plant.

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None

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Author contributions
Conceptualization was done by EOB and BA. BA EOB, ML and AG participated in the writing and editing of the manuscript. EOB, ML, AG, and BA reviewed the manuscript. All authors approved the manuscript.

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Availability of data
Data for this work is available upon reasonable request from the corresponding author.

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