HSI Health Sciences Investigations Journal

share

Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

ISSN Online 2704-4890 | ISSN Print 2720-7609

Online first publication

Original Research Article

HSI Journal (2026) Volume 9 (Issue 1):1540-1555. https://doi.org/10.46829/hsijournal.2026.7.9.1.1540-1555

Open Access

Prevalence, phenotypes and ovulation induction outcomes of polyendocrine metabolic ovarian syndrome among women seeking infertility care in Kumasi, Ghana: a multi-centre observational study

Bernard K OKAI [1], Charles M SENAYA [1], Adu APPIAH-KUBI [2], Anthony K DAH [2], Wisdom M BOATENG [2], Michael Y AMOH [2*]

[1] Department of Obstetrics and Gynaecology, Komfo Anokye Teaching Hospital, Kumasi, Ghana; [2] Department of Obstetrics and Gynaecology, University of Health and Allied Sciences, Ho, Ghana

Received January 2026; Revised March 2026; Accepted May 2026

Abstract

Background: Polyendocrine metabolic ovarian syndrome (PMOS) represents a significant but understudied cause of anovulatory infertility in sub-Saharan Africa (SSA). Regionally, specific data on its prevalence and phenotypic distribution in SSA are scarce, despite its recognized impact on fertility.

Objective: To determine the prevalence and phenotypic distribution of polycystic ovary syndrome (PMOS) among women seeking infertility care in Kumasi, Ghana, and to evaluate dominant follicle selection following ovulation induction.

Methods: In a multi-centre observational study with a cross-sectional component and nested longitudinal follow-up, women aged 20–40 years presenting for infertility evaluation at three fertility centres in Kumasi were consecutively screened using the Rotterdam criteria. Women diagnosed with PMOS underwent ovulation induction with clomiphene citrate or letrozole. Dominant follicle selection was monitored via transvaginal ultrasonography. Firth's penalized logistic regression was used to identify independent predictors of dominant follicle selection, accounting for complete separation and sparse data in BMI and phenotype categories.

Results: Among 1,537 women seeking infertility care, 251 met Rotterdam criteria for PMOS, giving a clinic-based prevalence of 16.3% (95% CI: 14.5–18.2) with Phenotype D being most prevalent (51.8%). Dominant follicle selection occurred in 82.9% (199/240; 95% CI: 78.2–87.7) of women undergoing ovulation induction. Clomiphene citrate and letrozole showed similar follicular response rates in this non-randomized cohort although letrozole use was limited. Firth's penalized logistic regression identified Obesity class III (BMI ≥40 kg/m²) as the only BMI category independently associated with dominant follicle selection (aOR = 0.01; 95% CI: 0.00–0.21; p = 0.005). A linear ordinal BMI analysis confirmed that BMI variation significantly reduced the odds of dominant follicle selection (aOR = 0.26; 95% CI: 0.15–0.46; p < 0.001).

Conclusion: PMOS was common among women seeking infertility care in three specialist fertility facilities in Kumasi, Ghana, and phenotype D predominated. Ovulation induction with clomiphene citrate or letrozole was frequently associated with dominant follicle selection, but pregnancy and live-birth outcomes were not assessed, hence, findings should be interpreted as reflecting an intermediate ovulatory endpoint rather than definitive fertility success. Severe obesity (BMI ≥40 kg/m²) was independently associated with a significantly reduced likelihood of dominant follicle selection, highlighting the clinical importance of weight management in this population and the need for phenotype-informed, weight-sensitive fertility care in the region.

Keywords: polycystic ovary syndrome, phenotypes, infertility, ovulation induction, body mass index

Cite the publication as Okai BK, Senaya CM, Appiah kubi A et al. (2026) Prevalence, phenotypes and ovulation induction outcomes of polycystic ovary syndrome among women seeking infertility care in Kumasi, Ghana: a multi-centre observational study. HSI Journal 9 (1):1540-1555. https://doi.org/10.46829/hsijournal.2026.7.9.1.1540-1555

INTRODUCTION

Polyendocrine metabolic ovarian syndrome (PMOS) is recognized as the most prevalent endocrine disorder affecting women of reproductive age worldwide, with estimated prevalence rates ranging from 6% to 15% depending on diagnostic criteria and population characteristics [1,2]. It is the leading cause of anovulatory infertility and is a highly heterogeneous endocrine disorder associated with a spectrum of metabolic, reproductive, and psychological comorbidities, including insulin resistance

* *Corresponding author*
Email: mamoh@uhas.edu.gh

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

[3,4]. PMOS heterogeneous clinical presentation has necessitated the development of various diagnostic frameworks, with the Rotterdam criteria being the most widely adopted. The Rotterdam criteria classify PMOS into four distinct phenotypes based on combinations of hyperandrogenism (HA), ovulatory dysfunction (OD), and polycystic ovarian morphology (PCOM) [5,6]. PMOS phenotypes include Phenotype A (HA+ OD + PCOM), Phenotype B (HA + OD), Phenotype C (HA + PCOM), and Phenotype D (OD + PCOM). Understanding these phenotypes is crucial for clinical practice, as they may influence treatment responses and long-term health risks, with varying prevalence reported across different regions of the world. For instance, Phenotype A is often associated with more severe metabolic and reproductive complications, while Phenotype D may present with milder symptoms [5,6].

Although PMOS is well characterised in high-resource settings, there is a marked scarcity of population-based and clinical data from sub-Saharan Africa (SSA) [7]. Historically, infertility in West Africa has been predominantly attributed to tubal factors, accounting for over 40% of cases, largely due to infections and post-inflammatory sequelae [7,8]. However, evolving demographic and lifestyle transitions characterized by urbanization, sedentary behaviour, dietary shifts towards processed foods, and escalating obesity rates are reshaping the infertility landscape, with increasing recognition of ovulatory disorders, particularly PMOS resulting in a double burden of infertility in SSA driven by both tubal factors and ovulatory disorders [9,10].

In Ghana, comprehensive data on PMOS prevalence, phenotypic distribution, and treatment outcomes are virtually non-existent, creating a critical knowledge gap that hampers evidence-based clinical practice and public health policy formulation. Emerging evidence suggests that PMOS phenotypic expression may exhibit ethnic and geographic variations. While Phenotype A predominates in Caucasian and many Asian populations [11,12], preliminary studies from Nigeria and Sudan indicate a higher prevalence of Phenotype D in SSA [13,14]. These variations may stem from genetic polymorphisms, differences in androgen metabolism, environmental factors, or diagnostic practices, underscoring the importance for region-specific research.

First-line pharmacological management of PMOS-related infertility typically involves ovulation induction with clomiphene citrate (CC) or letrozole (LTZ) [15]. Although both agents have demonstrated efficacy in improving ovulation and pregnancy rates, their effectiveness across different PMOS phenotypes, particularly in African populations, remains poorly characterized. Most existing studies focus primarily on pregnancy or live birth outcomes, with limited attention to intermediate endpoints such as dominant follicle selection, which is a crucial predictor of treatment success [16,17]. Furthermore, the influence of metabolic factors, particularly obesity, on phenotype-specific treatment responses warrants investigation given the high prevalence of overweight and obesity among women in SSA [18]. This study aimed to assess the prevalence of PMOS among women seeking infertility treatment, classify diagnosed cases into phenotypic subtypes using the Rotterdam criteria, and examine ovulation induction outcomes, specifically dominant follicle development across PMOS phenotypes following treatment with CC or LTZ in Kumasi, Ghana. The findings from this study are expected to provide foundational data for developing context-appropriate diagnostic and management guidelines for PMOS in Ghana and similar SSA settings. The study population was drawn from specialist fertility clinics thus, the resulting prevalence estimates reflect a clinic-based infertility population. It may not represent all reproductive-age women in the community.

MATERIALS AND METHODS

Study Design and Setting

This was a multi-centre observational study comprising a cross-sectional component with a nested longitudinal follow-up**,** conducted from February 2024 to January 2025 in three fertility centres within the Kumasi Metropolitan Assembly, Ghana. The cross-sectional component evaluated prevalence and phenotypic distribution of PMOS at a single time point, while the nested longitudinal component enabled prospective evaluation of ovulation induction outcomes following CC and LTZ administration.

The study sites included one public tertiary referral hospital Komfo Anokye Teaching Hospital and two private fertility centres (Trustcare Specialist Hospital/Fertility Centre and Ruma Fertility/Specialist Hospital). These centres were selected based on their representativeness, accessibility, expertise, and logistical feasibility. As high-volume referral facilities, they serve patients from both urban and rural areas, as well as from public and private healthcare settings, ensuring a diverse study population. This broad patient base captures women with varying socioeconomic backgrounds, clinical profiles, and access to fertility care, making the study findings more applicable to the wider population.
Komfo Anokye Teaching Hospital: A 1,200-bed tertiary referral hospital and teaching facility primarily serving the Ashanti Region and surrounding communities. The Reproductive Endocrinology and Infertility (REI) clinic attends to approximately 60–70 new infertility patients monthly.

Trustcare Specialist Hospital and Fertility Centre: A premier private healthcare facility with a dedicated fertility unit that receives approximately 80–100 new infertility clients monthly.
Ruma Fertility and Specialist Hospital: A specialized fertility hospital providing advanced ART services and attends to approximately 100–120 new infertility clients monthly.

Study Population and Eligibility Criteria

During the screening stage, we enrolled women aged 20 to 40 years who visited the study centres for infertility evaluation and gave written consent to partake in the study. Infertility was defined as failure to achieve a clinical pregnancy after at least 12 months of regular unprotected heterosexual intercourse [17]. This age group

was to eliminate confounding effect from hormonal changes present in teenagers or women approaching menopause. In the second stage, we focused on women diagnosed with PMOS according to the Rotterdam classification and receiving ovulation induction with either CC or LTZ. We excluded participants using donor eggs, undergoing IVF, who had previous ovarian surgery, and those with confirmed bilateral tubal blockage. Participants whose male partners had abnormal semen results, based on WHO 2021 criteria [19] were also excluded, as well as those with severe medical conditions prohibiting pregnancy or ovulation induction.

Sample Size Determination and Sampling Strategy

The sample size was calculated to meet all three study objectives: estimating PMOS prevalence, comparing phenotypic subgroups, and evaluating fertility treatment outcomes. For the primary objective (prevalence estimation), using Cochran's formula for a single population proportion, with an anticipated PMOS prevalence (p) of 25% (based on SSA literature) [13,14], a 95% confidence level ($Z_{\alpha/2} = 1.96$, for a 95% confidence interval), and a desired precision (d) of 3%, a minimum sample of 800 participants was required.

$$n = \frac{Z\alpha_{/2}{}^{2} x\ p\ x\ (1-p)}{d^2}$$

Recognizing the significant heterogeneity of PMOS, the sample size was inflated to ensure adequate statistical power for comparisons across the four phenotypic subgroups (A, B, C, D). Assuming a near-equal distribution of phenotypes, an inflation factor of 1.5–1.6 was applied. This increased the required sample size from 800 to an average of 1,250 participants (range: 1,200–1,300), ensuring sufficient power to detect clinically meaningful differences in metabolic and clinical profiles between subgroups. For the secondary analysis comparing dominant follicle selection rates following ovulation induction, a two-sample proportion power calculation was used:

$$n = 2 \times \left(\frac{Z\alpha_{/2} + 2\beta}{p_1 - p_2}\right)^2 \times \bar{p}(1-\bar{p})$$

where p_1 and p_2 are the expected proportions in comparison groups, and $\bar{p}$ is their average. Preliminary data suggested even modest differences in dominant follicle selection rates (e.g. 5-15%) would require several hundred participants per group. Given the need to compare treatment outcomes across four PMOS phenotypes, the required sample size exceeded the cross-sectional estimate, further justifying the inflated sample of ~1,250.

A conservative attrition rate of 20% was anticipated for the longitudinal fertility component, accounting for loss to follow-up, treatment discontinuation, and incomplete data. The adjusted sample size was calculated as:

$$n_{adjusted} = \frac{n_{calculated}}{1 - attrition\ rate} = \frac{1250}{0.8} \approx 1563$$ participants

Hence, after integrating all objectives and adjustments the final target sample size was 1,563 participants. A non-probability consecutive sampling technique was used for both parts of the study. The sample size of 1,563 was calculated with a 20% attrition adjustment. Recruitment was consecutive: all eligible women presenting at the three centres during the nine-month study period were enrolled. At the end of the recruitment period, 1,537 of the 1,563 allocated slots had been filled; the 26-participant shortfall reflects the difference between the inflated target and actual enrolment and not study participation refusals. All eligible women who attended were enrolled. Among these, women diagnosed with PMOS who underwent ovulation induction with CC or LTZ formed the longitudinal treatment cohort.

Participants were recruited proportionally across the three centres based on each site's average monthly new infertility case received as follows: Komfo Anokye Teaching Hospital (KATH): 386 of 390 allocated (25.1%); Trustcare Specialist Hospital and Fertility Centre: 509 of 520 allocated (33.1%); Ruma Fertility and Specialist Hospital: 642 of 653 allocated (41.8%). Site-level clustering was accounted for in all regression analyses using robust sandwich standard errors with study site as the cluster unit.

Data Collection Instruments and Procedures

Data were collected using a structured, pretested questionnaire adapted from instruments used in previous Nigerian PMOS studies [13] and modified to align with local context and study objectives. Hyperandrogenism was assessed clinically (based on hirsutism) rather than clinical laboratory findings. Biochemical hyperandrogenism (e.g., serum testosterone) was not routinely assessed because assays were inconsistently available and not standardized across sites. Therefore, for phenotypic classification, hyperandrogenism was defined primarily on the basis of clinical hirsutism using the modified Ferriman–Gallwey (mFG) score. This approach may have missed women with biochemical but not clinical hyperandrogenism.

The questionnaire was administered electronically using the KoboCollect mobile application, which allowed for real-time data entry, validation checks, and secure cloud storage. The instrument comprised five sections: Section A: Sociodemographic data (age, marital status), Section B: Anthropometric (height, weight for body mass index [BMI], clinical assessment for hirsutism), Section C: Clinical and diagnostic criteria (transvaginal ultrasound [TVUS] findings for PCOM, and results of hormonal assays for prolactin), Section D: Primary reason for clinic visit and Section E: Ovulation induction details

(agent used, dose, start day) and TVUS monitoring results (dominant follicle presence, number, size). Section E was

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

assessed for participants diagnosed with PMOS and were due for ovulation induction with oral ovulogens.

Three research assistants (registered nurses/midwives) and the principal investigator underwent a two-day standardized training program covering study protocol, ethical conduct, accurate administration of the questionnaire, and clinical measurement techniques (e.g. mFG scoring, BMI calculation). To ensure comprehension among participants with varying literacy levels, interviews were conducted in either English or Twi (the predominant local language), based on participant preference. The Interviews were conducted in private rooms to ensure confidentiality without personal identifiers. Clinical data (TVUS reports, lab results) were extracted from patient records and cross-verified with participant interviews. Electronic datasets were encrypted, access-restricted, and

de-identified before analysis, ensuring participants' autonomy, privacy and confidentiality. PMOS was diagnosed according to the 2003 Rotterdam consensus criteria [5], requiring the presence of at least two of ovulatory dysfunction (OD), polycystic ovarian morphology (PCOM), and hyperandrogenism (HA) after exclusion of other causes of HA such as thyroid disorders and hyperprolactinemia. OD is defined clinically as menstrual cycle intervals of less than 21 days or more than 35 days, or fewer than eight menstrual cycles in the preceding year. For women with amenorrhea, a progestin challenge test was performed to confirm oestrogenised endometrium and anovulation. HA was assessed clinically using the mFG scoring system [20]. Nine body areas (upper lip, chin, chest, upper abdomen, lower abdomen, arm, thigh, upper back, lower back) were evaluated, with each area scored from 0 (no terminal hair) to 4 (frank virile growth). A total score of ≥8 was considered diagnostic of clinical hirsutism, consistent with thresholds validated in African populations [21]. Biochemical hyperandrogenism (e.g., elevated serum total or free testosterone) was not routinely assessed because hormone assays were inconsistently available and not uniformly standardized across study sites. To enhance diagnostic specificity, thyroid dysfunction and hyperprolactinemia were excluded by reviewing thyroid-stimulating hormone (TSH) and prolactin levels when available. Non-classical congenital adrenal hyperplasia was considered unlikely in the absence of a suggestive history and was not routinely screened for.

PCOM was defined as the presence of ≥12 follicles measuring 2–9 mm in diameter in at least one ovary, and/or an ovarian volume exceeding 10 ml on TVUS according to the 2003 original Rotterdam criteria. This definition was chosen to ensure consistency in results across study sites and comparability with earlier studies from SSA, given variations in the quality of ultrasound equipment for counting the follicles. Newer guidelines may require high-frequency ultrasound transducers, which were not available in some centres. All ultrasound examinations were performed by experienced sonographers using a standardized scanning protocol and reporting format to reduce interobserver variation and measurement error.

Specific transducer frequencies varied across sites depending on locally available equipment; the original Rotterdam PCOM threshold (≥12 follicles, 2–9 mm) was deliberately chosen over newer criteria to ensure comparability across sites with differing equipment capability. [15]. Based on the combination of these features, participants diagnosed with PMOS were classified into one of four phenotypes: Phenotype A, Phenotype B, Phenotype C, and Phenotype D.

Participants diagnosed with PMOS who desired pregnancy and met the eligibility criteria for the longitudinal component were prescribed ovulation induction. Treatment choice (CC versus LTZ) and starting dose were decided by the attending consultant, based on clinical judgement and patient characteristics, rather than by random allocation. Only the first monitored ovulation-induction cycle per woman was included in the analysis, hence there was no within-patient clustering by cycle. For participants undergoing ovulation induction, standard protocols were followed. CC was administered orally at doses of 50 mg, 100 mg, or 150 mg daily for five consecutive days, starting on day 2 or 3 of the menstrual cycle. LTZ was administered orally at doses of 2.5 mg, 5 mg, or 7.5 mg daily for five consecutive days, also beginning on day 2 or 3 of the menstrual cycle. For women with amenorrhea or prolonged oligomenorrhea (>35 days), withdrawal bleeding was first induced with oral medroxyprogesterone acetate or norethisterone (5-10 mg/day). A baseline TVUS was performed on day 2 or 3 of the induced cycle once withdrawal bleeding occurred, followed by initiation of ovulation induction therapy.

Starting doses were selected by the clinician based on patient age, BMI, and any prior ovulation-induction history. In women who did not develop a dominant follicle (≥16 mm) by cycle day 21, the dose was escalated stepwise in the subsequent cycle (CC 50 → 100 → 150 mg; LTZ 2.5 → 5 → 7.5 mg), up to the maximum permitted dose. Women who failed to respond at the maximum dose were considered for second-line management at clinician discretion. Only the first monitored cycle per woman was included in the present analysis, so the reported estimates reflect first-cycle

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

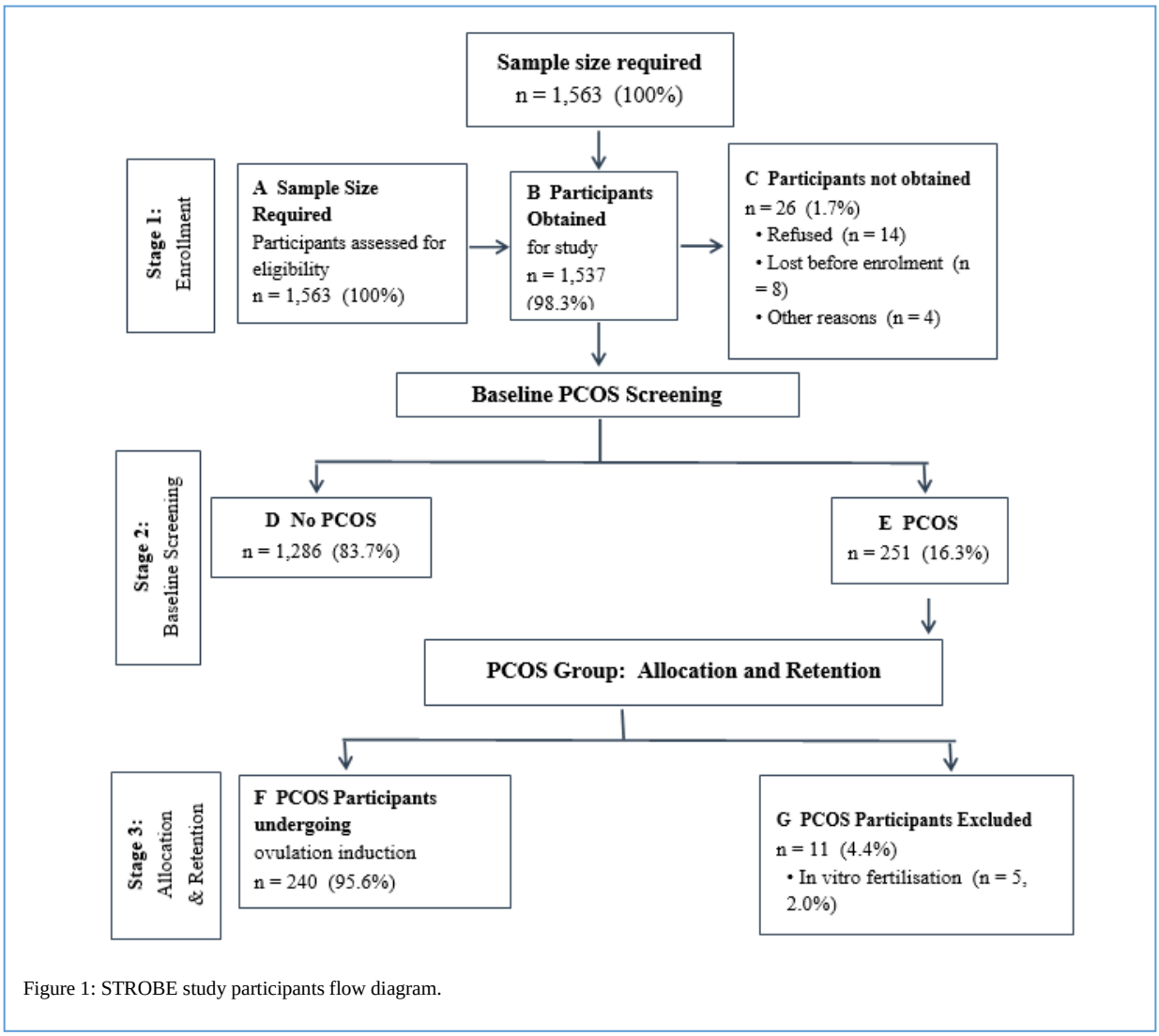

Figure 1: STROBE study participants flow diagram.

response and do not capture within-patient effects of dose escalation.

Monitoring and Outcome Assessment: Follicular response was monitored via serial TVUS beginning on cycle day 10 and continuing alternate days until at least one dominant follicle (≥16 mm in mean diameter) was identified, or until cycle day 21 if no follicular growth occurred. The primary outcome measure was dominant follicle selection, defined dichotomously as the presence of at least one follicle ≥16 mm. Secondary outcomes included the number of dominant follicles (categorized as 0, 1, 2, or ≥3) and the association between specific drug doses and ovulation success. Endometrial thickness was recorded but not analysed as a primary outcome. Participants who did not develop a dominant follicle by day 21 were classified as non-responders for that cycle.

Data Management and Statistical Analysis

Collected data were downloaded from KoboCollect into Microsoft Excel 365 for initial cleaning, which involved checking for missing values, inconsistencies, and outliers. The cleaned dataset was then imported into Stata version 17 and IBM SPSS Statistics version 27 for analysis.

Descriptive Statistics: Continuous variables with normal distribution were summarized as means ± standard deviations (SD), while skewed variables were reported as medians with interquartile ranges (IQR). Categorical variables were presented as frequencies and percentages (n, %). Normality was assessed using the Shapiro-Wilk test and visual inspection of histograms. Inferential Statistics: For Objective 1 (Prevalence): The prevalence of PMOS was calculated as the proportion of women meeting Rotterdam criteria among the total study population, with a 95% confidence interval (CI). For Objective 2 (Phenotype Distribution): The distribution of phenotypes

among PMOS cases was described using proportions. A chi-square goodness-of-fit test was employed to test the null hypothesis that phenotypes were equally distributed and specifically to determine if Phenotype D constituted a significantly larger proportion than expected by chance. For Objective 3 (Ovulation Induction Outcomes): The proportion of women achieving dominant follicle selection was calculated. Differences in ovulation success rates (a) between CC and LTZ, and (b) across the four PMOS phenotypes were analysed using Pearson's chi-square test. Post-hoc pairwise comparisons between phenotype groups were conducted using Fisher's exact test, with Bonferroni correction for multiple testing.

To identify independent predictors of dominant follicle selection, a multivariable logistic regression model was constructed. The model initially included variables with $p<0.20$ in univariable analysis or deemed clinically relevant: age (continuous), BMI category (underweight/normal, overweight, obesity class I, II, III), ovulation induction agent (CC vs. LTZ), and PMOS phenotype (with Phenotype D as the reference category (the largest subgroup, n = 130)). Results were reported as Firth adjusted odds ratios (aOR) with 95% confidence intervals. Variance inflation factors (VIF) were checked to rule out multicollinearity. To handle complete separation and sparse data in the multivariable model, Firth's penalized logistic regression (penalized maximum likelihood with Jeffreys prior) was implemented as the primary analytical approach. This method produces finite, stable estimates in the presence of zero-event cells and small subgroups.

The BMI reference category was defined as BMI <25 kg/m² (combining Underweight [n = 3] and Normal weight [n = 25]), as the Normal weight group alone had zero non-responders (complete separation). Phenotypes B (n = 9) and C (n = 19) were excluded from the adjusted model owing to sparse cells (<50 participants); crude Firth odds ratios for these phenotypes are reported. Two pre-specified sensitivity analyses were performed: (i) collapsing Phenotypes B and C into a single non-A/non-D category; and (ii) modelling BMI as an ordinal linear trend (0–4 scale) to test the overall direction of the BMI–outcome association. For all statistical tests, a two-tailed p-value of <0.05 was considered statistically significant. All analyses accounted for the clustered nature of the data by study site using appropriate techniques (e.g., robust standard errors).

RESULTS

Of the target 1,563 sample, 1,537 women were recruited and screened, yielding a response rate of 98.3%. The overall prevalence of PMOS among women seeking infertility care based on the Rotterdam criteria in Kumasi was 16.3% (251/1537; 95% CI: 14.5–18.2). Of the PMOS cohort, 240 women proceeded to ovulation induction and were included in the treatment outcome analysis (11 were excluded- 5 converted to IVF, 4 lost to follow-up, 2 converted to intrauterine insemination).

The study flowchart is presented in Figure 1

Table 1 presents the sociodemographic and menstrual characteristics of the total study population (N = 1,537) and the PMOS subgroup (n = 251). The mean age of all participants was 36.4 ± 2.1 years, while the PMOS subgroup was significantly younger (31.4 ± 3.1 years, $p<0.001$). The majority of participants were married (82.5% overall, 87.6% PMOS) and nulliparous (87.1% overall, 96.4% PMOS). Educational level was relatively high, with 65.6% of all participants and 69.3% of the PMOS group having tertiary education. Regarding menstrual history, a stark contrast was observed: 78.8% of all participants reported regular cycles (21–35 days), whereas 92.4% of the PMOS group reported irregular cycles. Similarly, 92.4% of PMOS women had cycle lengths >35 days compared to 18.4% in the general cohort.

The prevalence of overweight and obesity was high in both groups but more pronounced in the PMOS cohort as seen in Table 1. Among all participants, 34.9% were overweight and 52.4% obese. In the PMOS group, 31.9% were overweight and 57.0% obese, with 34.7% classified as Obesity Class I (BMI 30.0–34.9 kg/m²). Clinical hyperandrogenism (mFG score ≥8) was present in 10.7% of all participants and also present in 48.2% of the PMOS group. PCOM was identified in 30.6% of all participants via TVUS, but in 96.4% of the PMOS cohort, with bilateral involvement in 69.7%. The overall prevalence of PMOS among women seeking infertility care in Kumasi was 16.3% (251/1537). The 95% confidence interval was 14.5% to 18.2%. (Table 2). Among the 251 women diagnosed with PMOS, phenotypic classification revealed a distinct distribution pattern: Phenotype D was the most prevalent, accounting for 51.8% of cases (n = 130; 95% CI: 45.6–58.0), whereas

Phenotype A comprised 37.1% (n = 93; 95% CI: 31.1–43.0). The less frequently observed subtypes were Phenotype C (7.6%, n = 19; 95% CI: 4.6–11.6) and Phenotype B (3.5%, n = 9; 95% CI: 1.7–6.7) as seen in Table 2. A chi-square goodness-of-fit test was performed to test the null hypothesis of an equal distribution across the four phenotypes (expected count = 62.75 per phenotype and found to be statistically significant (χ^2 = 163.199, df = 3, $p < 0.001$). The standardized residuals were +30.3 for Phenotype A, -53.8 for Phenotype B, -43.8 for Phenotype C, and +67.3 for Phenotype D. The largest positive residual was observed in Phenotype D (Table 2). Table 3 summarizes the ovulation induction protocols and outcomes for the 240 PMOS women who underwent treatment.

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

Table 1. Sociodemographic and clinical characteristics of the participants

Characteristic	Total cohort (N = 1,537)	PMOS subgroup (n = 251)
	Frequency (%)	Frequency (%)
Age (years), mean ± SD	36.4 ± 2.1	31.4 ± 3.1
Marital status		
Married	1,268 (82.5%)	220 (87.6%)
Single	189 (12.3%)	27 (10.8%)
Other	80 (5.2%)	4 (1.6%)
Parity		
Nulliparous	1,339 (87.1%)	242 (96.4%)
Parous	198 (12.9%)	9 (3.6%)
Education		
Primary	91 (5.9%)	5 (2.0%)
Junior high school	66 (4.3%)	4 (1.6%)
Senior high school	349 (22.7%)	62 (24.7%)
Tertiary	1,008 (65.6%)	174 (69.3%)
Postgraduate	23 (1.5%)	6 (2.4%)
Menstrual cycle length		
< 21 days	43 (2.8%)	0 (0.0%)
Characteristic	**Total cohort (N = 1,537)**	**PMOS subgroup (n = 251)**
	Frequency (%)	**Frequency (%)**
21–35 days	1,211 (78.8%)	19 (7.6%)
> 35 days	283 (18.4%)	232 (92.4%)
BMI category		
Underweight (<18.5 kg/m²)	28 (1.8%)	3 (1.2%)
Normal (18.5–24.9 kg/m²)	168 (10.9%)	25 (10.0%)
Overweight (25.0–29.9 kg/m²)	536 (34.9%)	80 (31.9%)
Obesity class I (30.0–34.9 kg/m²)	539 (35.1%)	87 (34.7%)
Obesity class II (35.0–39.9 kg/m²)	195 (12.7%)	37 (14.7%)
Obesity class III (≥40.0 kg/m²)	71 (4.6%)	19 (7.6%)
Clinical hyperandrogenism (mFG ≥8)	165 (10.7%)	121 (48.2%)
PCOM on TVUS, n (%)	470 (30.6%)	242 (96.4%)
Bilateral PCOM	303 (19.7%)	175 (69.7%)
Unilateral PCOM	167 (10.9%)	67 (26.7%)

* BMI = body mass index; mFG = modified Ferriman–Gallwey score; PCOM = polycystic ovarian morphology; TVUS = transvaginal ultrasonography. Percentages are column percentages. Denominators: total cohort N = 1,537; PMOS subgroup n = 251 unless otherwise stated. Missing data: BMI = 0; mFG = 0 in this table (one value missing in the clomiphene arm, noted in Table 6); TVUS = complete for all participants who underwent ultrasound.

Among the 240 women with PMOS who underwent ovulation induction and completed follicular monitoring, dominant follicle selection occurred in 82.9% (199/240; 95% CI: 78.2–87.7). Among responders, 84.9% (169/199) developed a single dominant follicle, 14.6% (29/199) developed two, and 0.5% (1/199) developed three follicles. No cases of ovarian hyperstimulation syndrome were reported. CC was the most commonly prescribed

agent (87.1%, n = 209), with the 100 mg dose being the most frequent (90.4% of CC users). LTZ was used in 12.9% (n = 31) of cases, predominantly at the 5 mg dose (69.7%). The ovulation success rate in terms of dominant follicle selection was 83.7% (175/209; 95% CI: 78.7–88.7) in the CC group and 77.4% (24/31; 95% CI: 62.7–92.1) in the LTZ group. This difference was not statistically significant (χ^2 = 0.759, p = 0.383). Similarly, no significant differences in success rates were found between different dose levels within each drug category (CC 50 mg vs. 100 mg: p = 1.000; LTZ 2.5 mg vs. 5 mg: p = 0.254) although interpretation is limited by small subgroup sizes, particularly for LTZ dose categories.

Post-hoc pairwise comparisons (Table 4) revealed that Phenotype A had significantly lower success rates compared to Phenotype C (p < 0.001) and Phenotype D (p < 0.001). No other pairwise comparisons reached significance; notably, Phenotype C and Phenotype D did not differ significantly (p = 0.596), consistent with their similarly high success rates of 100.0% and 94.6%, respectively. Table 5 presents the results of the univariable and multivariable logistic regression analyses. Although age was significantly associated with ovulation success in univariable analysis, this association was not statistically significant after adjustment for BMI category, ovulation induction agent, and PMOS phenotype.

In the unadjusted (crude) analysis, Phenotype A was strongly associated with a lower likelihood of ovulation success compared to Phenotype D. Phenotypes B and C were excluded from the multivariable regression analysis because each subgroup contained fewer than 50 participants, which resulted in sparse cell counts and unstable model estimates. In an exploratory sensitivity analysis that collapsed Phenotypes B and C into a single non- A / non- D category (n = 28; 27 events; observed dominant-follicle selection rate 96.4%) and refitted the adjusted model, the association between Phenotype A and reduced dominant follicle selection was preserved and remained substantial in magnitude (aOR = 0.51; 95% CI 0.14–1.82; p = 0.299 versus Phenotype D as reference). The combined B/C category did not differ significantly from Phenotype D (aOR = 1.05; 95% CI 0.17–6.72; p = 0.956), with a wide confidence interval reflecting the limited number of women in this stratum. These findings support the robustness of the primary inference that Phenotype A is associated with poorer follicular response, and they do not alter the substantive conclusions of the study.

Table 2. Prevalence and phenotypic distribution of polycystic ovary syndrome among study participants

Category	Frequency (%)	Additional statistics
Overall PMOS Status (N = 1,537)		
Diagnosed with PMOS	251/1537(16.3%)	95% CI:14.5%-18.2%
Not diagnosed with PMOS	1286/1537(83.7%)	-
PMOS Phenotypes (n = 251)		
Phenotype A	93/251(37.1%)	95% CI: 31.1–43.0
Phenotype B	9/251(3.5%)	95% CI: 1.7–6.7
Phenotype C	19/251(7.6%)	95% CI: 4.6–11.6
Phenotype D	130/251(51.8%)	95% CI: 45.6–58.0
Chi-square goodness-of-fit	χ^2 =163.199, df=3, p<0.001*	Phenotypes not equally distributed

* p < 0.05 considered statistically significant; df = degrees of freedom ; χ^2 = chi square : CI= confidence interval. Phenotype percentages are based on all women diagnosed with PMOS (n = 251). Confidence intervals for Phenotypes A and D were calculated using the Wald method; exact Clopper–Pearson confidence intervals were used for Phenotypes B and C owing

Age was a significant predictor in unadjusted analysis (Firth OR per SD = 0.50; 95% CI: 0.37–0.70; p < 0.001), attenuated after adjustment (aOR = 0.78; 95% CI: 0.51–1.19; p = 0.247). In the adjusted Firth model, the association between Phenotype A and dominant follicle selection was similarly attenuated and non-significant (aOR = 0.51; 95% CI: 0.14–1.82; p = 0.299).

BMI was categorized according to WHO standards. The reference category was BMI <25 kg/m² (Underweight and Normal weight combined, n = 28), as the Normal weight group alone had zero non-responders (complete separation). BMI was retained in categorical form to facilitate direct clinical comparisons. Compared to women with BMI <25 kg/m², only Obesity Class III (BMI ≥40 kg/m²) reached statistical significance in the adjusted model (aOR = 0.01; 95% CI: 0.00–0.21; p = 0.005), representing a 99% reduction in the odds of dominant follicle selection. Other BMI categories did not reach significance individually in the adjusted model. A linear ordinal BMI sensitivity analysis confirmed the directional trend: each step increase in BMI category was associated with lower odds of dominant follicle selection (aOR = 0.26; 95% CI: 0.15–0.46; p < 0.001).

The BMI <25 reference group was small (n = 28), contributing to wide confidence intervals for intermediate BMI category estimates.

All BMI category estimates from the Firth adjusted model are presented in Table 5. Baseline characteristics of women receiving CC and LTZ are summarized in Table 6. Women treated with CC comprised the majority of the ovulation-induction cohort, whereas a smaller subgroup received LTZ. Overall, the two groups were broadly similar in key clinical characteristics, although the limited size of the LTZ group reduces the precision of between group comparisons. Dominant follicle selection occurred in 83.7% of cycles in the CC group and 77.4% in the LTZ group, consistent with the crude and adjusted estimates reported in the regression models. The type of ovulation induction agent (CC vs. LTZ) was not a significant predictor in either model (crude Firth OR: 1.77; 95% CI: 0.74–4.22; p = 0.196; aOR: 3.40; 95% CI: 0.99–11.72; p = 0.052). Full model estimates are presented in Table 5.

DISCUSSION

This multi-centre study is, to the best of our knowledge, among the few to present detailed epidemiological and clinical treatment data on polycystic ovary syndrome (PMOS) among infertile women in Ghana. Considering that the study was conducted in clinic settings among women seeking infertility care, the reported prevalence of 16.3% should be interpreted as a clinic-based estimate rather than a reflection of the general population of reproductive-age women.

Our findings, particularly the 16.3% prevalence of PMOS, the predominance of Phenotype D, and the strong influence of BMI on ovulation success, provide meaningful insights for reproductive healthcare in SSA. Notably, the observed prevalence places Ghana at the higher end of global estimates (typically 6–15%) and is consistent with reports from neighbouring West African countries. Studies from Nigeria have reported prevalence rates of 16.7% in Port Harcourt [22], and 18.1% in Enugu [13]. These findings suggest that PMOS prevalence in Kumasi closely resembles that of other SSA populations, reinforcing its significant burden in the region. This prevalence is substantially higher than rates reported in some Asian populations (e.g., 5.6% in Chinese women[23], underscoring the influence of ethnic and regional factors. The high prevalence underscores PMOS as a major contributor to the infertility burden in SSA, though previously under-recognized. This finding therefore challenges the historical primacy of tubal factors and hence, necessitates a shift in diagnostic and resource allocation priorities.

The lack of statistical significance for age after multivariable adjustment suggests that its apparent effect was largely confounded by BMI and phenotypic characteristics rather than representing an independent predictor of ovulation response. This finding is consistent with existing literature suggesting that chronological age is not an independent determinant of ovulatory response in

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

Table 3. Ovulation Induction Protocols and Outcomes

Parameter	Category	Frequency	Dominant Follicle	p-value
Ovulation Agent				0.383
	CC	209 (87.1%)	175/209 (83.7%) (95% CI: 78.7–88.7)	
	LTZ	31 (12.9%)	24/31 (77.4%) (95% CI: 62.7–92.1)	
CC Dose				1.000
	50 mg	21 (10.0%)	18/21 (85.7%)	
	100 mg	188 (90.0%)	157/188 (83.5%)	
LTZ Dose				0.254
	2.5 mg	10 (32.3%)	6/10 (60.0%)	
	5 mg	21 (67.7%)	18/21 (85.7%)	
Overall Outcome		n = 240		
	Dominant Follicle Present	199 (82.9%) (95%CI:78.2–87.7)		
	1	169 (84.9%)		
	2	29 (14.6%)		
	≥3	1 (0.5%)		
	No Dominant Follicle	41/240(17.1%)		

* CC = clomiphene citrate; LTZ = letrozole; CI = confidence interval. Outcomes are based on the monitored ovulation cohort (n = 240): CC n = 209, LTZ n = 31. A dominant follicle was defined as a follicle ≥16 mm in mean diameter on transvaginal ultrasound. The p-values compare CC vs LTZ (Pearson χ^2 or Fisher's exact test as appropriate). Dose percentages are calculated as the proportion of users of that agent. Percentages for number of dominant follicles (1, 2, ≥3) are among responders (n = 199).

Table 4. Post – Hoc Pairwise Comparisons of PMOS Phenotypes

Comparison	Fisher's exact (p)	p-value	Significance (p<0.05)
Phenotype A vs. B	Fisher's	0.154	Not Significant
Phenotype A vs. C	Fisher's	<0.001*	Significant
Phenotype A vs. D	Fisher's	<0.001*	Significant
Phenotype B vs. C	Fisher's	0.321	Not Significant
Phenotype B vs. D	Fisher's	0.423	Not Significant
Phenotype C vs. D	Fisher's	0.596	Not Significant

* p < 0.05 considered statistically significant. Post-hoc pairwise comparisons of dominant follicle selection success rates between PMOS phenotypes, computed from raw participant-level data. Fisher's exact test was used for all six pairwise comparisons (appropriate given sparse cell counts in Phenotypes B and C). All p-values are two-sided and unadjusted; Bonferroni-corrected threshold for six comparisons is p < 0.0083. Note: Phenotype C had zero non-responders (19/19 = 100% success rate), representing complete separation; the Fisher's exact estimate for the C vs D comparison (p = 0.596) reflects this and indicates no statistically significant difference in success rates between these two phenotypes. Success rates: Phenotype A = 62.4% (58/93), B = 88.9% (8/9), C = 100% (19/19), D = 94.6% (123/130). * p < 0.05.

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

Table 5 Logistic Regression Analysis of Predictors for Dominant Follicle Selection

Variable	Crude		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (per 1 SD increase)	0.50 (0.37–0.70)	<0.001*	0.78 (0.51–1.19)	0.247
BMI Category				
BMI <25 kg/m² (Underweight + Normal, ref.)	1.00	–	1.00	–
Overweight (25.0–29.9 kg/m²)	9.74 (2.62–36.31)	0.001*	4.80 (0.88–26.24)	0.070
Obesity class I (30.0–34.9 kg/m²)	2.91 (1.25–6.73)	0.013*	1.52 (0.31–7.51)	0.610
Obesity class II (35.0–39.9 kg/m²)	0.40 (0.18–0.88)	0.023*	0.55 (0.09–3.47)	0.528
Obesity class III (≥40.0 kg/m²)	0.003 (0.000–0.055)	<0.001*	0.01 (0.000–0.21)	0.005*
Induction Agent				
Letrozole	1.00	–	1.00	–
Clomiphene Citrate	1.77 (0.74–4.22)	0.196	3.40 (0.99–11.72)	0.052
PMOS Phenotype				
Phenotype D	1.00	–	1.00	–
Phenotype A	0.10 (0.04–0.22)	<0.001*	0.51 (0.14–1.82)	0.299
Phenotype B	1.17 (0.18–7.54)	0.867	— (sparse cells)	—
Phenotype C	8.75 (0.48–NE†)	0.143	— (sparse cells)	—
Model Fit Statistics				
Method	Firth penalized logistic regression		Firth penalized logistic regression	
Events / n	199 / 240		199 / 240	
Sensitivity: BMI ordinal aOR (per step)	0.26 (0.15–0.46, p<0.001)		0.26 (0.15–0.46, p<0.001)	

* All estimates from Firth penalized logistic regression (Jeffreys prior). * p < 0.05. Reference categories: BMI <25 kg/m² (Underweight [n = 3] and Normal weight [n = 25] combined as the reference owing to complete separation in the Normal weight group); Induction agent = Letrozole; PMOS Phenotype = Phenotype D. Obesity class III (n = 19, zero responders) was included using Jeffreys-prior penalization. Phenotypes B (n = 9) and C (n = 19) excluded from the adjusted model owing to sparse cells (<50 participants); crude Firth ORs reported: Phenotype B = 1.17 (0.18–7.54), p = 0.867; Phenotype C = 8.75 (0.48–NE†), p = 0.143. †Upper CI not estimable owing to zero failures in Phenotype C. Sensitivity analysis i (Phenotypes B + C collapsed): Phenotype A aOR = 0.51 (0.14–1.82), p = 0.299. Sensitivity analysis ii (BMI as ordinal linear trend, 0–4): aOR per step = 0.26 (0.15–0.46), p < 0.001 — higher BMI is associated with lower odds of dominant follicle selection. BMI = body mass index; CI = confidence interval; NE = not estimable; OR = odds ratio; PMOS = polycystic ovary syndrome; SD = standard deviation.

women with PMOS once metabolic and treatment-related factors are accounted for. [24,25] The most striking finding of this study is the predominance of Phenotype D (non-hyperandrogenic PMOS), which accounted for over half (51.8%) of all cases.

This predominance should be interpreted cautiously, as biochemical androgen assays were not performed routinely. Some women classified as phenotype D may have had unrecognized biochemical hyperandrogenism and could have been reclassified as phenotype A or C if standardized hormonal testing had been available. Furthermore, the predominance of the non-hyperandrogenic phenotype suggests that, in SSA, diagnostic practice should be targeted at ovulatory dysfunction and PCOM, even when obvious clinical hyperandrogenism is absent. In contrast, Phenotype A (classic hyperandrogenic PMOS) is consistently reported as the most frequent presentation, comprising 60–70% of

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

cases in Caucasian, many Asian, and Middle Eastern populations [11,12, 26]. Our finding aligns with emerging SSA data: a Nigerian preliminary report identified Phenotype D in 52.8% of cases [27], and a Sudanese study reported a 52% prevalence [28]. This convergent evidence suggests a distinct phenotypic signature of PMOS in SSA, characterized primarily by ovulatory dysfunction and PCOM without prominent clinical hyperandrogenism. Several interrelated factors may explain this pattern.

First, genetic and ethnic variations in androgen sensitivity, metabolism, and sex hormone-binding globulin (SHBG) levels may result in a lower clinical expression of hyperandrogenism (e.g., hirsutism) in women of African descent despite similar biochemical profiles [21,29]. Second, diagnostic limitations in resource-constrained settings play a role. Our study, like many in SSA, relied on clinical mFG score rather than biochemical assessment of hyperandrogenism. The mFG threshold of ≥8, while validated in African populations, may still fail to detect milder or biochemical-only hyperandrogenism. Furthermore, limited access to standardized androgen assays means Phenotypes A and B may be under-ascertained. Also, lifestyle and metabolic context may be influential. The traditional Ghanaian diet may differ in glycaemic load and fatty acid composition compared to Western diets, potentially influencing insulin resistance and its androgen-driving effects differently [30].

Finally, considering that our sample comprised women actively seeking fertility treatment, it is possible that women with hyperandrogenic symptoms (Phenotypes A, B, C) but regular ovulation may not perceive an urgent fertility concern, whereas those with overt oligo/anovulation (Phenotypes A and D) are more likely to present to clinic, potentially inflating the proportion of Phenotype D. The very low prevalence of Phenotype B (3.5%) is notable. This phenotype, characterized by hyperandrogenism and anovulation but without PCOM, is often associated with significant metabolic dysfunction [31]. Its rarity in our cohort may reflect true pathophysiological differences, or it may be the phenotype most susceptible to misclassification when PCOM assessment is prioritized over biochemical HA.

Our study also demonstrates that standard ovulation induction is highly effective in this population, with an overall success rate of 82.9% for dominant follicle development. While dominant follicle selection is the primary outcome of this study, it is an intermediate ovulatory endpoint rather than a patient-centred outcome. Published data suggest that in PMOS, the per-cycle clinical pregnancy rate following documented dominant follicle development is approximately 8–15%, depending on phenotype severity, BMI, and induction agent, meaning that many ovulatory cycles do not result in conception [32,33]. Dominant follicle development is therefore a necessary but not sufficient condition for fertility success, and hence, the high ovulation rates observed must be interpreted in that context. This aligns with reported ovulation rates of 60–85% for CC and approximately 80% for LTZ in literature [32, 33]. The comparable efficacy between CC and LTZ in our setting (83.7% vs. 77.4%, p = 0.383) is an important practical finding. It is noteworthy that treatment allocation was clinician-directed and not randomized, and because the LTZ group was relatively small, the observed similarity in dominant follicle selection rates between CC and LTZ should be regarded as exploratory and subject to confounding by indication. While large RCTs like that of Legro et al. [34] have shown superior live birth rates with LTZ, our focus on the intermediate endpoint of follicular development suggests both drugs are viable first-line options in Ghana, where drug availability, cost, and clinician familiarity may guide choice of appropriate treatment.

The significant variation in ovulation success by phenotype, with Phenotype A performing poorest (62.4%) and Phenotypes C and D performing best (100% and 94.6%, respectively), initially suggests a phenotype-driven treatment response. This is consistent with studies from India and Iran, where Phenotype A showed higher rates of CC resistance [17,35]. The pathophysiology likely involves the more severe metabolic and endocrine disturbances (marked insulin resistance, hyperinsulinemia, and hyperandrogenism) in Phenotype A, which can impair follicular sensitivity to gonadotropins [36].

Firth penalized logistic regression identified Obesity Class III (morbid obesity, BMI ≥40 kg/m²) as the only BMI category independently associated with a significantly reduced likelihood of dominant follicle selection (aOR = 0.01; 95% CI: 0.00–0.21; p = 0.005). A linear ordinal BMI sensitivity analysis confirmed the overall directional trend: each step increase in BMI category was associated with a 74% reduction in the odds of dominant follicle selection (aOR = 0.26; 95% CI: 0.15–0.46; p < 0.001). This inverse BMI/ovulation success relationship is biologically plausible and consistent with literature linking obesity to impaired gonadotropin signalling, elevated insulin resistance, and follicular dysfunction. The BMI <25 reference group was small (n = 28), contributing to wide confidence intervals for intermediate BMI categories. Residual confounders, the small size of the BMI <25 reference group, possible treatment-selection effects (including dose adjustments), and unmeasured metabolic factors may partly explain this association.

The attenuation of the phenotype effect after BMI adjustment suggests that the poorer response in Phenotype A may be largely mediated by the higher prevalence and severity of obesity in that subgroup, rather than by the phenotypic features. This has profound clinical implications: it shifts the focus from phenotype classification alone to a weight-targeted management approach.

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

Table 6. Baseline demographic and clinical characteristics by ovulation-induction agent

Characteristic	clomiphene citrate (CC, n=218)	letrozole (LTZ, n=33)	p value
Age, years, mean ± SD	31.3 ± 3.0	31.9 ± 3.4	0.392
BMI category, n (%)			0.003
Underweight / normal (<25)	22 (10.1)	6 (18.2)	
Overweight (25.0–29.9)	62 (28.4)	18 (54.5)	
Obesity I (30.0–34.9)	84 (38.5)	3 (9.1)	
Obesity II (35.0–39.9)	34 (15.6)	3 (9.1)	
Obesity III (≥40)	16 (7.3)	3 (9.1)	
Nulliparous, n (%)	210 (96.3)	32 (97.0)	1
Cycle length >35 days, n (%)	201 (92.2)	31 (93.9)	1
Clinical hyperandrogenism (mFG ≥8), n (%)*	108 (49.8)	13 (39.4)	0.35
Bilateral PCOM, n (%)	150 (68.8)	25 (75.8)	0.543
PMOS phenotype, n (%)			0.757
Phenotype A	83 (38.1)	10 (30.3)	
Phenotype B	8 (3.7)	1 (3.0)	
Phenotype C	17 (7.8)	2 (6.1)	
Phenotype D	110 (50.5)	20 (60.6)	

* Baseline characteristics of all 251 PMOS-diagnosed women allocated to an induction agent (full PMOS cohort). Of these, 11 (5 converted to IVF, 4 lost to follow-up, 2 converted to IUI) were excluded from the dominant-follicle outcome analysis (Tables 3–5, n = 240); their characteristics are retained here to assess confounding by indication. Continuous variables compared by Welch t-test; categorical variables by Pearson χ^2 or Fisher's exact test. * mFG score missing for one woman in the CC arm; hyperandrogenism percentage uses n = 217 as denominator. mFG = modified Ferriman–Gallwey score; PCOM = polycystic ovarian morphology; CC = clomiphene citrate; LTZ = letrozole; IVF = in vitro fertilisation; IUI = intrauterine insemination.

Our study thus, reinforces the 2023 International PMOS Guideline [15] which places lifestyle intervention as the foundational therapy, suggesting that in our setting, weight optimization might be the most impactful strategy to improve ovulation induction success, especially for women with Phenotype A. This study has several notable strengths: its multi-centre design enhances representativeness; the large sample size provides robust estimates; the use of standardized Rotterdam criteria ensures diagnostic consistency and comparability; and the integrated evaluation of prevalence, phenotype, and treatment response offers a comprehensive clinical picture.

Several limitations must be acknowledged. First, the cross-sectional design for prevalence and phenotype analysis precludes causal inferences. Second, selection bias is inherent, as participants were women seeking infertility treatment at tertiary centres; thus, findings may not generally be applicable to women with PMOS in the community, particularly those with mild symptoms or no fertility desires. Third, the lack of biochemical hyperandrogenism assessment is a major limitation that likely led to under-ascertainment of Phenotypes A and B and misclassification of some cases. The mFG score is a validated clinical standard in low-resource settings, and

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

the large sample size can compensate for the use of the mFG only. Fourth, the small subgroup treated with LTZ limits the power to detect true differences between ovulation induction agents. Fifth, we did not collect data on long-term endpoints like pregnancy, miscarriage, or live birth, which are ultimately more clinically significant than follicular development. Sixth, other potential confounders such as dietary patterns, physical activity, insulin levels, and anti-Müllerian hormone (AMH) were not measured.

Variance inflation factors (VIF) were used to assess multicollinearity; no evidence of multicollinearity was identified. The Hosmer–Lemeshow goodness-of-fit test is not routinely applicable to Firth penalized logistic regression models and is therefore not reported; calibration was assessed descriptively through comparison of observed and model-predicted success rates by covariate subgroup. Formal calibration plots and out-of-sample validation were not performed; future studies with larger samples and pre-specified validation strategies should report calibration alongside discrimination metrics. The use of the original Rotterdam follicle threshold rather than newer ultrasound cut-offs may have influenced phenotype classification, particularly the proportion of non-hyperandrogenic Phenotype D. A major limitation is that we did not collect data on pregnancy, miscarriage, or live birth. Dominant follicle selection is a useful intermediate indicator of ovarian response but is not equivalent to achieving pregnancy or live birth. Our findings should therefore be interpreted as reflecting ovulatory response rather than definitive fertility success.

The findings from this study carry several important implications for healthcare delivery in Ghana and similar SSA settings. The high prevalence of PMOS at 16.3 percent indicates that it is a common condition among infertile women. Consequently, providers, especially in primary and secondary care, should be trained to recognize its varied presentations, including the non-hyperandrogenic Phenotype D, which may present with only irregular menses. Diagnostic protocols should mandate a combination of menstrual history, clinical hyperandrogenism assessment with awareness of ethnic variations in hirsutism, and transvaginal ultrasound, while efforts to improve access to basic hormonal assays such as testosterone and sex hormone-binding globulin (SHBG) are needed to refine phenotype classification.

The central role of BMI in predicting treatment success supports the systematic integration of structured lifestyle modification programs involving diet and exercise into fertility clinics and as such preconception counselling for women with PMOS should emphasize weight optimization. Both CC and LTZ are effective for ovulation induction, and national formularies and treatment guidelines should ensure the availability and affordability of both, with early consideration of adjunctive metformin or gonadotropins for women with Phenotype A or high BMI who fail first-line oral agents. The significant burden of PMOS warrants its inclusion in national reproductive health strategies, supported by public awareness campaigns to promote early diagnosis and destigmatize the condition. Further, policypolicy support for research into the genetic and environmental determinants of PMOS in African populations should be widely promoted. The baseline comparison in Table 6 shows that CC was used in most women (n = 218; 86.9%), with LTZ reserved for a smaller subset (n = 33; 13.1%), reflecting clinical preference and local availability. The two arms were balanced with respect to age, parity, cycle length, clinical hyperandrogenism, bilateral polycystic ovarian morphology and PMOS phenotype distribution (all $p > 0.30$).

However, BMI distribution differed significantly between the arms ($p = 0.003$): the LTZ arm contained a higher proportion of overweight women (54.5% versus 28.4% in the CC arm) and a lower proportion of women in Obesity Class I (9.1% versus 38.5%). This pattern is consistent with clinician preference rather than random allocation and represents a clear example of confounding by indication. Because the multivariable logistic regression model adjusts for BMI category, the adjusted estimates partially account for this imbalance. Nevertheless, residual confounding from unmeasured factors that may have driven treatment selection (for example, prior CC non-response, metabolic comorbidities, or ovulation-induction history) cannot be excluded.

Formal propensity-score adjustment or inverse probability of treatment weighting was not undertaken because of the modest size of the LTZ subgroup and limited covariate overlap between the two treatment arms. Comparisons between agents should therefore be interpreted as exploratory and hypothesis-generating. Larger prospective or randomized studies with adequate LTZ representation are needed to define their comparative effectiveness of CC and LTZ. From a clinical perspective, these findings support a shift toward phenotype-informed counselling and individualized care for infertile women with PMOS, rather than a generic approach. Improved diagnostic work-up with more standardized hormonal and ultrasound assessments may refine phenotype classification and guide treatment choices more precisely.

Given the clear association between severe obesity and impaired ovulation induction response, structured weight management and lifestyle interventions should be integrated into holistic preconception care. The finding that Obesity Class III is associated with a 99% reduction in odds of dominant follicle selection underscores the clinical importance of weight optimization in this subgroup. Dominant follicle selection should be viewed as an intermediate ovulatory outcome, and further longitudinal studies that incorporate pregnancy and live-birth endpoints are needed to determine how these

ovulation-induction responses translate into meaningful reproductive outcomes.

Conclusion

This study establishes that PMOS is a prevalent condition (16.3%) among women seeking infertility care in Kumasi, Ghana. It reveals a unique phenotypic distribution dominated by Phenotype D. Ovulation induction with CC or LTZ is effective, with success strongly influenced by BMI. These findings highlight the necessity for context-specific, phenotype-aware, and weight-sensitive approaches to diagnosing and managing PMOS. By integrating these insights into clinical practice and public health policy, healthcare providers can improve fertility outcomes and overall quality of life for the substantial number of women affected by this complex syndrome in the region.

DECLARATIONS

Ethical consideration

All procedures were performed in accordance with the ethical standards of KATH Institutional Review Board (KATH-IRB/AP/190/24) and with the 1964 Helsinki declaration and its later amendments. All participants provided written informed consent prior to enrolment.

Consent to publish

All authors agreed on the content of the final paper.

Funding

The authors received no specific funding for this work.

Competing Interest

The authors declare no conflict of interest

Author contributions

BKO designed the study with support from CMS. Data collection, validation and analysis were done by AAK and AD. WMB and MYA drafted the manuscript, which was reviewed for intellectual content by all authors. Three research assistants (registered nurses/midwives) and the principal investigator underwent a two-day standardized training program covering study protocol, ethical conduct, accurate administration of the questionnaire, and clinical measurement techniques (e.g. mFG scoring, BMI calculation). All authors read, reviewed, and approved the final version of the manuscript.

Study Limitations

A formal intracluster correlation coefficient (ICC) was not estimated, which we acknowledge as a limitation. Sonographers were not formally blinded to participants' clinical data, as clinical assessments and ultrasound examinations were conducted within the same consultation; this represents a potential source of ascertainment bias that we acknowledge. Formal interobserver reliability coefficients were not measured, which is also acknowledged as a limitation.

Acknowledgement

The authors express their profound gratitude to the management and staff of Komfo Anokye Teaching Hospital, Trustcare Specialist Hospital and Fertility Centre, and Ruma Fertility and Specialist Hospital for their invaluable support and facilitation of this study. We are deeply indebted to the research assistants for their dedication in data collection and all our participants.

Availability of data

De-identified datasets generated and analysed during the current study are available from the corresponding author on request, subject to institutional and ethical approval.

REFERENCES

1. Fauser BCJM, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, et al. Consensus on women's health aspects of polycystic ovary syndrome (PMOS): The Amsterdam ESHRE/ASRM-sponsored 3rd PMOS Consensus Workshop Group. *Fertility and Sterility*. 2012;97:28–38.e25. https://doi.org/10.1016/j.fertnstert.2011.09.024
2. Mumusoglu S, Yildiz BO. Polycystic ovary syndrome phenotypes and prevalence: Differential impact of diagnostic criteria and clinical versus unselected population. Current Opinion in Endocrine and Metabolic Research. 2020;12:66–71. https://doi.org/10.1016/j.coemr.2020.03.004
3. Palomba S, Santagni S, Falbo A, La Sala GB. Complications and challenges associated with polycystic ovary syndrome: Current perspectives. International Journal of Women's Health. 2015;7:745–763. https://doi.org/10.2147/IJWH.S70314
4. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society clinical practice guideline. Journal of Clinical Endocrinology and Metabolism. 2013;98:4565–4592. https://doi.org/10.1210/jc.2013-2350
5. Chang S, Dunaif A. Diagnosis of polycystic ovary syndrome: Which criteria to use when? Endocrinology and Metabolism Clinics of North America. 2021;50:11–23. https://doi.org/10.1016/j.ecl.2020.10.002
6. Bozdag G, Mumusoglu S, Zengin D, Karabulut E, Yildiz BO. The prevalence and phenotypic features of polycystic ovary syndrome: A systematic review and meta-analysis. Human Reproduction. 2016;31:2841–2855. https://doi.org/10.1093/humrep/dew218
7. Abebe MS, Afework M, Abaynew Y. Primary and secondary infertility in Africa: A systematic review with meta-analysis. Fertility Research and Practice. 2020;6:20. https://doi.org/10.1186/s40738-020-00090-3
8. Dalal R. Infection and infertility. In: Genital Infections and Infertility. InTech; 2016. https://doi.org/10.5772/64168

9. Fox A, Feng W, Asal V. What is driving global obesity trends? Globalization or modernization? Globalization and Health. 2019;15:32. https://doi.org/10.1186/s12992-019-0457-y

10. Steyn NP, Mchiza ZJ. Obesity and the nutrition transition in sub-Saharan Africa. Annals of the New York Academy of Sciences. 2014;1311:88–101. https://doi.org/10.1111/nyas.12433

11. Lizneva D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertility and Sterility. 2016;106:6–15. https://doi.org/10.1016/j.fertnstert.2016.05.003

12. Cao NT, Le MT, Nguyen VQH, Pilgrim J, Le VNS, Le DD, et al. Defining polycystic ovary syndrome phenotype in Vietnamese women. Journal of Obstetrics and Gynaecology Research. 2019;45:2209–2219. https://doi.org/10.1111/jog.14097

13. Ugwu GO, Iyoke CA, Onah HE, Mba SG. Prevalence, presentation and management of polycystic ovary syndrome in Enugu, south-east Nigeria. Nigerian Journal of Medicine. 2013;22:313–316.

14. Akpata CB, Uadia PO, Okonofua FE. Prevalence of polycystic ovary syndrome in Nigerian women with infertility: A prospective study of the three assessment criteria. Open Journal of Obstetrics and Gynecology. 2018;8:1212–1224. https://doi.org/10.4236/ojog.2018.812112

15. Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. European Journal of Endocrinology. 2023;189. https://doi.org/10.1093/ejendo/lvad096

16. Sachdeva G, Gainder S, Suri V, Sachdeva N, Chopra S. Comparison of the different PMOS phenotypes based on clinical, metabolic, and hormonal profile, and their response to clomiphene. Indian Journal of Endocrinology and Metabolism. 2019;23:326–331. https://doi.org/10.4103/ijem.IJEM-30-19

17. Ashrafi M, Golmohammadi S. Different phenotypes of polycystic ovarian disease and their effects on clomiphene resistance in infertile women. Journal of Obstetrics, Gynecology and Cancer Research. 2023;8:23–30. https://doi.org/10.30699/jogcr.8.1.23

18. Amoah C, Adageba RK, Appiah EK, Sefogah PE. Obesity and overweight and associated factors among women with infertility undergoing assisted reproductive technology treatment in a low-income setting. Scientific Reports. 2025;15. https://doi.org/10.1038/s41598-024-82818-5

19. World Health Organization. WHO Laboratory Manual for the Examination and Processing of Human Semen. 6th ed. Geneva: World Health Organization; 2021.

20. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. Journal of Clinical Endocrinology and Metabolism. 1961;21:1440–1447. https://doi.org/10.1210/jcem-21-11-1440

21. Joham AE, Piltonen T, Lujan ME, Kiconco S, Tay CT. Challenges in diagnosis and understanding of natural history of polycystic ovary syndrome. Clinical Endocrinology (Oxford). 2022;97:392–402. https://doi.org/10.1111/cen.14757

22. Oriji VK. Prevalence of polycystic ovary syndrome among infertile women attending a fertility clinic at a university teaching hospital in Nigeria. Journal of Gynecology and Women's Health. 2019;15. https://doi.org/10.19080/jgwh.2019.15.555922

23. Ding T, Hardiman PJ, Petersen I, Wang FF, Qu F, Baio G. The prevalence of polycystic ovary syndrome in reproductive-aged women of different ethnicity: A systematic review and meta-analysis. Oncotarget. 2017;8:96351–96358. https://doi.org/10.18632/oncotarget.19180

24. Areetheerapas T, Singwongsa A, Suwannarurk K, Pattaraarchachai J. Predicting factors of clomiphene citrate responsiveness in infertile women with normogonadotropic anovulation (WHO group II anovulation). Clin Exp Obstet Gynecol. 2022;49. https://doi.org/10.31083/j.ceog4902039

25. Tholiya S, Kumari A, Mahey R, Kalaivani M, Sati HC, Sharma M, et al. Evaluation of predictors of response to ovulation induction using letrozole in women with polycystic ovary syndrome: a prospective cohort study. J Hum Reprod Sci. 2024;17. https://doi.org/10.4103/jhrs.jhrs_133_24.

26. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. Journal of Clinical Endocrinology and Metabolism. 2004;89:2745–2749. https://doi.org/10.1210/jc.2003-032046

27. Balogun M, Coker O, Samuel T, Sluss P, Udenze C, Azziz R, et al. Clinical phenotypes of polycystic ovary syndrome in Nigerian women: Preliminary results of the Nigeria PMOS Epidemiology & Phenotype (Nigeria-PEP) study. Journal of the Endocrine Society. 2022;6:bvac150.1436. https://doi.org/10.1210/jendso/bvac150.1436

28. Elasam AN, Ahmed MA, Ahmed ABA, Sharif ME, Abusham A, Hassan B, et al. The prevalence and phenotypic manifestations of polycystic ovary syndrome among infertile Sudanese women: A cross-sectional study. BMC Women's Health. 2022;22:247. https://doi.org/10.1186/s12905-022-01762-6

29. Engmann L, Jin S, Sun F, Legro RS, Polotsky AJ, Hansen KR, et al. Racial and ethnic differences in the polycystic ovary syndrome metabolic phenotype. American Journal of Obstetrics and Gynecology. 2017;216:493.e1–493.e13. https://doi.org/10.1016/j.ajog.2017.01.003

30. Rashidi H, Ramezani Tehrani F, Bahri Khomami M, Tohidi M, Azizi F. To what extent does the use of the Rotterdam criteria affect the prevalence of polycystic ovary syndrome? A community-based study from southwest Iran. European Journal of Obstetrics and Gynecology and Reproductive Biology. 2014;174:100–105. https://doi.org/10.1016/j.ejogrb.2013.12.018

31. Myers SH, Montanino Oliva M, Nordio M, Unfer V. PMOS phenotype focus: Phenotype D under the magnifying glass. Archives of Gynecology and Obstetrics. 2024;309:1–9. https://doi.org/10.1007/s00404-024-07408-2

32. Sakar MN, Oglak SC. Letrozole is superior to clomiphene citrate in ovulation induction in patients with polycystic ovary syndrome. Pakistan Journal of Medical Sciences. 2020;36:1465–1470. https://doi.org/10.12669/pjms.36.7.3345

33. Liu Z, Geng Y, Huang Y, Hu R, Li F, Song Y, et al. Letrozole compared with clomiphene citrate for polycystic ovarian syndrome: A systematic review and meta-analysis. Obstetrics and Gynecology. 2023;141:523–534. https://doi.org/10.1097/AOG.0000000000005070

34. Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. New England Journal of Medicine. 2014;371:119–129. https://doi.org/10.1056/NEJMoa1313517

35. Washington JK, Manivasakan J, Gunasekaran Kala P, RS. Association of anti-Müllerian hormone and free androgen index levels on response to clomiphene citrate in PMOS infertile women. Gynecology and Obstetrics Clinical Medicine. 2022;2:100–106. https://doi.org/10.1016/j.gocm.2022.11.003

36. Dahan MH, Reaven G. Relationship among obesity, insulin resistance, and hyperinsulinemia in the polycystic ovary syndrome. Endocrine. 2019;64:685–689. https://doi.org/10.1007/s12020-019-01899-9