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Incidence and risk factors of steroid-induced ocular hypertension following pterygium excision with conjunctival autograft

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Abstract

Background: Topical steroids are used to reduce post-operative inflammation after ocular surgery with the potential risk of ocular hypertension, glaucoma and blindness. There is a paucity of published data globally and locally on steroid-induced ocular hypertension (SiOH) post pterygium excision (PE) with conjunctival autograft (CAG).

Objective: We aimed to determine the incidence and risk factors of SiOH post-PE with CAG in Korle-Bu Teaching Hospital, Accra, Ghana.

Methods: In this prospective observational study, the demographic and clinical data of patients undergoing PE with CAG were collected and analyzed. Post-operative intraocular pressures (IOP) were measured on days 1, 7, 14, 28, and 42. The cumulative incidence of SiOH (proportion of the increase in IOP ≥ 10mm Hg at six weeks compared to baseline) and mean change in IOP from baseline were computed. Risk factors of SiOH were determined using a multiple logistic regression model. The Kaplan-Meier survival curve was used in estimating the median time to develop SiOH.

Results: Overall, 101 patients participated in this study with a mean age of 46.8 ± 11.9 years. The majority (65.3%, n= 66/101) of participants were females. The mean pre-operative IOP in the study eyes was 15.3 ± 3.0 mm Hg. The overall mean post-operative IOP was 18.6 ± 2.8 mm Hg ($p = 0.001$). The overall incidence of SiOH six weeks post-PE with CAG was 32.7% (95% confidence interval (CI) = 23.7 - 42.7%). Male sex was the only independent factor associated with the development of SiOH [odds ratio (OR) = 3.3; 95% CI = 1.1 - 9.7; $p = 0.032$]. The median time to develop SiOH was 42 days (95% CI = 37.1 - 46.9 days, $p = 0.022$).

Conclusion: The study showed that SiOH post-PE is a common complication with an overall six-weeks post-excision incidence of 32.7%. Males are more likely to develop SiOH after PE with CAG. Patients undergoing PE with CAG should be closely monitored postoperatively to prevent complications associated with prolonged raised IOP.

Keywords: Pterygium excision, conjunctival autograft, steroid, intraocular pressure, ocular hypertension

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INTRODUCTION

Corticosteroids are used to reduce inflammation after ocular surgery. They suppress cellular infiltration, vascular permeability, fibroblast proliferation, leukocyte migration, collagen deposition and scar formation [1,2]. Ocular hypertension (OH) is a well-recognized complication of corticosteroid use [3]. The incidence of steroid-induced ocular hypertension (SiOH) varies with the potency, concentration and formulation of the steroid, frequency of dosing and duration of treatment [2]. The ocular hypertensive effects of steroids are caused by an increase in outflow resistance and a reduction in the outflow of aqueous humor through the outflow channels at the level of the trabecular meshwork [4]. The higher the potency of

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a corticosteroid preparation, the earlier the onset and the stronger its ocular hypertensive effect [3]. The predisposing factors for steroid-induced ocular hypertension (SiOH) include a history of primary open-angle glaucoma, glaucoma suspect, a first-degree relative of glaucoma patient, previous history of SiOH, very young (< 10 years of age) and older ages (>50 years of age), high myopia, type 1 diabetes mellitus, connective tissue disease, male sex, and genetic and racial factors [2-7]. Although the elevation of Post-operative intraocular pressures (IOP) reduces upon cessation of steroid therapy, it may lead to glaucoma and blindness if not detected early and treated appropriately [2]. Pterygium is a common eye condition with a higher prevalence reported in the tropics [8]. The definitive treatment is surgical. Recurrence following pterygium excision can be reduced using conjunctival autografts or amniotic membrane transplant [8]. Adjunctive therapy involving the use of chemotherapeutic agents or application of beta radiation to the scleral bed may also reduce recurrence but no technique is perfect [9,10]. In pterygium surgery, steroids have not only reduced the post-operative discomfort and inflammation but also the rate of recurrence [11]. Topical administration is the most common mode of application of steroids in ophthalmology. Few studies on SiOH after pterygium surgery have been reported [7,12,13]. The reported incidence of SiOH varies between 9.6% and 24% due to differences in definition and criteria [7,12,13]. Furthermore, there are no published studies of SiOH after PE with CAG in the West African sub-region. In this manuscript, we report the incidence and determinants of SiOH after pterygium excision with a conjunctival autograft at Korle-Bu Teaching Hospital (KBTH), Accra, Ghana.

MATERIALS AND METHODS

Study design and settings

This prospective cohort study aimed to evaluate the occurrence and factors associated with steroid-induced ocular hypertension (SiOH) following pterygium excision (PE) with conjunctival autograft (CAG). The study was conducted at the Lions International Eye Center (LIEC) of the KBTH from September 2019 through March 2021. The LIEC is a tertiary teaching facility and has a full complement of staff for effective Eye Health delivery. Ocular surgeries, laser procedures, and various ophthalmic diagnostic investigations and imaging are carried out at the facility. About 20 new cases of pterygium are recorded monthly at the clinic.

Study population

Adults who were diagnosed with primary pterygium and were over 18 years old, and who provided written informed consent, were enrolled in the study if they agreed to undergo PE with CAG and attend follow-up consultations as specified in the study protocol. Patients with pterygium requiring excision were excluded from the study if they had prior intraocular surgery in the affected eye, recurrent pterygium, previous history of SiOH, current use of steroids whether systemic or local and those who could not be examined using an applanation tonometer. The sample size for this observational study was calculated using the formula $N = 2(Z\alpha + Z\beta)(Z\alpha + Z\beta)(SD)^2 / [E]^2$ [14], where N is the total number of participants to be recruited in the study, Zα is the type 1 error set at 5% with a corresponding z score of 1.96, Zβ is the type 2 error set at 20% with a corresponding z score of 0.84, SD is the standard deviation of the 1-day post-operative mean IOP = 4.3 mm Hg based on the study by Wu et al. [7]. The effect size E is 2.3 based on the study by Wu et al. [7]. Accounting for a 20% loss to follow-up, a minimum of 66 participants were required.

Data collection

A pre-tested structured questionnaire was used to collect preoperative and postoperative data from the participants. Demographic characteristics of study participants obtained included; age, sex and occupation of patients. Medical history of participants was obtained and these included; the duration of pterygium (< 6 months, 6 months to 1 year, > 1 year), eyes affected (right, left or both), eye to be operated (right or left), the location of pterygium (nasal, temporal and both), history of previous eye trauma, history of previous eye surgery, wearing of spectacles, history of glaucoma, family history of glaucoma, antecedent use of steroids, use of other medications that may affect IOP, drug history, presence of diabetes, presence of hypertension, presence of connective tissue disease, and indication for surgery. The Snellen visual acuity chart was used to assess the visual acuity of all participants. Assessment of the adnexa, anterior segment, and fundi was examined by biomicroscopy using the slit lamp binocular microscope with a Volk™ +90D lens (Volk, USA). Clinical staging/grading of pterygium was performed and the date of the surgery was scheduled.

Intraocular pressure (IOP) measurement of both study and fellow eyes was done using a slit lamp binocular microscope with mounted calibrated Goldmann applanation tonometer (GAT) (Köniz, Switzerland) after instillation of fluorescein 2% with tetracaine 2% drops. One reliable GAT mounted on a Haag Streit Slit lamp was deployed for use at the designated study area with ergonomically comfortable arrangements for the work. To ensure consistency of readings, pre-test runs were conducted by comparing the readings of two experienced ophthalmologists. The goal was to achieve an acceptable level of interobserver variability, with readings correlated within 2 mmHg of each other. The GAT was calibrated each day before measurements began and an average of three readings within 1 mm Hg of each other was taken. The guidelines for measuring IOP using applanation tonometry were followed. If a reading required corroboration and confirmation, as in the recording of an outcome measure, the investigators referred it to another Ophthalmologist who was blinded to the reading of the PI. The confirmatory IOP reading, if in the agreement was used as the reading for the participant. The study began before the onset of the novel Coronavirus disease (COVID-19) pandemic. To ensure the safety of study participants and investigators

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during the COVID-19 pandemic, the following protocols were implemented: study investigators and participants were required to wear face masks, and hand washing was mandatory. The temperatures of participants and the investigators were taken with a non-contact thermometer gun before entry into the clinic. Participants were required to observe social distancing of at least 2 meters in the waiting area. Pens and tools used for consenting were sanitized with alcohol-based hand sanitiser. The investigators wore a face mask, gloves, gown and a plastic shield over the eyes. At the consulting room, study participants were given an alcohol-based sanitiser to sanitize their hands before the start of the examination. Appropriate physical distance was observed. A special plastic breath shield was fixed on the slit-lamp machine to protect investigators and participants from any possible contamination from an aerosol exchange. Participants were told to refrain from speaking during slit lamp procedures until completion. There was disinfection of instruments including slit lamp biomicroscope and applanation tonometer after examination of each patient using 70% alcohol.

Pterygium excision with conjunctival autograft

All participants were taken through the Eye Center's system of booking, listing and preparation for surgery. The blood pressure of participants was measured on the day of surgery. Participants were counselled on the surgical technique to be deployed and informed consent for surgery was obtained. In preparation for surgery, 0.4% gutt benoxinate hydrochloride (Benox®, Egypt) anaesthetic drops were instilled in the inferior fornix and the patient asked to close the eye. Then, a 10% povidone-iodine solution was used to prepare the skin of the eyelids and adnexa of the study eye. The eye was then draped with sterile towels with a hole for the eyelets. More drops of the topical anaesthetic were applied with a 5% povidone Iodine solution. A lid speculum was used to part the eyelids and expose the globe. Subconjunctival injection of 2% lidocaine with adrenaline with 0.5% bupivacaine in a 1:1 proportion was administered in the inferior fornix to raise a bleb and provide further anaesthesia. The pterygium was mobilized and excised at a variable distance from the limbus. The head and neck were removed from their cornea adherence with a size 15 scalpel blade mounted on a Bard Parker handle. The cornea was then polished with careful superficial keratectomy. Tenon's fascia was excised from the sclera and adjacent areas in the retracted segment of the pterygium, being careful to spare any fibres of the superior oblique and medial rectus muscles to obtain a clean and bare sclera. The anaesthetic solution of lidocaine and bupivacaine was then injected into the superior fornix and spread supero-temporally and evenly to raise a bleb for harvesting of the free graft. A pair of Westcott scissors and forceps were used to harvest the graft. This was estimated to meet the dimensions of the bare sclera defect. The graft was then sutured in place with size 8-0 braided absorbable ophthalmic suture. Guttae dexamethasone with chloramphenicol and tetracycline compound preparation was applied for an emollient effect and the eye was padded. Oral analgesic medications were prescribed after the surgery including acetaminophen 1g tablets three times a day and diclofenac tablets 75 mg twice daily, all for 5 days.

Follow-up and post-operative care

The participants were seen on the following day and the eye patches were removed. The eyes were cleaned, and Snellen visual acuity was recorded. The IOPs were then measured and recorded and guttae dexamethasone and polymyxin B compound preparation were given to the patients to be applied every three hours of their waking hours up to six times a day. The clients were given their follow-up date at the current visit and reminded of their appointment during the week before the visit. Post-operative visual acuities and intra-ocular pressures were further measured on days 7, 14, 28 and 42 by Goldmann applanation tonometry. The measured IOP values were documented, and any values that met the study limits were considered indicative of SiOH and flagged accordingly. To ensure accuracy, a team member was tasked with validating the SiOH diagnosis, which was then recorded. Treatment with steroids was discontinued upon confirmation of SiOH, and replaced with diclofenac, timolol, and tear substitutes. Participants had a follow-up review one week after the initial visit. If their IOP was normal, they had another review in a month and continued the same treatment. If their IOP was still normal after a month, they received tear substitutes and non-steroidal anti-inflammatory drug drops until the graft was fully taken. The participants were counselled on the potential risks associated with the use of steroids and advised to inform any physician who offers them steroid treatment about the risk of developing steroid-induced ocular hypertension and subsequent glaucomatous optic neuropathy. Subsequently, participants were referred to general ophthalmology clinics for scheduled monitoring. Participants who completed the study but did not record primary outcome measures were followed up for an additional month after completing the initial 42-day period. During this time, steroid treatment was gradually tapered off over the course of approximately one month, while participants were still monitored for adverse events. Participants were then put on tear substitutes. Adverse events were monitored on a visit-by-visit basis, and any patients experiencing adverse events were promptly managed.

Outcome measures

The primary outcome measure was the incidence of SiOH at 42 days postoperative. We defined SiOH as a clinically significant postoperative elevation of IOP by a reading of ≥ 10 mm Hg from baseline IOP measurement with a Goldmann applanation tonometer [7]. The secondary outcome measures included the incidence of SiOH on days 1, 7, and 28, as well as the mean IOP on days 1, 7, 28, and 42 post-operation. In this study, SiOH was classified based on its severity, with high responders being those with an IOP of ≥ 16 mm Hg, moderate responders having an IOP of 6 - 15 mm Hg, and non-responders having an IOP of ≤ 5

mm Hg [16]. Additionally, risk factors for SiOH and the median time to develop SiOH were also measured.

Statistical analysis

Data were analyzed with IBM SPSS Statistics for Windows, Version 23.0. The mean, standard deviation (SD), and independent t-test were used for comparing continuous data, and percentages to track IOP increase over time. The Chi-square test of independence was performed on categorical variables to determine if there was a significant association. The mean rise in IOP after treatment with topical steroids post pterygium excision with CAG was analyzed and presented as mean differences and percentages. The incidence of SiOH six weeks post-pterygium excision with conjunctival autograft was calculated and presented in percentage. Univariate and multivariate logistic regression analyses were performed to determine demographic characteristics and risk factors for SiOH in clients undergoing pterygium excision with conjunctival autograft. Corresponding odds ratios and confidence intervals (CI) were calculated. The Kaplan-Meier survival curves were used to estimate the median number of days for study participants to develop SiOH after the excision of pterygium with conjunctival autograft using various factors. The significance level was set at $p < 0.05$.

RESULTS

The demographics of study participants

Overall, 110 patients underwent pterygium excision with conjunctival autograft, and the analysis included 101 patients (91.8%) who completed their follow-up schedules. The mean age ± SD of the 101 participants was 46.8 ± 11.9 years (range, 18 - 75 years). The majority (65.3%, n= 66/101) of participants, were females and 53% (n = 54) of them were involved in an outdoor occupation. The majority (88.0%, n = 89) of participants had pterygium of more than one-year duration and 51.5% (n = 52) of them had pterygium in both eyes. Twenty-six (25.7%) participants had a pterygium in the right and 23 (22.8%) had a pterygium in the left eye. Five (5.0%) participants had previous eye trauma. One (1.0%) participant had connective tissue disease. Nineteen (18.8%) participants reported antecedent use of eye drops, including topical lubricants such as methylcellulose, which was used by 7 participants (6.9%, n = 7), steroids such as dexamethasone 0.1% with polymyxin B (3.0%, n = 3), fluorometholone acetate 0.1% (3.0%, n = 3), dexamethasone 0.1%, polymyxin B sulfate and neomycin sulfate (3.0%, n = 3), hydrocortisone acetate 1.5%, neomycin sulfate and polymyxin B sulfate (1. 9%, n = 2), and dexamethasone phosphate, neomycin sulfate (1%, n = 1). The duration since the last dose of steroid use before study entry was 2 to 6 weeks. Most (84.6%, n = 77) participants had pterygium located nasally. The majority (78.0%, n = 71) had grade 3 pterygium. Ocular surface discomfort (89.8%, n = 79), advice from a health worker (87.1%, n = 74), and cosmetic considerations (69.9%, n = 51) were the 3 most common reasons why participants presented to the eye centre for pterygium excision. Other reasons included participants' personal decisions, willingness to undergo surgery, and the fear of pterygium growth extending to cover the visual axis. The demographic and clinical characteristics of participants are summarized in Table 1.

Table 1: Demographic, clinical characteristics and incidence of SiOH six weeks post-pterygium excision with conjunctival autograft.

Factor	Number with SiOH in the group	Total number in the group	Incidence of SiOH (%)
Age:			
18-30	3	7	42.9
31-45	17	47	36.2
> 45	13	47	27.7
All ages	33	101	32.7
Sex			
Male	17	35	48.6
Female	16	66	24.2
Occupation			
Indoor	15	47	31.9
Outdoor	18	54	33.3
Location of pterygium			
Nasal	30	87	34.5
Temporal	1	3	33.3
Both	2	11	18.2
Grade of pterygium			
II	2	3	66.7
III	25	80	31.3
IV	6	18	33.3

*SiOH, steroid-induced ocular hypertension. The proportion of the overall incidence of SiOH for a 95% CI= 32.7% (range, 23.7 - 42.7%). The median age was 45.0 (range, 18 - 75) years. Pterygium duration: 6 months to 1 year (11.9%, n = 12), > 1 year (88.1%, n = 89). Pterygium location: both eyes (51.5%, n = 52), right eye (25.7%, n = 26), left eye (22.8%, n = 23). Previous eye trauma (5.0%, n = 5). Connective tissue disease (1.0%, n = 1). Antecedent use of eye drops (18.8%, n = 19). Duration since last dose of steroid use = 2 to 6 weeks. Reasons for presenting for pterygium excision: ocular surface discomfort (89.8%, n = 90), advice from a health worker (87.1%, n = 90), cosmetic considerations (69.9%, n = 70), participants' personal decision and willingness to undergo surgery (1.0%, n = 1), fear of pterygium growth extending to cover the visual axis (1.0%, n = 1).

Incidence of SiOH

The overall incidence of SiOH six weeks post-PE with CAG was 32.7% (range, 23.7 - 42.7%). The incidence for age, sex, occupation, location of pterygium, and grade of pterygium is shown in Table 1. Among the three age groups, the highest incidence (42.9%) of SiOH six weeks post-PE with CAG was recorded among those aged 18 to 30 years. Males had a higher (48.6%) incidence compared to females. Participants with outdoor occupation had a higher incidence (33.3%) compared to those with indoor occupation. Participants with pterygium located nasally had the highest incidence of 34.5% for SiOH six weeks post-PE with CAG compared to those with pterygium located elsewhere. We classified ocular response to steroids six weeks post-PE with CAG (Table 2). A total of 17 (16.8%)

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Table 2: Classification of ocular response to steroids six weeks post-pterygium excision with conjunctival autograft

Factor	High responders ≥16 mmHg	Moderate responders 6-15 mmHg	Non-responders ≤5 mmHg	Total (%)	*p* value
	Number (%)	Number (%)	Number (%)		
Age:					0.040
18-30	3 (3.0)	1 (1.0)	3 (3.0)	7 (6.9)	
31-45	11 (10.9)	16 (15.8)	20 (19.8)	47 (46.5)	
>45	3 (3.0)	24 (23.8)	20 (19.8)	47 (46.5)	
Total	17 (16.8)	41 (40.6)	43 (42.6)	101 (100.0)	
Sex:					0.071
Male	10 (9.9)	12 (11.9)	13 (12.9)	35 (34.7)	
Female	7 (6.9)	29 (28.7)	30 (29.7)	66 (65.3)	
Occupation:					0.595
Indoor	6 (5.9)	20 (19.8)	21 (20.8)	47 (46.5)	
Outdoor	11 (10.9)	21 (20.8)	22 (21.8)	54 (53.5)	
Location of pterygium					0.272
Nasal	15 (14.9)	38 (37.6)	34 (33.7)	87 (86.1)	
Temporal	1 (1.0)	1 (1.0)	1 (1.0)	3 (3.0)	
Both	1 (1.0)	2 (2.0)	8 (7.9)	11 (10.9)	
Grade of pterygium					0.202
II	2 (2.0)	-	1 (1.0)	3 (3.0)	
III	12 (11.9)	34 (33.7)	34 (33.7)	80 (79.2)	
IV	3 (3.0)	7 (6.9)	8 (7.9)	18 (17.8)	

%, percentage

Table 3: Univariate analysis of the association between demographic and clinical characteristics and the development of SiOH

Risk factor	With SiOH	Without SiOH	Total	*p* value
	Number (%)	Number (%)	Number (%)	
Mean age ± SD	45.1±12.1	47.6 ± 11.7	46.8 ± 11.9	0.312
Age group (%):				0.569
18-30	3 (3.0)	4 (4.0)	7 (6.9)	
31-45	17 (16.8)	30 (29.7)	47 (46.5)	
>45	13 (12.9)	34 (33.7)	47 (46.5)	
Sex (%):				0.013*
Male	17 (16.8)	18 (17.8)	35 (34.7)	
Female	16 (15.8)	50 (49.5)	66 (65.3)	
Total	33 (32.7)	68 (67.3)	101 (100.0)	
Occupation (%):				0.525
Indoor	15 (14.9)	32 (31.7)	47 (46.5)	
Outdoor	18 (17.8)	36 (35.6)	54 (53.5)	
Duration of pterygium:				0.549
6 months to 1 year	-	3 (3.1)	3 (3.1)	
> one year	33 (33.7)	62 (63.3)	95 (96.9)	
Pre-operated IOP for the eye to be operated (mean ± SD)	14.6 ± 3.0	15.6 ± 2.8	15.3 ± 3.0	0.131
Location of pterygium (%)				0.554
Nasal	30 (29.7)	57 (56.4)	87 (86.1)	
Temporal	1 (1.0)	2 (2.0)	3 (3.0)	
Both	2 (2.0)	9 (8.9)	11 (10.9)	
Previous eye trauma (%)	2 (2.2)	3 (3.3)	5 (5.5)	0.535
Previous eye surgery (%)	3 (3.3)	9 (9.9)	12 (13.2)	0.393
Wearing of glasses (%)	10 (11.0)	24 (26.4)	34 (37.4)	0.649
Family history of glaucoma (%)	6 (6.6)	7 (7.7)	13 (14.3)	0.342
History of diabetes (%)	2 (2.2)	6 (6.6)	8 (8.8)	0.473
History of hypertension (%)	15 (5.5)	18 (19.8)	23 (25.3)	0.211
Antecedent use of steroids (%)	7 (7.8)	12 (13.3)	19 (21.1)	0.786
Grade of pterygium (%)				0.438
II	2 (2.0)	1 (1.0)	3 (3.0)	
III	25 (24.8)	55 (54.5)	80 (79.2)	
IV	6 (5.9)	12 (11.9)	18 (17.8)	
Total	33	68	101	

*Statistically significant risk factors ($p < 0.05$); SD, standard deviation; SiOH, steroid-induced ocular hypertension

Table 4: Multivariate logistic regression analysis of risk factors for development of SiOH

Risk factor	Number with SiOH/total	Incident rate (%)	OR (95% CI)	*p* value
Age:				0.945
18-30	3/7	42.9	0.9 (0.1-7.2)	0.469
31-45	17/47	36.2	0.7 (0.2-2.0)	
>45	13/47	27.7	Reference	
Sex:				
Male	17/35	48.6	3.3 (1.1-9.7)	0.032*
Female	16/66	24.2	Reference	
Occupation:				
Indoor	15/47	31.9	1.1 (0.4-3.0)	0.861
Outdoor	18/54	33.3	Reference	
Location of pterygium:				0.197
Nasal	30/87	34.5	0.3 (0.1-1.8)	0.782
Temporal	1/3	33.3	0.6 (0.1-14.4)	
Both	2/11	18.2	Reference	
Previous eye trauma	2/5	40.0	0.8 (0.1-6.7)	0.801
Previous eye surgery	3/12	25.0	1.5 (0.2-9.8)	0.695
Family history of glaucoma	10/13	76.9	0.8 (0.2-3.0)	0.702
History of diabetes	2/8	25.0	0.9 (0.1-6.6)	0.972
History of hypertension	15/23	65.2	1.5 (0.4-5.8)	0.543
Antecedent use of steroids	7/19	36.8	0.8 (0.2-3.5)	0.800

SiOH, steroid-induced ocular hypertension; OR, odds ratio; CI, confidence interval; %, percentage

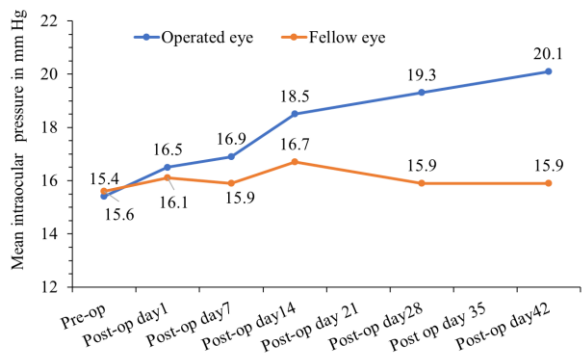

Figure 2: Line chart of mean rise in intraocular pressure between operated eye and fellow eye after treatment with topical steroids post pterygium excision. *Post-op, post-operation.

participants were high responders, 41 (40.6%) were moderate responders, and 43 (42.6%) were non-responders (Table 2).

Risk factors of SiOH

The univariate analysis showed that male gender (p = 0.013) was significantly associated with the development of SiOH in patients who underwent PE with CAG, as seen in Table 3. The multivariate logistic regression analysis revealed that male gender was the only risk factor for the development of SiOH in patients undergoing PE with CAG, with an odds ratio of 3.3 (95% CI = 1.1 - 9.7; p = 0.032). Males were 3 times more likely to develop SiOH compared with females (p = 0.032). The incidence of SiOH in males and females was 68.6 per hundred persons and 40.9 per hundred persons, respectively (Table 4).

Rise in intraocular pressure

Overall, there was a mean rise in intraocular pressure after treatment with topical steroids post-pterygium excision. At baseline, the mean pre-operative IOP was 15.3 ± 3.0 mm Hg (range, 10.0 - 21.0 mm Hg). The overall mean post-operative IOP was 18.6 ± 2.8 mmHg (range,13.8 - 25.4 mm Hg) with a 21.6% increase in IOP from baseline (p = 0.001). The intraocular pressure on day 1 post-operation was 16.4 ± 3.4 mm Hg, which represents a 7.2% increase from the baseline (p = 0.006). Similarly, the mean IOP for day 7 post-operation was 17.0 ± 3.7 mm Hg with an 11.1% increase from the baseline (p = 0.001). The mean intraocular pressure for day 14 post-operation was 18.6 ± 4.9 mm Hg, corresponding to an increase of 21.6% from the baseline (p = 0.001). On day 28, the mean post-operation intraocular pressure was 19.3 ± 7.4 mm Hg with a percentage rise of 26.1% (p = 0.001) and on day 42, the mean post-operation IOP was 20.2 ± 7.1 mm Hg with a percentage rise of 32.0% (p = 0.001). Figure 2 presents the average increase in intraocular pressure (IOP) between the operated eye and the fellow eye following treatment with topical steroids post-pterygium excision. Before surgery, there was no significant difference between the mean IOP of the operated eye and the fellow eye (p = 0.207). Also, no significant difference in mean IOP between operated eyes and fellow eyes was observed a day after the excision of pterygium (p > 0.05). Statistically significant differences in mean IOPs were observed from post-operation day one onwards (p < 0.05).

Survival analysis for time to develop SiOH

The median time to develop SiOH after PE with CAG was 42.0 days (Figure 3). The median time to develop SiOH

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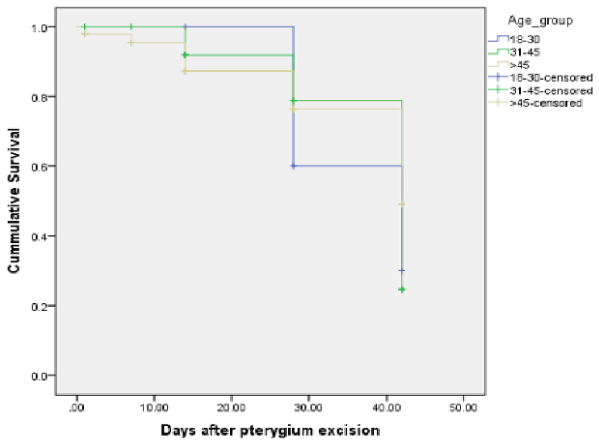
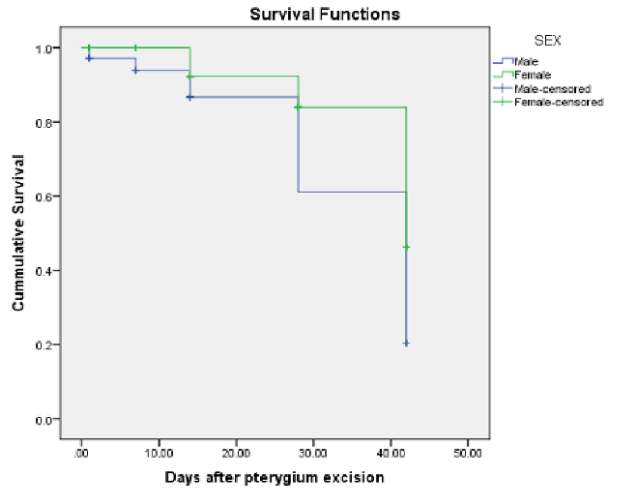


(a)



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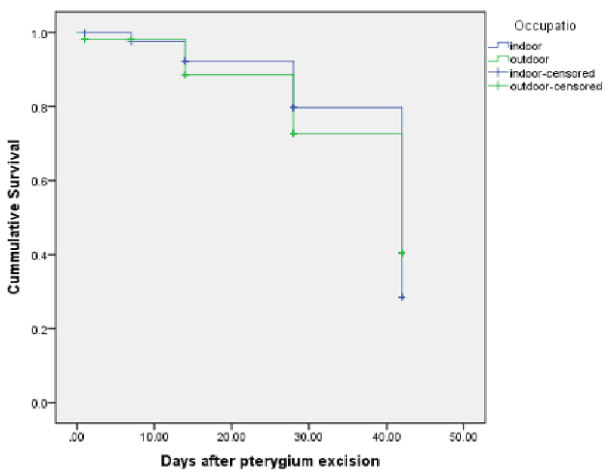
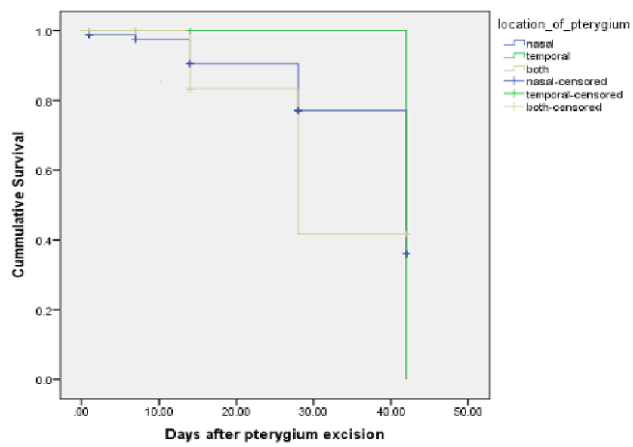
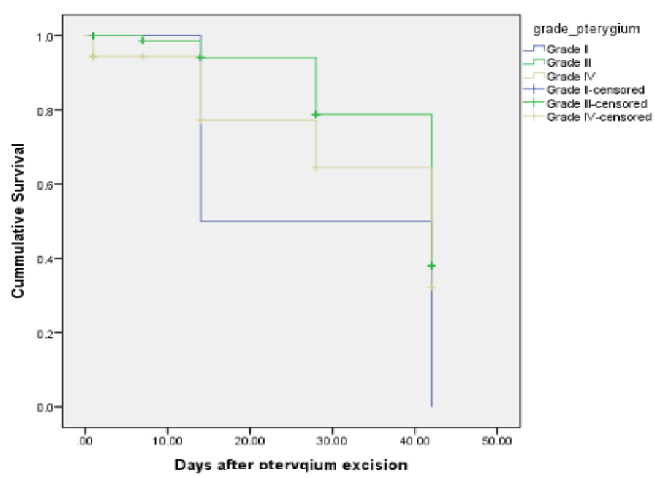


(c)



(d)



(e)

Figure 3: Kaplan-Meier survival curve for time to development of steroid-induced ocular hypertension (SiOH)
(a) among age groups
(b) between males and females
(c) *grades of pterygium*
(d) indoor and outdoor occupation
(e) location of pterygium

among males and females was 42.0 days, respectively. There was no statistically significant difference in the median time to develop SiOH between age groups (p = 0.712), sex (p = 0.202), grade of pterygium (p = 0.172), and occupation (p = 0.913). Participants with both nasal and temporal pterygia in the same eye had a median time to develop SiOH of 28 days compared to 42 days for those with either nasal or temporal pterygia only (p = 0.415).

DISCUSSION

This study is the first to determine the incidence and determinants of SiOH post-PE with CAG in Ghanaians. This study provides important epidemiological information about pterygium for the practice of eye health in Ghana and elsewhere. The overall incidence of SiOH (IOP ≥ 10mm Hg from baseline) six weeks post-operative PE with CAG was 32.7%. Few studies have reported the incidence of steroid-induced ocular hypertension post-PE [7,12,13,17]. Makornwattana et al. in Thailand [13] reported SiOH of 9.68% among 62 subjects following PE with amniotic membrane transplant. The outcome measure in the Makornwattana study was an increase in IOP of at least 10 mm Hg from the pre-operative level, which is similar to our study. However, there were differences between our study and the Makornwattana study in terms of the frequency of administration of dexamethasone eye drops, the duration of follow-up, and the population groups studied. Compared to our current study, participants in the study by Makornwattana et al. were older (55.4 ± 11.6 years versus 46.8 ± 11.9 years), had lower pre-operative IOP (13.1 ± 2.7 mm Hg versus 15.3 ± 3.0 mm Hg), and had fewer males. Although the mean increase in IOP week 1 post-operation was higher (25.8%) in the reports of Makorwattanna et al. [13] compared to our current study (11.0%), the values were similar at 1 month (21.3% versus 26.0%). In our current study, the percentage of moderate responders was similar to the findings of Makornwattana et al. (40.6% versus 37.1%). However, it is worth noting that none of the subjects in their study was a high responder [13].

In a retrospective study of 212 eyes, Wu et al. [7] observed ethnic differences in the rate of IOP rise post-PE. The Hispanic race had the highest incidence of IOP elevation (65.2%) followed by Africans (23.9%) [7]. The incidence rate of IOP elevation was significantly different between Hispanics and Caucasians (p = 0.031), but there was no statistically significant difference between Hispanics and Africans (p = 0.103) or Asians (p = 0.063) [7]. The observed differences in the incidence of IOP elevation post-PE may suggest differences in genetic predisposition to SiOH among different racial groups [7], an observation that needs to be examined in further studies. Kuryan et al. conducted a retrospective chart review of pterygium excision procedures performed by residents at an institution in New York and reported that 19.0% of eyes developed SiOH at 1 month. An increase in IOP > 5 mm Hg compared to baseline was observed in 30% of the patients [17]. Similar to our work, the study by Kuryan et al. reported a significant increase in mean postoperative IOP on day 1, 1 week, and 1 month compared to the mean pre-operative IOP [17]. Due to the significant increase in mean post-operative IOP observed on day 1 in our study and others [7,17], we hypothesize that IOP elevation observed in the immediate post-operative period may be due to factors other than steroid response. It has been proposed that this raised IOP may be because of the pterygium surgery on corneal biomechanics or the effect of the surgery on the downstream drainage of aqueous humour [7,17]. There are several reports of predisposing factors of SiOH [2-7]. Kuryan et al. [17] did not observe a significant association between possible risk factors and IOP rise following pterygium excision. Wu et al., on the other hand, found Hispanic race and subconjunctival injection of steroids to be significantly associated with SiOH post pterygium excision [7]. In the study by Wu et al., the male gender had a higher incidence of SiOH post-PE, but the difference was not significant [7]. Our current study supports previous findings by Busool et al. [5], Kanellopoulos et al. [6], and Manzoor et al. [18] that suggest males are more likely to develop SiOH than females after photorefractive keratectomy procedures. Further studies should be conducted to support our findings that the male gender is a risk factor for SiOH after pterygium surgery. The use of topical steroids induces ocular hypertension over the course of weeks [2]. Makornwattana et al. observed a peak rise in IOP post-pterygium excision occurring 1-month post-operation [13]. In our study, the median time to develop SiOH post-PE with CAG was 42 days. Patients will need to be monitored for elevated IOP beyond six weeks post-operation. In the retrospective study by Wu et al. [17], the probability of experiencing elevated IOP after pterygium excision was 10.91% for Africans at 1 week, 16.6% at 1 month, and 34.8% at 3 months.

This study had some limitations. The COVID-19 restrictions contributed to the prolongation of the study and missed appointments. Measurement of central corneal thickness would have given further validation to the IOP values that were obtained and would have provided an additional variable for investigating the risk factors for SiOH. A larger sample size would also have revealed other significant factors in the regression model. However, these limitations do not diminish the importance of the study and the results obtained. This study stands out as the first to determine the incidence of SiOH after pterygium excision with conjunctival autograft in Ghanaian adults.

Conclusion

SiOH post-pterygium excision with conjunctival autograft was a common complication with an overall six weeks post-operative incidence of 32.7%. The male gender was a risk factor for developing SiOH after PE with CAG. There is a need to closely monitor the intraocular pressure of all patients who undergo pterygium excision with conjunctival autograft with post-operative use of steroids to prevent post-operative complications associated with persistently increased intraocular pressure. A multi-centre study with a larger sample size and longer follow-up schedule is

recommended to explore other potential risk factors as well as monitor participants who develop a slower SiOH response.

DECLARATIONS

Ethical considerations
The study protocol was approved by the Institutional Review Board of Korle-Bu Teaching Hospital (KBTH-IRB/00066/2019). All procedures performed in studies involving human participants were by the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the participants at study enrolment and for surgery.

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

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

Author contributions
RDKT designed the study. RDKT, IZB, NNT, BA, YSA, EMD, VAE retrieved and analysed the data, and prepared the manuscript. All authors provided critical review 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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