GHANA COLLEGE OF PHYSICIANS AND SURGEONS

FACULTY OF OPHTHALMOLOGY

EFFECTS OF STEROID EYE DROPS ON INTRAOCULAR PRESSURE IN PATIENTS POST CATARACT SURGERY AND ASSOCIATED RISK FACTORS AT A TERTIARY FACILITY AND ITS OUTREACH CENTRE

A DISSERTATION SUBMITTED TO THE FACULTY OF OPHTHALMOLOGY IN PART FULFILMENT OF THE REQUIREMENTS FOR THE CONFERMENT OF A FELLOW OF THE GHANA COLLEGE OF SURGEONS (FGCS)

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ATTESTATION

We hereby certify that Dr Akosua Badu Mensa-Bonsu of the eye department of the Korle-Bu Teaching Hospital carried out this dissertation under our supervision.

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DECLARATION

I declare that except references to other people's work which I have duly acknowledged, this proposal is original. This dissertation has not been submitted in part or full for the award of any other degree.

Signed:.....

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STRUCTURED ABSTRACT

Introduction

Topical corticosteroids are routinely used after cataract surgery to decrease inflammation, relieve pain, and improve visual outcomes. However, they are known to have significant side effects, whether topically or systemically administered. Not much is known about the incidence of Steroid-Induced Ocular Hypertension (SiOH) in adult Ghanaians undergoing cataract surgery. Considering the immense negative impact visual impairment has on the quality of life of those affected, it is imperative to know the incidence of SiOH in the Ghanaian population. This would help in outlining preventive measures for potential ocular complications among patients undergoing cataract surgery.

General Aim

To determine the effect of steroid eye drops on intraocular pressure in patients post-cataract surgery and its associated risk factors.

Methods

This is a prospective cohort study of the effect of steroid eyedrops in patients post-cataract surgery at Korle Bu Teaching Hospital and Emmanuel Eye Centre. Patients undergoing cataract surgery were recruited into the study after informed consent. Demographic information, history and findings from ocular examinations were documented using a structured questionnaire. Baseline intraocular pressures were recorded. Post-operative intraocular pressures were measured on day one, weeks one, five and thirteen after surgery. Continuous numerical data were summarized as mean and Standard deviation (SD) and categorical data as percentages (%). Mean change in intraocular pressure from baseline was computed. Risk factors for SiOH were analysed using a Binary Logistic Regression Model and presented as Odds ratios and 95% Confidence Intervals. Kaplan-Meier survival function was used in calculating the average time (days) to develop SiOH among study participants. P-values less than 0.05 were considered statistically significant.

Results

A total of 124 patients participated in this study with a mean age of 66.1±13.6 years. Majority 75 (60.0 %) of the study participants were females. The overall mean pre-operative intra ocular pressure (IOP)in the study eyes was 17.8±4.4 mmHg with a 5.3% increase in IOP from baseline

which was not statistically significant (p = 0.061). The incidence of SiOH in the study was 29% on post-operative day one and reduced to 1.6% at 13 weeks. In a univariate and multivariate analysis, there were no risk factors associated with the development of SiOH . A sub analysis of the ocular responses however picked up age as a risk factor for responding to the use of topical steroids. Participants aged 70 years and above were more likely to respond to the use of topical steroids after cataract surgery though this did not translate to a significant likelihood of developing SiOH in this cohort of patients undergoing cataract surgery. From Kaplan-Meier analysis, the overall mean time (days) to develop SiOH among the study participants was 55.3 days (95% CI= 47.3 – 63.3 days).

Conclusion

SiOH post-cataract surgery is a common complication in this study cohort with an incidence of 36.3 %; most of which (29%) occurred within the first month post-operation. There were no risk factors associated with the development of SiOH in this study. Patients undergoing cataract surgery should have their IOP monitored closely during their early postoperative visits to prevent ocular complications associated with prolonged raised IOP.

Key words: steroids, cataract, cataract surgery, intraocular pressure, ocular hypertension.

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LIST OF ABBREVIATIONS

ABBREVIATION	FULL MEANING
BSS	Balanced Salt Solution
BCVA	Best Corrected Visual Acuity
COVID-19	Coronavirus-19
CCT	Central Corneal thickness
CME	Cystoid Macular Edema
CSR	Cataract Surgery rate
DCT	Dynamic Contour Tonometry
DNA	Deoxyribonucleic acid
DSEK	Descemet's Stripping Endothelial Keratoplasty
EEC	Emmanuel Eye Center
ECCE	Extra capsular cataract surgery
GAT	Goldmann Applanation Tonometry
GAGs	Glyco-amino glycans
FDA	Food and Drugs Authority
IBM SPSS	International Business Machines Statistical Package for the Social Science
IOP	Intraocular Pressure
ICCE	Intracapsular cataract surgery
IVTA	Intravitreal Triamcinolone Acetonide
KBTH	Korle Bu Teaching Hospital
LASIK	Laser in situ keratomileusis
MSVI	Moderate to Severe Visual Impairment
MSICS	Manual Small incision cataract surgery

NCT	Non-contact tonometry
ORA	Ocular Response Analyser
OVD	Ophthalmic Viscoelastic Devices
OPD	Outpatient Department
POAG	Primary Open Angle Glaucoma
SD	Standard Deviation
SICS	Small Incision Cataract Surgery
SiOH	Steroid Induced Ocular Hypertension
SSA	Sub Saharan Africa
TM	Trabecular Meshwork
WHO	World Health Organization

CHAPTER ONE
INTRODUCTION

1.1 Background

Topical steroid agents are used in the postoperative management of majority of ophthalmic surgeries including cataract surgery, which is the most performed operation in ophthalmology.[1]As a result of its routine use, people who have had cataract surgery may be exposed to the risk of topical steroid intra-ocular pressure response.

Cataract, the leading cause of visual impairment in the world is an opacification of the natural eye lens.[2] In 2010, cataract was the cause of visual impairment in 35.1 million people and the cause of blindness in an estimated 10.8 million people. In 2010, 33.4% of blindness and 18.4% of severe or moderate visual impairment worldwide was caused by cataracts.[3] These figures have increased. Currently, cataract accounts for 94 million people being visually impaired. [113]Greater than 90% of the estimated world prevalence of cataract is seen in lower to middle-income countries which describes most countries in the Sub-Saharan region of Africa.[3] Of the 285 million visually impaired people in the world, cataract accounts for half of this number. Out of this, 39 million (13.7%) are blind.[4] Twenty-six million people in Sub-Saharan Africa are visually impaired from cataracts, with 5.9 million (22.7%) people blind.[5,6]

In standard clinical care, steroid agents are routinely used as effective suppressants of postoperative ocular inflammation.[7] This reduces the complication rate since most patients now expect good vision after cataract surgery. Uncontrolled inflammation may cause further unwanted complications like cystoid macular edema, intraocular pressure (IOP) rise and excessive cicatrization .[8] The IOP rise after topical steroid application is usually modifiable and can be managed mostly with tolerable medical therapy. However, the IOP spikes may be elevated enough and protracted to cause ocular complications such as glaucomatous optic neuropathy, reduced wound strength and central retinal vein occlusion.[8]

The detection of possible steroid-induced IOP rise makes it key to measure IOP during postoperative visits after any intraocular surgical procedure.[9,10] In the ophthalmic community, aside from people who have been diagnosed with glaucoma or ocular hypertension, there are no universally acceptable risk factors for determining which people have a high probability of having a clinically significant topical steroid induced ocular hypertensive response.[4,7,10–14]

Cable et al, had the rate of increased intra ocular pressure in a series of twice daily dosing of difluprednate following a 100 uncomplicated cataract surgeries to be 5% with 100% in patients with open angle glaucoma.[15]

In fact, steroid induced ocular hypertension with its subsequent risk for steroid-induced glaucoma remain the major disadvantage of topical steroid therapy.[16] Some people, mostly glaucoma patients are known to develop a substantial rise in IOP when administered topical steroids in small doses or over short periods of treatment. In such individuals cautious monitoring of IOP is important.[7] Anecdotal evidence shows that clinicians in our tertiary facilities are not quick to taper patients off steroids postoperatively. There is a paucity of data and studies in our West African sub-region on IOP spikes after post-operative administration of steroids. There is also lack of evidence-based protocols on the use of post-operative steroids for use by clinicians at the centers of study, resulting in patients being on steroids for prolonged durations.

1.2 Problem statement

In Ghana, the prevalence of cataract is high in older people, with roughly 1 in 20 people who are 50 years or older reporting having been diagnosed with cataract before.[17] Cataract is the prevailing cause of blindness and visual impairment in Ghana with Glaucoma categorized as the second major cause of blindness among pensioners in Ghana. Glaucoma also accounts for a substantial number of pensioners with moderate-severe visual impairment (MSVI). It is the third leading cause of MSVI among pensioners in Ghana.[18]

In Ghana, cataract surgery is the most frequent surgery performed by Ophthalmologists with post-operative steroids given routinely to manage intraocular inflammation. Currently, steroids are considered the benchmark for the management of ocular inflammation, nonetheless, they are also associated with some side effects, including prevention of the immune system mechanisms, delay in wound healing process, and IOP spikes.[7]

Steroids also aid in the relief of analogous symptoms, such as pain on exposure to sunlight, conjunctival injection, chemosis, ocular pain, and tenderness. Mechanisms at the cellular level include, repression of cellular infiltration, dilation of capillaries, fibroblasts proliferation, deposition of collagen fibres and a resulting scar. [19]Considering the frequency at which steroid

drops are used post-operatively, it is imperative to know the effect it has on an African population.

Data on the sequel of steroid drops after cataract surgery is limited which could explain the acceptance and wide use of scientific research results from other regions as representative of our sub-regional experience. Local studies could enrich available data by corroborating existing research findings or making new findings.

1.3 Justification

Review of available literature suggests that steroid induced ocular hypertension is prevalent in the Caucasian population and may lead to glaucoma and its devastating consequences.[13,19,20,21] Topical steroids are routinely used post cataract surgery for a minimum of six weeks in the research centers.

There are practitioner-dependent variations in steroid therapy, with some doctors using a steroid regimen of 2 hourly and others four times daily with antibiotic drops four times daily starting from first post-operative day and then tapering the steroid over the following month if there are no complications. Antibiotics are usually discontinued within the first month for uncomplicated surgeries. Anecdotal reports at the centers under study show that some patients may remain on topical steroids for extended periods e.g., 3 months or more before steroids are stopped.

Paucity of data on the incidence of steroid-induced ocular hypertension (SiOH) after cataract surgery in Africa may be the cause of lack of standardized therapeutic use of steroids in our African sub region. A study by Easty et al showed that IOP in a small group of South African Bantus responds less dramatically than that of Caucasians to topical steroids.[22] This study, however, was done in a small population of 52 bedridden patients.

Due to the paucity of information on the prevalence of SiOH in the African population genetically predisposed to glaucoma after review of literature from PubMed, Google scholar, Ovid Medline, Web of Science, Scopus and lilacs,[23] it is essential to gather data on the effect of topical steroids post cataract surgery. This is especially important, since some studies have shown people of African descent to be more genetically predisposed to advanced primary open angle glaucoma.[24] Ghana has one of the highest prevalence of primary open angle glaucoma in

the world, [26,27] and with glaucoma being a risk factor for SiOH, it's imperative that the effects of steroids on intra ocular pressure is known in our setting to guide practitioners when administering this drug.[26] It's also essential since SiOH can lead to secondary glaucoma [9] especially in our already predisposed population. Korle Bu Teaching Hospital serves as a major referral center in Accra, the capital city of Ghana and is considered ideal for this research since they receive patients from all over Ghana and the neighbouring countries.

It is expected that the results of this study would highlight the risk factors for the development of SiOH post cataract surgery among Ghanaians. The finding of significant prevalence of SiOH could also draw attention to the problem in our population. This should influence the post operative management of cataract patients with steroid eye drops and reduce the risk of SiOH in post op cataract patients. It will also provide a platform for uniformity in the administration of post-operative steroid use i.e predforte applied four times daily after cataract surgery is sufficient to control inflammation. The findings of significant prevalence of SiOH may inform practitioners to modify their practice and aid in the training of allied eye care practitioners at outreach centers.

1.4 General aim

To determine the effect of postoperative steroid eye drops on intraocular pressure and associated risk factors at Korle Bu Teaching Hospital and the Emmanuel Eye Centre.

1.4.1 Specific objectives

1. To determine the mean rise in intraocular pressure following cataract surgery in patients at KBTH and EEC with post- operative use of topical steroids.
2. To determine the incidence of steroid induced ocular hypertension post cataract surgery.
3. To determine the demographic characteristics and risk factors associated with steroid induced ocular hypertension post cataract surgery.

1.5 Null hypothesis

Topical corticosteroids use after cataract surgery does not cause a statistically significant rise in intraocular pressure in Ghanaians.

CHAPTER TWO

LITERATURE REVIEW

2.1 Cataract

Cataract, an opacification of the normal transparent eye lens, is responsible for 50% of global blindness, with the incidence increasing with advancing age. Worldwide, the older a person gets the higher the likelihood of developing a cataract.[2] Cataract is the prevailing cause of blindness in Africa, it is said to affect approximately half of the seven million blind people in the continent.[25] In Ghana, cataract remains the prevailing cause of avoidable and reversible blindness, accounting for 40–60% of MSVI and blindness due to glaucoma being the number one cause of irreversible blindness.[17] An estimated 8.4% of people aged 30 years and above have glaucoma in Ghana.[26,27]

Globally, the main causative factors of blindness include age-related macular degeneration, glaucoma, corneal opacities, uncorrected refractive errors, and diabetic retinopathy.[18] In Ghana, the major causes of blindness can be ascribed to amenable causes such as cataract and refractive errors. According to the Ghana Blindness and Visual Impairment Study and various other studies done across the country, the main causes of visual impairment and blindness included cataract, refractive errors, glaucoma, and retinal pathologies. [17,18,28] In Ghana, cataracts account for 54.8% of those blind.[28] A measure of the volume of cataract surgeries performed in a population is the cataract surgery rate (CSR). In Africa it is about 500 per million per year. [17] The national cataract surgical rate reached 25% of the WHO target in 2018.[17] Considering the importance of cataract and glaucoma and the high number of cataract surgeries performed each year, it becomes imperative that the effect of steroids used post operatively is known to serve as a guideline during routine administration after surgery.

2.1.1 Types of cataract surgeries

Generally, the common terms for cataract surgery are intracapsular and extracapsular cataract surgery.

- *Intracapsular surgery*

Intracapsular cataract surgery involves the careful removal of whole lens while it remains within its lens capsule. [29] This method is not often practiced by most ophthalmologists (except

in rare instances) as the visual outcomes are not so good and the intraoperative and postoperative complication rates are higher than the other methods. [29] It is used in cases such as trauma or lens subluxation when extracapsular surgery is difficult. The extracted lens is replaced with an artificial lens (typically referred to as an intraocular lens (IOL) implant). There are two options for replacing the lens, it can either be placed in the anterior portion of the eye, fixed onto the iris or scleral fixated. Though it has a short learning curve, it remains the least preferred choice due to its high rate of post-operative complications that arise from the big incision that is made and alterations in the pressure of the vitreous. [29]

- *Cryosurgery*

This method of intracapsular cataract surgery was popular and used more commonly from the late 1960s to the early 1980s. [29] Currently, it is primarily used in the management of lens subluxation. It is form of ICCE that utilizes liquid nitrogen, a cryogenic substance, a cryoextractor/cryoprobe. In this technique the cryoextractor/probe with its refrigerated tip binds to and immediately freezes the lens, allowing for its extraction. [29]

- *Extracapsular surgery*

Extracapsular capsular surgery (ECCE) involves extracting the lens from within the capsule and leaving behind the posterior capsule which serves as a blockade between the anterior and posterior parts of the eye as well as providing a site for the implantation of an artificial lens.[29] There are various methods listed below:

- *Phacoemulsification*

Phacoemulsification, this is the most modern cataract surgery and involves the use of an ultrasound machine to pulverize the nucleus into a mixture of emulsion and small pieces that can be aspirated through a dual lumen system of irrigation-aspiration. [29]The small incision gives two main advantages. Firstly, there is less alteration to the corneal configuration (which accounts for more than half of the dioptric power in the eye), giving a good postoperative unaided vision. Secondly, due to the confined space in which the surgery is performed, there is more control with less fluctuation of intraocular pressure, etc.[29]

In phacoemulsification, the main incision is a small incision made at the limbus i.e. the outermost part of the cornea. An ophthalmic viscosurgical device (OVD) is injected into the anterior chamber of the eye to maintain the space and protect the endothelium of the cornea during the surgery. A round continuous capsulorhexis is made in the anterior part of the lens capsule, usually about 5 or 6 mm in diameter. This allows for the removal of the pulverized contents of the lens, with the phacoemulsification handpiece. Once the lens capsule has been

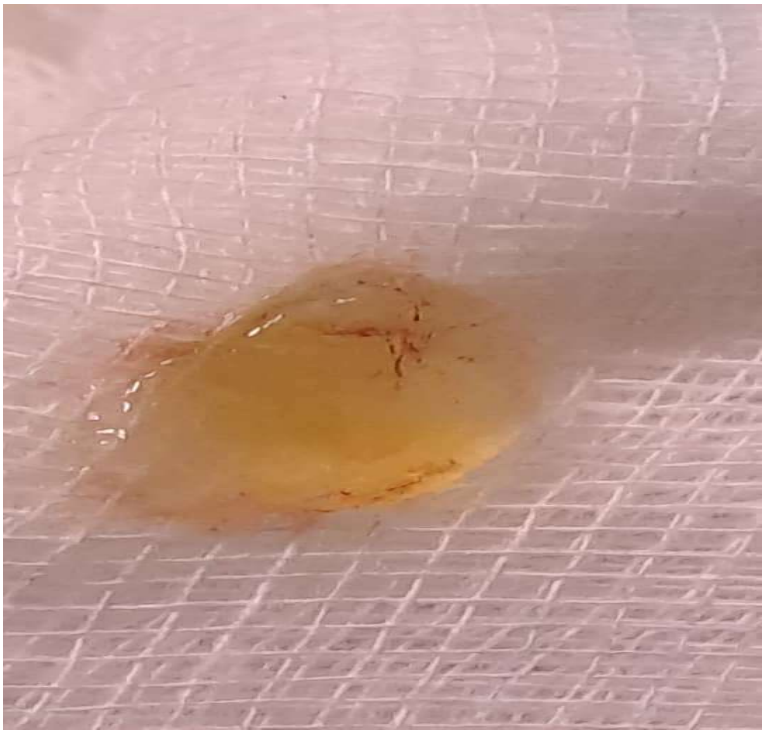
emptied, more OVD is placed into the capsule to create space for the foldable intraocular lens implant which is placed within the capsule. The surgeon then removes all remaining viscoelastic material and ensures a watertight incision. Usually, suturing is not required. [29]

- *Manual small incision cataract surgery (MSICS):*

This method involves removing the lens nucleus through a carefully made self-sealing scleral tunnel wound. It is an improvement of the previously popular ECCE and involves the construction of a watertight scleral tunnel which does not need to be sutured. The "small" in the name stems from the wound being smaller when compared to the original ECCE, though it is still relatively bigger than a phacoemulsification (phaco) incision. [29]

Trials comparing MSICS vs phaco in dense cataracts have found no significant differences in postoperative visual acuity, with MSICS being cheaper and being performed over a shorter duration.[33] This conventional method is suitable for patients with dense cataracts or in situations where phacoemulsification is inappropriate.

Figure 2. 1: Nucleus of a mature cataract after ECCE



Source: Picture by Researcher

2.2 Anaesthesia in ophthalmic surgery

General anaesthesia for surgery was introduced in the middle of the 19th century. Koller and Knapp are considered the pioneers of local anaesthesia for cataract surgery. [30]Topical cocaine was introduced as an anaesthetic agent by Koller in 1884 while retrobulbar anaesthesia for ocular surgeries was introduced by Knapp.[31] Orbicularis block was introduced by Van Lint, O'Briens, and Atkinson in the early 19th century. [30]

Local anaesthesia techniques have evolved in the last 25 years from posterior peribulbar to "no anaesthesia" methods. [30] The various anesthesia modalities in Ophthalmic surgery include

1. General anaesthesia
2. Local anaesthesia (with or without sedation).
3. Topical Anaesthesia
4. Intracameral anaesthesia
5. Cryoanalgesia

2.2.1 General anaesthesia

General anaesthesia is used when performing pediatric cataract surgeries and for other selected adult patients (i.e., mental retardation, autism etc.), where the patient may not be compliant for local anesthesia or remain still during the procedure. General anesthesia involves the use of diverse pharmacological agents for good anesthesia, i.e., for pain control, relaxation of muscles, inhibition of all reflexes including somatic reflexes, and somnolence. [31]

Overtime, with advancing research, we have moved away from the use of very potent, toxic, and long-acting agents. The drugs commonly used include Opioids (μ receptor agonist): Fentanyl, Remifentanil, Alfentanil, Benzodiazepine (sedative/hypnotic): Midazolam, anesthetic gases: Isoflurane, Sevoflurane, and intravenous anesthetic agent Propofol (which in low dose can be used as sedative with topical anesthesia). The risks and costs however make it less common for ophthalmic use. [30]

2.2.2 Local anaesthesia techniques

These include retrobulbar anaesthesia, peribulbar anaesthesia, sub tenon anaesthesia and subconjunctival injections. [30,31] These methods are able to achieve levels of analgesia and akinesia that facilitate surgical activity for the clients. The safety profiles of these methods have to be considered carefully in the option of anaesthesia to use. Retrobulbar and peribulbar anaesthesia risks retrobulbar hemorrhage, globe perforation and brainstem anaesthesia. [30-33]

Muscle injury can occur during the injection process for all the injectable anaesthetics with resulting strabismus. [31] These methods are the most commonly used at the study sites.

2.2.3 Topical anaesthetics

Topical anaesthesia for ocular surgery was reintroduced by Fichman in 1992. Topical anaesthesia provides anaesthesia by blocking the long and short ciliary nerves, nasociliary, and lacrimal nerves. [32] It has the advantage of avoiding the possible complications of retrobulbar anaesthesia which is given blindly. The methods include anaesthetic drops, gels or sponges soaked in the anaesthetic agent and placed in the fornix during surgery. [32] There has been a general trend toward this method because of safety and effectiveness in reducing pain in phacoemulsification surgery. This method does not relieve pain associated with traction of the iris, the zonule, and the ciliary body hence the need for intracameral anaesthesia. Occasionally the need arises to combine an injection method (like peribulbar) with the topical because of inadequacy of the topical to provide the needed anaesthesia. [32,33] Today, different agents are available on the market for topical anesthesia like Procaine (1%/2%/10%), Proparacaine (0.5%), Oxybuprocaine (0.4%), Tetracaine (0.5%/1%), Bupivacaine (0.25%/0.5%), Etidocaine (1%), Lidocaine (0.5%/1%), Prilocaine (4%), and Ropicacaine (0.2%/1%). [30,31]

2.2.4 Intracameral Anaesthesia

Intracameral technique of anaesthesia was introduced by Gills in 1992. [30,31,33] A small amount (0.2 mL) of preservative-free lidocaine hydrochloride (10 mg/mL/ 1%) is given into the anterior chamber of the eye at the onset of the surgery by the surgeon. More anaesthetics are given when the patient develops some amount of pain during the surgery. Either topical amethocaine hydrochloride (1%) drops and/or additional intracameral lidocaine hydrochloride (1%) is given. [33]

2.2.5 Cryoanalgesia

Cryoanalgesia for cataract surgery is a modification of the “no anaesthesia “ method introduced in 1999 by Gutierrez–Carmona. In this method, with the exception of povidone iodine drops all other solutions to be used during the surgical procedure are cooled to 4° C.[30,32] Pre-surgical procedures involve placing a cold gel over the eye for 10 minutes. Irrigation of the eye is done with cold balanced salt solution to provide an anaesthetic effect during the surgery. The cooling effect provided by the solutions serves as a form of anaesthesia. [30-33] Though this

has been shown to be a safe method for cataract surgery with good pain control, it is not appropriate for every cataract and for some patients.

2.2.6 No Anaesthesia

The "no anaesthesia" technique for cataract surgery was introduced in the late 90" s by Amar Agarwal. It involves performing cataract surgery without the use of any form of anaesthesia. No retrobulbar, topical or intracameral drugs are used. [33]Though it ensures surgery without any anaesthetic complications for the patient, it can be quite stressful for the surgeon due to the high level of patient compliance required. [30]

The main issues raised was how it is possible to do cataract surgery without any anaesthesia when the cornea is highly innervated. The explanations given are: The superior cornea is less sensitive than the central cornea due to the varying distribution of the density of nerve fibres supplying the cornea. [30,31]

The corneal sensitivity of blacks, Chinese and dark-brown eyed Indians is said to be four times less than blue-eyed Caucasians, an increased level of exposure to ultraviolet rays in people in developing countries is postulated to result in a significant loss of corneal sensitivity. [30] The "no anaesthesia" technique has not gained acceptance in the ophthalmic community due to the reliance on patient co-operation and the increased stress on the surgeon.

When deciding on the type of anaesthesia to use during cataract surgery several factors must be considered. This includes proper case selection and the experience of the ophthalmic surgeon who is going to operate. Different surgeons may choose different types of anaesthesia when evaluating the same patient. The surgeon's skill and expertise, level of patient co-operation, type of cataract, related ocular co-morbidity like corneal scars, weak zonules, etc. are prime factors to consider when deciding on which type of anaesthesia to use. [31]

2.3 Intraocular pressure /glaucoma

2.3.1 Normal intraocular pressure

Intraocular pressure (IOP) refers to the aqueous pressure inside the globe. Pressure is calculated as force per unit area; IOP is thus measured by calculating the amount of force exerted by the fluid inside the eye (aqueous humour) on the internal surface area of the anterior chamber of the eye.[34] The IOP in theory can be determined by the Goldmann equation, which is IOP = (F/C) +

P, where F represents aqueous flow rate, C represents aqueous outflow, and P is the episcleral venous pressure. [34,35]

IOP is altered when there are fluctuations in any of these variables. Aqueous humour dynamics consists of an interplay between production by the ciliary body of the eye and drainage of same from the posterior chamber to the anterior chamber and through the trabecular meshwork to Schlemm's canal and finally being drained into the episcleral venous network. [37]
There is a non-Gaussian distribution of IOP among populations. Large population studies in the United States indicate an average IOP between 15-16 mmHg with about 95% of people having an IOP between 10 and 21. This is like what pertains in Ghana and Nigeria, where the mean IOP is 15.5 in both countries. (normal range-10-21 mmHg). [36,37]

With increasing age, IOP tends to skew towards the higher pressures especially in persons forty years and above.[36-38] Approximately less than 2% of the population have IOPs higher than 21mmHg and lack any form of optic neuropathy or visual field defect (ocular hypertension).
Also, individuals within the normal range exhibit signs of optic nerve damage and visual field defects (normal tension glaucoma). Hence using IOP as a sole criterion for glaucoma screening would result in significant numbers of Glaucoma patients being missed and thus this position was revised.[38] Elevation of intraocular pressure is still seen as a key risk factor for the development and management of glaucoma considering that this is the sole parameter that is targeted in therapeutic interventions. [40-42]

In essence, normal IOP is the pressure at which there is no glaucomatous or visual field defect, [35] and this is found by a complex interrelationship between aqueous humour production and drainage in the eye as well as some environmental and genetic factors.
It has a circadian rhythm with highest figures during the early hours of the morning and the values reduce as the day wears on over a range of about 2 – 6 mmHg.[11] The higher figures for the early hours are attributed to the recumbent position during sleep which is associated with higher pressures. [35]

2.3.2 Glaucoma

Glaucoma is an optic neuropathy characterized by retinal ganglion cell damage and associated visual decline, which are seen clinically as enlargement of the optic disc cup and loss of visual fields.[35,46]

According to a study done in 2013 by Kyari et al, Ghana was ranked as one of the countries in Sub Saharan Africa (SSA) with a high prevalence of glaucoma.[39] Prevalence of glaucoma in an urban setting in Ghana was 6.8%. Prevalence in this study was higher in men and 96.7% of participants diagnosed with glaucoma were not aware they had the disease. [27] In a recent population-based study conducted in Ghana, glaucoma accounts for 19.4% of blindness.[28] A study in Ghana showed glaucoma as the second prevailing cause of blindness among pensioners and causing 12.9% of blindness. [18]Retinal diseases accounted for 4.8% of blindness. Age-related macular degeneration (3.2%), cornea opacities (2.7%), phthisis bulbi (2.7%), optic nerve related (2.2%), with other causes contributing to 9.1%. [18]

Also, the public health burden of glaucoma in Africa was emphasized at two major summits on glaucoma care in Africa, where a decision was made to enhance and involve glaucoma management, training and education into current programs. [39,41]

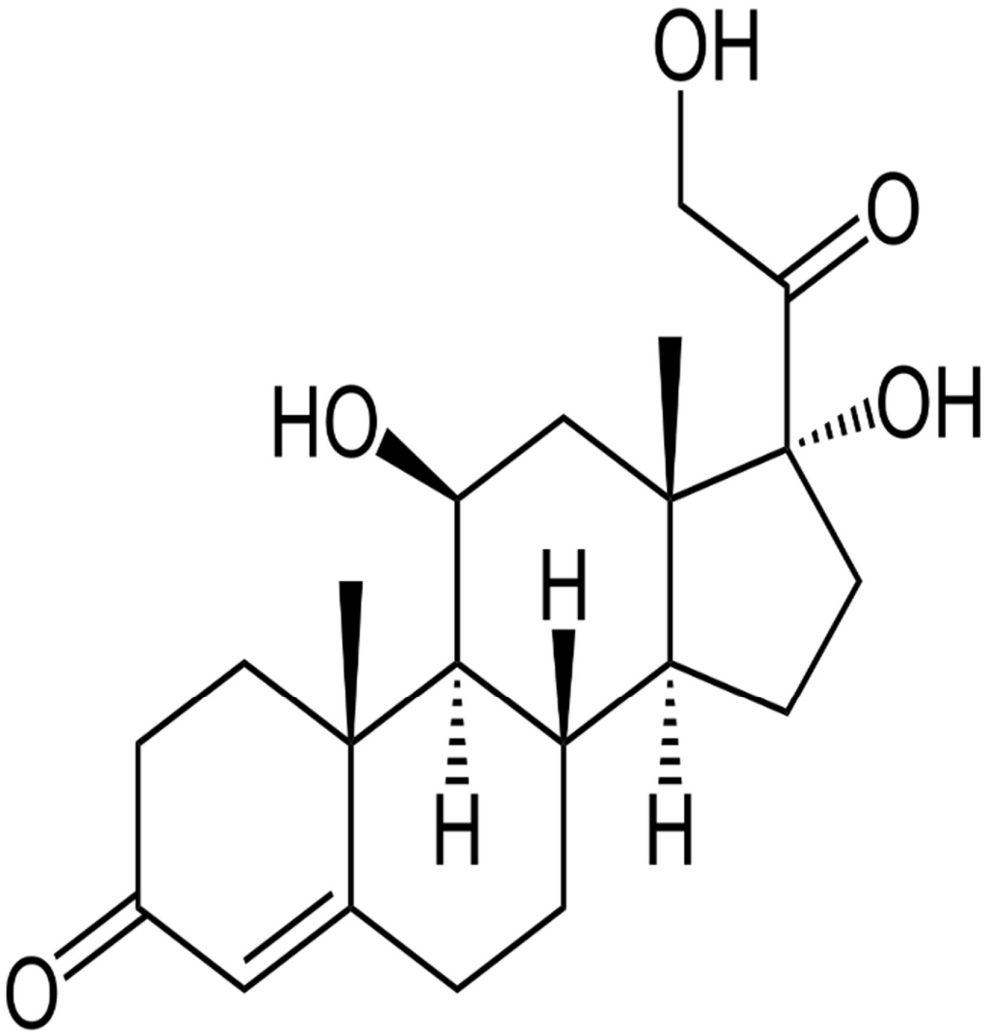
In the Upper East region of Ghana, one third of all the patients reported blind in both eyes while 50% were blind in one eye. Of those blind in one eye, over 70% had end stage disease.[42] Also, 52% of patients seen in northern Ghana in 1990 were blind and young.[42] In Southern Ghana, blindness from glaucoma has been recorded as 24%. [43] Up to 94% of glaucoma patients diagnosed in Akwapim South of Ghana were young and were unaware they had the disease. [26] These data serve to show the importance of glaucoma when considering visual impairment in our sub region and the need to take measures to detect and curb it.

2.4 Steroids

The advent of corticosteroids has seen it being applied in almost all aspects of medicine and with a wide variety of routes of application. [44] They are synthetic analogs of the naturally occurring steroid hormones produced by the adrenal cortex and comprise of glucocorticoids and mineralocorticoids. The synthetic analogs have various glucocorticoid and mineralocorticoid effects. Glucocorticoids are mainly involved in metabolism and are used in immunosuppression, controlling inflammation, and constriction of vessels. Mineralocorticoids on the other hand are involved in the regulation of water and electrolytes balance by modulating cell transport in the kidneys. [45]

The term corticosteroids when used, generally refers to the glucocorticoid effect. They are mainly stress hormones involved in the regulation of essential physiologic processes. [44,45]

Figure 2. 2: Chemical structure of corticosteroid [46]



Source: Barnes PJ. Inhaled Corticosteroids. Pharmaceuticals (Basel). 2010 Mar 8

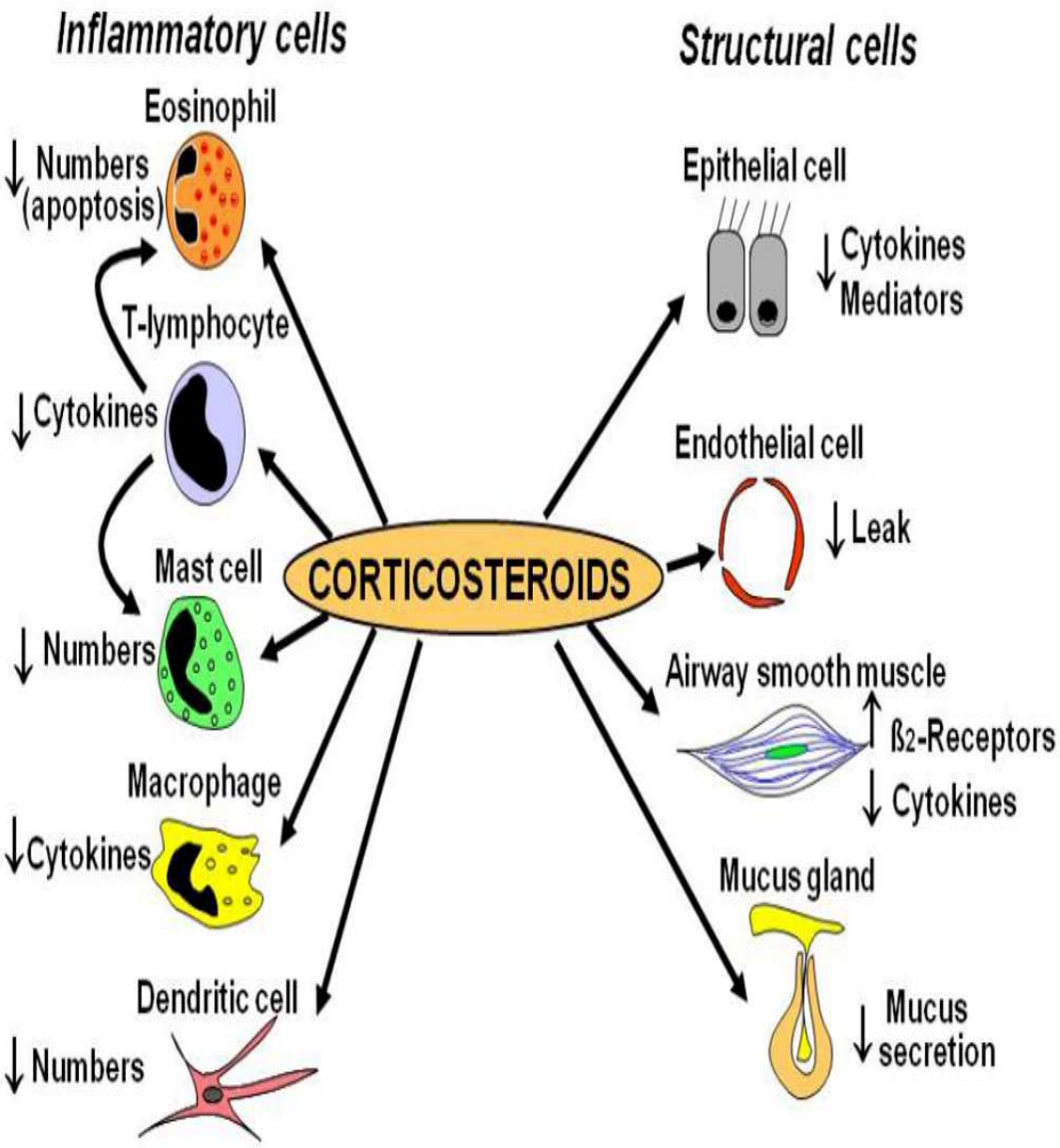
2.4.1 Mechanism of action

There are several pathways through which the effects of corticosteroids are manifested in the human body. These include, and arenot limited to their anti-inflammatory and immunosuppressive effects, their effects on protein and carbohydrate metabolism, water and electrolyte, central nervous system, and blood cells. [47] Their mechanisms of action can also be classified as either genomic or non-genomic. The former is primarily mediated through the glucocorticoid receptor and contributes to the anti-inflammatory and immunosuppressive effects of steroids in the human body.[45]

Scientist have stipulated that the glucocorticoid receptor is located within the cellular cytoplasm and, upon binding, moves rapidly into the nucleus of the cell, where it affects gene transcription and impedes gene expression and translation for inflammatory and structural cells. [44,45] As a result, there is a retardation in pro-inflammatory cytokines and mediators along the inflammatory response cascade. [45]

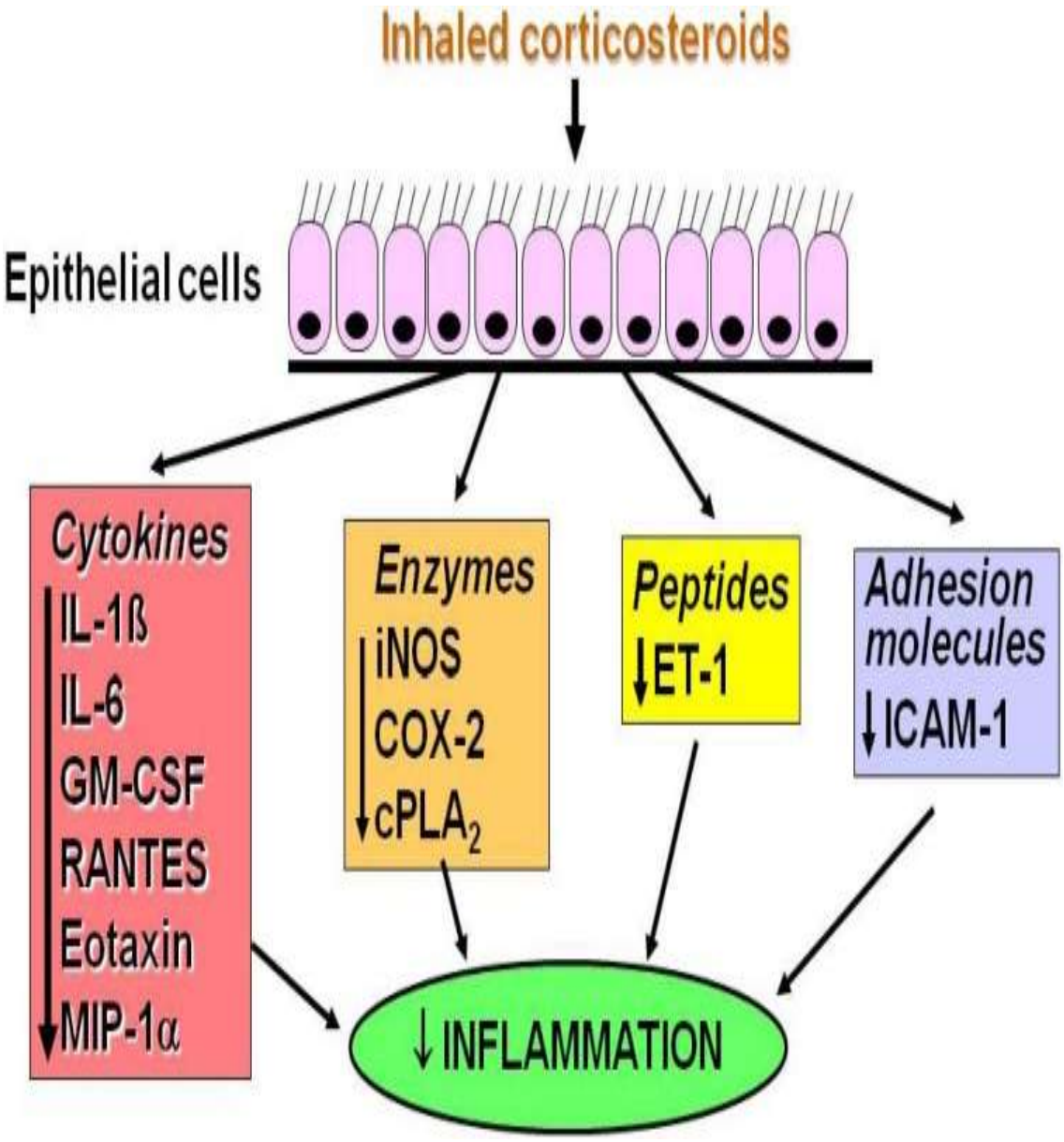
The latter, that is the non-genomic response occurs more rapidly as compared to the former. Its pathway is through interactions between either the intracellular glucocorticoid receptor or a membrane-bound glucocorticoid receptor. [44] When a receptor is activated, it immediately, initiates a cascade of events, which includes the suppression of phospholipase A2. This step is important for producing inflammatory cytokines, suppression of arachidonic acid, and regulation of cell death in immune cells. [44,46] Corticosteroids also have the potential to suppress the production of B cells and T cells involved in the inflammatory process when present at high concentrations. [44]

Figure 2. 3: Mechanism of action of steroids [46]



Source: Barnes PJ. Inhaled Corticosteroids. Pharmaceuticals (Basel). 2010 Mar 8

Figure 2. 4: Inflammation suppression by steroids



Source: Barnes PJ. Inhaled Corticosteroids. Pharmaceuticals (Basel). 2010 Mar 8

2.4.2 Formulations, routes of administration and management

Various factors come into play when deciding the route of administration for corticosteroids with the main target being the disorder treated. There are various routes such as intravenous, oral, inhalational, topical, injected and suppositories.[44] Healthcare workers must consider many factors when choosing steroid therapy. These include the route of administration, concentration, frequency of use, and length of therapy.[48]

Commonly used routes of steroid treatment in cataract surgery include topical and intracameral instillation. The latter being used in situations where there are complications such as intra-operative vitreous loss. [48]

The ocular hypertensive effect has been noted to be remarkable with topical application but elevation of the IOP has been established with all the formulations. [48,49] SiOH has been reported with topical eyelid administration, nasal and inhaled corticosteroids as well as local injection of steroids. [52] The use of repositories or depot preparations of steroids has the potential to give extended doses of the drug at local concentrations but this particularly raises the risk of long term increases in IOP and a heightened risk of glaucomatous optic neuropathy. [114] This is because the steroids are not easily removed and their effects not fully counteracted by antiglaucoma medications: intravitreal administration of triamcinolone has been reported to produce mild to moderate IOP elevations which were treated with one or two topical antiglaucoma medications. [114]

2.5 Steroid induced ocular hypertension and other ocular complications of steroid usage

The use of steroids is accompanied by several ocular side effects. SiOH following steroid use has been recorded in several studies. [48-52] This may sometimes be avoided after cataract surgery by replacing them with the nonsteroidal/anti-inflammatory options and in situations where this cannot be done, monitoring the IOP is important no matter the dose and length of the steroid therapy. Other side effects from steroid usage include cataract formation (usually a posterior subcapsular cataract which forms at the back of the lens), delayed wound healing (due to the inhibition of growth factors critical in wound healing), increased susceptibility to infections, tear film instability and epithelial toxicity[8,52.]

2.5.1 Complications of cataract surgery and steroid usage.

Cataracts surgery complications associated with ocular inflammation include corneal oedema, IOP rises, cystoid macular edema, and opacification of the posterior lens capsule. With increase in knowledge, majority of patients have expectations of a 6/6 vision after cataract surgery without any complications, it is standard practice to use anti-inflammatory substances especially in the following situations:

- Frequent topical steroids in cases of severe inflammation such as retained cortical matter.
- Intracameral use of steroids to help visualize and control inflammation when vitreous loss occurs following posterior capsular rent
- Subconjunctival steroid injection to control post-op inflammation.

2.5.2 Potency of Steroid, time of onset and duration of therapy.

The more potent the preparation, the higher the ocular hypertensive effect and the earlier the onset of action. [52] Stewart et al determined that it took topical Dexamethasone a mean of 22.7 days to effect a response of > 10 mmHg from baseline compared to 29.5 days with Fluorometholone Acetate, a one week difference which showed statistical significance ($p = 0.015$). [73] This is taken into consideration in the deployment of depot preparations of steroids because use of potent preparations are associated with high intraocular pressures.

Increase in IOP of ≥10 mmHg over baseline is seen to be clinically significant.[7,10,11,19,22,49] It has been shown that there are generally three groups of responders. Three categories of steroid responders were suggested from the IOP response to topical application of betamethasone and dexamethasone by Armaly and Becker [50,51]:

1. High responders (4 to 6% of the population) – developed an IOP greater than 31 mm Hg or a rise of more than 15 mm Hg from baseline.
2. Moderate responders (about 1/3 of the population)- developed an IOP between 25-31 mm Hg or a rise of 6-15 mm Hg from baseline.
3. Non-responders (about 2/3 of the population) – found to have an IOP less than 20 mm Hg or a rise of less than 6 mm Hg from baseline.

Topical steroids though used routinely, can produce various side effects, such as IOP spikes, cataract formation (in phakic individuals), and decreased wound healing.[8] It has been shown

that elevated IOP, if not managed, may lead to progressive optic neuropathy and visual field loss, leading to steroid-induced glaucoma.[16,19] The intraocular hypertensive response resolves in 1- 4 weeks [(11)] after cessation of steroid treatment and is said to be reversible and can be managed with careful monitoring to detect early changes and prevent vision threatening complication.[10,11]

Dexamethasone and Prednisolone are associated with higher steroid response than Fluometholone which is a less potent steroid. [73] The duration of therapy affects the steroid response with a higher response observed after a six-week treatment period compared with a 4 week period. [73]

2.5.3 Steroid induced glaucoma

In 1950 SiOH was reported, when prolonged use of systemic adrenocorticotrophic hormone was proven to cause an elevation of intraocular pressure (IOP).[16] Prolonged use of steroids through any route with raised IOP can result in optic nerve damage and hence steroid-induced glaucoma.[52]

Steroid-induced glaucoma is an induced and preventable disease. [10,11]The frequent use of steroids by health providers and abuse by patients themselves in developing countries points to a low level of knowledge about the disease.

Steroid-induced glaucoma can be prevented by taking precautionary measures such as the identification of risk factors. Monitoring for risk factors (like glaucoma or ocular hypertension, family history of glaucoma, high myopia, diabetes mellitus, and connective tissue disorder) can lower the incidence of glaucomatous optic nerve damage.[52]

2.5.4 Aetiology/Genetics

Stern in 1953 and Francois' in 1954 were the first to publish reports on steroid response. This was followed a decade later by two independent researchers, Armaly and Becker, who published results that changed significantly the importance of steroid response in the ophthalmic community. [50,51]

They proposed that topical steroid response followed a simple mendelian pattern of inheritance. The inheritance of this gene was closely associated with the inheritance of primary open-angle glaucoma. [50,51]

Following studies of first-degree relatives of patients, they demonstrated a trimodal frequency distribution of the steroid pressure response. Both group of workers used different variables to record the level of steroid response, and categorized them as low, intermediate, and high-pressure response, representing phenotypic expressions of the three genotypes. Later work by Kersey [11] concluded that eyes with trabecular meshwork insult are more likely to develop SiOH and the use of topical steroids should be avoided in patients with glaucoma, especially after ocular surgery when they are frequently prescribed.[11] Intraocular pressure should be monitored regularly in cases where they are required to be used for long periods.

Steroid induced ocular hypertensive effect is believed to have a genetic basis. Trabecular meshwork inducible glucocorticoid response or TIGR gene (recently renamed the myocilin gene) product with a molecular weight of 55kDa is inducible in invitro cultured trabecular meshwork cells with a 2–3-week exposure to dexamethasone.[53,54,55] The case for Myocilin's role in steroid-induced ocular hypertension is made stronger by the observation that steroid exposure leads to increased expression of the gene in TM cells. Furthermore, this rise in expression directly corelates with the rise in IOP with both rising after a period of latency referred to as a delay. Lastly, raised IOP and increased gene expression occur at similar doses of steroids.[54]

The trabecular meshwork has been shown to have a resistance to the outflow of aqueous humor in steroid-induced glaucoma. [48] This increased resistance is believed to be due to alterations in the extracellular matrix. Steroids modulate glucocorticoid receptors in the trabecular meshwork cells resulting in an increased resistance in the egress of aqueous humor and an IOP spike.[48]

Steroids cause an increase in resistance to trabecular outflow by the repression of the breakdown of extracellular matrix proteins and increasing their deposition in the trabecular meshwork.[63] Drainage of aqueous humor in the eye occurs through two main pathways i.e trabecular outflow which accounts for more than 70% of the outflow and the uveoscleral pathway. [35] Hence changes in the trabecular meshwork (main drainage site) leading to an increase in resistance is most likely to cause a rise in IOP. Evaluation at the cellular level of

the trabecular meshwork in steroid-induced glaucoma shows an increase in extracellular matrix protein in the meshwork.[61,66]

Changes intype IV collagen has been found in the trabecular meshwork of people with steroid-induced glaucoma.[63] Steroids cause accumulation of debris in the trabecular meshwork by prevention of phagocytosis by endothelial cells.[60] Steroids have been implicated in changes to the trabecular meshwork cell structure by its effect at nuclear level.[61]

Clark and Wordinger[61] proposed that steroid-induced glaucoma resulted from alterations in the trabecular meshwork which cause IOP spikes. [61] Myocilin gene which has been implicated in steroid-induced IOP increase,[53-55] has different mutations resulting in phenotypic changes.
Fan et al. [56] studied the effect of steroids on gene expression of human trabecular meshwork cells. They established the induction or repression of the same genes by triamcinolone acetonide and dexamethasone. This translates into a common mechanism of action for SiOH. [56] Tissue penetration and half-life may account for different steroids causing varying degree of IOP rise.[56]

Other mechanisms involved in steroid response include:

- Glycosaminoglycans (GAGs) are thought to play a major role in steroid induced raised IOP. The steroids cause polymerization of GAGs which imbibe water and swell up thus increasing resistance in the trabecular meshwork. [56-58]

- Intravitreal triamcinolone acetonide (IVTA) injections used in the management off retinal conditions has been shown to increase trabecular obstruction by the deposition of particles in the trabecular meshwork.[62]

2.5.5 Risk Factors for SiOH.

The following are considered to increase the probability of steroid-induced glaucoma after topical steroid treatment:

1. Patients with primary open angle glaucoma (POAG), their first-degree relatives and glaucoma suspects. [13]
2. Age. [14]
3. Others:

High myopia [64]

Eyes with history of corneal transplant.[65]

Laser in situ keratomileusis (LASIK)[66]

Autoimmune conditions such as diabetes mellitus or rheumatoid arthritis.[13]

2.5.5.1 Patients with primary open angle glaucoma (POAG), their first-degree relatives and glaucoma suspects

Patients with glaucoma and glaucoma suspects have a higher probability of developing SiOH. Some studies have shown glaucoma and glaucoma suspect as a risk factor for SiOH. [11,13] Becker and Mills[11] documented a high IOP response after application of steroids in glaucoma and glaucoma suspects. This was after the steroids had been applied for over a long duration of time.

The glaucoma group had a mean rise in IOP of 16.9 to 32.1 mmHg and the glaucoma suspect had a mean rise of 17.1 to 28.3 mmHg. Participants who did not have glaucoma or were not suspects had a lower mean rise of 13.6 to only 18.2 mmHg. Participants in the normal group were categorized into two groups. Those with a moderate increase and those who had no effect of the steroids on their IOP. Steroid therapy was associated with a decreased trabecular outflow in steroid responders. Stopping steroid therapy resulted in a fall of IOP to preoperative levels or within the normal range.[11]

2.5.5.2 Age

Age has been shown to be a risk factor for SiOH. A study by Armaly showed age and glaucoma to be risk factors for SiOH. Older eyes had a higher steroid response when compared to younger eyes and glaucomatous eyes had a higher response when compared to non- glaucomatous eyes.[14]

2.5.5.3 Other risk factors.

Other risk factors are: -High myopia-Chang et al demonstrated that younger patients with high myopia had a higher risk for a postoperative steroid response after uneventful cataract surgery and may require more frequent IOP monitoring or alternative topical anti-inflammatory medications. [64]

-Eyes with history of corneal transplant- Glaucoma after corneal transplantation is a leading cause of ocular morbidity after penetrating keratoplasty. [65] The incidence reported is highly variable with IOP elevation occurring after procedures such as deep lamellar keratoplasty (DALK), Descemet's striping-automated endothelial keratoplasty (DSAEK), and keratoprosthesis (KPro). [65]

2.6 Africans and glaucoma

A genetic association of advanced POAG in the *ENO4* locus was identified in people of African ethnicity in the ADAGES trial.[67] People of African Descent compared to European descent had higher IOP's, worse visual acuity and worse visual fields results. [67]

In the U.S., African Americans have the highest prevalence of glaucoma, 3.4% when compared to other races i.e 1.7% in Caucasians, and 1.5% in Hispanics.[23] African Americans with glaucoma have a higher risk of vision loss and blindness when compared to other populations in the U.S.; this is because they usually have a higher mean IOP and deficit in visual fields. [23,24] Due to their low socioeconomic background, majority of African Americans have limited access to medical care coupled with their higher risk of getting glaucoma earlier in life, they usually present with advanced glaucoma at medical facilities.[23] This can be likened to the situation in Ghana where a study in the Upper East region showed that 50% of people reporting to a health facility were already blind in one eye with over 70% having advanced glaucoma. [49] This is also the situation in Sub–Saharan Africa where there is increased prevalence of glaucoma with a reduction in access to medical treatment. [23]

A genetic study in Ghana investigated the association of genetic variants of the optineurin gene (OPTN, GLCIE) with POAG. One hundred and fortyPOAG and 130 non-glaucoma controls were evaluated. Several coding variants were identified such as E322K, S321S, V147L etc. but there were no statistically significant differences when cases and controls were compared. Two of the variants showed a relatively early onset of glaucoma and high IOP, > 30 mmHg. The study identified seven coding variants of the optineurin gene out of which three were unique to the Ghana population.[68]

2.7 Incidence of SIOH

Few studies have looked at the incidence of steroid induced ocular hypertension after cataract surgery. A study by Lorenz et al.[69] investigated the effect of prednisolone acetate 0.5% on the

intraocular pressure of 62 patients who underwent phacoemulsification. Patients were given either prednisolone acetate 0.5% four times a day or placebo for the first 48 hours and then given prednisolone acetate 0.5% four times daily for the remaining 14 days. Mean IOP was within the normal range in both groups, but three patients (4.8%) showed an increase in IOP.[69]

Korenfield et al[70] compared the effectiveness and ocular hypertensive effect of difluprednate 0.05% with placebo. [70] Four hundred and thirty-eight patients after ocular surgery were started on difluprednate 0.05% twice daily or four times daily or placebo twice daily or four times daily in the operated eye for the first 14 days post-surgery. The drops were then tapered off over a 14 days period and a 7-day safety evaluation period. The study results showed that difuprednate 0.05% when given twice daily or four times daily was effective in suppressing ocular inflammation and pain. [70] Three percent of patients in both difluprednate groups had a steroid-induced ocular hypertension as compared with 1% in the placebo group. The criteria for a clinically significant rise in IOP was an increase in IOP of greater than10 mmHg from baseline and an IOP of $\geq$ 21 mmHg. [70]

Smith et al.[71] did a similar study on 121 patients undergoing cataract surgery. They compared the efficacy of once daily dosing of difluprednate 0.05% to twice daily placebo in controlling postoperative inflammation and pain as well as the effect on intra ocular pressure. The drops were started a day prior to surgery and given over a period of 16 days. This was followed by a 14 day tapering off drops.[71]

Difluprednate was more effective in controlling postoperative inflammation and pain (74.7%) as compared to placebo (42.5%). However, three patients (3.7%) in the difluprednate group had a significant IOP rise (IOP > 10 mmHg and $\geq$21 mmHg) with no patients in the placebo group exhibiting a significant IOP rise.[71]

An evaluation of the effect of twice daily difluprednate 0.05% on the intraocular pressure of 100 open angle glaucoma patients undergoing phacoemulsification was done by Cable et al. Analysis showed that the incidence of ocular hypertension (IOP $\geq$ 10 mmHg) was 5% with majority of the IOP rise occurring on POD1 60% and 40% by POD7. Average increase in IOP was 17.8 mmHg.[15]

The early rise in IOP is postulated to be due to several factors I.e presence and type of glaucoma, the viscoelastic agent and surgical procedure. [114]To exclude the effect of viscoelastic, careful irrigation and aspiration of viscoelastic material from the anterior chamber but also from the capsular bag behind the implanted IOL was done.Akingbehin compared the ocular hypertensive response of fluorometholone 0.1% and dexamethasone 0.1% instilled four-times daily in 24 patients. Twenty-two eyes had provocative testing with dexamethasone 0.1% and followed 6 months later with fluorometholone 0.1%. Simultaneous bilateral testing with dexamethasone (right eye) and fluorometholone (left eye) was done in two patients. The provocative testing was stopped if patients showed an increase in IOP of 15 mmHg over baseline. The mean increase in IOP was 8.58 mmHg with dexamethasone treatment as compared to 2.96 mmHg with fluorometholone treatment. In this study steroid response of >10 mmHg was observed in 45.8% of dexamethasone- treated eyes and 4.2% of fluorometholone-treated eyes.[72]

Stewart et al. evaluated the steroid response of 17 patients when treated with fluorometholone 0.1% for 6 weeks, this was followed by treatment with dexamethasone 0.1% after a one-month washout period. All patients had a history of being steroid responders. The mean time taken to effect a steroid response of >10 mmHg as compared to baseline was longer, 29.5 days in the fluorometholone group when compared with 22.7 days in the dexamethasone group .[73]
From this study, an increase in IOP of >10 mmHg over baseline was proposed to be considered clinically significant. [73]

A study by Mohan et al found no statistically significant rise in intraocular pressure after administration of steroid eye drops following cataract surgery in an Asian population.[74] These studies show that SiOH is a common occurrence after cataract surgery with an incidence ranging from 3% to 60%. [15,69-73]

2.8 Cataract surgery and IOP

Currently, the common methods of cataract surgery in our sub region are manual small incision cataract surgery and phacoemulsification surgery. Many studies have shown a drop in IOP after either procedure of cataract surgery.[75-80] Studies have shown improved control of IOP after cataract surgery in patients with acute and chronic angle-closure glaucoma and the benefits are universally accepted. [80] Though the exact process of this IOP lowering effect is still not clearly

understood, substantial literature supports a modest long term drop in IOP after uncomplicated cataract surgery with implantation of a posterior chamber intraocular lens (PCIOL).[75-80]

Shingleton et al in a retrospective analysis of 148 patients who underwent cataract removal by phacoemulsification demonstrated a small but significant decrease in IOP at 3 and 5years post-surgery. Patients comprised of 3 groups: glaucoma patients, glaucoma suspects and no glaucoma. All groups demonstrated a drop in IOP after cataract surgery. [76]

Poley et al demonstrated that cataract surgery was effective in reducing and sustaining the reduction in intraocular pressure over a long duration (10 years). Cataract surgery with PCIOL may help in the management of adult glaucoma.[77]

Poley et al demonstrated a 17% decrease in mean IOP after comparing final postoperative intraocular pressure (10 years post-surgery) to baseline in 124 eyes. There was a proportional reduction in postoperative IOP reduction when compared to the preoperative IOP. Eyes with high baseline IOP had the greatest IOP decrease and eyes with lowest baseline IOP having a slight increase. There was a 34% drop in IOP at the last visit in the group with the highest mean preoperative IOP (24.7 mmHg). The IOP increased by 16% in those with low mean baseline IOP values. [77]

Another study did a follow up of 385 eyes after uneventful phacoemulsification surgery for 6 to 8 months. Participants were divided into glaucoma group, glaucoma suspects group, and no glaucoma group. Phacoemulsification was associated with a 1.1 to 2.5 mmHg drop in IOP at the end of the study period. There were no significant differences between the groups. Follow up was done for 6 to 8 months. Clear corneal and scleral tunnel techniques had similar results.[79]
Various explanations have been proposed for the reduction in IOP seen after cataract surgery. Comparing the anterior chamber in a unilateral pseudophakic eye with the contralateral phakic eye, the anterior chamber is seen to be visibly deeper in the former.[80] Using Scheimmpflug video photography, it was observed that the anterior chamber of open angle glaucoma patients was deeper (1.51 mm) than controls (1.35mm) 1 year post phacoemulsification. The surgery was also associated with widening of the chamber angles.[80]

Cataract surgery in patients with angle closure glaucoma was associated with a significant drop in IOP and a widening of the anterior chamber angle width. It was postulated that the postoperative widening of the anterior chamber angle may also cause an expansion of the

trabecular meshwork and thus enhance aqueous outflow and a drop in IOP. [80] Contraction of the lens capsule with a resultant zonular traction on the ciliary body was also suggested to play a role in IOP reduction in pseudophakic eyes. Traction on the ciliary body could cause a reduction in aqueous humor production and stability of the schlemm's canal.[79]The evidence for IOP lowering effect post cataract surgery supports that any intraocular pressure rises attained during uncomplicated cataract surgery in this study may be due to the steroid administration.

2.9 Measurement of IOP

Intraocular pressure measurement is done routinely in ophthalmic examinations and a precise measurement is required in glaucoma management. Tonometers are instruments used in the measurement of IOP. Measurements taken using an ideal tonometer should have the features of being accurate, reproducible, and repeatable. Additionally, an ideal tonometer should be portable, easy to use, simply calibrated, and standardized. [81-88]

There are a variety of tonometers currently available such as,

1. Indentation tonometry: Schiotz tonometer
2. Applanation tonometry: Goldmann Applanation Tonometer (GAT)
3. Noncontact tonometer: Pneumotonometer
4. Mackay-Marg tonometer and Tono-Pen tonometry
5. Transpalpebral tonometry
6. Manometry
7. Rebound tonometry

2.9.1 Schiotz tonometry

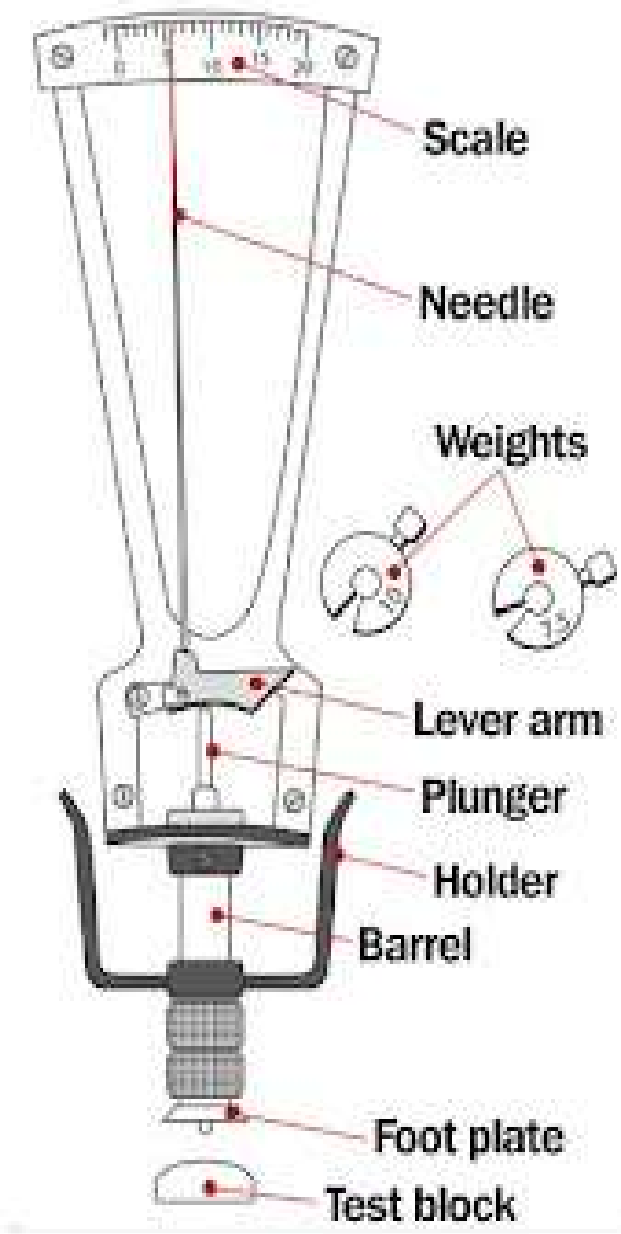
The Schiotz tonometer is a type of indentation tonometry which consists of a cylindrical barrel attached to a concave footplate and a holder which comprises of a needle and a horizontal scale numbered 0-20 (Figure 2. 4). A free-floating, cylindric-like plunger which is attached to a weight fit inside the barrel. The instrument is held vertically over the anterior portion of the eye, the plunger indents the cornea, and the minute amplitude movement is magnified by a lever arm to move a needle that gives a reading on a horizontal scale. A softer eye, with lower IOP, will result in a higher indentation and a higher reading on the scale.[88]

A conversion table that is provided by the manufacturer enables these readings to be converted to IOP in mmHg. To enable measurement of a wide range of pressure, various weights

(typically 5.5 g, 7.5 g and 10 g) are included in the set and can be added on to the plunger when required.

The advantage is that it's a small portable device which can be readily utilized in the field as well as in the recumbent position. This makes it ideal for screening and outreach teams. The effect of scleral rigidity tends to underestimate the intraocular pressure in subjects. Its readings are considered less accurate than the other tonometry methods. [88]

Figure 2. 5: Schiøtz tonometer [88]



Source: Editor: Syed Shoeb Ahmad;, Sub-Editor: Ghuncha Khatoon. Glaucoma Specialist Blog:The“Glog”:October2019[Internet].

2.9.2 Goldmann applanation tonometry (GAT)

The Goldman Applanation Tonometer is the gold standard for checking IOP since its introduction in 1955. Goldman Applanation Tonometry (GAT) is based on the Imbert–Fick principle, which states that for a dry thin-walled sphere, the pressure (P) inside the sphere equals the force (F) necessary to flatten its surface divided by the area (A) of flattening (i.e., P = F/A). It applies to surfaces which are perfectly spherical, dry, flexible, elastic and infinitely thin. Theoretically, average corneal rigidity (taken as 520 μm for GAT) and the capillary attraction of the tear meniscus cancel each other out when the flattened area has the 3.06 mm diameter contact surface of the Goldman prism.[88,89] The Goldman tonometer tip is applanated to the cornea with a measurable amount of force which translates into IOP. Each millimeter is equivalent to 10 mmHg.[81]

Errors in GAT do exist but most of the sources of error can be overcome when it is performed by an experienced person and adhering to available guidelines.[89] Some limitations or sources of error include:

1. Holding the eyelid to widen the palpebral fissure
2. Accommodation by patient
3. Holding of one's breath
4. Decentration of the tonometer tip
5. Prolonged contact of the tip with the cornea.

It has a limitation on the restriction of IOP measurement within a 1mm error. Other factors that place limitations on its results are poor technique, intra- and inter-observer variability, central corneal thickness, corneal curvature, hysteresis as well as tear film characteristics which have a direct effect on the measurements take. Thicker corneas may overestimate the IOP with thinner corneas underestimating IOP. Corneal oedema may cause a reduction in IOP readings. Guidelines for applanation tonometry help in minimizing errors in the measurement of IOP.[81] To minimize errors in the results from GAT, strict adherence to guidelines for applanation tonometry was applied throughout the study. Intra- and inter-observer variability was taken care of by limiting the measurement of IOP to only two ophthalmologists. An average of three readings within 2 mmHg reading of each other was used and in the event that there was a reading that required corroboration and confirmation, the Principal Investigator referred it to the other Ophthalmologist who was blinded to the reading of the PI. The confirmatory IOP

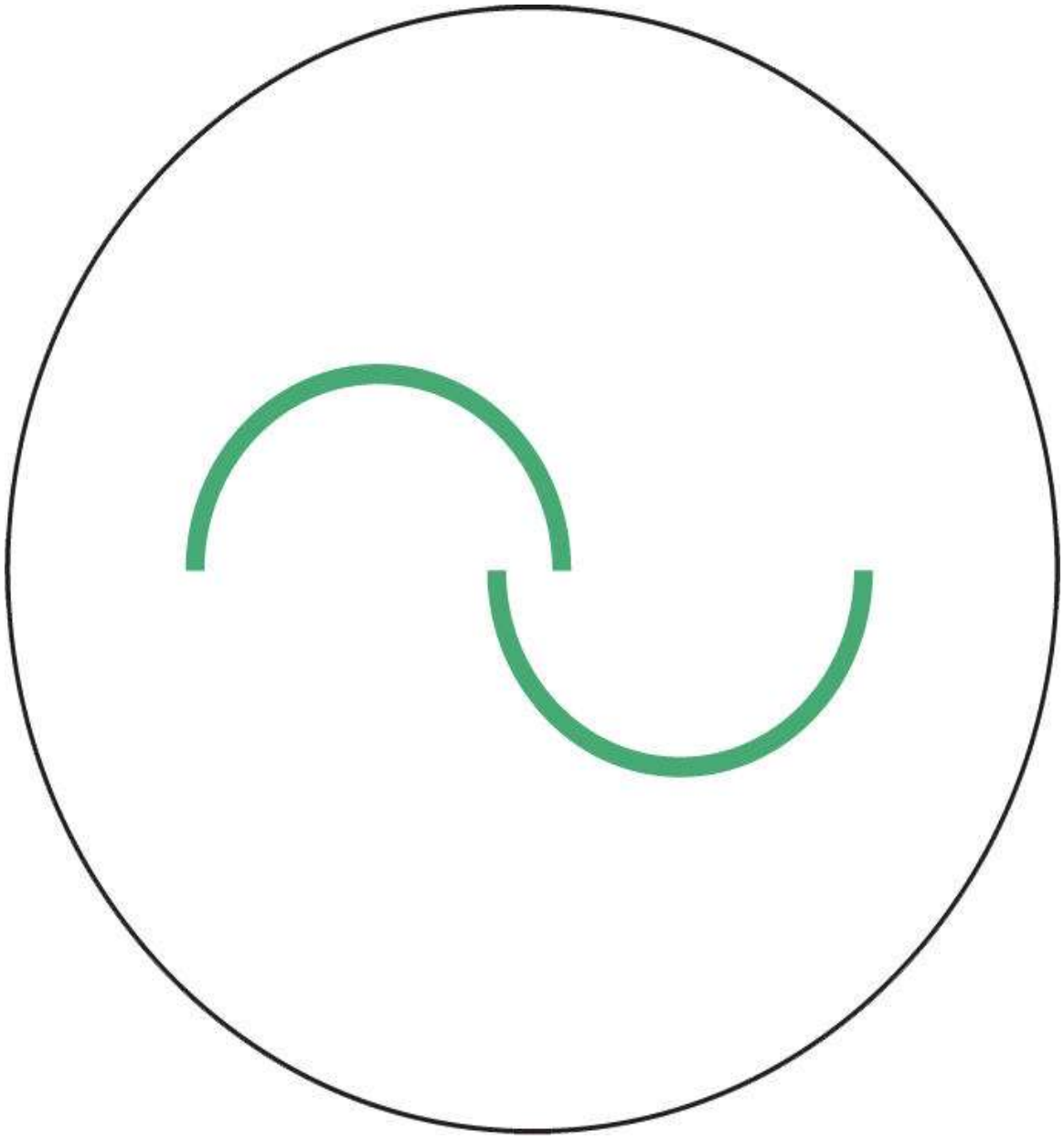
reading, if in agreement was used as the reading for the participant. GAT is routinely used in the eye clinic except in situations such as trauma or corneal ulcer.

Figure 2. 6: Goldman Applanation Tonometer [81]

Source: Stevens S, Gilbert C, Astbury N. How to measure intraocular pressure: applanation tonometry. Community eye Health

Goldmann Applanation Tonometer (GAT) is an instrument usually attached onto a slit lamp microscope. Fluorescein eye drops are instilled in the eye. The operator then gently applies the prismatic probe against the cornea and observes an optical pattern through the microscope. Two semicircular patterns termed as mires are adjusted till the semicircles' inner edges touch each other. The IOP (in mmHg) is then taken as ten times the contact force (in grams) needed to achieve this configuration. [81,89]

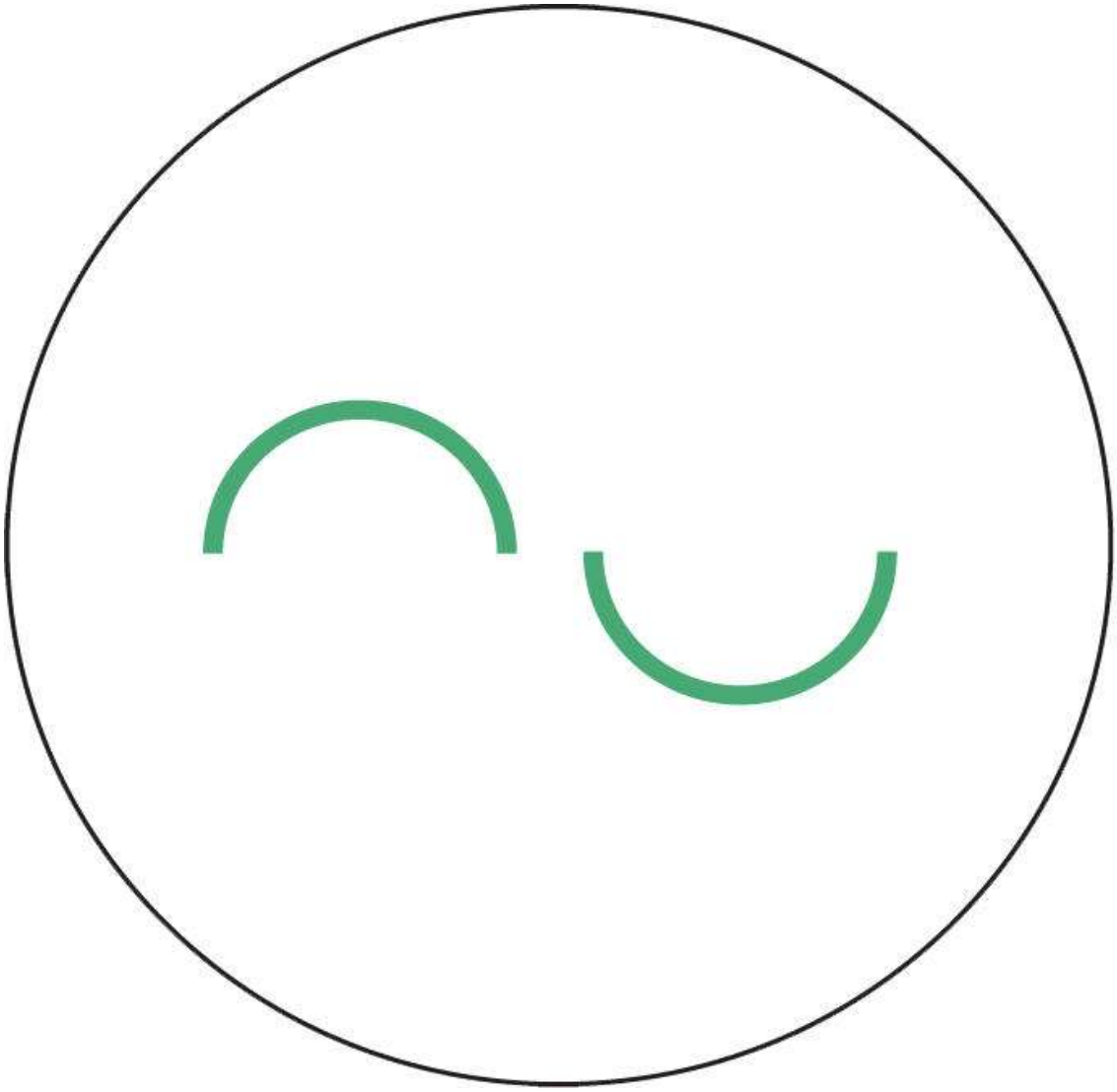
Figure 2. 7: IOP Measurements (overestimating)



High intraocular pressure before the end point is reached will result in this image. Continue to turn the calibrated dial on the tonometer clockwise to reach the correct end point.

Source: Stevens S, Gilbert C, Astbury N. How to measure intraocular pressure: applanation tonometry. Community eye Health.

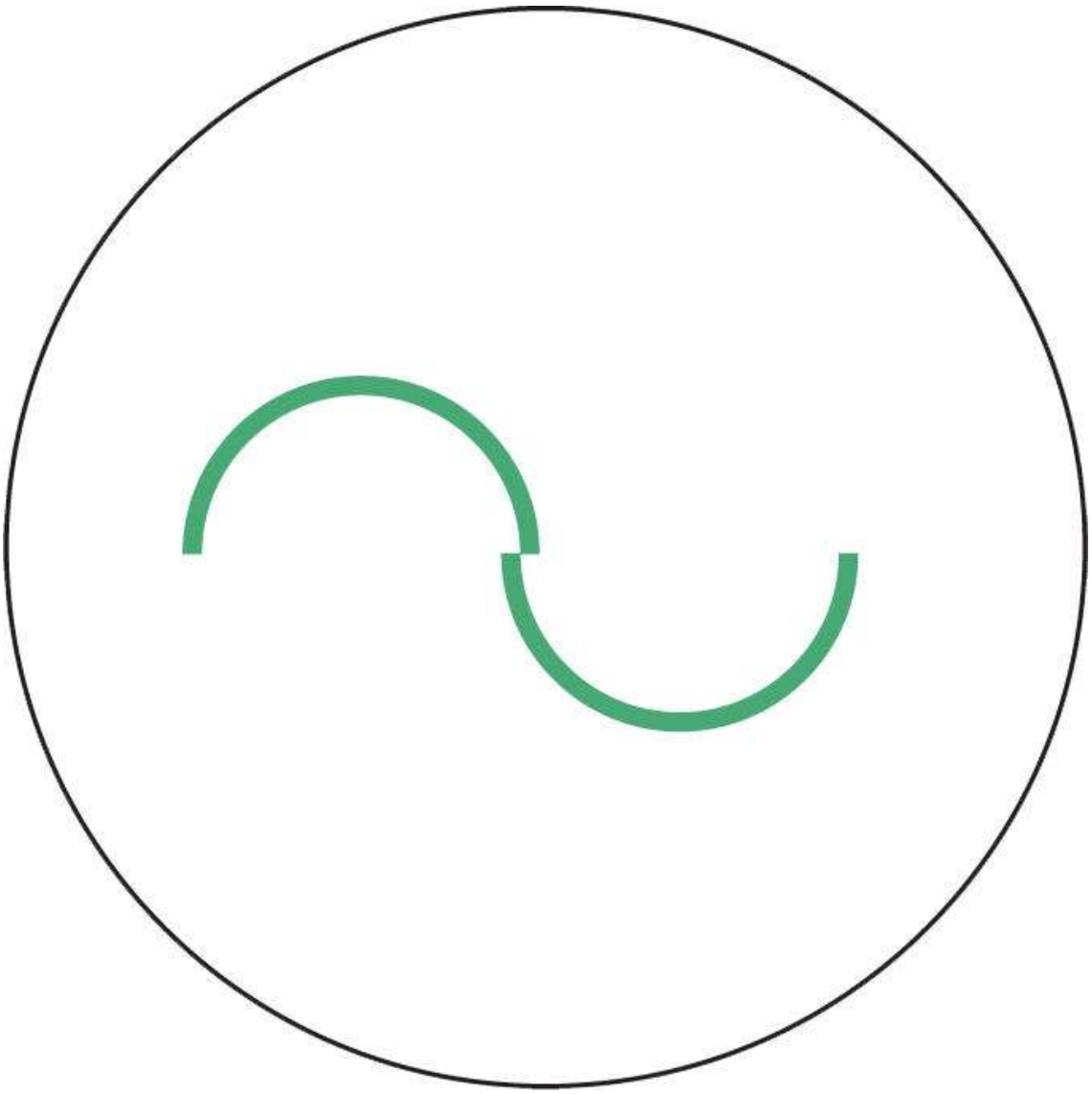
Figure 2. 8: IOP Measurement (underestimating)



Low intraocular pressure will result in this image. Turn the calibrated dial on the tonometer anticlockwise to reach the correct end point.

Source: Stevens S, Gilbert C, Astbury N. How to measure intraocular pressure: applanation tonometry. Community eye Health

Figure2. 9: IOP Measurement (normal)



This is the correct end point - the inner edges of the rings are just touching. This will give a correct reading of intraocular pressure.

Source: Stevens S, Gilbert C, Astbury N. How to measure intraocular pressure: applanation tonometry. Community eye Health

Figure 2. 10: Goldman Tonometer

Source: Stevens S, Gilbert C, Astbury N. How to measure intraocular pressure: applanation tonometry. Community eye Health

2.9.3 Perkins Tonometer

The Perkins tonometer is a portable version of the GAT which makes it suitable for measurement of IOP in upright or supine positions. [83]It is particularly useful in the measurement of IOP in children who are less likely to sit still or cannot be positioned behind a slit-lamp biomicroscope and in the field/outreach situations where the slit-lamp may be impractical. [81,83]

2.9.4 The Pneumotonometer and Tonopen

The pneumotonometer and tonopens are technologically built such that they combine the principles of indentation and applanation.[83,89] The pneumotonometer utilizes a jet of air to push

a silicone tipped piston to indent the cornea. The IOP is measured by the amount of pressure required to push the tip forward and flat on the cornea.[105]

The Tonopen is a small, portable, hand-held battery-operated tonometer. As described earlier, it is based on the principle of indentation and applanation, such that the tonometer has an applanating footplate with a tiny plunger protruding minimally from the center. As the tonometer contacts the eye, the plunger receives resistance from the cornea. The force is distributed to the foot plate and the plunger,causing a decrease in the continuously increasing force. An electronic system records the point of applanation and averages several readings. The IOP is then calculated based on a previous knowledge of the area of applanation. [105]

Figure 2. 11: Tonopen *[88]*

Source: Editor: Syed Shoeb Ahmad;, Sub-Editor: Ghuncha Khatoon. Glaucoma Specialist Blog:The"Glog":October2019[Internet].

2.9.5 Non-contact tonometry (NCT)

In non-contact tonometry, a jet of air is emitted with gradually increasing intensity to flatten the cornea. [83]The emitted air is cut off at the point where it causes flattening of the cornea, and the force required at that point is measured and converted into pressure (mmHg). An average of at least 3 readings is taken to estimate the mean IOP, as IOP may vary with the cardiac cycle. [81,83] The value of IOP obtained doesn't correlate well with GAT as it underestimates it in the high

ranges and overestimates them in the lower ranges. [83] This method of tonometry is convenient when performing mass screening of IOPs.[81]

Figure 2. 12: Non-contact tonometer

Source: Picture by Researcher

2.9.6 Rebound Tonometry

The latest innovation in this category of rebound tonometer is the ICare device. The device is modelled such that a 1.8mm diameter plastic ball on a stainless-steel wire is held in place by an electromagnetic field in a handheld battery-powered device. [84] In rebound or impact tonometry the deceleration of a ball attached to a wire is measured electronically as it encounters the cornea.[84,85] At the push of a button, a spring thrusts the wire and ball forward rapidly. As the ball makes contact and hits the cornea, the ball and wire decelerate; a high IOP causes a more rapid deceleration, with a slower deceleration if the IOP is low. The device converts the speed of deceleration into IOP readings. [84,85]

Unlike other contact tonometers such as GAT, there is no requirement for the use of topical anesthetic agents. Measurements taken with this device are comparable to that taken with Goldmann and Tonopen. [83] Additionally the central corneal thickness of the patients' eyes has been demonstrated to affect IOP readings with this instrument. Thicker corneas tend to produce higher IOP readings and vice versa.[84,85] Corneal hysteresis and corneal resistance factor have also been documented to influence IOP readings from this device. The iCare Pro can assess the IOP in a recumbent person.[89]

Figure 2. 13: iCare Tonometer

Source: Picture by Researcher

2.9.7 Dynamic Contour Tonometry (DCT)

Some researchers have purported that it is necessary to have a tonometer that can obtain the intraocular pressure directly (ie, without relying on calculations based on the amount of force applied). A tonometer that eliminates operator bias and bias due to the individuals' corneal features. The dynamic contour tonometry (DCT) gives a continuous IOP measurement through a trans corneal approach. The contour in the name refers to the pressure-sensitive tip that is curved and closely resembles the convexity of the cornea.

Pascal Dynamic Tonometer is built such that it utilizes a piezoelectric sensor embedded in the tip of the tonometer to measure the changing pulsatile fluctuations in IOP.[87] The developers of the DCT determined, given that the average radius of most corneas is 10.5mm, the radius of curvature of the tonometer needed to also be 10.5 mm to get reliable readings. [83]

The shell-shaped tip of the tonometer is embedded with a 1.7mm diameter pressure sensor. [87] In the accurate use of the tool, the examiner places the centre of the cornea into the curvature of the DCT tip. The examiner then measures the intraocular pressure directly from the external surface of the cornea.

In using the DCT, IOP taken is defined as the mean diastolic IOP during the period of contact between the tonometer and the eye. In comparison to the Goldmann tonometer, IOP values with the DCT are said to be affected to a lesser degree by corneal thickness, curvature and hysteresis. In this way it circumvents the biases of the individual operator and the characteristics of the cornea like thickness, curvature and rigidity.[87,89]

Goldmann applanation tonometry readings are potentially influenced by central corneal thickness (CCT), whereas in pneumotonometry and DCT measurements, CCT is less likely to affect the values. Correlation between CCT and GAT is not linear. Hence, using a correction formula usually does not give a true reflection of the IOP. [83] Dynamic contour tonometry is a novel technology that may provide more accurate IOP measurements and, thus, allow better management of ocular hypertension and glaucoma. [86]

Figure 2. 14: Pascal Dynamic contour Tonometer [88]

Source: Editor: Syed Shoeb Ahmad;, Sub-Editor: Ghuncha Khatoon. Glaucoma Specialist Blog:The"Glog":October2019[Internet].

2.9.8 The Ocular Response Analyzer (ORA)

The ocular response analyzer is a more modern contactless type of tonometer. The applanating force like the non- contact tonometer is a jet of air of increasing intensity. The ocular response analyzer measures the moment of applanation, but emission of the jet of air continues till there's indentation of the cornea.

There is a subsequent decrease in the force of air until the cornea is once again at a point of applanation. The difference in the pressures at the two applanation points is a measure of the corneal elasticity (e.g., hysteresis). It allows for corneal compensated IOP measurements and

estimates cornea bio-mechanical factors such as cornea hysteresis and corneal resistance factor. Factors are used in correcting for differences in elasticity.

It also gives measurements that are less influenced by CCT compared to other applanation tonometers. [83] For instance GAT is affected by CCT. The ocular response analyzer measures the IOP as well as the corneal hysteresis with correction of IOP for these factors. [83]

Figure 2. 15: Ocular Response Analyzer *[88]*

Source: Editor: Syed Shoeb Ahmad;, Sub-Editor: Ghuncha Khatoon. Glaucoma Specialist Blog:The“Glog”:October2019[Internet].

The deformability of the cornea is captured in terms of corneal hysteresis and corneal response factor which are reflective of the "viscoelastic" properties of the cornea. The ability of the cornea to absorb and dissipate energy forms the basis on which the device applies a correction factor to obtain the "corneal compensated IOP (IOPcc). The corneal response factor relates to the central corneal thickness and IOP and indicates the overall resistance of the cornea.[88]
Disadvantages of the device mainly arise from the relative immobility of the machines since they are fixed to a table. Additionally, they are not widely available and published data on corneal hysteresis and corneal response factor in relation to glaucoma is not fully established.[88]

2.9.8.1 Trans-palpebral Tonometry

Trans palpebral tonometry refers to the method of measuring IOP through the eyelid and over the sclera and thereby avoiding contact with the cornea. Diaton is the commercially available version of this type of tonometer. The trans palpebral tonometer is designed such that the acceleration of a freely falling rod is determined as it rebounds against the eyelid.[89]

The main advantages of this type of tonometer include the fact that in evaluating the IOP of a patient, the cornea is completely avoided, and topical anesthesia is not required. In various conditions such as corneal trauma or surgery, or in patients who are immobile, this device comes in handy for the above stated reasons. For immobile patients, their relatives or caregivers, can be taught how to use the device and monitor IOP.

Figure 2. 16: Diaton trans-palpebral tonometer [89]

Source: Editor: Syed Shoeb Ahmad;, Sub-Editor: Ghuncha Khatoon. Glaucoma Specialist Blog:The“Glog”:October2019[Internet].

The newer tonometers such as the non-contact, pneumo-tonometer and I-care have been designed to overcome the short coming of the GAT. However, most of these instruments are not widely available in our setting with the Goldmann tonometer being the most common tool available and considered the gold standard.[89]

CHAPTER THREE

METHODOLOGY

3.1 Study design

This is a prospective cohort study of the effects of steroid eye drops on intraocular pressure and associated risk factors in patients post cataract surgery in KBTH and EEC.

3.2 Study site

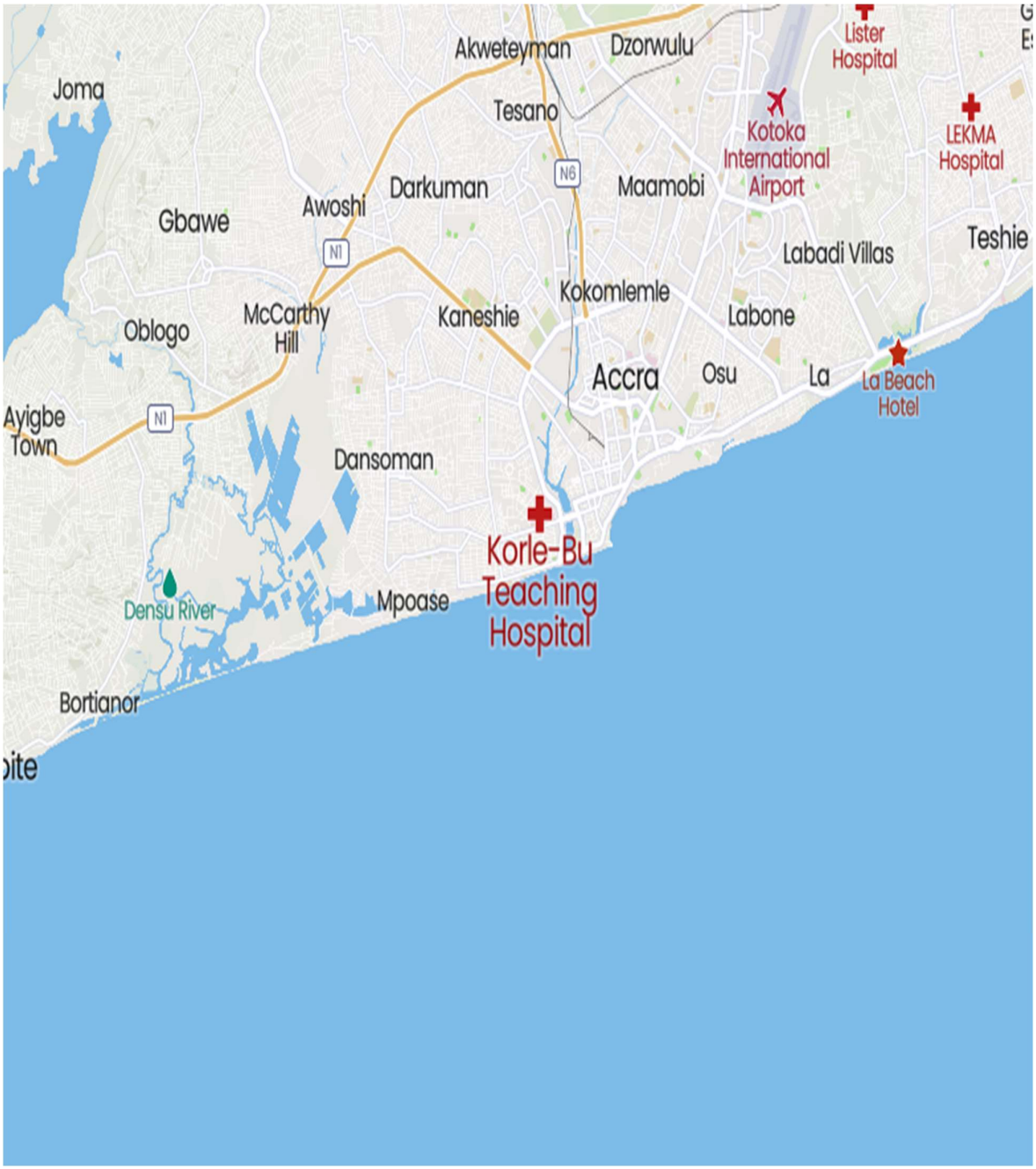
The study was conducted at the Lions International Eye Centre of the Korle-Bu Teaching Hospital (KBTH) and the Emmanuel Eye Centre (EEC) located in Accra, the capital city of Ghana, in the Greater Accra Region. Greater Accra Region is the most urbanized region in the country with 87.4% of its population living in urban centers. It is also the most populous region with a population of 4.2 million. [106.] Accra is located on the southern coast at the Gulf of Guinea, which is part of the Atlantic Ocean. [106]

The Lion International Eye Center is in the KBTH. It is a tertiary teaching facility and has a full complement of staff for effective Eye Health delivery. It has twenty (20) consulting rooms with Slit lamps equipped with Goldmann Applanation tonometers, Perkins tonometers and I-Care tonometers for in-clinic and outreach use. It has a complement of nine consultant eye surgeons with residents studying at varying levels of proficiency. There is a dedicated theatre complex with two operating suites and two modern Zeiss Ophthalmic Operating microscopes. It also has two Scanoptics microscopes which are deployed for outreach purposes. The center records an average daily Outpatient Department (OPD) attendance of 150 old cases and 30 new cases respectively. Averagely, 30 newly diagnosed cases of glaucoma are recorded monthly. In 2019, 458 adult cataract surgeries were performed at the Centre.

The Emmanuel Eye Centre is a Christian Health Facility located in East Legon a suburb of Accra, in the Greater Accra Region of Ghana. It is registered by the Ministry of Health as a mission hospital and a member of Christian Health Association of Ghana. The center has 3 ophthalmologists and 4 ophthalmic nurses. It is equipped with a theatre and 2 operating microscopes. It was set up to manage various ophthalmic cases that require an

ophthalmologist's evaluation. In 2019, 405 adult cataract surgeries were performed at Emmanuel Eye Centre.

Figure 3. 1: Target population



Source: *"Ghana"*. *The World Factbook*. *Central Intelligence Agency*. *Archived* from the original on 9 May 2022.

3.3 Inclusion criteria

1. All adult patients aged 18 years and above with or without glaucoma undergoing cataract surgery at the Korle Bu Teaching Hospital and Emmanuel Eye Centre.

2. Patients agreeing to attend follow up consultations for the study period.

3.4 Exclusion criteria

1. Adult participants aged 18 years and above who have had previous intraocular surgery.
2. Patients with intraoperative complications such as hyphaema, uveitis or postoperative complications such as endophthalmitis or toxic anterior segment syndrome were excluded from the study.
3. Adult patients aged 18 years and above with a history of Steroid-Induced Ocular Hypertension.
4. Patients who could not be examined accurately with Applanation Tonometry (e.g. participants with corneal scars and corneal growths).
5. Adult patients who had been on steroid treatment within 2 months prior to the cataract surgery.

3.5 Sample size determination

The study used 80% power (β) and a significance level of 0. 05 (α) to detect a statistically significant change in intraocular pressure from pre-operative baseline, to post cataract surgery. A 10% attrition rate was considered in this study. A previous study by O'Brien et al[89] to determine risk factors for a postoperative intraocular pressure spike after cataract surgery recorded a mean preoperative baseline IOP of 14.5 (SD=3.4) mmHg and 24-hours post-operative mean IOP of 17.0 (SD=6.0) mmHg which was a significant change from baseline IOP (P <0.002). [89]

Using the sample size formula presented below[90]:

$N = 2[Z\alpha + Z\beta]\,[Z\alpha + Z\beta\,][SD]^{\wedge 2} / [E][E]$

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 24-hours post-operative mean IOP of 17.0 (SD=6.0) mmHg (from the study by O'Brien et al) =6.0

E is the effect size (17-14.5) = 2.5

N=2(1.96+0.84)^2(6)^2/2.5^2

N=90.3

Substituting the variables into the above equation gives N = 90.3 and accounting for 10% loss to follow-up will yield;

N = 99.31

Therefore, the minimum sample size required for this study was 100.

3.6 Sampling procedure

All consecutive adult patients 18 years and above presenting with or without glaucoma undergoing cataract surgery were recruited into the study and examined after informed written consent. Patients with bilateral cataracts had the eye with the poorer vision done first and included in the study. Subsequent surgery for the second eye was not included in the study due to the requirement of washout period of steroid and time constraints for the study. Patients were booked into a diary with a maximum of 12 cataract surgeries per booking. Patients were recruited from the 24th of July to the 17th of October and followed up for thirteen weeks.

3.7 Procedures for the study

Ethical clearance and administrative study approval was obtained from the Institutional Review Board at the Korle Bu Teaching Hospital and college approval from Ghana College of Physicians and Surgeons (GCPS). Participants who qualified to be part of this study were recruited into the study after obtaining informed consent from them.

There was strict observation of anti-COVID-19 protocols. This was because, evidence-based studies show the virus to be spread by aerosols. It is transmitted when people come into close contact with an infected person. Transmission can also occur when there is contact with the mucous membrane or tears which drain through the nasolacrimal ducts and into the respiratory tract.[91] Hence the measures below (section 3.7.5) were considered during examinations of study participants.

3.7.1 Team Members (Constitution)

Two Ophthalmic nurses were recruited to help with the recruitment and flow of patients during the study at each study site. They were briefed on the scope, ethical concerns, goals and tenets of the study and how patients are expected to be approached, received, handled and managed with emphasis on courteous interaction with the clients. Two certified ophthalmologists (principal investigator and a specialist ophthalmologist at EEC) also performed SICS at the two study sites with the principal investigator performing surgeries at both study sites.

3.7.2 Roles of team members

The Principal Investigator had oversight responsibility for and was responsible for supervising the study. This included but was not limited to:

1. Interviewing, examining, and performing the surgeries on the clients at both study sites. She was also responsible for the day-to-day measurement of the intra-ocular pressure as stipulated in the protocol.
2. Overall protection of the rights and welfare of the study participants.
3. Overseeing the successful execution of the study.
4. Delegating duties considered appropriate and within the capacity of the study team members such as counselling of patients and checking of visual acuity.
5. Provide oversight for the research goals and the team. This included adherence to standards, protocol procedures and provision of training when needed.
6. Ensure resources earmarked for the study were always available.
7. Gathering and analyzing the data and write up of the dissertation.

Ophthalmologist at EEC:

1. Performing cataract surgeries at EEC.
2. Measuring of IOP and examination of patients for ocular pathologies during follow up visits.

Ophthalmic Nurse roles included:

1. Recognizing a patient with cataract requiring surgery.
2. Counselling of Patient with cataract for informed consent.
3. Following the study's inclusion and exclusion criteria.

4. They also checked the visual acuities of patients during the initial visit and at subsequent visits.

3.7.3 Pre-study preparations

3.7.3.1 General Guidelines

There was a preliminary training and orientation session for all the team members at the study sites involving the various cadres of staff as stated above. The scope, goals and conduct of the study were discussed. Their roles were spelt out and a session for questions-and-answers was created to address potential issues that may occur during the conduct of the study.

3.7.3.2 Instruments

The instruments to be deployed were assessed for optimum functioning and the necessary pre-test runs of the questionnaire and instruments were done. Instruments deployed included slit lamp bio-microscopes with mounted Goldmann Applanation Tonometers (Haag Streit, Inami). Efforts were made to secure comfortable work and seating arrangements that would facilitate gathering of data.

3.7.3.3 Validation of instruments

The Goldmann Applanation Tonometers were manually calibrated each day before measurements begun by the biomedical engineer of the clinic. Uniformity of IOP and elimination of inter-observer variability were reduced by restricting the measurements to only 2 ophthalmologists and adherence to guidelines for the measurement of IOP (Applanation Tonometry) was followed. Pre-test runs were undertaken before each scheduled review (I.e day one,weeks one ,five and thirteen) to ensure uniformity of readings. Pre-test runs were done by correlating the readings of the Principal Investigator with that of another Ophthalmologist to within 2 mmHg of each other as acceptable interobserver variability.

3.7.4 Clinical Examination Protocols for COVID 19:

1. The researcher wore face mask and gloves.
2. At the consulting room, study participants were given an alcohol-based sanitizer to sanitize their hands before the start of examination.
3. There was a special plastic breadth shield on the slit-lamp machine to protect principal investigator and participants from any possible contamination from droplets.

4. Participants were requested to refrain from speaking during slit lamp procedures until completion. Participants were allowed to talk and answer questions at a safe physical distance from each other.
5. There was disinfection of instruments daily as per the hospital protocols with disinfecting of the tonometer tip after every patient with 70% ethyl alcohol.

3.7.5 Flow Pathway

Demographic characteristics and detailed clinical history (including ocular and systemic conditions such as previous eye surgeries and collagen vascular diseases) of participants were documented on a structured questionnaire (Appendix II) after informed consent.

Participants were educated on some minimum risks in participating in this study. There was dilation of eyes to aid in the fundus examination. The use of dilating eye drops may cause mild irritation of the eyes, transient blurring of vision and glare lasting between six and eight hours. This does not require treatment. Participants were therefore advised to take extra care until they regain their usual vision. No experimental procedures were involved. They were informed of lack of compensation or any form of reward for participating in the study.

Pre-operative baseline clinical data on the ocular findings (best corrected visual acuity, slit lamp examination of the anterior segment of the eye, fundus examination and IOP were done to rule out other ocular pathologies causing visual loss) after examination were recorded. Vertical cup to disc ratios were subjectively measured using a 90 dioptre fundus lens before surgery. In patients with dense cataracts that precluded fundal view, a bimodal scan was done to rule out other vision impairing ocular pathologies. Cataract surgery was done by certified ophthalmologists. Post-operative intraocular pressures were measured during post-operative follow-up visits by an applanation tonometer (Slit-lamp mounted Goldmann Applanation Tonometer).[65]Two IOP measurements were taken, and the average recorded. In cases where the difference was more than 2 mmHg, a third reading was taken and the mean of the 2 closest readings taken.

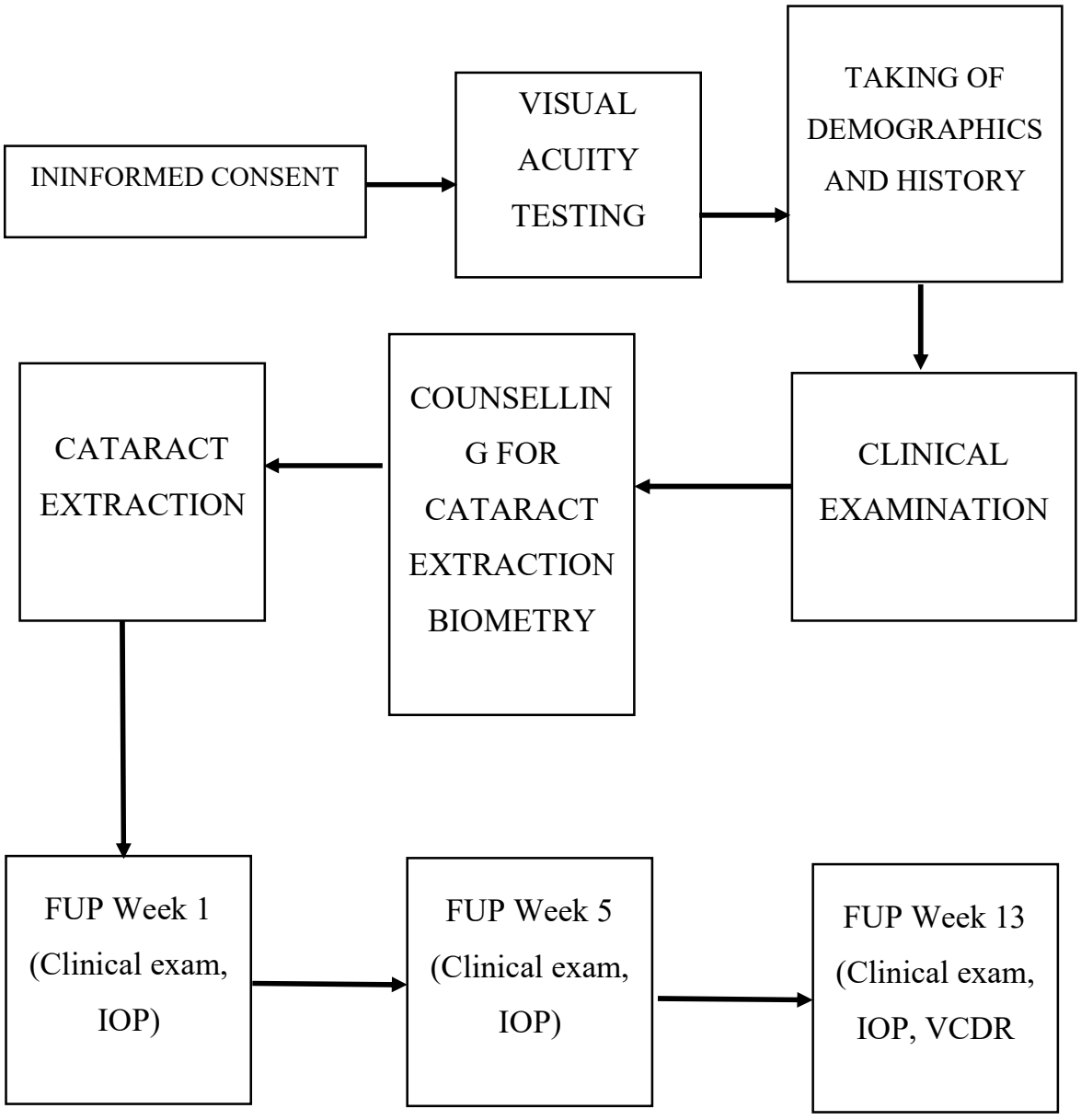
Surgery was performed in a standardized way as described below. Manual small incision cataract surgery was chosen as the preferred method for the study after considering the surgeons experience, relatively shorter period of surgery and good visual outcomes.

The pupil was dilated with a combination of tropicamide 1% and 2.5% phenylephrine hydrochloride (Auromide Plus) drops. The conjunctival sac was instilled with 5% povidone iodine solution. Anaesthesia was administered using 1% tetracaine hydrochloride (Tetracaine) drops followed by a peribulbar injection of about 6 ml of an equal mixture of bupivacaine 5 mg/ml (Marcaine) and lignocaine (lidocaine) 20 mg/ml with epinephrine 12.5 µg/ml (Xylocaine adrenaline). For this study peribulbar anesthesia was chosen since it was the preferred choice amongst surgeons at the study sites and has been proven to provide suitable akinesia and anaesthesia during surgery. It was given through the lateral 1/3 of the lower lid at the orbital margin. A scleral tunnel incision (approximately 6-7 mm) was performed centered at 12 o'clock, with a 1.5 mm extension into clear cornea to create a self-sealing incision. Light cautery was used. Viscoelastic was injected and a continuous circular capsulorhexis and/ or can opener capsulorhexis of about 6 mm diameter was made. Hydro dissection and hydrodelineation was done and nucleus was delivered through the incision. The irrigation fluid was ringers lactate with 0.5 mg of epinephrine per 500 ml ringers lactate. Aspiration of cortical matter was done, viscoelastic was injected into the lens capsule and a polymethylmethacrylate (PMMA) IOL with a 5.0 mm optic and an overall diameter of 12.0 mm was implanted into the capsular bag/ sulcus. Viscoelastic was washed out of the anterior chamber thoroughly with ringers' lactate. Suturing of the wound with 8-O vicryl using three interrupted sutures was done in four cases that had unstable wounds. Subconjunctival injection of 2mg dexamethasone and 40mg gentamycin with a steroid/antibiotic combination drop were given at the end of the operation.

Patients were put on topical prednisolone 1%(predforte) 6 hourly for 4 weeks and then tapered off as follows; three times a day for a week, two times a day the following week and then once daily for the subsequent and 7th week. Intraocular pressure measurements were taken over a 13-week period as per the questionnaire schedule (Appendix II) with subjective measurement of the cup to disc ratio at the last visit. Baseline best corrected visual acuity (BCVA) and post-operative BCVA were recorded using the Snellen chart by trained nurses before all examinations and categorized as good, borderline and poor per the World Health Organization (WHO)criteria. [93] It has also recommended targets aimed at achieving good uncorrected visual acuity greater than80% and poor less than 5% and corrected visual acuity good in 90 % and poor in 5%. [93]This criterion was used in evaluating the visual outcomes of patients in this study.

All patients who required intervention for increased intraocular pressure (i.e. IOP spikes defined as that above or equal to 10mmHg from baseline as well as patients with IOP greater than21mmHg)[68-72]during this study were treated as having steroid induced ocular hypertension and started on anti-glaucoma medications alongside steroid treatment . Beta blockers and/or carbonic anhydrase inhibitors were the preferred initial choice. Patients who developed SiOH on the first day were placed on oral Diamox 250mg three times a day for 5 days and had their IOP's dropped to ≤ 20 mmHg by the subsequent visit. Patients who later developed SiOH were put on timolol as first line therapy and monitored weekly till their IOP's dropped to ≤ 20 mmHg. All glaucoma patients were kept on their glaucoma medications throughout the study. SiOH was also grouped under high responders (≥16mmHg), moderate responders (6-15mmHg) and non-responders (≤5mmHg).

Figure 3. 2: Flow pathway of patients undergoing cataract surgery at Korle Teaching Hospital and Emmanuel Eye Centre. FUP – follow up, IOP - intraocular pressure, VCDR – vertical cup disc ratio



Patient Flow pathway

3.8 Data handling

The study was done in keeping with the Declaration of Helsinki for human subjects in medical research. For this study, data security, quality assurance and confidentiality of participants' information were held paramount. Consequently, the principal investigator was responsible for ensuring that adequate, accurate and relevant data was collected and not excessive for the purposes of the study to uphold quality assurance.

The principal investigator ensured appropriate archiving of data generated during the study and at the end of the study. Identities of study participants were concealed by codes. The researcher assigned codes to each questionnaire or participants' information. Information of study participants were treated as confidential. To ensure confidentiality of participants' information, names of participants did not appear on any write-up.

All hard copies of research data were stored in locked filling cabinets and it was ensured this was accessible only to authorized persons. All unwanted documentation or paper which contained confidential data were disposed appropriately. However, at the end of the study, all documentation or data connected with the study will be kept for five years in a secured cabinet. The principal investigator and the Institutional Review Board (IRB) of the Korle Bu Teaching Hospital will be the only authorized persons who will have access to the stored data.

3.9 Statistical analysis

Analysis of data was done using International Business Machines, Statistical Programme for Social Sciences Statistics software version 20. Continuous numerical data were summarized as mean and Standard deviation (SD) and categorical data as percentages (%). Data were presented using frequency diagrams, tables and pie charts as appropriate. Demographic characteristics of study participants such as age and sex were analyzed and presented as mean and standard deviations and counts and percentages, respectively. Chi-square test was used to compare proportions in the demographic and clinical characteristics of study participants. Kaplan -Meier analysis was used in calculating the time taken to develop SiOH.

Demographic characteristics and risk factors associated with steroid induced ocular hypertension post cataract surgery were analyzed using a Binary Logistic Regression Model and presented as Odds ratios and 95% Confidence Intervals. The mean rise in intraocular

pressure above baseline after treatment with topical steroids post cataract surgery were calculated and presented as a mean (standard deviation). The prevalence of steroid induced ocular hypertension 13 weeks post cataract surgery was presented as a percentage. To prove significant outcomes, t-test, and ANOVA were used to compare means in intraocular pressure elevations. P-values less than 0.05 were considered statistically significant.

CHAPTER FOUR

RESULTS

4.0 Introduction

Data analysis was done descriptively followed by the application of inferential statistics. Data on demographic and clinical characteristics of study participants were analyzed and presented as frequencies, proportions, means and standard deviations. Inferential statistics such as Chi square test, paired t test and Kaplan Meier were used to examine associations and significant differences. P-values less than 0.05 were considered statistically significant.

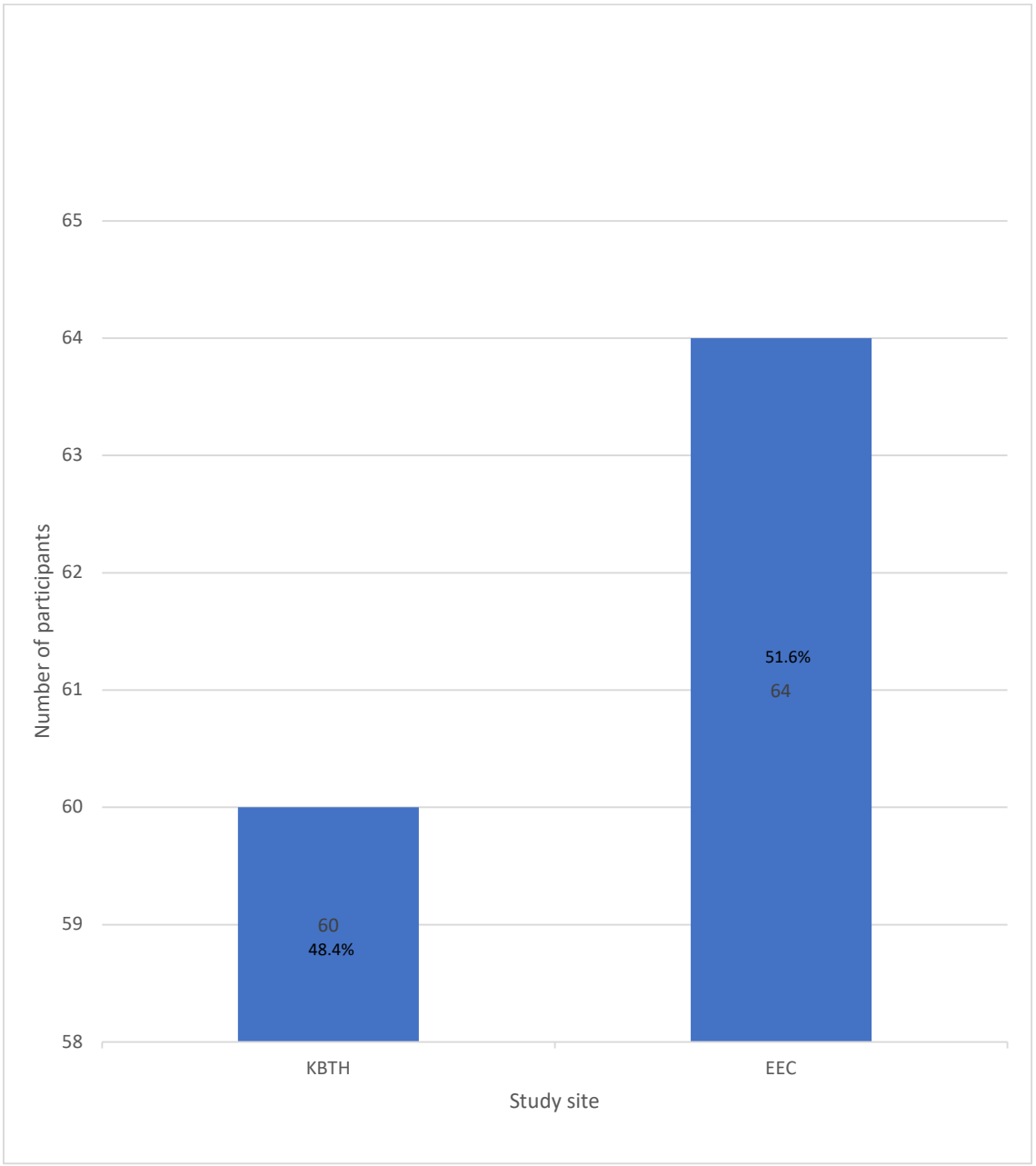
4.1 Socio-demographic characteristics of study participants

A total of 132 participants had cataract surgery in this study. Out of the 132, 6 (4.5 %) participants were excluded from the analysis because they were lost to follow-up. A participant who had endophthalmitis and another participant who passed away from complications of diabetes and hypertension were excluded from the study. Hence, the results reported was based on the outcome from 124 participants who completed the study(Sixty-four from Emmanuel Eye Centre and sixty from Korle Bu Teaching Hospital).

4.1.1 Study sites of participants

The Eye Centre at the Korle Bu Teaching Hospital and the Emmanuel Eye Clinic were the main study sites. A total of 64 (51.6 %) participants were from the Emmanuel Eye Centre and 60 (48.4 %) were from the Eye Centre at the Korle Bu Teaching Hospital.

Figure 4. 1: Study sites of participants undergoing cataract surgery at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.



4.1.2 Age

From the study, the mean age and standard deviation (SD) of the participants was 66.1±13.6 years. The ages ranged from 26 years to 89 years. The median (interquartile range) age was 68.0 (61.0-73.8) years. Most (67, 54.0 %) of the study participants were below 70 years.

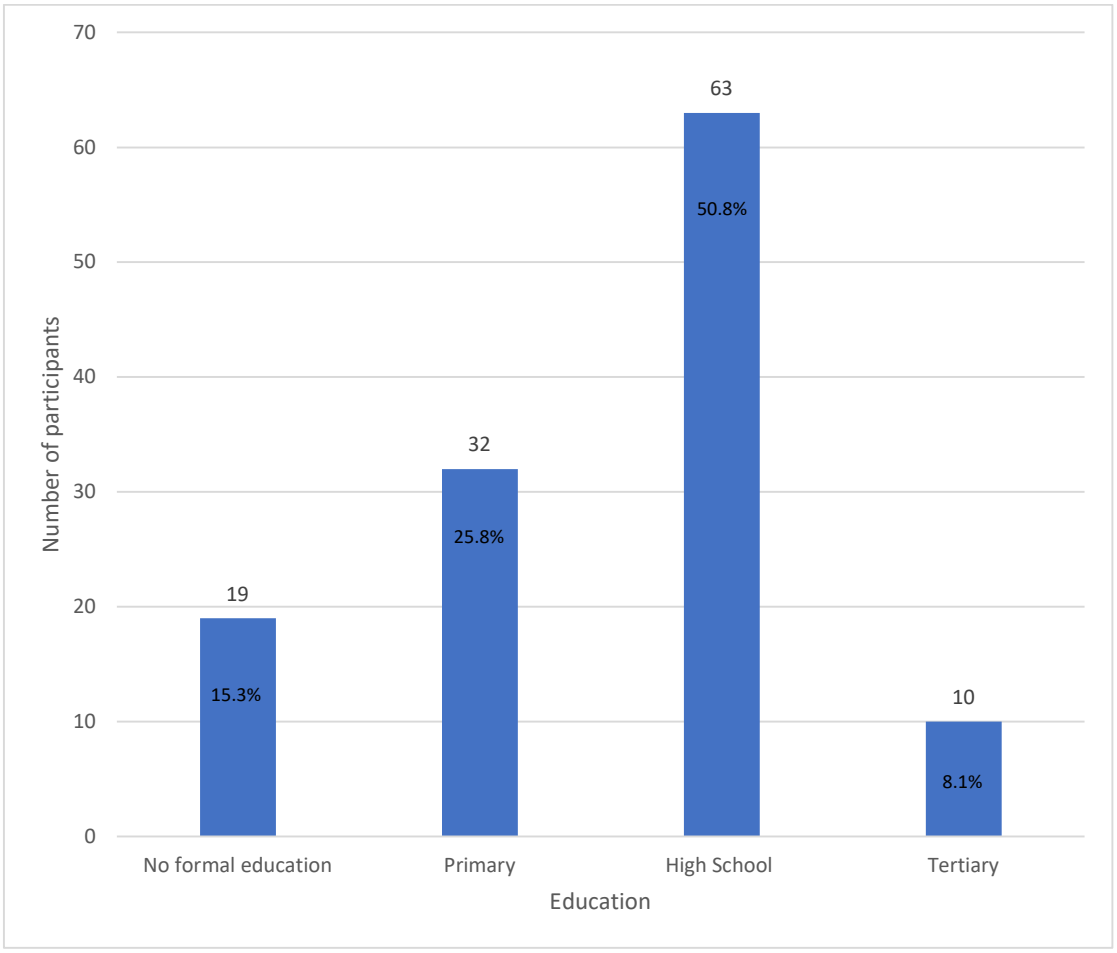
4.1.3 Sex

Majority (75, 60.0 %) of the study participants were females.

4.1.4 Educational Status

Most (63, 50.8%) of the participants had attained high school level of education, as shown in Figure 4.2.

Figure 4. 2: Educational status of participants undergoing cataract surgery at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.



4.2 Clinical characteristics of study participants

Clinical characteristics of study participants are presented on the tables (Table 4.1) and Figures (Figures 4.5 and 4.6) below.

4.2.1 Presenting ocular complaints of the study participants

From table 4.1 below, the presenting ocular complaints of the study participants are shown as follows:

Table 4.1: Presenting ocular complaints of study participants undergoing cataract surgery at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

Ocular complaints	**Right eye N (%)**	**Left eye N (%)**
Reduced vision	94(78.3)	122(72.8)
Seeing rainbow rings around lights	2(1.6)	2(1.6)
Ocular pain	2(1.6)	2(1.6)
Burning sensation	1(0.8)	1(0.8)

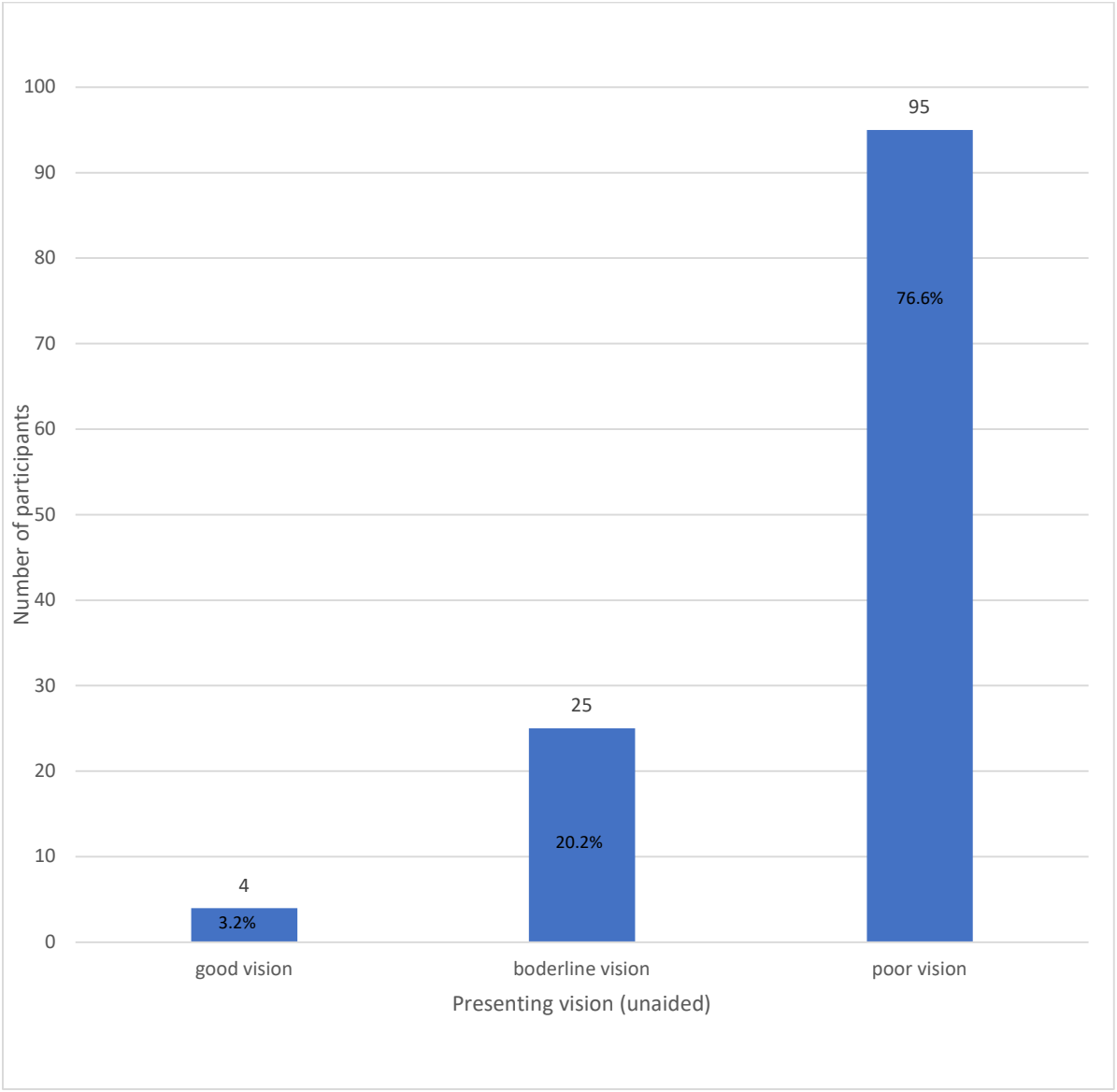
4.2.2 Study participants with glaucoma

A total of 29 (23.0%) participants had pre-existing glaucoma and were on treatment before recruitment. Figure 4.5. The mean age at diagnosis of glaucoma as reported by study participants was 68.6±10.1 years.

4.2.3 Study participants with family history of glaucoma

Twenty (16.1 %) participants in the study had family history of glaucoma.

Figure 4. 3: Presenting distance vision (unaided) of eyesoperated among participants. undergoing cataract surgery at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.



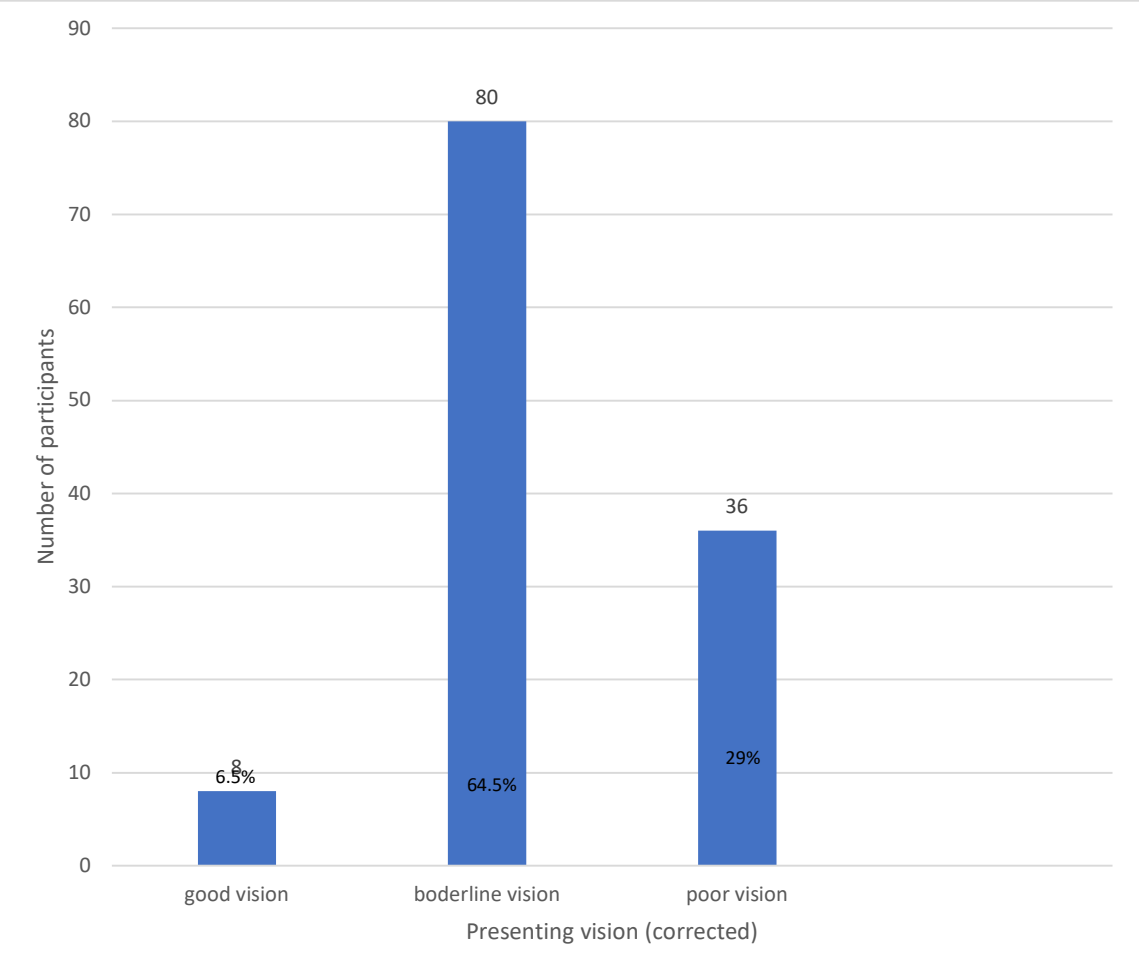
4.2.4 Presenting distance vision (unaided) of eyes operated among participants

Presenting distance visual acuity (unaided) of the eyes operated among the participants was assessed and is shown in Figure 4.6. There were 95 (76.6 %) participants with poor vision.

4.2.5 Presenting distance vision (best corrected) of eyes operated among participants

Presenting distance visual acuity (best corrected) of the eyes operated among the participants was assessed and is presented in Figure 4.4.

***Figure 4. 4*: Presenting distance vision (best corrected) of eyes to be operated among participants.**



4.2.6 Distance Vision assessment (unaided) at thirteen weeks post cataract surgery

Table 4.2 below displays the distance visual acuity, unaided and best corrected of the operated eyes among the participants.

Table 4.2: Presenting distance Vision assessment (unaided/best corrected) of patients thirteen weeks post cataract surgery at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

Visual impairment categorization	Number unaided	Number best corrected	Percent unaided	Percent best corrected
Good vision [6/12 or better]	62	101	50	88.7
Borderline [VA worse than 6/18 to 6/60]	53	11	42.7	8.9
Poor vision [VA worse than 6/60]	9	3	7.3	2.4
Total	124	124	100.0	100

4.2.7 Distance Vision assessment (best corrected) at thirteen weeks post cataract surgery

Table 4.3 below shows the distance visual acuity (best corrected) of the operated eyes among the participants. These figures may however change with some patients gaining more Snellen lines, since some patients were not refracted at 13 weeks. In these cases, best corrected refers to visual acuity with pin hole. Patients who had severe visual impairment after correction were seen on fundoscopy to have either a glaucomatous optic atrophy (2 people i.e1.6%) or severe macular atrophy from age related macular degeneration (1 person i.e 0.8%).

4.2.8 Participant's eyes operated at Korle-Bu Teaching Hospital and Emmanuel Eye Centre

Out of the 124 eyes operated, 65 (52.4 %) were left eyes and 59 (47.6 %) were right eyes.

4.3 Incidence of SiOH

Table 4.3 presents the incidence of SiOH per day post-operatively.

The overall incidence of SiOH in the study was 36.3%.

Findings from the table shows that the incidence of SiOH post-op day one (POD-1)was 29.0%. Week one, five and thirteen recorded an incidence of 4.0%, 1.6% and 1.6% respectively. Patients who developed SiOH on POD-1 were placed on oral Diamox 250mg three times a day and reviewed again on POD-5. All but 4 patients had their IOP's within the normal range. These patients were put on timolol eye drops and monitored weekly. IOP's were < 22 mmHg by week 3 and they were taken of timolol. Subsequent patients who developed SiOH were put on timolol as first line and pressures normalized within three weeks. Patients were off glaucoma medications by the time IOP measurements were due. Due to the small number of patients who had to be on ocular hypotensive treatment for longer than 5 days, these patients were included in the analysis.

The incidence of SiOH after thirteen weeks post-cataract surgery was also calculated for age, sex, education, study site, presence of glaucoma and family history of glaucoma. The results are shown in Table 4.3.

For the age groups, participants who were 70 years and above had the highest incidence (42.1%) of SiOH.

Females had higher (41.3%) incidence of SiOH compared to males (28.6%). Participants with high school level of education had the highest incidence (44.4%) of SiOH.

Participants from the Korle Bu Teaching Hospital had the lowest incidence of 33.3% for SiOH thirteen weeks post-cataract surgery compared with those from the Emmanuel Eye Clinic (39.1%).

Participants with glaucoma had an incidence of 44.8% and those with family history of glaucoma had an incidence of 40.0%.

Table 4.3: Incidence of SiOH thirteen weeks post-cataract surgery in patients at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

Factor	Number with SiOH in the group	Total number in the group	Incidence of SiOH (%)
Age:			
<70	21	67	31.3
(≥70	24	57	42.1
Total	45	124	36.3
Sex:			
Male	14	49	28.6
Female	31	75	41.3
Education:			
No education	8	19	42.1
Primary	6	32	18.8
High school level	28	63	44.4
Tertiary	3	10	30.0
Study site:			
KBTH	20	60	33.3
EEC	25	64	39.1
Presence of glaucoma:			
Yes	13	29	44.8
No	32	95	33.7
Family history of glaucoma:			
Yes	8	20	40.0
No	37	104	35.6

*Statistically significant difference

4.4 Mean rise in intraocular pressure after treatment with topical steroids post cataract surgery

The mean rise in intraocular pressure (IOP) after treatment with topical steroids post cataract surgery was analyzed. Table 4.4 shows the time relationship of the mean IOP at baseline for the eye to be operated and the mean IOP at post-operative follow-ups for study participants.
At baseline, the mean pre-operative IOP was 16.9±4.3 mmHg with minimum and maximum IOPs; 10.0mmHg and 30.0mmHg respectively.

The intraocular pressure for 1st day post-operative was 20.5±9.9 mmHg with a 21.3% increase from the baseline IOP measured. This showed a statistically significant difference in mean IOP between the baseline and 1st day post-operative IOP ($p = 0.001$).
The mean post-operative intraocular pressure for week one was 17.0±6.7 mmHg with 0.6 % increase from the baseline IOP. This mean difference in IOP was not statistically significant ($p = 0.936$).

Mean intraocular pressure for the week five post-operative was 17.2±5.9 mmHg. This was an increase of 1.8% from the baseline IOP and was not statistically significant ($p = 0.587$).
At week thirteen, the mean post-operative intraocular pressure was 16.2±4.3 mmHg with a percentage decrease of 4.1%.

The overall mean IOP in the study eyes was 17.8±4.4 mmHg with a 5.3% increase in IOP from baseline. This overall mean IOP was not statistically significant ($p = 0.061$). This affirms the null hypothesis that topical corticosteroids after cataract surgery does not cause a statistically significant rise in intraocular pressure in Ghanaians.

Table 4.4: Mean rise in intraocular pressure from baseline with treatment with topical steroids post cataract surgery in patients at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

Day	Mean±SD IOP (mmHg)	Mean Rise IOP (mmHg)	% Rise in IOP (%)	Minimum IOP (mmHg)	Maximum IOP (mmHg)	P-value
Baseline	16.9±4.3	-	-	10.0	30.0	-
Post-op day 1 IOP Baseline IOP	20.5±9.9	3.6	21.3	4.0	54.0	0.001*
Post-op week1 IOP Baseline IOP	17.0±6.7	0.1	0.6	6.0	42.0	0.936
Post-op week 5 IOP Baseline IOP	17.2±5.9	0.3	1.8	10.0	54.0	0.587
Post-op week1 13 IOP Baseline IOP	16.2±4.3	-0.7	-4.1	6.0	30.0	0.092
Overall mean Difference: Post op IOP Baseline IOP	17.8±4.4	0.9	5.3	9.5	33.5	0.061

*Statistically significant difference (p-values < 0.05), IOP = intraocular pressure, SD = standard deviation.

4.5 Difference in mean intraocular pressure between operated eye and fellow(phakic) eye before cataract surgery

Table 4.5 below shows the difference in mean intraocular pressure between the eye to be operated and the fellow eye (phakic) before cataract surgery. Findings did not show any significant difference in mean intraocular pressure between the eye to be operated and the fellow eye before cataract surgery (p-value = 0.265).

Table 4.5: Difference in mean intraocular pressure between the operated and fellow (phakic) eye before cataract surgery in patients at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

Statistic	IOP before cataract surgery		Difference	95% Confidence Interval of the Difference	P-value
	eOperated eye	Fellow eye			
Mean±SD IOP (mmHg)	16.9±4.3	17.3±4.8	0.4	0.3-1.0	0.265
Minimum IOP (mmHg)	10.0	10.0	0.0		
Maximum IOP (mmHg)	30.0	34.0	4.0		
Standard error of the mean IOP	0.4	0.4	0.0		

IOP = intraocular pressure, SD = standard deviation.

4.6 Difference in mean intraocular pressure between operated eye and fellow phakic eye thirteen weeks post cataract surgery

Table 4.10 below shows the Difference in mean intraocular pressure between operated eye and fellow eye (phakic) thirteen weeks post cataract surgery. Findings shows a significant difference in mean intraocular pressure between operated eye and fellow phakic eye thirteen weeks post cataract surgery (p-value = 0.002). The fellow phakic eye had an IOP (17.5 mmHg)

greater than the operated eye (16.2 mmHg) thirteen weeks after surgery. This shows a drop in IOP in the operated eye. Table 4.10.

Table 4.6: Difference in mean intraocular pressure between operated eye and fellow phakic eye thirteen weeks post cataract surgery Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

Statistic	IOP Thirteen weeks post cataract surgery		Difference	95% Confidence Interval of the Difference	P-value
	operated eye	fellow phakic eye			
Mean±SD IOP (mmHg)	16.2±4.3	17.5±5.1	1.3	0.5-2.1	0.002*
Minimum IOP (mmHg)	6.0	10.0	4.0		
Maximum IOP (mmHg)	30.0	42.0	8.0		
Standard error of the mean IOP	0.4	0.5	0.1		

*Statistically significant difference (p-values < 0.05), IOP = intraocular pressure, SD = standard deviation.

4.6.1 Descriptive summary of intraocular pressures (IOPs) and cup-to-disc ratio of participants

Table 4.7 presents a descriptive summary of intraocular pressures (IOPs) and cup-to-disc ratio (CDR) of participants. No changes in vertical cup to disc ratios were noted pre and post operatively for patients in whom fundoscopy was possible. Three patients who had very dense cataracts were excluded from this analysis.

Table 4.7: Descriptive summary of intraocular pressures (IOPs) and cup-to-disc ratio of participants

Parameter	Mean	Standard deviation	Minimum	Maximum	Median	Lower quartile	Upper quartile
Preoperative right IOP	17.1	4.9	10.0	34.0	16.0	14.0	19.0
Preoperative left IOP	17.1	4.1	10.0	32.0	17.0	14.0	19.0
Operated eye preoperative IOP	16.9	4.3	10.0	30.0	16.0	14.0	19.0
Operated eye postoperative IOP	17.8	4.4	9.5	33.5	16.8	15	20.8
Right eye cup-to-disc ratio	0.5	0.2	0.2	0.9	0.4	0.3	0.6
Left eye cup-to-disc ratio	0.5	0.2	0.2	0.9	0.4	0.3	0.6

4.7 Ocular responses after treatment with topical steroids post cataract surgery

Table 4.8 presents the ocular responses (change in IOP above baseline) after treatment with topical steroids post cataract surgery. SiOH was grouped under high responders (≥16mmHg), moderate responders (6-15mmHg) and non-responders (≤5mmHg). Findings from the study shows that majority 73 (58.9 %) were non-responders. Association between demographic and clinical characteristics and ocular responses after treatment with topical steroids post cataract surgery shows that age was the only factor associated with the development of SiOH post cataract surgery ($p = 0.036$). Table 4.8.

Table 4.8: Ocular responses (change in IOP above baseline) after treatment with topical steroids post cataract surgery

Factor	High responders(≥16 mmHg) N(%)	Moderate responders (6-15 mmHg) N(%)	Non-responders (≤5 mmHg) N(%)	Total N(%)	P-value
Age:					
< 70 years	9(7.3)	12(9.7)	46(37.1)	67(54.0)	0.036*
(≥ 70 years	9(7.3)	21(18.9)	27(21.8)	57(46.0)	
Total	18(14.6)	33(26.6)	73(58.9)	124(100.0)	
Sex:					
Male	8(6.5)	10(8.1)	31(25.0)	49(39.5)	0.445
Female	10(8.1)	23(18.5)	42(33.8)	75(60.5)	
Study site:					
KBTH	5(4.0)	20(16.1)	35(28.2)	60(48.4)	0.080
EEC	13(10.5)	13(10.5)	38(30.6)	64(51.6)	
Presence of glaucoma:					
Yes	2(1.6)	12(9.7)	15(12.1)	29(23.4)	0.084
No	16(12.9)	21(16.9)	58(46.8)	95(76.6)	
Family history glaucoma:					
Yes	1(0.8)	8(6.5)	11(8.9)	20(16.1)	0.207
No	17(13.7)	25(20.2)	62(50.0)	104(83.9)	

*Statistically significant risk factors (p-values < 0.05), N= number.

4.7.1 Other clinical findings before cataract surgery

Rheumatoid arthritis was found in one participant (0.8%) and two patients (0.16%) had very advanced glaucoma.

4.8 Association between demographic and clinical characteristics and the development of SiOH

The association between demographic and clinical characteristics and the development of SiOH was examined using univariate and multivariate analyses to determine the risk factors for developing SiOH. Findings from the univariate and multivariate analysis are captured inTable 4.9 and 4.10 respectively.

Table 4.9: Association between demographic and clinical characteristics and the development of SiOH post cataract surgery

Factor	With SIOH N(%)	Without SIOH N(%)	Total N(%)	P-value
Age:				
< 70 years	21(16.9)	46(37.1)	67(54.0)	0.262
(≥ 70 years	24(19.4)	33(26.6)	57(46.0)	
Total	45(36.3)	79(63.7)	124(100.0)	
Sex:				
Male	14(11.3)	35(28.2)	49(39.5)	0.183
Female	31(25.0)	44(35.5)	75(60.5)	
Study site:				
KBTH	20(16.1)	40(32.3)	60(48.4)	0.577
EEC	25(20.2)	39(31.5)	64(51.6)	
Presence of glaucoma:				
Yes	13(10.5)	16(12.9)	29(23.4)	0.280
No	32(25.8)	63(50.8)	95(76.6)	
Family history glaucoma:				
Yes	8(6.4)	12(9.7)	20(16.1)	0.801
No	37(29.9)	67(54.0)	104(83.9)	

KBTH-Korle-bu Teaching Hospital EEC-Emmanuel Eye Centre

Table 4.10: Multivariate adjusted odds ratio of risk factors for development of SiOH post cataract surgery

Factor	Odds ratio	95% Confidence Interval	P-value
Age:			0.206
< 70 years	Reference		
(≥ 70 years	0.6	0.2-1.3	
Sex:			0.128
Male	Reference		
Female	0.5	0.2-1.2	
Study site:			0.281
KBTH	Reference		
EEC	0.7	0.3-1.4	
Presence of glaucoma:			0.263
Yes	Reference		
No	2.1	0.6-8.0	
Family history glaucoma:			0.542
Yes	Reference		
No	0.7	0.1-2.8	

4.9 Kaplan-Meier analysis of time taken to develop SiOH

The Kaplan-Meier survival curve was used in estimating the mean time taken to develop SiOH in days. The results of the Kaplan-Meier analysis of time to develop SiOH are presented in table 4.13 and figures 4.11, 4.12 and 4.13 below.

The mean survival time (days) among males and females was 3.4 days and 8.9 days respectively. There was no statistically significant difference in the mean survival time between males and females (p = 0.226).

Participants who are aged below 70 years had a mean survival time of 1.6 days. Those aged 70 years and above had a mean survival time of 12.1 days. There was a significant difference in mean survival time between the age groups (p = 0.040).

Participants from the Korle Bu Teaching Hospital had a mean survival time of 10.9 days compared with those from the Emmanuel Eye Clinic (4.2 days). The difference in mean survival time between the two centers was not statistically significant (p-value = 0.285).
The overall mean time (days) to develop SiOH among study participants was 55.3 days (95% CI= 47.3 – 63.3 days).

Table 4.11: Kaplan-Meier analysis of mean survival time taken to develop SiOH

Factor	Mean survival time (days)	95% CI	P-value
Sex:			
Male	3.4	0.0 – 8.2	
Female	8.9	0.8 – 16.9	
Overall	7.2	1.4 – 12.9	0.226
Age group:			0.040*
< 70 years	1.6	0.8 – 2.3	
(≥ 70 years	12.1	1.6 – 22.5	
Study site:			0.285
KBTH	10.9	0.0 – 22.9	
EEC	4.2	0.5 – 7.9	

*Statistically significant difference

Figure 4. 5: Kaplan-Meier survival curve of mean time to develop SiOH (males/females) in patients undergoing cataract surgery at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

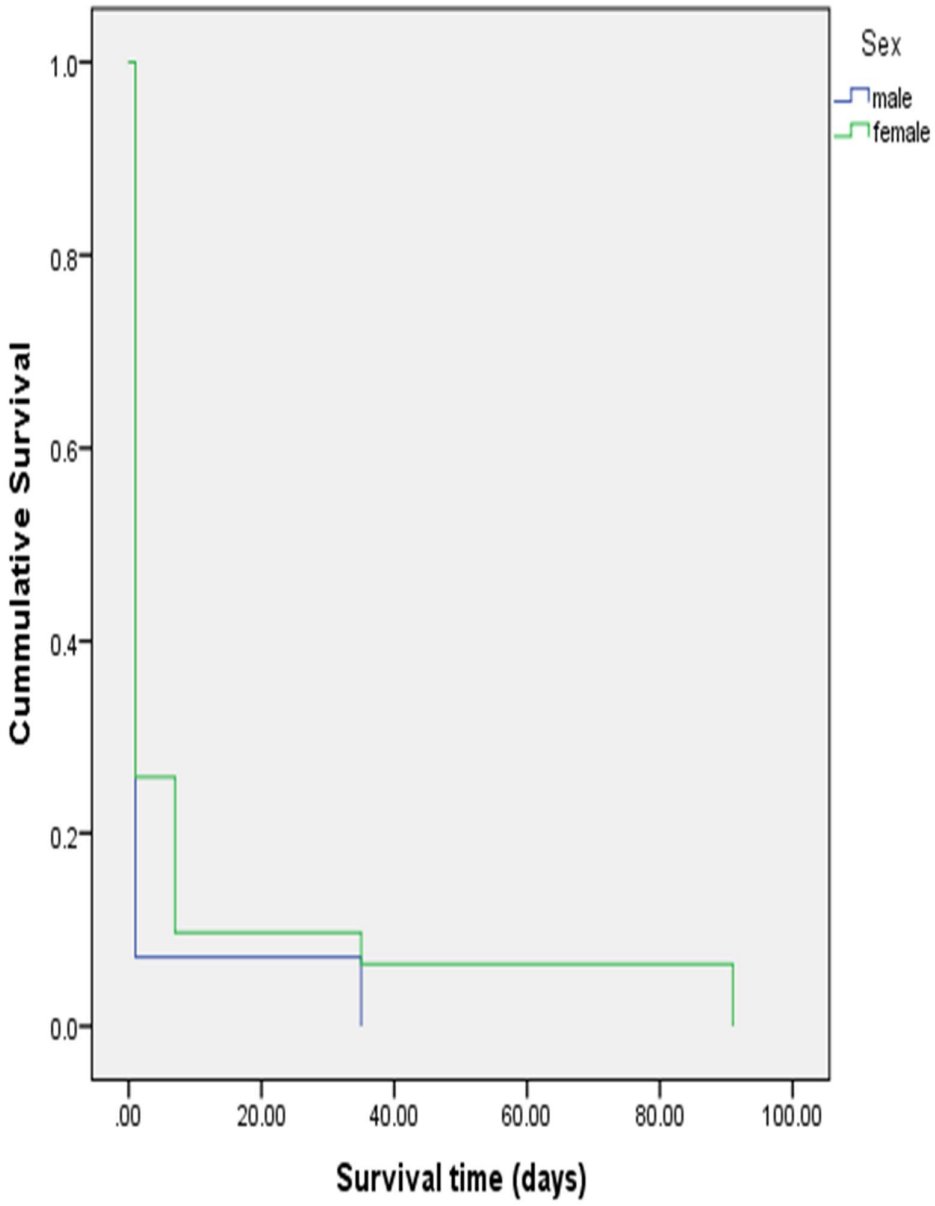


Figure 4. 6: Kaplan-Meier survival curve for mean survival time taken to develop SiOH between participants aged below 70 years and those 70 years and above at Korle-Bu Teaching Hospital and Emmanuel Eye Centre.

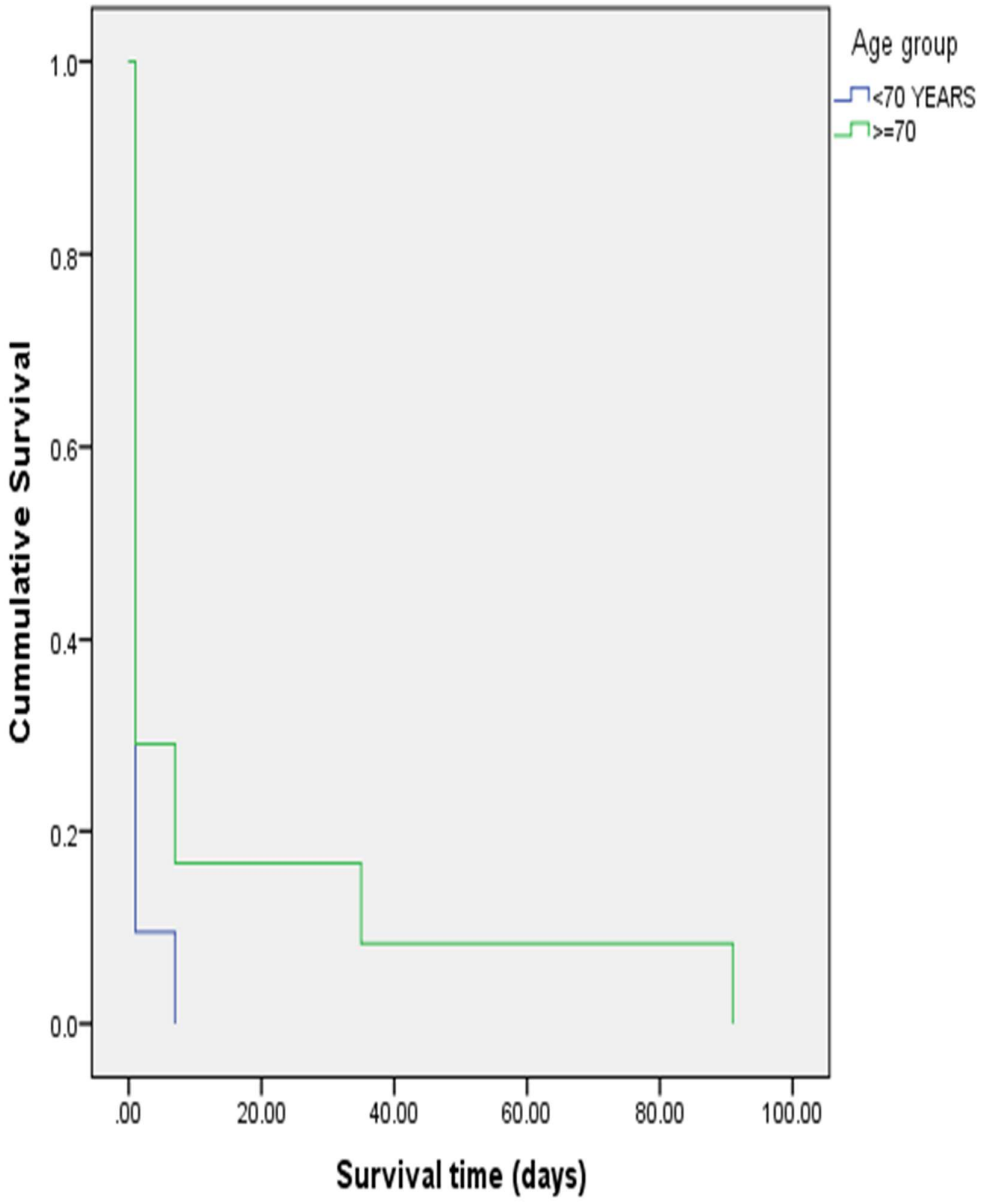
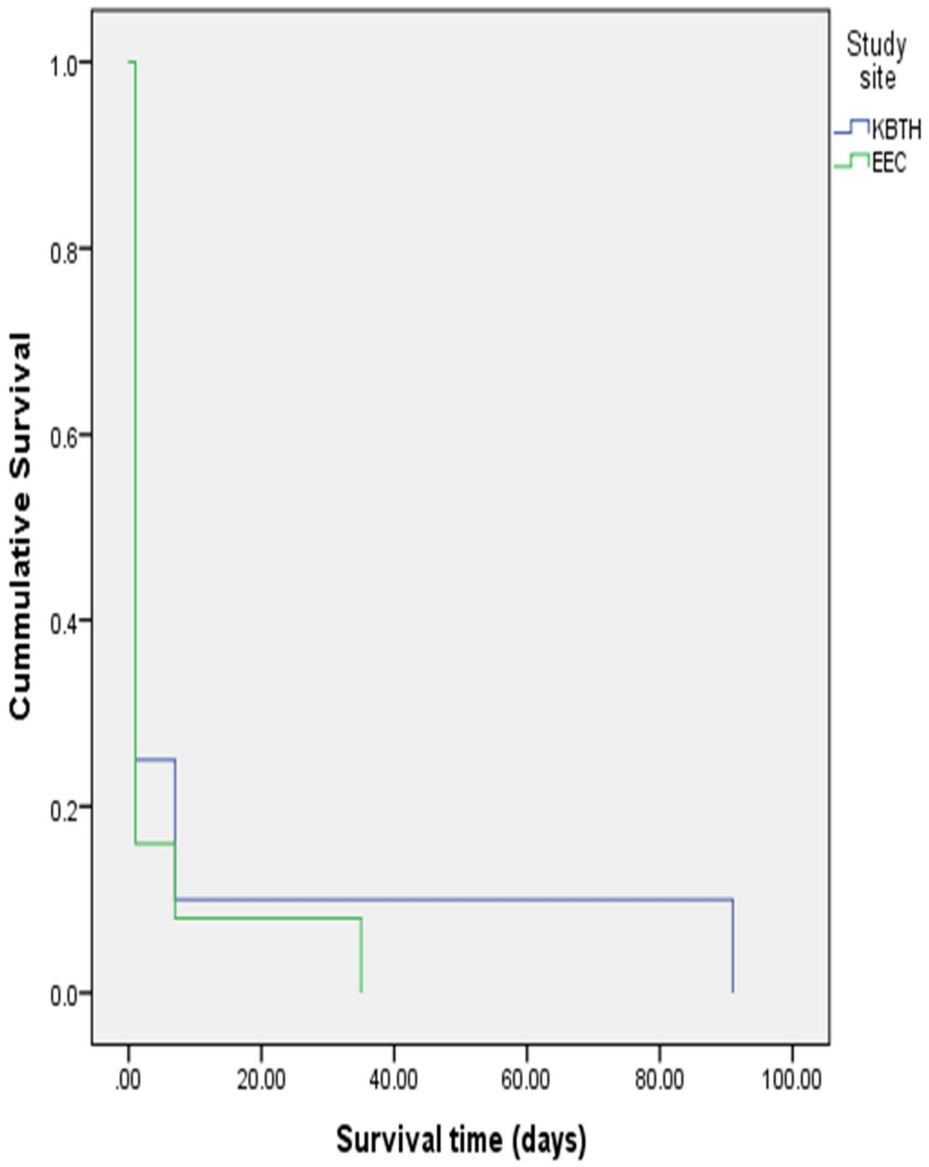


Figure 4. 7: Kaplan-Meier survival curve for mean survival time (i.e. time taken to develop SiOH) at the Korle Bu Teaching Hospital (KBTH) and the Emmanuel Eye Clinic (EEC).



4.10 Post-operative cataract surgery adverse event monitoring

Typical complaints amongst most participants included ocular pain, blurred vision and foreign body sensation during the first day and first week post-operative visits. However, these symptoms resolved after treatment with steroids and pressure lowering medications. Three

participants developed posterior capsular opacities after the first month and were treated with YAG laser capsulotomy after week thirteen.

CHAPTER FIVE

DISCUSSION

5.0 Introduction

This chapter discusses the results of the study and compares them with those of similar studies in the literature. The study was designed to determine the effect of steroids when used in the post operative management of cataract surgeries in our African Sub-Region.

There were more female participants (60%) than males. Half, 50.8% of the participants had attained high school level of education, with 15.3 % having no formal education. This may reflect the study site which is in an urban setting or an awareness of cataract and its treatment amongst those with some level of formal education.[17]

5.1 Cataract Surgical Outcome

Post cataract surgery, unaided visual acuity testing showed 50 % of participants had good vision, 42.7% had borderline vision, and 7.3 %) had poor vision as shown in Table 4.2. After correction with pinhole or refraction, there were significant improvements such that, 88.7 % participants had good vision, 8.9 % had borderline vision, 2.4 % had poor vision These post-surgical refractive errors may have been due to surgeon factors such as site of incision or to inaccuracies in biometry readings pre-op.

The World Health Organization (WHO) categorizes the outcome of cataract surgeries into 3 groups: good (visual acuity of 6/ 6 to 6/ 18), borderline (visual acuity of <6/18 to 6/60) and poor (visual acuity of <6/60).[93] It has also recommended targets aimed at achieving good uncorrected visual acuity >80% and poor < 5% and corrected visual acuity good in 90 % and poor in 5%. This points to the need for good biometry and proper case selection. Proportion of patients with good vison (90%) for this study meets the WHO recommendation. This is much higher than other studies done in Ghana and the sub region. [94,95]A retrospective study of 1288 unilateral cataract surgeries at two referral centres in southern Ghana by Ilechie et al[100] reported 41.2 % with good visual outcomes. Ashaye et al [101] in their study also reported 78.8 % of their study subjects having good vision 8 weeks post operatively. This percentage of patients with good corrected visual acuity in this study may also have improved in the long run since corrected visual acuity was done by pinhole at thirteen weeks in patients who declined

refraction. The value of 2.3 % of poor vision falls within the WHO guidelines of <5% having poor vision. These patients had optic atrophy from glaucoma and severe macular atrophy from wet age-related macular degeneration.

There was no change in cup to disc ratios pre and post operatively. Thus translating into no glaucomatous damage from the use of topical steroids after cataract surgery. This may suggest that most patients can tolerate a transient postoperative rise in IOP with no significant deficit on visual function. [98] However, a more detailed and objective assessment of ganglion cell loss from raised IOP such as using optical coherence tomography or visual fields was not done.

5.2 Incidence of steroid-induced ocular hypertension

The incidence of SiOH on the first postoperative day was 29% which decreased on week one, five and thirteen to 4%,1.6% and 1.6% respectively. The overall incidence was 36.3%. An overall mean time (days) to develop SiOH among study participants being 55.3 days (95% CI= 47.3 – 63.3 days). This was determined using the definition of SiOH of IOP ≥ 10mmHg from baseline and ≥ 21 mmHg. Majority of the steroid response occurred on POD-1(29%). This is higher than reported by Kim et al who reported an incidence of 22% on the first post-operative day. This difference could be explained by lower cut off of IOP of 21 in this series and the surgical method used in this study (MSICS which has been shown in some studies to have higher associated post op IOP when compared to phaco) [112] They used a cut off of >23 mmHg but had more than 80% of the surgeries being phacoemulsification[106]There is controversy regarding the pathophysiology of early IOP elevation after cataract surgery. Intraocular pressure elevation was named Healon-block glaucoma, because of obstruction of the trabecular meshwork by high-molecular-weight viscoelastic material.[40] Mechanical deformation of angle structures before or during surgery, inflammation, hemorrhage, pigment dispersion, and retained lenticular materials are also theorized to cause early IOP rises. [102]

An incidence SIOH of 4% at 5 weeks was much lower than an incidence of 45.8% [72] and 21% [98] reported at 6 weeks by Akingbehin and Kamal respectively. The lower incidence in this current study may be attributed to the type of steroid used i.e., prednisolone which causes a lower rise in IOP when compared to dexamethasone which was used in the other listed studies. On the other hand, the incidence in this study is higher than that recorded by a study in Washington by Bojikian. Bojikian et al did a retrospective study on 472 eyes of 472 non-glaucoma patients and 191 eyes of 191 glaucoma patients.[103] Ten (2.1%) non-glaucoma eyes

and 16 (8.4%) glaucoma eyes were diagnosed as steroid responders. Another study had an incidence of 0.42% after evaluating Postoperative IOP of patients placed on prednisolone acetate after cataract surgery.[106] This disparity can be explained by the surgery type i.e., phacoemulsification which was used as the mode of surgery in majority of the cases and may have contributed to the lower pressures unlike the MSICS used in this study which is associated with a high IOP 24 hours after surgery.[78,79]

Findings from the study shows that a total of 14.6 % were high responders, 26.6 % were moderate responders and 59 % were non-responders. This is consistent with literature which shows that about 2/3 of the population are non-responders. [(9,10)] These figures are comparable to the Armalys study in a Caucasian population (USA) which had moderate responders 29% and non-responders 66% of the population but a lower incidence of high responders (5%).[14]

A sub analysis of the data using this classification picked up age as a risk factor for SiOH. Patients 70 years and older have a higher risk of SiOH. Age was not identifiedas a risk factor in this study since this classification includes non-responders in the analysis. Unlike this study, Wu et al picked-up age as a risk factor for SiOH after pterygium surgery. [108]

This demonstrates that patients on steroids need to be monitored closely in the early post operative period. Long follow-up appointments may result in missed periods of raised intraocular pressures especially during the first month after surgery and may result in optic nerve damage. Long term use of steroids should be discouraged due to the risk of optic neuropathy. A baseline measurement of IOP should be taken prior to commencement of steroid therapy. Patients on topical therapy should then have their IOP measured regularly after initiation of treatment especially those at risk of SiOH.
The ocular hypertensive effect wears off after stopping the steroids as demonstrated in this study and other previous studies. [11,82]

5.3 Mean rise in intraocular pressure after treatment with topical steroids post cataract surgery

Intraocular pressure rise after steroid therapy has been commonly identified as a complication with topical administration than systemic administration. [11] Drops or ointment applied directly to the eye or over the skin of the eyelids is associated with an IOP rise.[72,83]

The overall mean IOP in the study eyes post-op was 17.8±4.4 mmHg with a 5.3% increase in IOP from baseline. The mean post op IOP was not statistically significant (p = 0.061) and fell within the normal range <21 mmHg. This compares with other studies on the topic conducted in Asia, United States of America and Europe. [20,49,55,80,102] Studies have shown similar increase in IOP in the early post-operative period. Cable et al did a study in the United States and had an overall mean IOP of 17.8 mmHg after reviewing 100 uncomplicated cataract surgeries with a twice daily dosing of difluprednate eye drops post operatively. Sixty percent of IOP spikes were noted on POD 1 and 40% on POD 7.[15] Lorenz et al studied the effects of prednisolone acetate 0.5% and placebo given four times daily till postoperative day two. Patients were all continued on prednisolone acetate four times daily till day 14 after phacoemulsification.[69] Their study also showed a similar increase of 4.8 % after steroid usage and like this study the overall mean IOP was considered normal (<21 mmHg).

The highest percentage rise in mean IOP (21.3%) occurred on the first post-operative day. The mean intraocular pressure for 1st day post-operative was 20.5±9.9 mmHg with a 21.3% increase from the baseline IOP measured. This showed a statistically significant difference in mean IOP between the baseline and 1st day post-operative IOP (p = 0.001). This increase in IOP may be due to the inflammatory reaction caused by surgery with disruption of the blood-aqueous barrier, remaining lens cortical matter blockage of the trabecular meshwork by cortical matter, viscoelastics, inflammatory cells, and iris pigments. [97,98] Thorough irrigation of viscoelastic was done intra- operatively, any remaining viscoelastics may take up to 48 hours to be completely resorbed. Also, cohesive viscoelastics that were used are more difficult to remove completely during surgery and has the potential effect of intraocular pressure rise and may be a confounder in the IOP recorded on day 1. The rise in IOP is similar to other studies which show the highest rise in IOP on post-operative day 1. [102-104]

In a study by Kamal et al in an Asian population incidence of raised intraocular pressure above 25 mmHg was 12% on the first post operative day. [98] Unlike this study, steroids (0.1 % prednisolone or 0.1% dexamethasone) were given 6 times a day for one week and then four times a day for five weeks and surgical methods was both MSICS and phacoemulsification.

Another study in Nigeria showed the highest IOP's for patients who underwent MSICS followed by steroid therapy was recorded on POD 1. The study did not indicate the type of steroid and post-op regimen that was used. [112]Other studies did not show a significant rise in IOP on POD1. Shingleton *et al*. did a retrospective study of patients who underwent clear corneal phacoemulsification with PCIOL with a minimum follow up period of 1 year. The patients were divided into three groups - no glaucoma, glaucoma suspect and glaucoma. IOP changes occurred in all groups though but there were no significant changes in IOP on POD1. [38] This may have been due to the method of surgery, phacoemulsification, which is associated with less inflammation and fewer IOP spikes and also the post- operative use of non steroidal anti inflammatory drops instead of steroids.[101]

Patients who had SiOH were treated with oral and/ or topical pressure lowering drops resulting in a drop in mean IOP in subsequent weeks. As the steroids were tapered the IOPs also declined. These results agree with studies in India and New Zealand in the literature.[98,104] The rise in mean IOP during the first week suggests a benefit for rigorous monitoring of IOP within the first week for patients considered to be at risk of steroid induced ocular hypertension to enable early detection of SiOH.

The lowest mean IOP occurred on week 13, at which mean post-operative intraocular pressure was 16.2±4.3 mmHg indicating a percentage decrease of 4.1%. This effect was seen after clients had been off steroid drops for 6 weeks giving sufficient time for the steroids to be washed out. [58] This goes to support studies which have shown that cataract surgery may cause a decrease in IOP. [106,107] A randomized prospective study was done on cataract patients who had undergone ECCE or phacoemulsification with PCIOL implantation. The study evaluated the IOP pre-operatively and post-operatively up to 6 months. [108]There was a mean decrease in IOP of 1.1 mm Hg (5.72%) in the ECCE group (15 eyes) and 0.6 mm Hg (4.16%) in the phaco group. [102]Although in the current study the drop of 0.7 was not significant. This may have changed if the follow up period was longer.[107,108]

5.3.1 Difference in mean intraocular pressure between operated eye and fellow eye thirteen weeks post cataract surgery

Findings shows a significant difference in mean intraocular pressure between operated eye and fellow phakic eye thirteen weeks post cataract surgery (p-value = 0.002). The fellow eye had a mean IOP (17.5 mmHg) which was greater than the operated eye (16.2 mmHg) thirteen weeks after surgery as compared to no significant difference in mean intraocular pressure between the eye to be operated and the fellow eye before cataract surgery. This is supported by previous studies.[103,106,108]

A recent study of 353 patients who underwent cataract surgery with measurement of intraocular pressures pre and post operatively showed a statistically significant drop in IOP after the surgery at days 7, 30 and 90 days.[71] In the study by Shingleton *et al.*[38] patients were categorized as; non- glaucoma(NG), glaucoma suspect (GS) and glaucoma(G). IOP changes occurred in all groups. In the NG group, the pre-operative IOP was 16.42 ± 2.77 mm Hg and post-operative IOP on 1st day, 6th week, 6th month and 1 year was 16.75 ± 4.82 mm Hg, 15.30 ± 3.15 mm Hg, 14.38 ± 2.47 mm Hg and 14.37 ± 2.97 mm Hg respectively. Showing a successive reduction in IOP. [38] Another study demonstrated that cataract surgery by clear cornea phacoemulsification in glaucoma patients, glaucoma suspects, and normal patients results in a small but significant decrease in IOP that is sustained at 3 years and a mean of 5 years in all groups. [76] Possible reasons for the reduction in IOP after cataract surgery with posterior chamber lens implantation is increased anterior chamber depth (removal of the bulky lens) resulting in decreased resistance to aqueous outflow. Also, increased levels of prostaglandins (F2) in aqueous humor may result in a reduction in the IOP. Reduced IOP may also be due to fibrosis and contraction of the posterior lens capsule leading to traction on the ciliary body and a resultant hypo-secretion of aqueous humor.[107]

5.4 Demographic characteristics and risk factors for SiOH in clients undergoing cataract surgery

The demographic and risk factors of any disease process is important in most epidemiologic studies. This enables us to know the people who are most likely to get the condition and put preventive measures in place.

There were no risk factors for SiOH in this study. The mean age of study participants was 66.1±13.6 years. The ages ranged from 26 years to 89 years. This ensured a wide range in terms of age, to help detect any influence of topical steroids on various age groups. Rajendrababu et al[92] with a mean age of 59.49 ± 7.25 years in their study cohort was similar to this current study. This also reflects the higher prevalence of cataract in the older age group. [2,17]

Participants who were 70 years and above had a higher incidence (52.6%) of SiOH when compared with those younger than 70 years. However, this was not statistically significant so age was not picked up as a risk factor for SiOH.This compares to a study in New Zealand by Kusne et al which did not find age to be a risk factor for developing SiOH, though like this study patients with more advanced age (>75 versus ≤75) showed an increase in IOP which was not statistically significant. [104] Other studies found age to be a risk factor for SiOH. [4,13,14,21,50,103] A study in a Caucasian population reported that the steroid-induced effect was greater in older compared with younger eyes, and greater rise in glaucomatous compared with non-glaucomatous eyes.[50]

Diabetes and hypertension were not identified as risk factors for the development of SiOH. Some studies have found diabetes as a risk factor. [13,14,105] The mechanism of the association between hyperglycemia and elevated lOP is not clear. It is postulated that the elevated blood glucose level in diabetes mellitus may induce an osmotic gradient and attract fluid into the intraocular space, which may result in an elevated IOP. [13] There were no significant differences seen in the presence of glaucoma, family history of glaucoma and sex of clients after multivariate analysis and were not risk factors in this study. In other anterior segment studies, Wu et al did not find presence of glaucoma, sex and age as a risk factor for SiOH. [108]Other studies have found glaucoma to be a risk factor for the development of SiOH. [4,56,9850] Boijekan et al found presence of glaucoma to be a risk factor for the development of SiOH they included 472 eyes of 472 nonglaucoma patients and 191 eyes of 191 glaucoma patients. [103]Ten (2.1%) nonglaucoma eyes and 16 (8.4%) glaucoma eyes were diagnosed as steroid responders. The findings of this current study (i.e., glaucoma not being a risk factor) may have been due to the relatively small number of glaucoma clients included in the study.

Females had a slightly higher (44.0%) incidence of SiOH compared to males (36.7%). This was however not statistically significant and corroborates findings from other studies in Europe and Asia which did not identify gender to be a risk factor for SiOH. [13,108]

This female preponderance is difficult to explain and further prospective studies with a larger sample size and longer follow-up may confirm the results of this study. Steroid induced glaucoma does not follow a mendelian inheritance hence future studies on the genetics of corticosteroid induced IOP and gene loci involved maybe beneficial.[11,23,24,59,53] Better identification of patients at risk of steroid induced IOP rises would allow them to be more closely monitored.

In standard clinical care, steroid agents are routinely used as effective suppressants of postoperative ocular inflammation.[7] This reduces the complication rate since most patients now expect 6/6 vision after cataract surgery. Uncontrolled inflammation may cause unwanted complications like cystoid macular edema, intraocular pressure (IOP) rise and excessive cicatrization. Chronic administration of steroids post cataract extraction may result in elevated intraocular pressures and hence steroid-induced ocular hypertension, [11] especially with topical steroids over the course of weeks after cataract extraction.[66,77] Although increases in IOP after cataract surgery are usually uneventful, they can cause further damage to retinal ganglion cells in patients who have an already been compromised optic disk. In addition to individuals with glaucoma, those prone to anterior ischemic optic neuropathy are at increased risk for further optic nerve damage. SiOH may result in optic neuropathy and hence steroid induced glaucoma. [11,52]

Other morbidities associated with extremely high or prolonged ocular hypertension also include severe corneal edema, pain, anterior ischemic optic neuropathy, and central retinal vein occlusion. There are some interventions used by eye surgeons to control early IOP spikes including removing all viscoelastic materials at the end of surgery, prophylactic use of intracameral acetylcholine, and use of systemic or topical ocular hypotensive medications.[106] Currently, the situation of elevated intraocular pressures after cataract extraction has not been fully studied in the Ghanaian population. To the best of our knowledge, this study is the first to determine the incidence and determinants of SiOH post-cataract extraction in Ghanaians. The study provides essential and relevant epidemiological information about the effect of

steroids after cataract surgery and the effect of the surgery on intraocular pressures within a 3-month period in Ghana.

As is the current norm in all medical conditions, prevention is considered ideal. Eye care providers should aim to prevent or reduce the occurrence of irreversible optic nerve damage by doing a thorough Preoperative patient assessment and applying judicious use of steroids. It is particularly important, whenever possible, to avoid use of steroids in patients with pre-existing glaucoma, unless necessary since these patients are prone to steroid-responsiveness and may be tipped into a state of significant visual loss by such therapy.[11]

Early identification of patients who have a steroid induced pressure rise is key in order to prevent them from developing permanent visual loss. In the majority of cases, SiOH can be treated successfully by topical or oral ocular hypotensive therapy, although the ideal management is to cease steroid therapy. [11]

5.5 Study limitations

1. The study could have evaluated the visual fields and retinal nerve fibre layer thickness instead of relying on the vertical cup/disc ratios used, this will give a better indication of optic neuropathy.
2. A hospital-based study hence cannot be used as a representative of the general population.
3. A larger number of glaucoma clients would have helped to elucidate glaucoma as a risk factor.
4. The novel coronavirus pandemic (COVID 19) restrictions and difficulties with follow-up contributed to attrition.

Despite its limitations, this current study found the incidence of SiOH at 13 weeks to be 36.3% with a steep rise in IOP occurring within the first 24 hours after surgery. There were no risk factors for the development of SiOH in this study.

CHAPTER SIX

CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusion

1. The outcome of this study affirms the null hypothesis that topical corticosteroids after cataract surgery does not cause a statistically significant rise in intraocular pressure at the study sites when using the current study's regimen. There is however a high incidence of ocular hypertension (29%) during the early post operative period.
2. Administration of prednisolone 4x daily for one month followed by gradual tapering over the subsequent month is adequate to control post operative inflammation.
3. There were no risk factors for the development of SiOH. Participants aged 70 years and above however had a slightly higher but insignificant rise in intraocular pressure.
4. SiOH can develop in the early period post steroid administration, with about a third of participants, 29% occurring within the first 24 hours post-surgery and with effect wearing off after stopping steroids.
5. Cataract surgery causes a drop in IOP at 3 months post-op.
6. Transient rise in IOP does not cause a significant change in the vertical cup to disc ratio.

6.2 Recommendations

1. It is imperative that the intraocular pressures of patients post cataract surgery is monitored especially during the first month post-surgery. This is the period where most IOP spikes occurred and where measures will have to be instituted to prevent steroid induced glaucoma.
2. All eye care professionals should be educated and provided with the means (provision of tonometers at peripheral facilities) of taking accurate measurements of IOP to aid in the management of these cases. Emphasis on education should be given to eye care professionals in district hospitals to improve on early detection and patient referrals.
3. We recommend a study to evaluate the precision of biometric measurements to ensure good unaided visual acuity post operatively. This will reduce the high number (47.6%) of patients who still require spectacles for distance vision after cataract surgery seen in this study. Proper training of staff to ensure quality biometric readings should be undertaken at all eye centres that offer cataract surgery.

4. We recommend a multi-centre study with a longer follow up period to evaluate the use of cataract surgery as a means of achieving IOP control in glaucoma patients in our setting and the long-term sustainability of this IOP lowering effect on patients. This will enhance literature on the possible benefit of this procedure which is done by almost every ophthalmologist.
5. We recommend a multi-centre, highly powered study on the incidence of steroid induced ocular hypertension and its associated risk factors. This would provide further evidence that may inform national policy on prevention and management of patients with SiOH.

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APPENDICES

APPENDIX I

INFORMED CONSENT FORM FOR STUDY PARTICIPANTS

Personal details of study participants:

NAME:		
Place of birth	Date of birth	Gender
		Male [ ] female[ ]
Phone number(s)	e-mail address	

Home address	Postal address

Nationality: Ghanaian [ ] Foreigner [ ]. If foreigner, State Country:
Occupation:

Person to notify in case of emergency	
Name:	Telephone:

Principal investigator's information:

Project title: Effect of steroid eye drops on intraocular pressure in patients post cataract surgery and associated risk factors in a West African population
Name of Principal Investigator: Dr. Akosua Badu Mensa-Bonsu
Address: Eye Department, Korle-Bu Teaching Hospital. Tel.: +233244750168.

General information about the research:

The general objective of this study is to determine the prevalence and risk factors associated with steroid induced ocular hypertension in glaucoma and non-glaucoma patients post cataract surgery. Steroids are drugs which are commonly used after cataract surgery to decrease inflammation and improve visual outcomes. However, they are known to have

significant side effects, such as increased intraocular pressure (IOP). At the end of this study, the prevalence of and the risk factors for steroid induced ocular hypertension following

cataract surgery would be determined for appropriate interventions to be instituted.

Procedures of the study:

The study involves the completion of a set of questionnaires to assess study participants' demographic (age, sex, history of symptoms) and clinical (ophthalmic, and other medical) history. The eyes of study participants will be examined (the usual eye examination done for patients with glaucoma; distance vision testing, examining the back of the eyes, visual fields testing and checking of eye pressures. The eyes of study participants will be examined again during the next visit as a follow up on the previous exams done.

Possible Risks and Discomforts:

There may be some minimum risks in participating in this study. There will be dilation of eyes to aid in the examination of the back of the eyes. The use of dilating eye drops may

cause mild irritation of the eyes, transient blurring of vision and glare lasting between six and eight hours, which do not require treatment. Participants are advised to take extra care till they regain their usual vision. No experimental procedures are involved. There is no documentation of participants' name.

Possible Benefits:

At the end of this study, the prevalence of and the risk factors for steroid induced ocular hypertension following cataract surgery would be determined for appropriate interventions to be instituted. This would lead to an improved care and a significant impact in the management of glaucomatous eyes and non-glaucomatous eyes with cataract. The outcome of this study may also contribute to the body of knowledge relating to the management of glaucoma.

Confidentiality:

Information obtained from study participants would be treated as confidential and kept in a file which will not have the participant's name on it but a code number assigned, which will not be disclosed to anyone. Outcome of this study would be submitted to an academic body, but the name of study participants will not be reported.

Compensation:

There is no financial compensation or any form of reward for participating in this study.

Voluntary Participation and Right to Leave the Research:

Study participants have the right to voluntarily participate or refuse to participate in this study which will not offend the principal investigator in any way. Thus, participating in this research is voluntary and participant can withdraw without penalty.

Contacts for Additional Information:

This proposal has been reviewed and approved by the Institutional Review Board (IRB) at the Korle-Bu Teaching Hospital which has the mandate to protect participants from harm. In case of any research-related injury or pertinent questions about the rights of study participants,

participants may contact the IRB Office between the hours of 8am-5pm through the landline below. Study participants may also contact the principal investigator with the address and telephone numbers below for further information about the study.

Contact Information:

The Chairman,

Institutional Review Board,

Korle-Bu Teaching Hospital, Accra.

0302666766

Email addresses: rdo@kbth.gov.gh

The Principal Investigator,

Dr. Akosua Badu Mensa-Bonsu,

Eye Department,

Korle-Bu Teaching Hospital.

Tel.: +233244750168.

Volunteer Agreement:

The above document describing the benefits, risks and procedures for the research titled (Effect of steroid eye drops on intraocular pressure in glaucoma and non-glaucoma patients post cataract surgery in a West African population has been read and explained to me. I have been given an opportunity to have any questions about the research answered to my satisfaction. I agree to participate as a volunteer.

……. ……..

Name and signature/ Thumbprint of study participant Date

If volunteers cannot read the form themselves, a witness must sign here:

I was present while the benefits, risks and procedures were read to the volunteer. All questions were answered and the volunteer has agreed to take part in the research.

……. .....……

Name and signature of witness Date

I certify that the nature and purpose, the potential benefits, and possible risks associated with participating in this research have been explained to the above individual.

……. …….

Name signature of person who obtained consent Date

APPENDIX II

CATARACT SURGERY CONSENT FORM

Cataract is a clouding of the lens which causes blurred vision. It may also cause changes in your glasses measurements, glare and doubling of the image. Surgery for cataract is usually indicated when it interferes with your day-to-day activities such as driving, reading and watching TV.

Cataract surgery is usually performed under local anaesthetic with sedation. An anaesthetist is present during the procedure. A small incision is made, the cloudy lens is removed and replaced with an artificial lens implant. Before surgery, measurements are done to determine what power implant will be most suitable for your eye.

RISKS AND COMPLICATIONS

While we cannot list every possible complication of surgery you should be aware of the following risks:

- Adverse reactions to local anaesthetic, sedation or general anaesthetic
- Infection, pressure in the eye, clouding of the cornea, dislocation of the implant, changes to the shape of the pupil, swelling of the macula, detachment of the retina.
- Calculations for the implant power are not “an exact science.” We might not get exactly the focus that we aimed for, although we are usually close. You must still expect to need glasses to get your best vision.
- A membrane behind the implant, called the capsule may become cloudy, usually some years after surgery and it may be necessary to clear this with a simple laser treatment.
- Some effects of the surgery, while not dangerous, may be distressing to the patient, these include light reflections off the surface of the implant, awareness of shapes or flashes in the peripheral vision, floaters, streaks around lights or increased sensitivity to bright lights. These usually do not last.
- Surgery may not improve the vision if there are other eye problems, such as macular degeneration.

In signing below, I acknowledge that I have read this form. I accept that complications, although rare, can occur and the outcome of surgery can never be guaranteed.

VOLUNTARY CONSENT

I consent to have CATARACT surgery performed on my RIGHT / LEFT eye

……..	……
Patient Name and Signature/ Thumbprint	Date

I certify that I have explained the nature of the operation and the possible risks involved.

……...	……
Surgeon	Date

APPENDIX III

DATA COLLECTION TOOL

A. Demographic information

Date of Examination……

1. Patient identification number:..….....
2. Folder number:…… …….
3. Address/ phone no:……..
4. Age …….
5. Education: [ ] Illiterate [ ] Primary [ ] High School level and higher
6. Sex: [ ] male [ ] female
7. Have you been told you have glaucoma? [ ] Yes. [ ] No
8. Date of diagnosis of glaucoma if answer above is yes …….....
9. Date of first examination.....
10. Age at diagnosis (age at onset of glaucoma) .....
11. Family history of glaucoma [ ] Yes [ ] No

B. History

1. Presenting ocular complaint (please tick as appropriate)

Presenting ocular complaint	RE	LE
a. Reduced vision (please state eye)		
b. Redness of eyes		
c. Sudden and severe eye and head pain		
e. Nausea or vomiting following severe eye pain		
f. Seeing rainbow rings around lights		
g. No ocular complaints		
h. Others (Please specify)		

C. Examination

Visual acuity			
RE(unaided)	**BCVA(RE)**	**LE(unaided)**	**BCVA(LE)**

Feature	**RE**	**LE**
Initial IOP		
CDR (Cup-to-disc ratio)		

D. Diagnosis: ……

E. Medication/ treatment given

……

……

……

……

……

G. Date/time for next visit:……

FOLLOW UP VISITS

Date……

Patient identification number…..

Number of Visits	Visit #FUday1		Visit #FU1 week		Visit #FU 5 weeks		Visit# FU 13 weeks	
Date								
Eye(tick operated eye)	OD	OS	OD	OS	OD	OS	OD	OS
Visual acuity (unaided)								
Visual acuity (best corrected)								
IOP								
CDR (Cup-to-disc								

Ratio @ 13 weeks)								
Medications given								
Duration of medication								
Number of times a dose was missed								

Diagnosis / Other comments:

.....

.....

.....

APPENDIX IV

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/IMS/03/21
Your Ref. No......

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: Info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

16th July, 2021

DR. AKOSUA BADU MENSA-BONSU
EYE DEPARTMENT
KORLE BU

INSTITUTIONAL APPROVAL: KORLE BU TEACHING HOSPITAL-SCIENTIFIC AND TECHNICAL COMMITTEE/INSTITUTIONAL REVIEW BOARD (KBTH-STC/IRB/00089/2021

Following approval of your study entitled "Effects of steroid Eye drops on intraocular pressure in patients post cataract surgery and associated risk factors in a West African Population" by the Korle Bu Teaching Hospital-Scientific and Technical Committee/Institutional Review Board.

I am pleased to inform you that institutional approval has been granted for the conduct of your study in Korle Bu Teaching Hospital.

Please contact the Heads of Departments to discuss the commencement date of the study.

Please note that, this institutional approval is rendered invalid if the terms of the Institutional Reviewed Board/Scientific and Technical Committee approval are violated.

Sincere regards,

Dr. Ali Samba
Director of Medical Affairs
For: Chief Executive

APPENDIX V

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/MD/C3/21
Your Ref. No......

KORLE BU TEACHING HOSPITAL
P. O. BOX KB 77,
KORLE BU, ACCRA.

Tel: +233 302 667759/673034-6
Fax: +233 302 667759
Email: Info@kbth.gov.gh
pr@kbth.gov.gh
Website: www.kbth.gov.gh

15th July, 2021

DR. AKOSUA BADU MENSA-BONSU
EYE CLINIC
KORLE BU

EFFECTS OF STEROID EYE DROPS ON INTRAOCULAR PRESSURE IN PATIENTS POST CATARACT SURGERY AND ASSOCIATED RISK FACTORS AT A TERTIARY FACILITY AND ITS OUTREACH CENTRE

KBTH-IRB /00089/2021

INVESTIGATOR: Dr. Akosua Badu Mensa-Bonsu

The Korle Bu Teaching Hospital Institutional Review Board (KBTH IRB) reviewed and granted approval to the study entitled: "**Effects of Steroid Eye Drops on Intraocular Pressure in Patients Post Cataract Surgery and Associated Risk Factors at a Tertiary Facility and Its Outreach Centre**"

Please note that the Board requires you to submit a final review report on completion of this study to the KBTH-IRB.

Kindly, note that, any modification/amendment to the approved study protocol without approval from KBTH-IRB renders this certificate invalid.

Please report all serious adverse events related to this study to KBTH-IRB within seven days verbally and fourteen days in writing.

This IRB approval is valid till 30th June, 2022. You are to submit annual report for continuing review.

Sincere regards,

DR. DANIEL ANKRAH
VICE CHAIR (KBTH-IRB)
FOR: CHAIR (KBTH-IRB

Cc: The Chief Executive Officer, KBTH
The Director of Medical Affairs, KBTH

In case of reply the number
And the date of this
Letter should be quoted
My Ref. No. KBTH/MS/0781/21
Your Ref. No......

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21st June, 2021

DR. AKOSUA BADU MENSA-BONSU
EYE DEPARTMENT
KORLE BU TEACHING HOSPITAL

SCIENTIFIC AND TECHNICAL COMMITTEE APPROVAL
PROTOCOL IDENTIFICATION NUMBER: KBTH-STC 00089/2021

The Korle Bu Teaching Hospital Scientific and Technical Committee (KBTH-STC), on 21st June, 2021 approved your submitted study protocol.

TITLE OF PROTOCOL: "Effects of Steroid Eye Drops on Intraocular Pressure in Patients Post Cataract Surgery and Associated Risk Factors in a West African Population"

PRINCIPAL INVESTIGATOR: Dr. Akosua Badu Mensa-Bonsu

This approval requires that you **forward your approved document to Korle Bu Teaching Hospital –Institutional Review Board (KBTH-IRB) for the ethical aspect of the proposal to be assessed before the project can be initiated.**

This STC approval is valid till 30th December, 2021

You may, however, request extension of the approval period, or renewal as the case may be, should the study extend beyond the stated period.

Upon completion, you are required to submit a final report on the study to the STC. This is to enable the STC ensure among others that, the project has been implemented as per the approved protocol. You are also required to inform the KBTH-STC and Research Directorate of any publications that may emanate from the research findings.

Kindly note that, should the need arise, the KBTH-STC or IRB may institute appropriate measures to satisfy itself that study is being conducted according to the highest scientific and ethical standards.

Please note that any modification to the study protocol without Scientific Technical Committee (STC) approval renders this approval invalid.

Sincere regards,

Prof. G. Obeng Adjei
Chairman, KBTH-STC

Cc: The Chairman, KBTH-IRB

EMMANUEL EYE MEDICAL CENTRE

TOTAL QUALITY EYE MEDICAL CARE

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East Legon, Accra
DA: GA 288-1122

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Tel: +233 0302 500578/500778
emmanueleyecentre@gmail.com
eemc@lukemissions.org
www.lukemissions.org

Our Ref: EEMC/ADM/028/21
Your Ref:

Date: 20th July, 2021

Dr. Akosua Badu Mensa-Bonsu
Eye Clinic
Korle-Bu.

Dear Dr. Mensa-Bonsu,

RE: PERMISSION TO CONDUCT A REASEACH.

We write with reference to your letter received 16th July, 2021 on the above subject.

We wish to inform you that, your request to conduct a research on **"Effects of Steriod Eye Drops on Intraocular Pressure in Patients Post Cataract Surgery and Associated Risk Factors at a Tertiary Facility and Its Outreach Centre"** has been approved.

Thus, the centre will make available the necessary data / information that will be needed to conduct the research.

We are hopeful that the findings from the study will be made available to the Centre at the end of the study and it will help improve the services we render to our clients.

Yours Sincerely,

EMMANUEL EYE MEDICAL CENTRE
P. O. BOX GP 8967, ACCRA-GHANA
LOC. EAST LEGON
TEL: 0302500578/0302500778

Dr. Fobi Oduro-Boateng
(Dep. Executive Director)

Cc: The Medical Director, EEMC
Finance and Administrative Manager, EEMC