OUTCOMES OF SURGERY FOR PRIMARY CONGENITAL GLAUCOMA IN KENYA: A MULTICENTRE RETROSPECTIVE CASE SERIES

PRINCIPAL AUTHOR:

DR. JALIKATU MUSTAPHA

UNIVERSITY OF NAIROBI

A THESIS SUBMITTED IN PARTIAL FULFILMENT FOR THE AWARD OF DEGREE OF MASTER OF MEDICINE (OPHTHALMOLOGY), UNIVERSITY OF NAIROBI

DECLARATION

I declare that this dissertation is my original work and has not been presented for the award of a degree in any other university.

PRINCIPAL INVESTIGATOR:

Dr. Jalikatu Mustapha M.B.Ch.B., MSc. GHD

H58/69441/2013

Signed: _____ Date: _____

SUPERVISORS

Professor KARIMURIO Jefitha

M.B.Ch.B., M.MED (Nairobi). MSc.CEH (London), FEACO, PhD (Melbourne)

Associate Professor, University of Nairobi

Signed: _____ Date: _____

Dr. MARCO Sheila

M.B.Ch.B., M.MED (Ophthalmology), FEACO

Senior Lecturer, University of Nairobi

Glaucoma Specialist

Signed: _____ Date: _____

Dr. MUNDIA Daniel

M.B.Ch.B., M.MED (Ophthalmology), FEACO

Consultant Ophthalmologist, PCEA Kikuyu Hospital

Paediatric Ophthalmologist

Signed: _____ Date: _____

DEDICATION

I dedicate this dissertation to my family, my fiancé Dr. Brian Shiramba and my best friend, Mrs. Sallay Gulama.

ACKNOWLEDGEMENTS

I wish to thank the following:

1. The Almighty God, for His grace, wisdom and strength during my residency and in carrying out this thesis.

2. My supervisors, Professor Karimurio, Dr. Marco and Dr. Mundia for their critical review, input and support during this study.

3. Dr. S. Gichuhi, for his valuable contribution to my analysis.

4. All lecturers of the Department of Ophthalmology, University of Nairobi, for their input during proposal and results presentation of this study.

5. Kenyatta National Hospital, Kikuyu Eye Unit, Sabatia Eye Hospital and Tenwek Mission Hospital for allowing me access to their records and enabling my data collection for this study.

6. Sightsavers International for funding my training.

7. Mrs. Smart of Sightsavers Sierra Leone, for all her help during my residency.

8. Family members and friends who were always there for me when I needed them.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

ACRONYMS AND ABBREVIATIONS

5-FU	5-Fluorouracil
AC	Anterior Chamber
AL	Axial Length
ABC	Ahmed Baerveldt Comparison
AGV	Ahmed Glaucoma Valve
AVB	Ahmed versus Baerveldt
BCVA	Best Corrected Visual Acuity
BIG	British Infantile and Childhood Glaucoma
CAI	Carbonic Anhydrase Inhibitors
CCT	Central Corneal Thickness
CPC	Cyclophotocoagulation
CYP1B1	Cytochrome P4501B1
CTT	Combined Trabeculotomy-Trabeculectomy
GDD	Glaucoma Drainage Device
HCD	Horizontal Corneal Diameter
IAPB	International Agency for the Prevention of Blindness
IOP	Intraocular Pressure
KEU	Kikuyu Eye Unit
KNH	Kenyatta National Hospital
MMC	Mitomycin C

NLP	Non-light Perception
PCG	Primary Congenital Glaucoma
PCEA	Presbyterian Church of East Africa
PGA	Prostaglandin Analogue
SCH	Suprachoroidal Haemorrhage
TET	Trabeculectomy
TVT	Tube versus Trabeculectomy
VA	Visual Acuity
VCDR	Vertical Cup Disc Ratio
WHO	World Health Organization

SUMMARY

Introduction: Primary congenital glaucoma (PCG) is a childhood developmental eye disorder associated with elevated IOP. It is the leading cause of childhood glaucoma and an important cause of childhood blindness worldwide. The condition is difficult to manage and ultimately requires surgical intervention. In Kenya, there are several surgical options available for PCG, but no published studies evaluating the effectiveness of such procedures. This study aimed to assess the outcomes of these procedures, thus facilitating evidence-based practice in the management of PCG.

Methods: This was a retrospective case series conducted in 4 tertiary hospitals in Kenya (Kenyatta National Hospital, PCEA Kikuyu Hospital, Tenwek Mission Hospital and Sabatia Eye Hospital). Eyes of children <16 years of age who were operated for PCG from 2005 to 2014, were followed up to a maximum of 2 years. Post-operative IOP was the primary outcome measure. Surgical success and complication rates were calculated for each type of surgery. Kaplan Meier (KM) survivor curves were used to assess the cumulative probability of surgical success.

Results: The number of primary surgeries performed was 213 in 131 patients. Repeat surgeries were done in 33 eyes of 26 patients. Most patients were males and were diagnosed before 1 year of age. 52.6% of surgeries were conducted at the Kikuyu Eye Unit (KEU).

Majority of primary surgeries were trabeculectomies (TET- 40.8%) and combined trabeculectomy-trabeculotomies (CTT- 38%). Qualified success was obtained in 73.3% of eyes and complete success in 23% of eyes. KM probability of success at 1 month, 3 months, 6 months, 1 year and 2 years were 95%, 86%, 81%, 76% and 71% respectively. Ahmed Glaucoma Valve (AGV) and CTT had the highest success rates, at 83.3% and 81.8% respectively, whilst TET had the lowest (59.7%). The only significant predictor of surgical failure was a large pre-operative cup disc ratio (CDR). There was no change in the mean number of glaucoma drugs used between pre- and post-operative period. Serious complications were endophthalmitis (1), suprachoroidal haemorrhage (2) and retinal detachment (2). The most common repeat procedure

was AGV. Repeat surgeries achieved a percentage reduction in median IOP of only 21.9% from baseline at final follow-up visit.

Conclusion: The most frequently-performed surgical procedures for PCG are TET and CTT. Surgical intervention was successful up to a period of 2 years post-operatively. CTT and AGV achieved the highest rates of surgical success as primary procedures. A large pre-operative CDR was a risk factor for surgical failure.

1. INTRODUCTION

1.1 PCG and Childhood Blindness

Primary congenital glaucoma (PCG) is a rare but potentially blinding condition affecting children globally.[1] It is the commonest type of glaucoma in childhood and an important cause of childhood blindness worldwide.[2] For this reason, PCG is a major public health problem that requires addressing if VISION 2020 goals are to be achieved. VISION 2020: The Right to Sight Global Initiative is an action plan developed jointly by the World Health Organization (WHO) and the International Agency for the Prevention of Blindness (IAPB) in 1999. Its overall goal was elimination of avoidable blindness by 2020. Childhood blindness is one of its main priorities.[3] The initiative aims to reduce global prevalence of childhood blindness from 0.75 per 1000 children to 0.4 per 1000 children by 2020. This is to be achieved through specific targets including the control of specific diseases associated with childhood blindness, of which glaucoma is one.

Glaucoma in childhood is targeted in the VISION 2020 initiative as a condition that could be treated early to prevent blindness in children.[4] As a result of causing blindness at an early age, this disease can lead to a lifetime of dependency and loss of productivity in the affected children.[5] It also places substantial emotional, social and economic costs to the families of these children and to the society as a whole.[4]

1.2 Epidemiology of PCG

Worldwide incidence of PCG is reported at approximately 1 in 10,000 live births.[6] However, the incidence varies across regions and is said to be higher in developing countries. For instance, it ranges from 1 in 10,000-12,500 in the western world to 1 in 2,500 in Saudi Arabia.[1,7] Similarly, an incidence of approximately 1 in 3300 has been reported in some states of India, where PCG is said to account for 4.2% of all childhood blindness.[8] The greater incidence reported in developing countries has been attributed to the higher rates of consanguinity in these

populations.[9] Additionally, it has been suggested that in such populations, the disease is more severe and the patients frequently present with advanced disease.[8,10] Currently, there is no population prevalence data for PCG in Africa. One hospital based study from Ethiopia estimated that PCG accounted for 2% of all cases of glaucoma.[11] In Cameroon, an estimated prevalence of 0.4% has been reported for juvenile-onset glaucoma.[12]

A positive family history may be seen in some cases of PCG. The British Infantile and Childhood Glaucoma (BIG) Eye Study reported a positive family history in 11% of PCG patients.[13] PCG appears to affect male children more than females, with an approximate male: female ratio of 3:2.[7,13] Nonetheless, the distribution by sex may also vary across regions, with no difference in sex predilection reported in the BIG study[13], whilst a male: female ratio of 2.3:1 has been described in a Chinese population.[14] When familial, the prevalence of PCG may in fact be equal between males and females.[15,16]

1.3 Challenges in the Management of PCG

PCG presents ophthalmologists worldwide with one of the most challenging diseases to manage in childhood.[17] Untreated or poorly treated, the outcome is usually poor. The condition is refractory to medical therapy and surgery is the mainstay of management.[18] Early and prompt microsurgical intervention has been advocated for by several researchers.[1,19,20] This is important to prevent permanent eye damage associated with raised intraocular pressure (IOP) and thus improve visual outcome. Fortunately, the prognosis of PCG has been significantly improving with the development of and advancement in surgical procedures used to manage this condition.[13] Examples of these procedures include angle surgery, trabeculectomy, drainage devices and cycloablative therapy.

Even with successful surgery, long-term visual potential of these patients may be limited by serious complications such as amblyopia, astigmatism, myopia, dislocation of the lens, retinal detachment and optic atrophy.[21] An important determinant of outcome of PCG is thought to be the severity of disease at presentation. Children with advanced disease typically carry a poorer prognosis despite surgical intervention.[1] Additionally, several socio-demographic characteristics of patients may play a role in the final outcome. For instance, age at presentation may be an

important contributing factor to the prognosis of PCG. Studies have reported a worse prognosis in children reporting later compared to their counterparts who present earlier.[22,23] For example, Mandal et al. found that children who had surgery before the age of 6 months had higher success rates than those operated on after 6months of age.[24] This is probably because such patients will present with advanced disease. Similarly, cases with a history of consanguinity have been described as having a more severe and accelerated clinical course.[25] Sex may also play a role in the outcome, with a higher rate of failed surgical management reported in female patients in one Tanzanian study.[26]

PCG is a complex and life-long disease which requires strict and regular follow up for adequate management. This adds to the difficulty in the treatment of this disease.[27] In developing countries especially, there is usually delay in presentation and suboptimal follow up.[26] There may be several barriers to these patients seeking and accessing care consistently. These may include cultural and financial barriers, ignorance, fear, misconceptions, distance to health facility and paucity of ophthalmologists in these regions of the world.[23,28] Successful management of this condition may therefore require collaboration between the families of patients, the health sector, social workers, the community as well as the government.

2. LITERATURE REVIEW

2.1 Definition

PCG is a developmental disorder of childhood associated with elevated IOP and its subsequent effect on the eye. The underlying pathology is said to be an isolated trabeculodysgenesis, which is a maldevelopment of the anterior chamber angle without any other ocular abnormalities.[28] In this regard, it differs from paediatric glaucoma associated with other ocular anomalies or systemic diseases. Several mechanisms have been proposed to explain the pathogenesis of PCG. The presence of an anomalous membrane (Barkan Membrane) mechanically covering the trabecular meshwork has been suggested, whilst other researchers propose a more widespread abnormality of the anterior segment.[29] Generally, a developmental arrest of the anterior chamber angle during embryonic development is thought to be the primary anomaly.

2.2 Inheritance

PCG appears to be sporadic in most cases.[6,30] However in approximately 10% of cases, it is inherited in an autosomal recessive pattern with variable penetrance.[6] In this case, several genes have been linked to the disease, including the cytochrome P4501B1 (CYP1B1) gene on chromosome 2p21 (GLC3A locus).[31] This gene may occur in up to 87% of familial cases of PCG.[29] Familial cases are reportedly more frequent in areas where incidence of the disease is high due to parental consanguinity.[15,30] This could be because consanguinity allows clustering of the genes linked to the disease.

2.3 Clinical Presentation

The clinical features of PCG are usually evident at birth or within the first few years of life. Most cases (60-70%) present within the first 6months of life, with 80% presenting by 1 year of age.[13] However, later presentations may be seen in developing countries.[10] In terms of laterality, most studies propose that the disease occurs bilaterally in an estimated 70-80% of children.[13]

However, recent data from Turkey suggests that the disease may occur bilaterally in up to 92.3% of cases.[27] Even when bilateral, the stage of disease is usually asymmetrical between the two eyes.[29]

PCG is characterized by optic neuropathy associated with a raised IOP and accompanying clinical signs of optic disc cupping, disc asymmetry, enlarged corneal diameter, corneal oedema, Haab striae, increasing axial length and progressive myopia.[6,32] The classical triad of presenting signs are blepharospasm, photophobia and epiphoria.[6] However, studies from developing countries have reported that buphthalmos and corneal oedema may be more common presenting features.[32] This is probably because in these regions, patients typically present with more advanced and severe disease.[22,24]

2.4 Management

2.4.1 Surgical Management

Surgery is the mainstay of management of PCG. There are several options, the chosen procedure usually depending on the patient characteristics as well as surgeon's personal preference and experience. Traditionally, angle surgery (goniotomy and trabeculotomy) had been the first line of management of PCG, with other procedures saved for when angle surgery failed.[18,32] Nonetheless, with development of several newer interventions, there has been considerable debate on the best surgical options for the management of PCG.[18,19,24,32] However, there is paucity of data regarding the effectiveness of these procedures, especially in the African continent.

Several studies have been done in the Western and Arab countries evaluating PCG surgical outcomes.[5,21,33] Conversely, few similar studies have been done in Africa. For instance, Essuman et al. assessed the outcome of combined trabeculectomy trabeculotomy (CTT) in PCG in Ghana[34] whilst Onwasigwe et al. in Nigeria looked at the success of trabeculectomy as an initial procedure.[35] However, these studies only assessed one particular type of procedure. Due to the rarity of PCG, they had very small sample sizes and so the results cannot be generalized to the African continent. Currently, there are very few studies in East Africa evaluating surgical

management of PCG. Bowman et al. in Tanzania looked only at goniotomy outcomes in a rural population.[26]

In Kenya, 6 types of procedures are used to treat PCG. These include:

- Goniotomy
- Trabeculotomy
- Trabeculectomy (TET) with or without anti-fibrotic agents
- Combined Trabeculotomy-Trabeculectomy (CTT)
- Tube Shunt Surgery/Glaucoma Drainage Devices (GDD)
- Cyclodestruction

Goniotomy

Goniotomy is the oldest and one of the most widely used procedures for PCG.[18] It involves incising the trabecular meshwork under visualization with a gonio lens, thus facilitating aqueous outflow.[31] For this reason, it requires corneal clarity to allow good visibility of the anterior chamber. It is thought to be a very effective procedure with few complications. Success rates have been reported between 70-100%.[18] In Tanzania, the authors reported that 86% of children in their study achieved IOPs of <21mmHg at 3months follow up after 1 or more goniotomies.[26] Success of surgery apparently increases with the number of goniotomies done, with Gramer et al. reporting success rates of 72% after 1 goniotomy, which increased to 100% after 3 goniotomies.[36] Outcome of goniotomy is also dependent on patient characteristics. For instance, goniotomy is inappropriate for advanced cases of PCG due to associated corneal clouding and poorer outcomes.[10] A more recent study described endoscopic goniotomy which overcomes the need for corneal clarity.[33] This study reported only a 50% success in PCG and concluded that a bigger study was needed to properly evaluate the safety and efficacy of this procedure.

Trabeculotomy

Trabeculotomy involves making a conjunctival incision, and accessing Schlemm's canal using a rigid probe called a trabeculotome.[37] As such, it has the advantage of not requiring a clear cornea.[31] However, since it uses conjunctiva, it does not leave the conjunctiva intact in the event that future filtering surgery is required. It is also a procedure that requires a high level of skill and appropriate training. Furthermore, it is not always possible to find Schlemm's canal, especially in eyes with distorted anatomy due to buphthalmos.[18] In this case, another advantage of trabeculotomy is that it can easily be converted to trabeculectomy. Several researchers have claimed that success rates of trabeculotomy are comparable with those of goniotomy.[38,39] On the other hand, more serious complications have been reported with trabeculotomy, such as creation of false passages in the eye and haemorrhage.[37]

Newer forms of trabeculotomy have been described such as the illuminated microcatheter-assisted trabeculotomy and suture trabecuolotomy. These procedures are said to overcome some of the disadvantages of trabeculotomy. For instance, suture trabeculotomy allows more flexibility than the rigid trabeculotome, thus allowing up to 360 degrees incising of Schlemm's canal.[40] Nevertheless, this procedure may be associated with the devastating complication of suture misdirection into the suprachoroidal or subretinal space.[18] On the other hand, microcatheter-assisted technique avoids the problem of misdirection by the illuminated microcatheter confirming the location of the probe inside Schlemm's canal.[41] Success rates of around 90% has been reported for both these procedures. However, these procedures require expensive equipment which is not currently available in Kenya.

Trabeculectomy

TET or filtering surgery is not routinely used as first line therapy for PCG. This is because it is thought to be associated with poorer outcomes due to the higher chance of scarring in children.[17,18] The use of adjunctive anti-fibrotic agents, mitomycin-C (MMC) and 5-Fluorouracil (5-FU), may improve the success of this procedure, although evidence about their effectiveness is conflicting.[18,42] A Nigerian study reported a 40% reduction in mean IOP in children who had primary TET for PCG over a 5year period.[35]

TET has also been associated with higher complication rates in the paediatric population, especially when used with anti-fibrotic agents. Sidoti et al. reported that the incidence of bleb-related infections may be as high as 17% in children.[43] There are also concerns about the possibility of anti-fibrotic agents being carcinogenic in children in the long term.[44]

Combined Trabeculectomy-Trabeculotomy

CTT involves performing both trabeculotomy and TET in one sitting, with or without the use of anti-fibrotic agents. Some researchers argue that it has improved outcomes compared to each procedure done singly.[42] In India, a success rate of 75.5% was reported at 1year follow up for CTT alone, even in eyes with advanced disease.[10] However, lower success rates were obtained in Ghana by Essuman et al., who reported an initial high success rate in the first 9 months after surgery, which then dropped to below 45% at 1 year follow up.[34] The authors suggested that racial or genetic influences may account for the difference in success rates and recommended further studies into this possibility. Conversely, in Saudi Arabia, Al Hazmi et al. found the success rate for CTT was high in patients with PCG (~80%), regardless of severity of disease.[22] They reported that compared to trabeculotomy, CTT augmented with MMC gave the best success rates for moderate (80%) and severe (70%) cases of PCG.

Tube Shunt Surgery/GDD

In this procedure, a glaucoma drainage device with a silicone tube in the anterior chamber (AC) is used to shunt aqueous humor to the subconjunctival space, thus bypassing Schlemm's canal.[31] The shunt may be implanted with or without the use of anti-fibrotic agents. There are non-valved and valved devices such as Baerveldt implant and the Ahmed Glaucoma Valve (AGV) respectively. It has been argued that tube surgery offers the best long-term control of IOP in patients with refractory PCG.[17]

The AGV has a unidirectional flow-restriction mechanism which allows aqueous outflow only when IOP is more than 8mmHg, thus reducing complications associated with post-operative hypotony.[45] This finding was confirmed by the Ahmed Baerveldt Comparison (ABC)[46] and

Ahmed versus Baerveldt (AVB)[47] Studies which showed that compared to AGV, patients with Baerveldt implant had more serious post-operative complications. However, these authors also reported a higher success rate with Baerveldt implant with better long-term IOP control.

Current published evidence on the success of AGV implants in the treatment of PCG after other surgeries have failed is controversial. For example, some researchers have reported success rates as high as 90% in eyes with refractory PCG after AGV implantation.[48,49] On the other hand, Chen et al. described a high failure rate of 55% in AGV implantation for refractory PCG compared with children with other types of glaucoma.[50] In a randomized control trial, Beck et al. found that compared to TET with MMC, children who had AGV implants for PCG had higher complication rates.[51] They described complications such as serious hypotony, tube-corneal touch and cataract formation. Conversely, in the Tube versus Trabeculectomy (TVT) study, there were more early postoperative complications in the TET group (60%) compared with the tube group (34%). [52] These authors noted that there was a higher rate of failure and reoperations for glaucoma in patients who underwent TET with MMC.

There have been few studies in Africa looking into the use of AGV in childhood glaucoma. In Kenya, Kiage et al. found that the most common indication for AGV implantation was congenital glaucoma.[53] They reported a high complication rate in 44% of eyes (11 of 25 eyes), including the potentially dangerous complication of blebitis with extrusion of implant in one patient.

Cyclodestruction

Cyclodestructive therapy is usually reserved for patients who have had multiple failed surgeries with uncontrolled IOPs and low visual potential. Several types have been described including cyclocryotherapy, transcleral cytophotocoagulation (CPC) and endoscopic CPC.[18] These procedures all lower IOP through the reduction of aqueous humor production by ciliary body ablation.

Cyclocryotherapy involves freezing the ciliary body, thus destroying the epithelium. This procedure is very aggressive and associated with devastating side effects such as phthisis, retinal

detachment and sympathetic ophthalmia.[54] For this reason, it is not the preferred method of cyclodestruction in refractory PCG and is reserved for eyes with very low visual potential. Success rates are also reportedly poor when used as primary procedure in PCG.[55]

CPC uses laser therapy to destroy the ciliary body. It is preferred to cyclocryotherapy due to less inflammation and complications.[56] In Kenya, diode laser (810nm) is used for CPC. Research has shown that diode laser CPC can satisfactorily control IOP especially in the short-term with a low complication rate.[57] However, most patients will need to be re-treated, with retreatments rates of up to 70% reported in the literature.[58] These authors reported that when it failed, this usually happened within the first 6months of treatment.

Transcleral CPC estimates the location of the ciliary body. For this reason, it may be difficult to do accurately in eyes with buphthalmos due to the distorted anatomy. Endoscopic CPC overcomes this problem by allowing direct visualization of the ciliary body.[17] However, this procedure is invasive and is currently not offered in Kenya.

Other Procedures

There are other procedures reported in the literature which are used in the management of PCG. For example, deep sclerectomy has been described as effective and safe in dealing with advanced cases of PCG in Saudi Arabia.[59] It involves deroofing of Schlemm's canal through a deep scleral flap.[60] As such, theoretically, it should reduce the complications of overfiltration and hypotony as well as serious post-operative infections. However, currently this procedure is not used to treat PCG in Kenya.

2.4.2 Medical Management

PCG is a complex condition that is difficult to manage. As previously stated, medical therapy is often ineffective and surgery is the ultimate management. However, medical therapy still has a role, usually to lower the IOP and clear the cornea enough to allow angle surgery.[28] Drugs can also be used when surgery is inappropriate or high risk, for instance in life-threatening contraindications to anaesthesia.[17] The usual agents, such as β-adrenergic antagonists or carbonic

anhydrase inhibitors (CAI) have been employed as provisional therapy before surgery.[28] However, these drugs have a limited long-term role in the management of PCG. Medical therapy is relatively ineffective and also poorly tolerated long term in children due to serious potential side effects.[18] For instance, alpha adrenergic agonists may cause severe central nervous system depression whilst carbonic anhydrase inhibitors (CAI) could result in serious metabolic disturbances.[18] Adequate knowledge of the side effects of the various medications in the paediatric population and their appropriate management presents additional challenges in the use of drugs to treat PCG.

3. JUSTIFICATION

PCG had been surgically managed in Kenya for years, but there were no published studies evaluating the success of these procedures. This study was expected to provide vital information for both ophthalmologists and patients with regards to the outcome of the various management options available for this disease. This may enable ophthalmologists to tailor management options for particular patients aimed at achieving the best possible outcomes. It may also help hospitals decide which procedures to focus their resources on, since most of the procedures used for PCG management are highly technical and require special training and equipment.

It was anticipated that this study will provide the baseline information needed to facilitate future research in this area and hopefully enable evidence-based practice in the management of PCG.

4. OBJECTIVES

4.1 Broad Objective:

The broad objective of this study was to evaluate the outcomes of surgical management of PCG in 4 tertiary eye hospitals in Kenya.

4.2 Specific Objectives:

The specific objectives of the study included:

I. To establish the surgical procedures currently used in the management of PCG in Kenya.
II. To determine the surgical success of these procedures.
III. To document any additional treatment required after these surgical procedures during the study period.
IV. To determine the rate of surgical complications and identify clinically relevant factors associated with a poor outcome.

5. MATERIALS AND METHODS

5.1 Study Design

This was a retrospective case series.

5.2 Study Setting

The study was conducted in four tertiary hospitals in Kenya, where most surgeries for PCG are performed. These are:

- Kenyatta National Hospital
- PCEA Kikuyu Hospital
- Tenwek Mission Hospital
- Sabatia Eye Hospital

5.3 Target Population:

Records of all children aged <16 years, diagnosed with and surgically managed for PCG in the above hospitals, over the 10-year period of 2005-2014.

5.4 Inclusion Criteria

All available records of children diagnosed with PCG and managed surgically in any one of the institutions within the study period.

5.5 Exclusion Criteria

The following were excluded from the study:

I. Missing records.

II. Eyes who had visual acuity (VA) recorded as non-light perception (NLP) in the pre-operative period and remained NLP post-operatively.

III. Records which did not indicate the type of surgical procedure done.

5.6 Outcome Measures

Primary Outcomes

The primary outcome of this study was the post-operative IOP at the final follow-up visit.

Secondary Outcomes

These included:

1. Proportion of patients achieving surgical success or failure, defined as:
   - **Complete success:** IOP >5mmHg and <21mmHg without glaucoma medications or further glaucoma surgery.
   - **Qualified success:** IOP >5mmHg and <21mmHg with glaucoma medications, without further glaucoma surgery.
   - **Failure:** will include any of the following criteria:
     - IOP ≤5mmHg or ≥21mmHg at the last visit
     - Need for additional glaucoma surgeries
     - The development of NLP vision

2. Change in visual acuity over time.

3. Change in mean horizontal corneal diameter (HCD), axial length (AL), vertical cup disc ratio (VCDR) and the number of patients with corneal clouding.

4. The proportion of surgical complications during the post-operative period.

5. Change in mean/median number of glaucoma medications over time in each group.

6. Number of additional laser or surgical procedures required in each group during the study period.

5.7 Data Collection Tool

A pre-designed data collection form (Appendix I), was used.

5.8 Sample Size

The following formula was used to calculate the minimum required sample size for the study:

$$N = \frac{Z\alpha/2^2\{P(1-P)\}}{d^2}$$

$$= \frac{1.96^2(0.3x\ 0.7)}{0.1^2}$$

$$= 80.1$$

Where:

- $Z\alpha/2$ is critical value for 95% confidence interval, that is 1.96
- P is estimated proportion of population value, in this case estimated failure rate = 30%
- d is margin of error = 10%

After correcting for finite population, N = 78.9

This was done using the following formula $= \frac{N\ x\ X}{X + N\text{-}1}$

Where:

- N is population size (assumed to be 100,000 if you don't know the actual value)
- X is previous sample size calculated

The minimum sample size required for this study to have adequate power of 80% is 40.

This was calculated using the formula: $n = \frac{n}{1+n/N}$

Where:

- n is sample size after population correction
- N is previous sample size calculated

5.9 Sampling Plan

The above sample size gave the minimum required sample (eyes) for the study to have adequate power. However, all eyes of patients who met the inclusion criterion from all the hospitals were included in the study. This was so as to get the true picture of surgical success of these procedures in the various hospitals.

5.10 Data Collection Procedure

A research assistant was employed to assist in the retrieval of files in Sabatia, Tenwek and Kikuyu Hospital. These were qualified ophthalmic clinical officers (OCO) who work in these hospitals. They were trained on day 1 of data collection on the search words and key parameters to look for in the outpatients, ward and records. The patients IP numbers were gotten from these records and use to retrieve their files from the main medical records department of each hospital. In Tenwek, the records were digital whereas it was manual for the remaining hospitals. I resided near/in each of these 3 hospitals for the week during which data were collected. For KNH, data were collected after working hours.

The following search words were used: glaucoma, congenital, EUA, IOP, Trab, TET and buphthalmos.

All information relevant to the study were collected and entered into the data collection form. Data included:

- Demographic details: such as age, sex, race and residence

- Clinical Presentation:
    - Age of onset of symptoms, age at presentation, age at diagnosis , pre-operative VA, HCD, corneal clarity, IOP, VCDR, refractive errors, age at which surgery was performed. Eyes were classified in terms of disease severity according to the classification employed by Al-Hazmi et al.[22]
    - Any coexisting ocular abnormalities, a history of consanguinity and a positive family history of glaucoma
    - Number of glaucoma medications used pre-operatively
- Outcome measures:
    - Post-operative VA, VCDR, HCD, corneal clarity, IOP, medications used, complications and their subsequent management if any, refractive errors and duration of follow up
    - Follow up period was divided into day 1, month 1, month 3, month 6, year 1 and year 2
    - Outcome measures were collected at each follow-up visit
    - For patients not presenting on the exact scheduled date for follow-up visit, an acceptable window was used as indicated in Table 1 below[61]

Table 1 indicates the timing of post-operative follow-ups for children operated for PCG.

Table 1: Ideal, preferred and acceptable time period of follow-up after PCG surgery

Follow-up visit	Ideal time (days)	Preferred time (days)	Acceptable time (days)
Day 1	1	1	1-3
Month 1	30	23-37	15-59
Month 3	90	76-104	60-120
Month 6	182	161-203	121-270
Year 1	365	305-425	271-455
Year 2	730	670-790	638-912

5.11 Data Analysis

Stata IC 12 statistical software was used for data analysis.

The primary surgeries were the basis of this study. The repeat surgeries were analyzed separately at the end of the results section.

Descriptive analysis was done to determine the frequencies and proportions of the variables and presented in tables and graphs where appropriate. The normality of the data was assessed using histograms. For those not normally distributed, transformation of the data was attempted, when appropriate, to find the best possible normal fit. The mean with standard deviations were reported for data which was normally distributed. However, majority of the data was not normally-distributed without any best normal fit even on attempted transformation. As such, medians and interquartile ranges were used to summarize the data. Students' t-test or the equivalent was used to study the statistical significance of differences between pre- and post-operative measurements at each follow up visit in these patients. Statistical significance was set at a p-value of <0.05 with a confidence interval of 95%.

Univariate regression analysis was used to determine correlations between outcome measures and demographic characteristics and presenting features of the patients.

Due to the rarity of PCG, patient numbers were expected to be low. As such, the only factor related to outcome of surgery that this study had adequate power to test, based on the sample size, was whether or not the patient had had prior glaucoma surgery. The study lacked adequate power to test other factors linked to outcomes of surgery such as age at diagnosis, age at surgery, family history of consanguinity, axial length, horizontal corneal diameter and surgeons' experience. However the analysis was still done to give an overall picture of the possible factors which may predict failure of surgery in these eyes.

Kaplan-Meier analysis was used to calculate the cumulative probability of surgical success for the different follow-up periods.

5.12 Ethical Consideration

Ethical permission was sought and obtained from Kenyatta National Hospital/ University of Nairobi Ethics and Research Committee. Permission to conduct the study was also obtained from the administrative heads of the other hospitals.

Patient details and identity were kept anonymous at all times through the use of coded data collection forms with matching codes on the patient's file. The information on the data collection forms was only accessible to the primary investigator who maintained confidentiality and adhered to data protection standards.

This study aimed to produce results which would contribute towards evidence-based practice in the management of PCG. As such, patients with PCG in this setup will benefit from the safest, most successful and appropriate therapy geared towards preserving their vision.

During this study, the data was stored only in a computer and was encrypted to ensure confidentiality. Only the primary investigator had access to this electronic data. The coded data collection forms and all digital records of the data will be destroyed after publication to ensure confidentiality is maintained. The primary investigator had no conflict of interest.

5.13 Work Plan

This study was conducted from December 2014 to January 2016. Table 2 below gives a summary of the time line for the study.

Table 2: Study timeline

Period	Activity
December 2014	Proposal development
March 2015	Proposal presentation
April 2015	Submission for ethical approval
September-October 2015	Data collection
October-December 2015	Data analysis
December 2015	Report writing
January 2016	Dissemination of results

6. RESULTS

Figure 1 below gives a flow chart of this study. It also shows the total number of patients and eyes studied and the surgeries done.

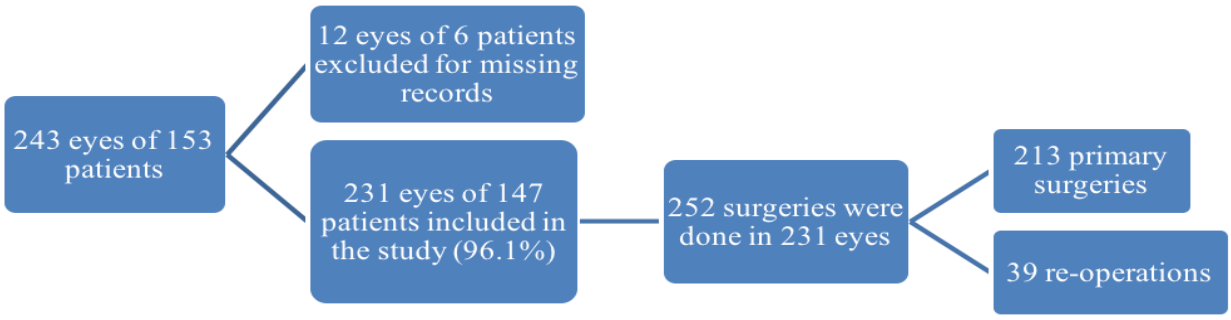


Figure 1: Flow chart of files

Figure 2 shows the annual distribution of the surgeries reported in this study.

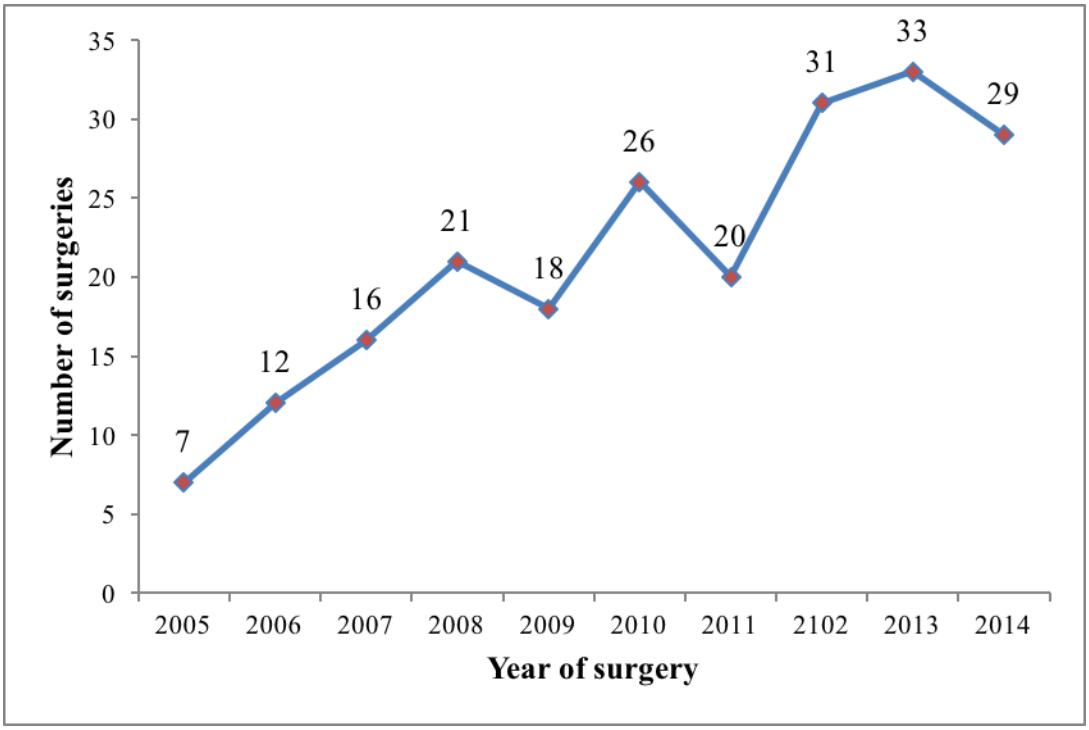
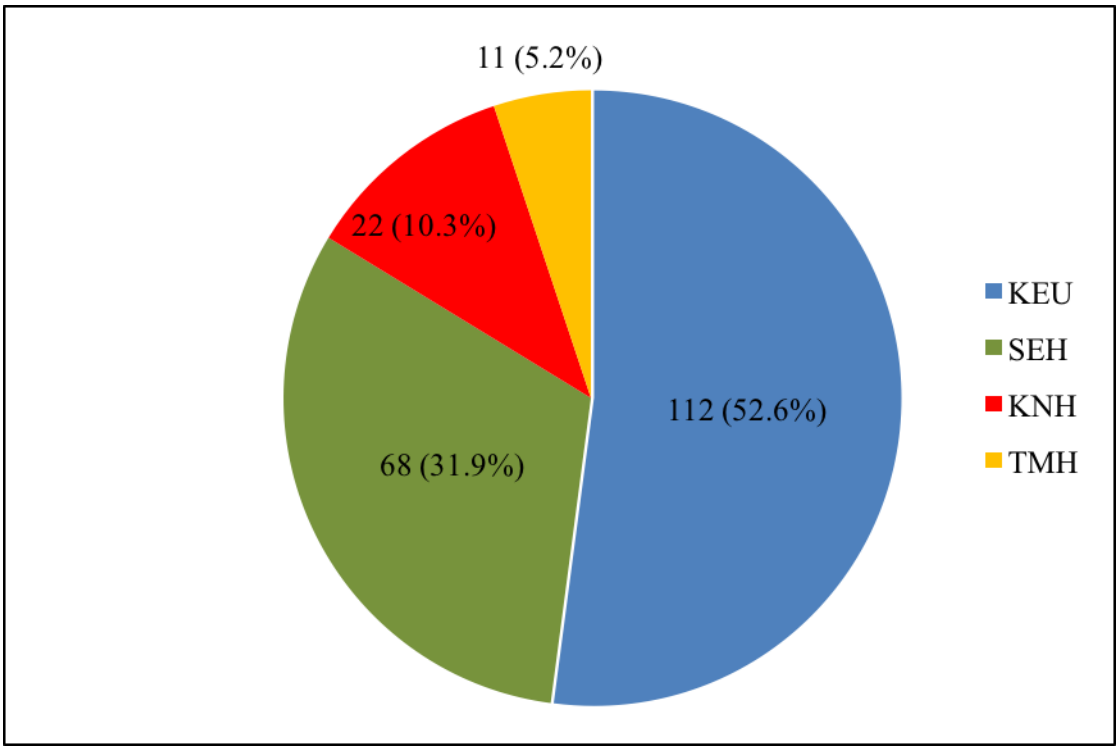


Figure 2: Annual trend of primary surgeries done (n=213)

Overall, there was a steady rise in the number of surgeries being done for PCG over the 10 years. Most of the surgeries (65.3%) were done from 2010-2014.

Figure 3 below illustrates the hospitals included in the study and the surgeries that were done in these hospitals.



Key
KEU: Kikuyu Eye Unit
SEH: Sabatia Eye Hospital
KNH: Kenyatta National Hospital
TMH: Tenwek Mission Hospital

Figure 3: Surgery distribution by hospital

Most (52.6%) of the surgeries were done at PCEA Kikuyu Hospital, followed by Sabatia Eye Hospital at 31.9%.

Figure 4 below illustrates the number of eyes seen during each follow-up visit.

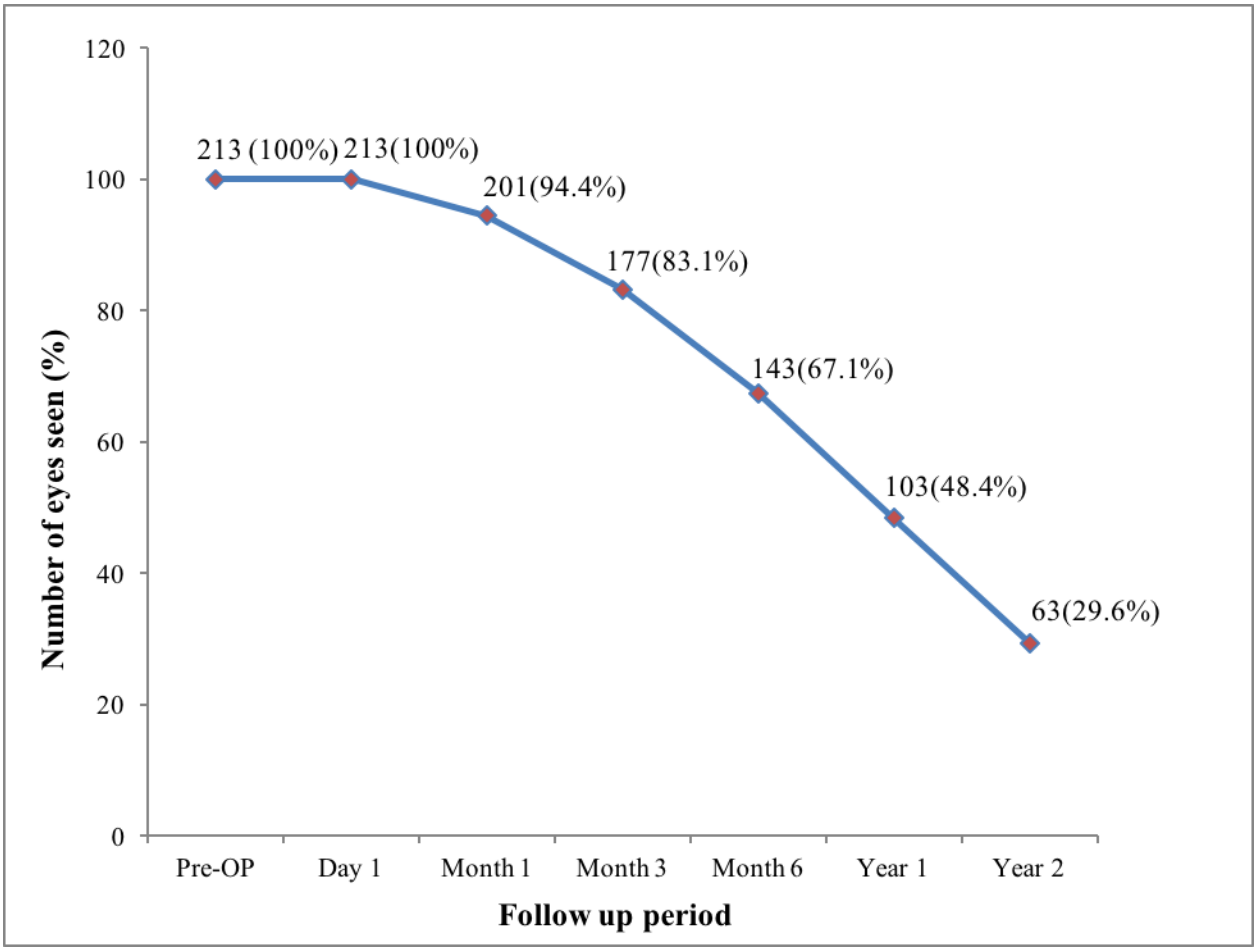


Figure 4: Compliance to follow-up appointments (n=213)

All eyes were reviewed on the first post-operative day. However the percentage gradually declined in subsequent follow-up visits, with only 29.6% of eyes being examined during the 2-year follow-up visit.

Table 3 gives the baseline characteristics of the children who had primary surgery.

Table 3: Distribution of the study population by sex and laterality

Patients	**Number (n=131)**	**Percentage**
Sex		
Male	93	71
Female	38	29
Laterality		
Bilateral	108	82.4
Unilateral	23	17.6
Eyes	**Number (n=213)**	**Percentage**
Right vs. Left		
Right	106	49.8
Left	107	50.2
Classification of Disease Severity[22]	**Number (n=213)**	**Percentage**
Mild	6	2.8
Moderate	134	62.9
Severe	71	33.3
Not recorded	2	0.9

All the 131 patients were of African descent. Only one patient recorded a positive family history of congenital glaucoma (older brother). There was no mention of a history of consanguinity for any of the patients. The male: female ratio was 2.4:1 and 82.4% of patients (108) had bilateral PCG.

Most eyes (96.2%) had moderate to severe disease (see Appendix II).

Figure 5 below shows the age at diagnosis of the patients managed for PCG in these institutions.

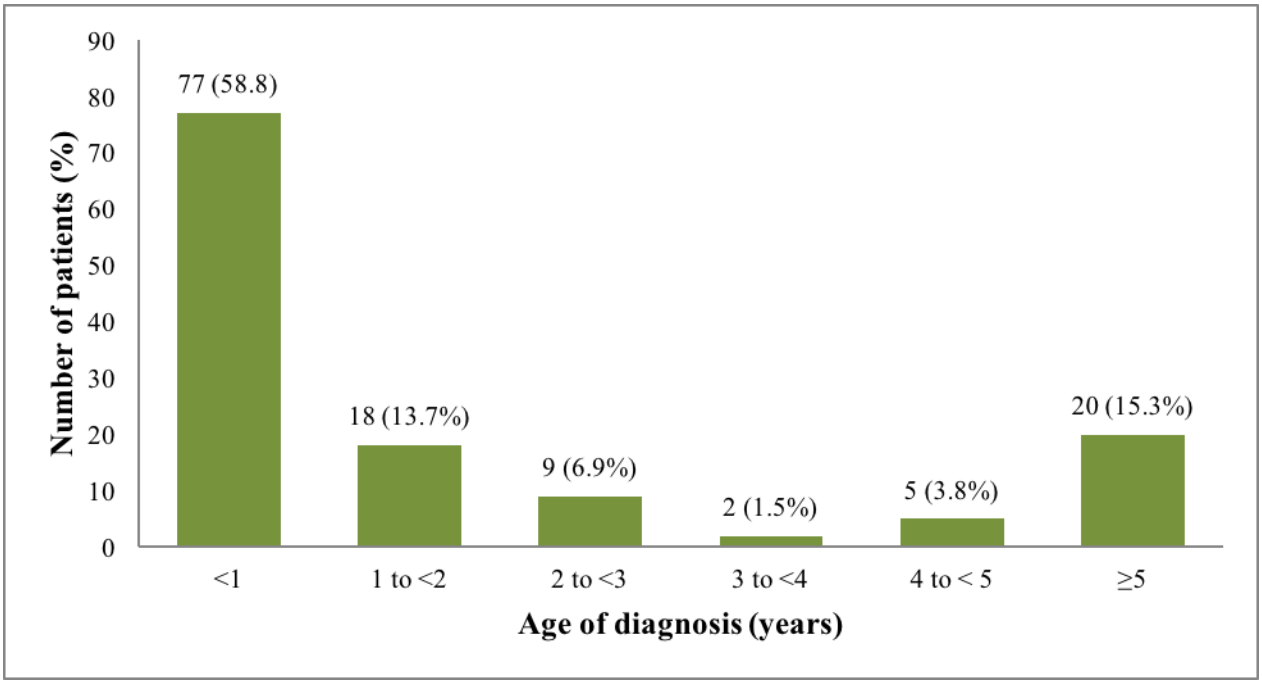


Figure 5: Distribution of the 131 patients by age at diagnosis

Majority (58.8%) of the patients were diagnosed before 1 year of age and approximately 80% before 3 years of age. The median age at diagnosis was 9 months (3-12), with a range of 3 weeks to 15years, whilst mean age was 23.1 months (SD 33.1).

Figure 6 shows the signs of PCG in the studied eyes. Some eyes presented with more than one sign/symptom.

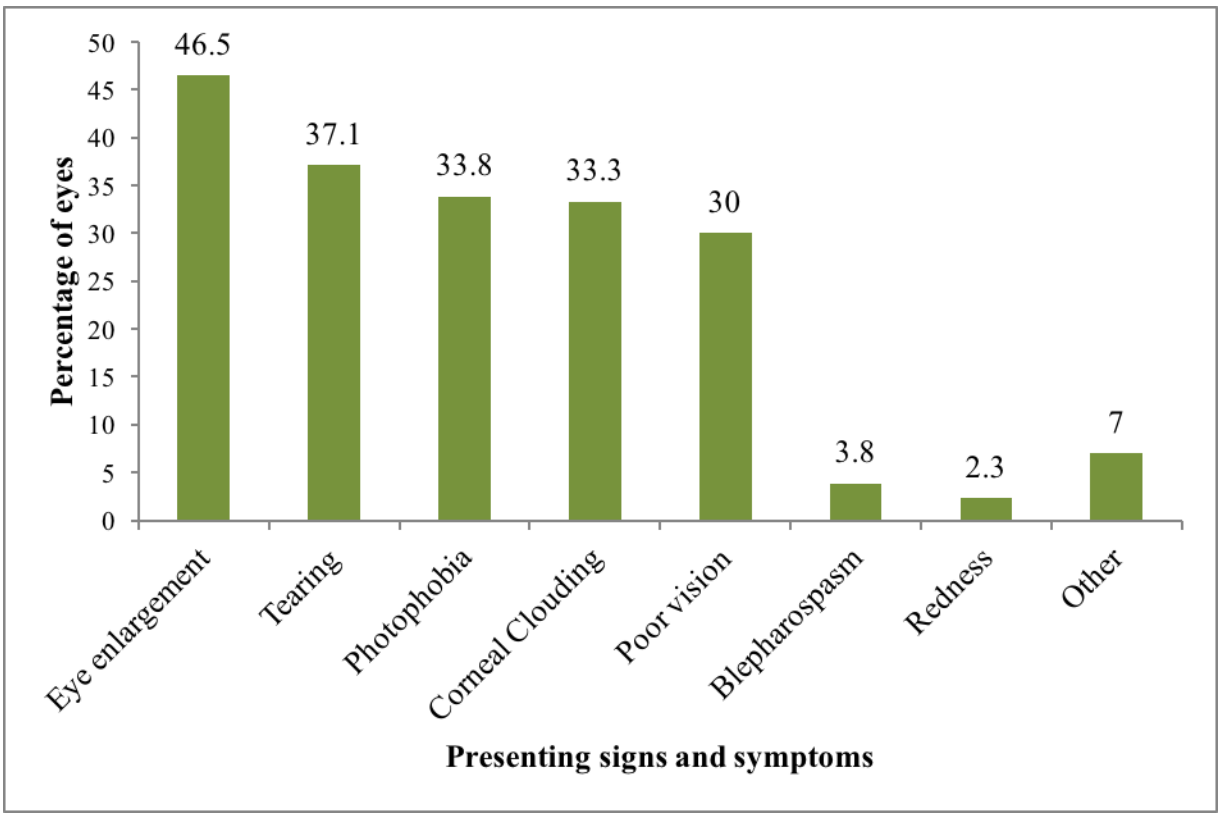


Figure 6: Presenting signs and symptoms (n=213)

Buphthalmos was the most common presenting complaints, seen in 46.5% of eyes. The signs and symptoms listed as other included pain (10 eyes), discharge (3 eyes) and proptosis in 1 eye.

The clinical features of the study eyes which were elicited at examination are described in table 4 below.

Table 4: Pre-operative clinical features at examination

Examination findings	Eyes (n=213)	
	Number	Percentage
Buphthalmos	179	84
Cornea		
Clear	12	5.6
Haze	187	87.8
Oedema	8	3.8
Scar	1	0.5
Striae	2	0.9
Subluxated lens	8	3.8
Other	4	1.9
Clinical findings not recorded	3	1.4

Majority of the eyes (84%) already had buphthalmos at presentation. Only 12 out of the 213 eyes had clear corneas. The examination findings listed as others included descemetocoele (1 eye), vitreous haemorrhage (1 eye) and retinal detachment (2 eyes).

Table 5 indicates the various methods of recording pre-operative visual acuity that was used for the study eyes.

Table 5: Pre-operative visual acuity

Visual acuity test (n=213)	Number of eyes	Percentage
Logmar	11	5.2
Others	156	73.2
Not recorded	46	21.6
Others (n=156)	**Number of eyes**	**Percentage**
Picks 100s & 1000s	6	3.8
Picks objects	24	15.4
Follows objects	21	13.5
Hand motion	5	3.2
Follows light	67	42.9
Perception of light	13	8.3
Blink reflex	4	2.6
Not following light	12	7.7
No light perception	4	2.6

Only 11 eyes had logmar equivalent visual acuity recorded pre-operatively. Majority (73.2%) of the eyes had VA recorded in other ways. VA was not recorded for 21.6% of eyes.

The distribution of pre-operative IOP of study eyes is given in figure 7 below.

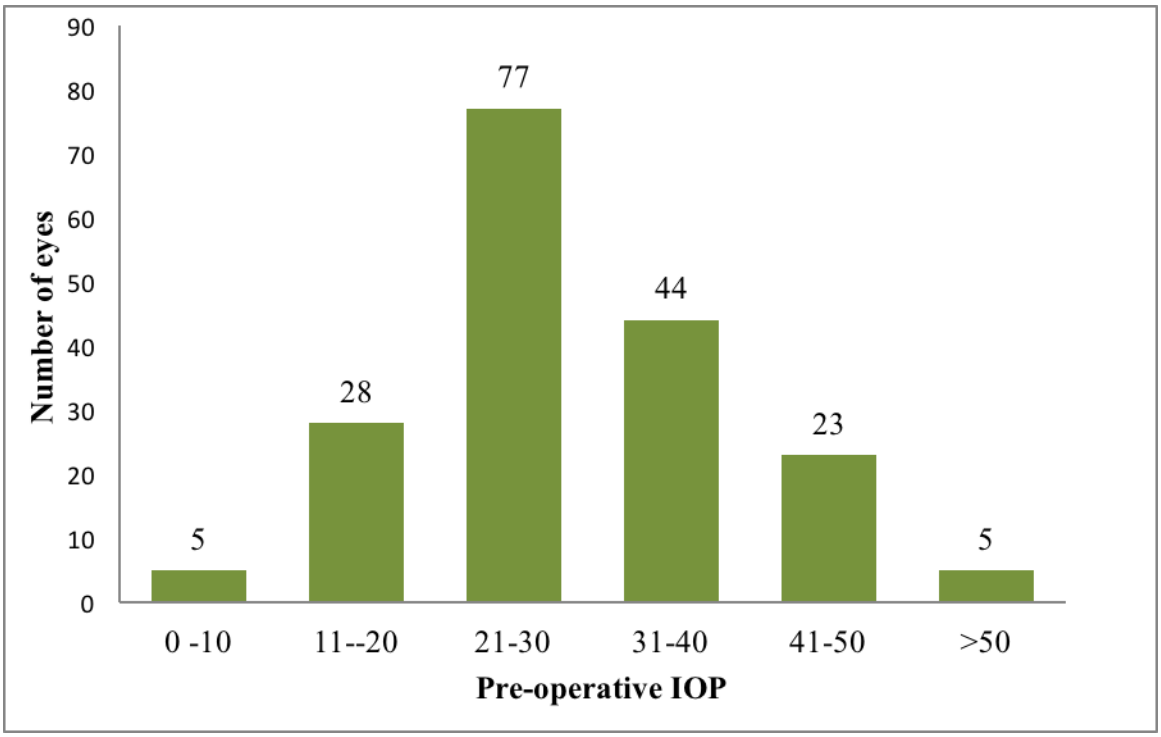


Figure 7: Pre-operative IOP (n=186)

Most of the eyes (82.3%) had a pre-operative IOP recorded as ≥21mmHg. The median pre-operative IOP was 29mmHg (21-31) and the mean was 29.9mmHg (11.4). Pre-operative IOP values ranged from a minimum of 7mmHg to a maximum of 70mmHg.

Pre-operative IOP was not recorded for 27 eyes (12.7%).

Table 6 gives the summary statistics of other pre-operative examination findings of the study eyes.

Table 6: Other pre-operative clinical features

Variable	Number of eyes (n)	Median	Inter quartile range	Range
Pre-op HCD	150	13.5	12.5-14	10-20
Pre-op AL	22	22.4	19.8-23.7	18.9-28.8
Pre-op CCT	16	538	477.4-563	259.4-965
Pre-op CDR	76	1.0	0.6-0.9	0.2-1
Pre-op Refractive error	10	-6.1	-9.1 to -5.1	-10.25 to 1

HCD was the most common pre-operative examination done with values ranging from 10 to 20mm.

Table 7 below describes the type of anti-glaucoma drugs that were used pre-operatively for IOP control in this study. Some eyes were on more than one anti-glaucoma drug.

Table 7: Pre-operative use of anti-glaucoma medications

Pre-operative glaucoma drugs	Distribution by eyes	
Number of drugs	**Number of eyes (n=213)**	**Percentage (%)**
0	74	34.7%
1	93	43.7%
2	41	19.3%
3	3	1.4%
4	2	0.9%
Type of drug	**Number of eyes (n=139)**	**Percentage**
Beta-Blocker	128	92.1%
Prostaglandin Analogue	9	6.5%
Oral Carbonic Anhydrase Inhibitor (Diamox)	20	14.4%
Topical Carbonic Anhydrase Inhibitor	35	25.2%

Most of the eyes were on 1 anti-glaucoma drug in the pre-operative period (43.7%). 34.7% of eyes were not on any anti-glaucoma medications pre-operatively. The median number of drugs used pre-operatively was 1 (0-1) and mean was 0.9 (0.82).

For eyes on anti-glaucoma drugs, beta-blockers were the most commonly used for IOP control (92.1%). Of note is that none of the eyes were on an alpha-2 agonist or pilocarpine during this period.

Figure 8 below illustrates the type of surgeries done as a primary procedure for PCG in the study eyes.

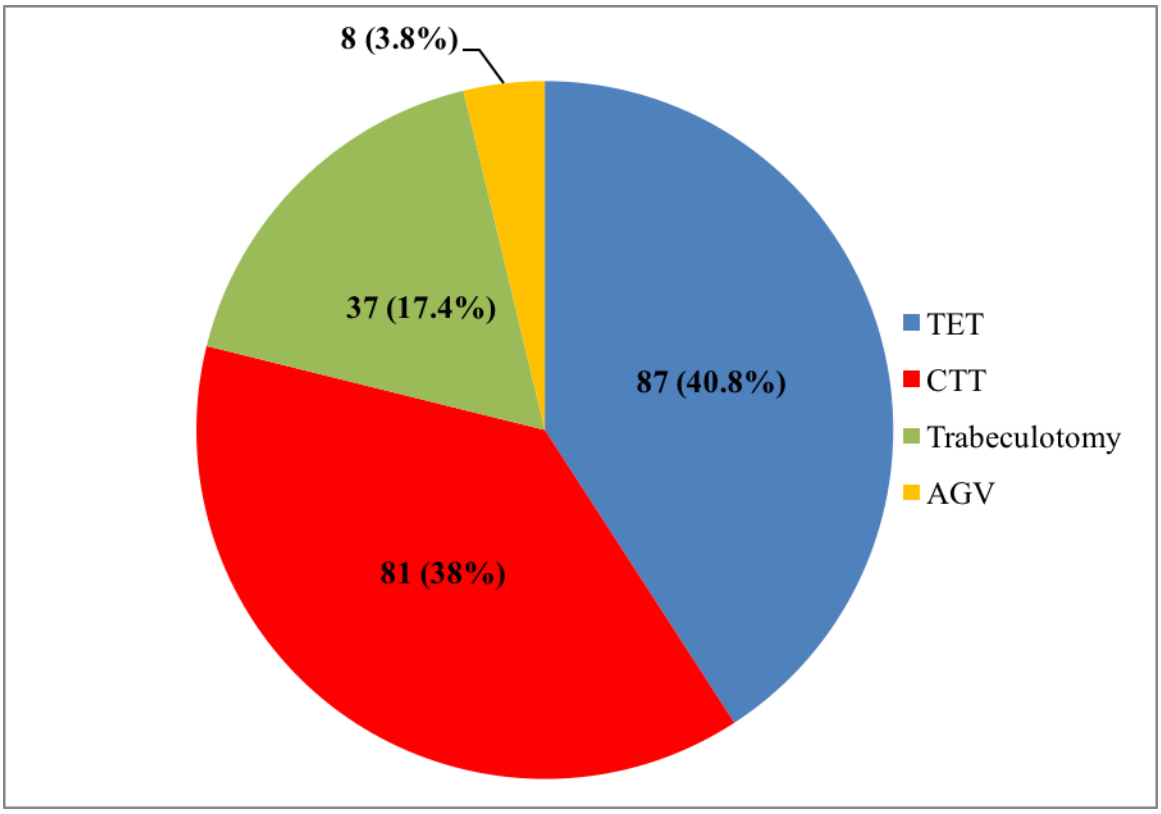


Figure 8: Types of primary glaucoma surgeries (n=213)

TET and CTT were the most common types of surgeries done, in 40.8% and 38% of eyes respectively. 37 TET's (42.5%) were performed with 5-FU, whilst 13 CTT's (16%) were performed with anti-fibrotic agents (1 with 5-FU and 12 with MMC).

Table 8 below describes a comparison between the median pre- and post-operative IOP for the different follow-up periods in this study. This was done using only eyes which had both pre-operative and post-operative IOP values for each follow-up period (n).

Table 8: Comparison of median pre-operative and post-operative IOP for different follow-up visits

Follow-up period	Pre-operative median IOP (IQR)	Post-operative median IOP (IQR)	p-value
Day 1 (n=28)	37 (26-40)	12 (5-12)	**0.00**
Month 1 (n=82)	30 (21-32)	17 (13-20)	**0.00**
Month 3 (n=67)	30 (21-35)	18.5 (10-21)	**0.00**
Month 6 (n=63)	25 (21-29)	15.5 (10-17)	**0.00**
Year 1 (n=60)	25 (20-30)	13 (10-16)	**0.00**
Year 2 (n=53)	24 (21-29)	13 (11-15)	**0.00**

There was a statistically significant reduction in the median IOP for all follow-up periods.

Figure 9 shows the steady reduction of median IOP from the pre-operative period over the various follow-up visits.

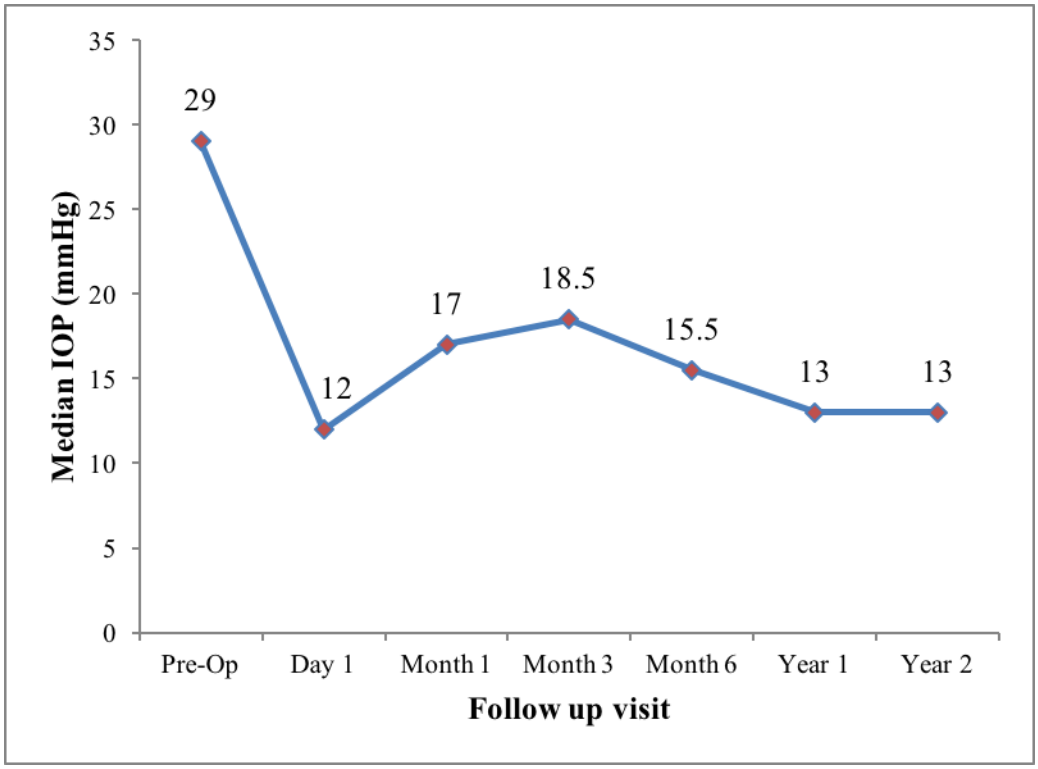


Figure 9: Reduction in median IOP post-operatively

The peak reduction in median IOP was seen on the first post-operative day.

Figure 10 shows the percentage reduction in median IOP from the baseline pre-operative period over the various follow-up visits.

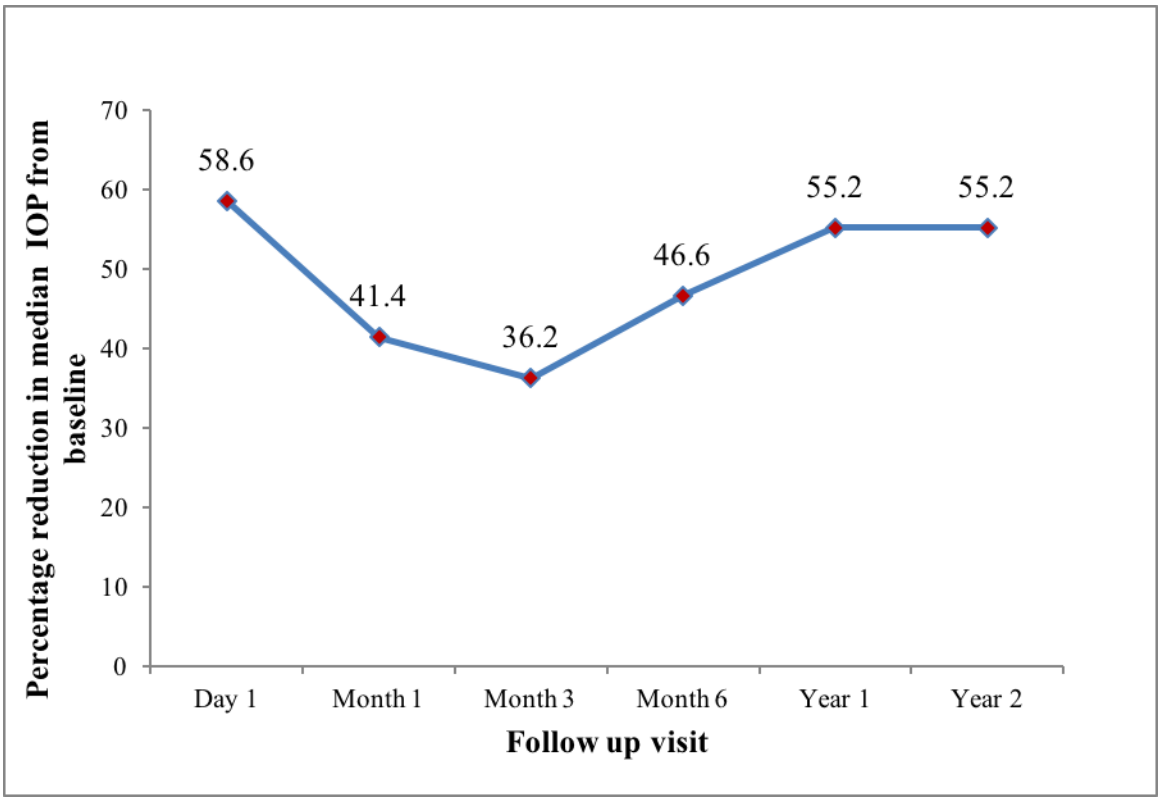


Figure 10: Percentage reduction in IOP from baseline

The highest percentage reduction in median IOP from baseline was seen on the first post-operative day. The percentage reduction in median IOP from baseline was >30% for all follow-up visits.

Table 9 below shows the reduction in median IOP as well as the percentage reduction in median IOP from baseline at the final follow-up visit, for the different types of glaucoma surgeries done for PCG in this study.

Table 9: Comparison of pre-operative and post-operative median IOP for different types of surgery

Surgery Type	Pre-operative median IOP (IQR)	Post-operative median IOP (IQR)	p-value	Percentage reduction in median IOP
TET (n=52)	32 (24-36)	17.5 (10-21)	**0.00**	**45.3**
CTT (n=61)	24 (21-26)	13 (10-15)	**0.00**	**45.8**
Trabeculotomy (n=23)	28 (16-30)	17 (11-17)	**0.00**	**39.3**
AGV (n=4)	41.5 (30-42)	19 (15-19)		**54.2**
p-value	0.39			

There was a statistically significant reduction in median IOP for TET, CTT and trabeculotomy. For AGV and CPC, the number of eyes was too small to accurately calculate a p-value.

When percentage reduction in median IOP from baseline is considered, AGV had the highest reduction at 54.2%.

Of note, there was no statistically significant difference between the median pre-operative IOP of the different surgical groups (p=0.39).

Table 10 below shows the comparison between pre- and post-operative median IOP for surgeries in which anti-fibrotic agents were used and those without use of anti-fibrotic agents. This comparison is only made with eyes that had an IOP value at final follow-up visit

Table 10: Comparison of pre- and post-operative median IOP between surgeries done with and without anti-fibrotic agents

Surgery type	Pre-operative median IOP (IQR)	Post-operative median IOP (IQR)	p-value	Percentage reduction in median IOP
Without anti-fibrotics (n=132)	29 (21-31)	16 (11-18)	**0.00**	**44.8%**
With anti-fibrotics (n=30)	29 (20.5-31.5)	12 (8.5-13)	**0.00**	**58.6%**
p-value	0.27	0.18		

Surgeries with anti-fibrotic agents achieved a higher percentage reduction in median IOP from baseline (58.6%) compared to those without anti-fibrotic agents (44.8%). However there was no statistically significant difference between the post-operative median IOP for both groups (p=0.18).

Figure 11 describes the post-operative IOP at final follow-up visit.

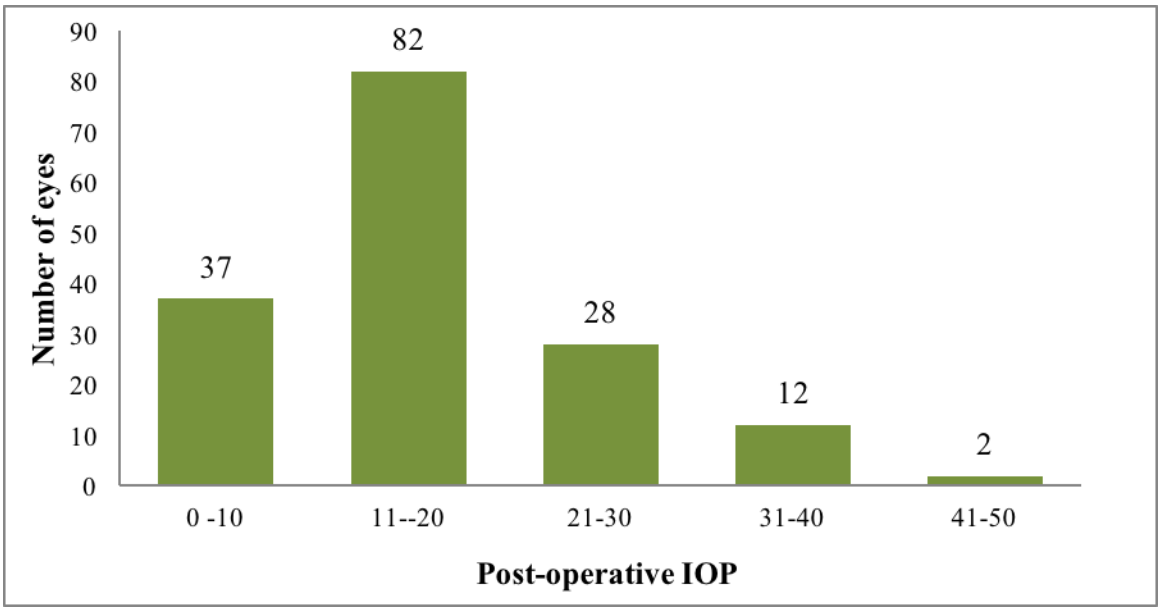


Figure 11: IOP at final follow up visit (n=161)

At final follow-up visit, most of the eyes (73.9%) had IOP values <21mmHg. The median IOP at final follow up visit was 15mmHg (10-17) and the mean was 17mmHg (8.6). The IOP values ranged from 3mmHg to 44mmHg.

Table 11 shows the percentage of eyes with surgical success/failure at the final follow-up visit.

Table 11: Surgical success (n=161)

Qualification	Number of eyes	Percentage
Complete success (IOP >5 and <21 without additional anti-glaucoma drugs)	37	23
Qualified success (IOP >5 and <21 with or without additional anti-glaucoma drugs)	118	73.3
Failure (IOP ≤5 and ≥21 or loss of NLP vision)	43	26.7

Qualified success was seen in 73.3% of eyes at final follow-up visit.

Figure 12 shows the cumulative probability of qualified surgical success for the different follow-up periods as shown by the Kaplan Meier survival curve.

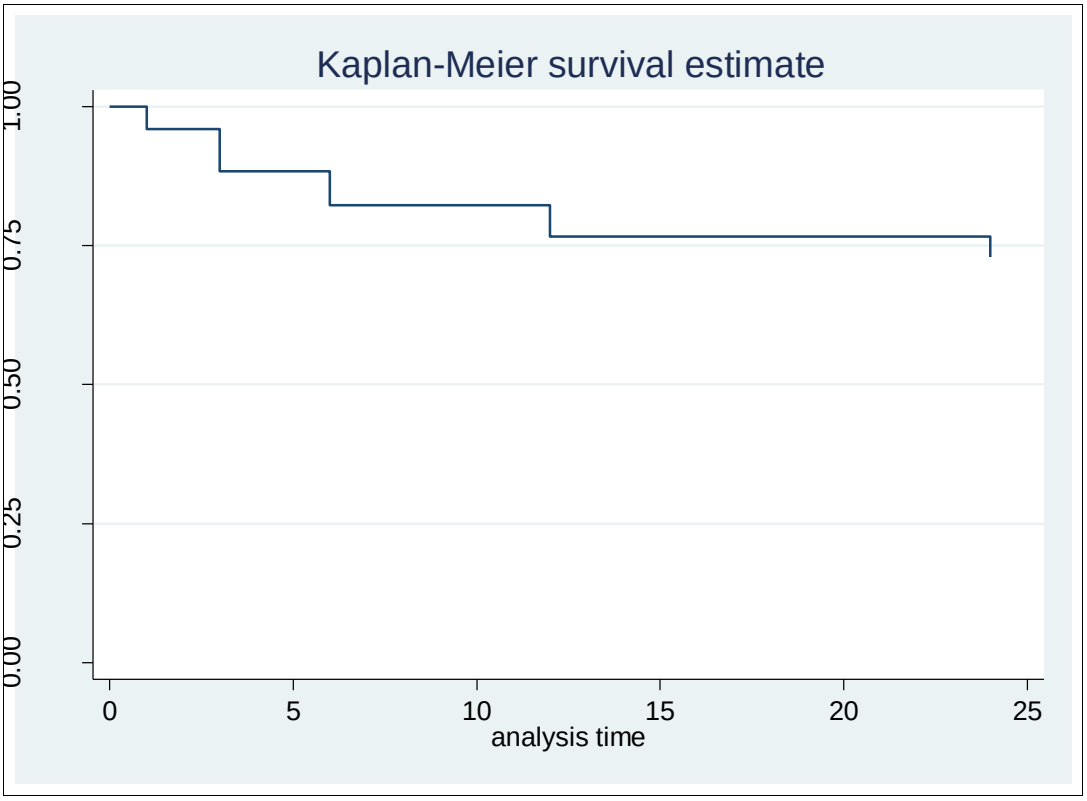


Figure 12: Kaplan Meier survival estimate for final IOP

Kaplan Meier survival function showed a probability of IOP success of >90% at month 1, decreasing to about 70% by year 2 post-operative visit.

Table 12 below gives the rates of qualified surgical success and failure for the different types of glaucoma surgeries analyzed in this study.

Table 12: Qualified surgical success for the different types of surgeries at the final follow-up visit

Type of surgery	5>IOP<21	Success (%)
TET (n=62)	37	**36 (58.1%)**
CTT (n=66)	55	**54 (81.8%)**
Trabeculotomy (n=27)	21	**21 (77.8%)**
AGV (n=6)	5	**5 (83.3%)**

At final follow-up visit, AGV and CTT had the highest rates of surgical success at 83.3% and 81.8% respectively. Of note is that 2 eyes (1 post CTT and 1 post TET), despite having an IOP of <21mmHg, still developed NPL vision and so were regarded as failure.

Table 13 below gives the rates of surgical failure for the different types of glaucoma surgeries analyzed in this study.

Table 13: Surgical failure for the different types of surgeries at the final follow-up visit

Type of surgery	No. of eyes with failure	Percentage
TET (n=62)	26	41.9
CTT (n=66)	12	18.2
Trabeculotomy (n=27)	6	22.2
AGV (n=6)	1	16.7

At final follow-up visit, TET had the highest rates of surgical failure at 41.9%.

Figure 13 illustrates the cumulative probability of qualified surgical success for the different types of surgeries at each follow-up period as shown by the Kaplan Meier survival curve.

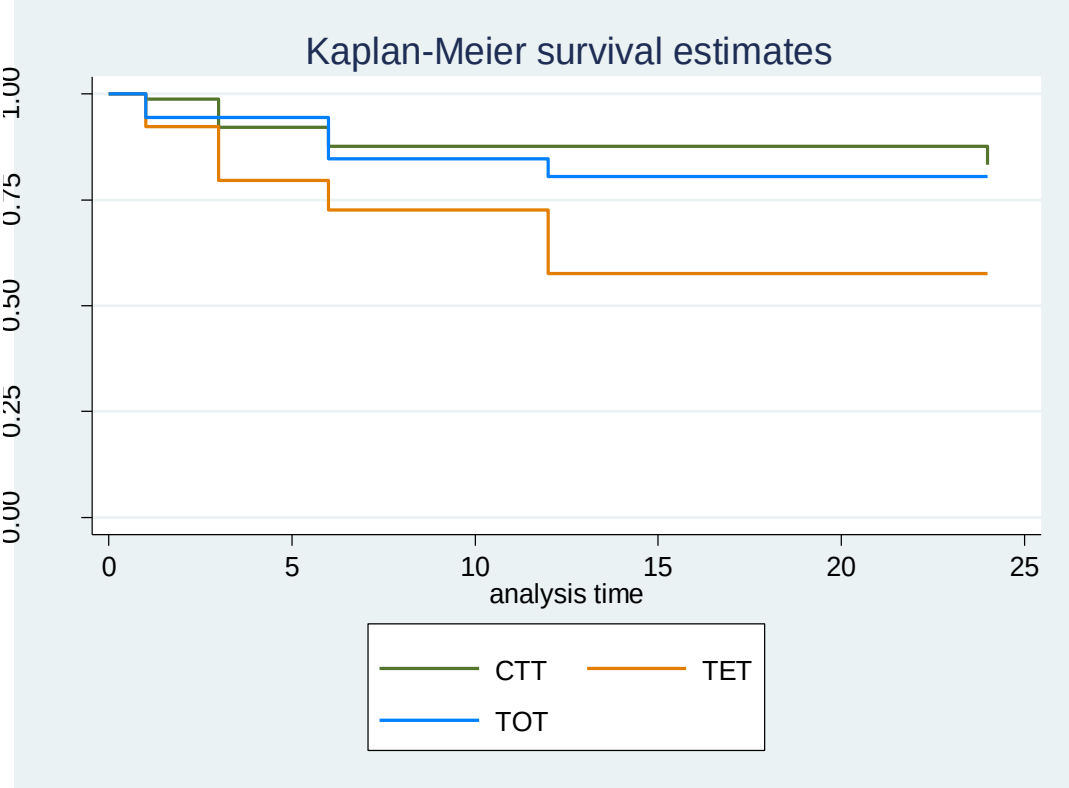


Figure 13: Kaplan Meier survival estimate for final IOP by type of surgery

CTT had the highest probability of success at 2 years follow-up visit, followed closely by trabeculotomy. The number of eyes with IOP values at final follow-up visit was too few for AGV to construct Kaplan Meier curves.

Table 14 below gives the VA recorded at the final follow-up visits for all study eyes.

Table 14: Visual acuity tests at final follow-up visit

Visual acuity test	Number of eyes (n=213)	Percentage
Logmar test	28	13.1
Others tests	163	76.5
Not recorded	22	10.3
Others (n=163)	**Number of eyes**	**Percentage**
Picks 100s & 1000s	31	19
Picks objects	39	23.9
Follows objects	30	18.4
Hand motion	8	4.9
Follows light	27	16.5
Perception of light	18	11
Not following light	3	1.8
No light perception	5	3.1

Only 28 eyes (13.1%) had logmar or equivalent reported VA. The majority of eyes (76.5%) had other forms of VA reporting. VA was not recorded for 22 eyes (10.3%)

Table 15 below indicates the change in corneal status of eyes from pre- to post-operative period. Data on corneal clarity status was absent for 3 eyes pre-operatively and for 8 eyes postoperatively. A corneal status of "not clear" included corneal haze, oedema, striae and scar.

Table 15: Change in corneal status

Corneal clarity	No. of eyes pre-op (n=210)	No. of eyes post-op (n=205)	p-value
Clear	12 (5.7%)	126 (61.5%)	**0.01**
Not clear	198	79	

There was a significant increase in the number of eyes with clear cornea from the pre-operative period to post-operative period (p=0.01).

Table 16 shows the change in the clinical features of the study eyes from the pre-operative values to the post-operative values at final follow-up visit. This is done with eyes for which both pre-operative and post-operative values could be compared for the different variables.

Table 16: Change in clinical characteristics of the eyes

Variable	Pre-operative median (IQR)	Post-operative median (IQR)	p-value
CCT (n=6)	546 (477.4-570.8)	490 (452-494)	**0.03**
HCD (n=65)	13.5 (12.5-14)	13.3 (12.5-13.5)	0.12
AL (n=8)	22.5 (19.8-23.7)	22.2 (20.3-23.9)	**0.03**
CDR (n=57)	1.0 (0.6-0.9)	0.7 (0.3-0.8)	**0.00**
Refractive Error (n=9)	-6.1 (-9.1 to -5.1)	-4.2 (-9 to -3.5)	0.86
VA (n=6)	0.78 (0.48-0.8)	0.6 (0.3-0.8)	0.39

There were statistically significant reduction between the pre-operative and post-operative medians for CCT, axial length and CDR.

Table 17 below shows the number of anti-glaucoma drugs used for IOP control during each follow-up visit.

Table 17: Post-operative use of anti-glaucoma drugs for each follow-up visit

Follow-up period	Mean number of drugs used post-operatively
Day 1 (n=213)	0.2 (0.4)
Month 1 (n=201)	0.45 (0.5)
Month 3 (n=177)	0.46 (0.54)
Month 6 (n=143)	0.51 (0.55)
Year 1 (n=103)	0.83 (0.62)
Year 2 (n=63)	0.84 (0.45)

Figure 14 describes the change in use of anti-glaucoma medications from the pre-operative period to post-operative period, calculated for eyes present at each follow-up visit.

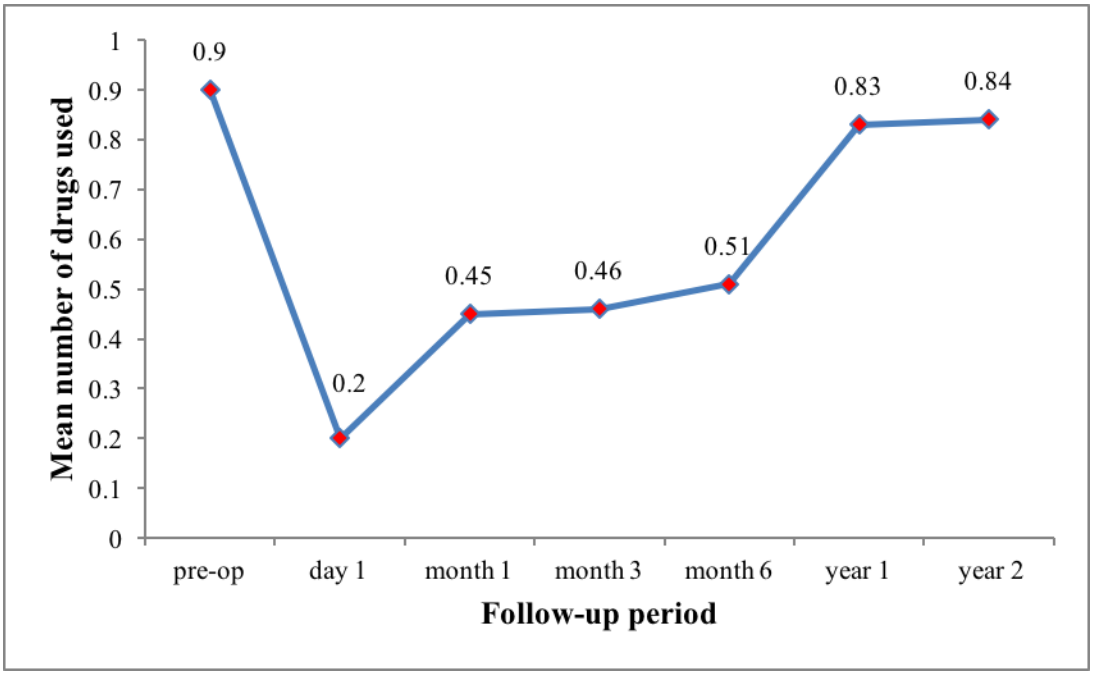


Figure 14: Change in mean number of glaucoma drugs used

The peak reduction in mean number of drugs used was seen in the first post-operative day. After that, there was a gradual increase in the mean number of drugs used.

Table 18 indicates the number of additional glaucoma procedures that were needed for each type of primary surgery done.

Table 18: Number of additional laser/surgical glaucoma procedures needed for each type of surgery

Surgery type	Additional procedures per surgery type	
	Number	Percentage
TET (n=87)	6	6.9%
CTT (n=81)	6	7.4%
Trabeculotomy (n=37)	1	2.7%
AGV (n=8)	2	25%

AGV had the highest rate of re-operations at 25% whilst trabeculotomy had the lowest at 2.6%.

Table 19 gives the number of eyes which were re-operated in this study as well as the previous glaucoma surgeries that had been done in these eyes.

Table 19: Re-operations for PCG (n=39)

Surgery	Previous surgeries	Re-operations
AGV	8	15
TET	14	8
CPC	-	8
CTT	10	4
Trabeculotomy	5	2
Goniotomy	-	2

A total of 39 re-operations were done in 33 eyes (14.8%), 12 eyes achieved IOP <21mmHg (36.4%). 5 eyes (2.2%) needed 2 or more re-operations, only 1 achieved IOP<21mmHg.

The most common previous surgery done was TET, and the most common re-operation was AGV.

The median pre-operative IOP was 32mmHg (26-34) and median post-operative IOP was 25mmHg (15-26). The percentage reduction in median IOP from baseline was 21.9% at final follow-up visit.

Table 20 below describes the various complications and their subsequent interventions, if any, for this study in the early and late post-operative period.

Table 20: Complications by post-operative period

Complications	Distribution by eyes (n=213)			
	<30 days	>30days	Total	Percentage
None	-	-	164	77
Flat/shallow AC	20	0	20	9.4
Hyphaema	11	1	12	5.6
Cataract	2	2	4	1.9
Tube-corneal touch	0	3	3	1.4
Hypotony	2	0	2	0.9
Bleb leak	1	0	1	0.5
Endophthalmitis	0	1	1	0.5
Suprachoroidal haemorrhage	2	0	2	0.9
Retinal detachment	1	1	2	0.9
Descement strip	2	0	2	0.9
Choriodal effusion	1	0	1	0.5
Vitreous loss	2	0	2	0.9
Iridodialysis	2	0	1	0.9
Iris prolapse	1	0	1	0.5
Subconjunctival haemorrhage	1	0	1	0.5

23% of eyes (49) had complications in total, 19.7% in the early post-operative period and 3.3% in the late post-operative period.

The most common complications were shallow/flat AC (20 eyes) and hyphaema (12 eyes). The most serious complications were endophthalmitis (1 eye), suprachoroidal haemorrhage (2 eyes) and retinal detachment (2 eyes).

Table 21 describes the type of interventions done for the surgical complications encountered in this study.

Table 21: Surgical interventions for complications

Intervention	<30 Days	>30 Days
Tube shortening	0	1
AC reformation	5	0
Scleral flap revision	1	0
Bleb Revision	1	0
AC washout	2	0
Iris repositioning	1	1
Lensectomy/ Lens washout	0	2
Anterior vitrectomy	2	0
Evisceration	0	1

1 eye was eviscerated for endophthalmitis 2 years after CTT.

Table 22 below shows the complications for each type of surgery employed for PCG in this study.

Table 22: Complications by surgery type

Complications	Type of surgery (n)				
	All (213)	TET (87)	CTT (81)	AGV (8)	Trabeculotomy (37)
Yes	**49**	**22**	**16**	**3**	**8**
No	164	65	65	5	29
Percentage of eyes with complications	23%	25.3%	19.8%	37.5%	21.6%

AGV had the highest proportion of eyes with complications at 37.5%. The number of eyes with complications was similar for the other types of surgeries.

Table 23 below describes univariate regression analysis to show associations between various clinical characteristics of the eyes and risk of failure to achieve good IOP control.

Table 23: Univariate regression analysis showing predictors of IOP failure at final follow-up visit

Variable	Odds ratio	95% Confidence interval	p-value
Age at diagnosis (n=161)	1	0.99 to 1.01	0.8
Sex (n=161)	1.33	0.9 to 1.96	0.15
Pre-op CCT (n=15)	0.98	0.96 to 1.01	0.13
Pre-op AL (n=20)	1.23	0.84 to 1.81	0.29
Pre-op CDR (n=64)	**0.04**	**0.002 to 0.6**	**0.02**
Pre-op HCD (n=110)	1.16	0.87 to 1.55	0.3
Buphthalmos (n=159)	1.74	0.71 to 4.29	0.23
Corneal clarity (n=158)	1.63	0.34 to 7.85	0.55
Pre-op use of drugs (n=161)	0.48	0.23 to 1	0.05
Complications(n=161)	1.4	0.62 to 3.19	0.42

Pre-operative CDR was the only significant predictor of failure to achieve good IOP control.

7. DISCUSSION

This study established that in Kenya, the types of surgical procedures conducted for PCG were mostly CTT and TET. The surgical success of these interventions lasted up to a period of 2 years after the surgery.

There was a steady increase in the annual surgical output for PCG from 7 operations per year in 2005 to over 30 surgeries per year in 2013. This increase was attributed to the training of paediatric ophthalmologists for 3 out of 4 study sites (KNH, SEH and KEU). AT KNH, there was either a qualified paediatric ophthalmologist or glaucoma specialist from around 2009-2011. In TMH, patients' record keeping was changed from files to electronic data in 2012 and it is impossible to retrieve records of surgical procedures conducted before 2012. The missed records may have led to under-estimation of the workload of TMH. Most surgeries were done in KEU and SEH, possibly because they got large number of referrals from peripheral clinics. Furthermore, since 2007, the "Seeing is Believing" program (a Standard Chartered Bank Initiative), has sponsored cataract, glaucoma and trauma related surgeries for needy children under the age of nine at TMH, SHE and KEU. This may have enabled these institutions to handle greater patient loads.

7.1 Compliance to Follow-up Appointments

Sixty-seven percent of the studied eyes were examined at 6 months follow-up period and 29% at 2 years. This very poor follow-up pattern is similar to those reported by other studies from the continent. In Ghana, only 3 out of 19 eyes were seen at the 2 years follow-up period.[34] Similarly, in neighboring Tanzania, Bowman et al. reported that out of 47 children, only 23% had more than 1 year duration of follow-up. [26] They stated that this was in fact improved follow-up rates from previous studies, due to different methods that they had earlier employed to reduce presentation delay and increase follow-up for childhood eye conditions. These included research into the reasons for presentation delays, liaising with community eye and child health workers and trying the "key informant" strategy reported as effective for childhood blindness in other developing countries. In this approach, lay people in the community were trained to recognize and be responsible for children with eye problems. Parents of these children were also called

regularly to check on progress and encourage compliance to follow-up appointments as well as being reimbursed for travel expenses. It will be interesting to evaluate if any of these approaches can be tried in our setting and if they would improve on follow-up and reduce presentation delays of PCG patients to these institutions.

7.2 Patient Demographics

There were 131 patients for whom primary glaucoma surgeries were done in this study. There was a male: female ratio of 2.4:1, similar to findings from other studies in this patient population. In neighboring Tanzania, Bowman et al. looked at 47 children who had primary goniotomy for PCG and found a male: female ratio of 3:1. [26] As expected, majority of children in this study had bilateral disease at 82.4%. Onwasigwe et al. in Nigeria assessed the success of primary TET in 32 children with PCG and reported that 81% of these children were bilaterally affected.[35] In India, Mandal et al. assessed 360 children who had primary CTT and found that 73% of children had bilateral disease. [24]

In this study, only one patient recorded a positive family history of congenital glaucoma in an older brother and there was no mention of a history of consanguinity for any of the patients. Similarly, Bowman et al. reported no family history in any of their patients and suggested that consanguinity was not a common practice in their population. [26] This is in contrast to studies from other developing countries where high rates of consanguinity were found in the families of PCG patients. In Turkey for instance, Tamcelik et al. examined 311 patients with developmental glaucoma, of which 63% had PCG.[27] They reported a positive family history of PCG in 13% of patients and a history of consanguinity in 49%. It is not clear if the findings of this study reflect low rates of consanguinity or of positive family history in Kenya, or whether they were not specifically asked for or recorded during the history taking. The health workers who took the history may not have been aware of the reported contribution of consanguinity and a family history of PCG to the development and pathogenesis of PCG.

Majority (96.2%) of eyes had moderate to severe disease. This classification was derived from the method used by Al-Hazmi et al. when they examined 820 eyes of 532 patients with PCG and reported that 70% of eyes had moderate to severe disease.[22] However, they only looked at

children <1 year of age, whilst this study had children ranging from 3 weeks to 15 years of age at the time of presentation. This delay in presentation could explain why almost all eyes in this study had moderate to severe disease.

Approximately 60% of patients were diagnosed before 1 year of age and 80% before 3 years of age. However, some children presented as late as 15 years old, with 20% of patients being diagnosed after 3years of age. The eyes of these children were still included in this study due to the presence of buphthalmos. Raised IOP must have been present before the age of 3 years when scleral stretching was still possible for buphthalmos to develop. Median age was 9 months (3-12) whilst the mean was 23.1months (33.1). This is similar to findings described by Bowman et al. who reported a mean age of 19 months with a range of 1 month to 17years.[26]

Of note is that in this study, age of presentation was essentially the same as age of diagnosis and age at surgery for all patients. In all the institutions, PCG was diagnosed on the same day the children presented to hospital, and the surgery was done within weeks of this diagnosis. This is a major finding, indicating that there was no delay in the diagnosis and management of PCG once these children present to hospital. Therefore, if the delay in presentation is addressed, then progression of PCG in these children will be halted at an earlier stage to prevent development of severe disease.

7.3 Presenting Signs and Symptoms

Buphthalmos was the most common presenting symptom, seen in 46.5% of eyes. This is similar to other reports from developing countries. For instance, Tamcelik et al. reported that buphthalmos and corneal clouding were the most common presenting complaints of children with PCG.[27] In contrast to developed nations where children with PCG classically present with the triad of blepharospasm, tearing and photophobia, in developing regions, children are more likely to present late and with advanced disease.[22]

At examination, 84% of eyes had buphthalmos whilst 5.6% had clear corneas. This reflects the advanced stage of disease at presentation in patients in this study. These findings correlate well with those of studies from other developing nations. For example, in Ghana, Essuman et al.

looked at 19 eyes of 12 children with PCG undergoing primary CTT and reported that all eyes had significant corneal oedema before surgery.[34] Similarly, in India, Mandal et al. assessed success of CTT in 121 eyes of 74 patients with an age range of 3days to 14 years and described the presence of significant corneal oedema/scarring with buphthalmos in 87.4% of patients.[10]

7.4 Pre-operative Characteristics

Pre-operative Snellen VA (or equivalent) was recorded for only 11 eyes. For majority of eyes, other qualitative ways of measuring VA were used and VA was not recorded for about a quarter of eyes. This could be due to the young age of the majority of the patients and challenges in recording visual acuity in this age group in this setting. Also most of these eyes had clouded corneas and many had photophobia, which may have made it either difficult or impossible to measure VA.

Median pre-operative IOP was 29mmHg (21-31) and mean was 29.9mmHg (11.4), with 82.3% of eyes presenting with an IOP ≥21mmHg. These values are similar to those described by other studies in the continent. Essuman et al. and Onwasigwe et al. reported mean presenting IOP values of 30.3mmHg and 28.3mmHg respectively. [34, 35] Generally, for PCG, IOP is recorded under anaesthesia due to the young age of the patients. This was the case for majority of eyes in this study. However, for most patients, there was no mention at what point during anaesthesia this IOP was recorded. In this setting, halothane is typically used for induction of anaesthesia. Halothane has a well-documented IOP-lowering effect.[62,63] Therefore, the actual IOP may even be higher than recorded for these children.

The other examination findings in this study reflect the advanced nature of disease at the time of presentation of these patients. For instance, the median pre-operative HCD was 13.5 (12.5-14) and median CDR was 1.0 (0.6-0.9). The pre-operative axial length and CCT were only measured for 22 eyes and 16 eyes respectively. Only one institution recorded these values routinely and even then, only after 2011 when they got a glaucoma specialist. Pre-operative refraction was only done in 10 eyes. This was probably because most eyes presented with clouded corneas.

Majority of eyes were on at least 1 anti-glaucoma drug pre-operatively. This is because once these patients were diagnosed, at least one drug was prescribed immediately for IOP control whilst awaiting surgery. The most commonly used drug was timolol, probably because it is relatively cheap and available in these institutions. Alpha agonists were not used in any eyes pre-operatively, probably due to the documented adverse effects in children.

7.5 Surgeries

TET and CTT were the most commonly performed primary surgeries for PCG, followed by trabeculotomy. AGV was done in only 8 eyes. No eyes had goniotomy as a primary procedure in this study. Usually for PCG, goniotomy and trabeculotomy are preferred primary procedures, with the other procedures are typically reserved for when these have failed. Al Hazmi et al. explained that in developing countries, TET and CTT may be preferred due to advanced nature of the disease at presentation. [22] Zhang et al. also reported that TET, CTT and trabeculotomy were preferred first options for surgical management of PCG, with other procedures being employed only in suitable cases.[64] AGV is not generally used as primary options for PCG. The 8 cases of primary AGV implantation were all done in TMH, where the surgeon preferred this procedure due to the poor socioeconomic status of the patients and thus expected poor compliance to follow-up appointments.

7.6 Post-operative IOP

In this study, there was a statistically significant drop from pre- to post-operative IOP for all follow-up periods. The drop in median IOP was significant for TET, CTT and trabeculotomy. Nevertheless, AGV still recorded the highest percentage reduction in final IOP from baseline. This is an important finding indicating that there might be a role for primary AGV insertion if a greater drop in IOP is desired. However, the number of eyes with final IOP readings for AGV was too few to draw definite conclusions.

Several studies have reported an improved success rate when antifibrotic agents are used in surgeries for PCG.[42,43] In this study, some of the TET's and CTT's were done with anti-fibrotic

agents. In KNH, typically Mitomycin-C (MMC) was used whilst in other centres, 5-fluorouracil (5-FU) was more commonly used. These surgeries achieved a greater percentage reduction in median IOP from baseline compared with surgeries done without antifibrotic agents. However, the difference between median IOP at final visit was not significantly different between the two groups. This is similar to findings by Rodrigues et al. who retrospectively compared results of trabeculectomy in PCG with and without the use of MMC and reported no difference between the two groups. [65]

7.7 Surgical Success/Failure

Overall, qualified success was achieved in 73.3% of eyes and complete success in 22.8% of eyes. Despite having a final post-operative IOP <21mmHg, 2 eyes developed a post-operative VA of no perception of light, 1 at 1year post CTT and the other at 6months post TET. As such, these eyes were regarded as failures. Zhang et al. assessed success of TET, trabeculotomy and CTT in 81eyes of 48 patients and reported 1 year and 3 years success rates of 92.6% and 77.8% respectively.[64] All their patients were < 4 years of age at the time of diagnosis and so may have presented with less advanced disease. This may explain their slightly higher surgical success rates.

For specific procedures, AGV and CTT achieved the highest success rates whilst TET achieved the least. When the Kaplan Meier curves were assessed, the cumulative probabilities of success were similar for CTT and trabeculotomy, remaining at approximately 80% at 2 years. On the other hand, the cumulative probability of success for TET dropped much faster remaining at about 55% at 2 years. These findings correlate well with similar studies from literature. Autrata et al. looked at 83 eyes of 47 patients who underwent either primary trabeculotomy or TET for PCG and reported 2-year success rates at 76% and 47% respectively. [66] In China, Zhang et al. similarly reported highest success rates for CTT compared to other procedures.[64] This was also the case for Al Hazmi et al. in Saudi Arabia.[22] Of note is that for these 2 countries, patients also presented late with advanced disease, comparable to patients in our set-up. These findings are expected since TET in children has been associated with increased risk of failure due to an aggressive fibrotic response in this age group. [18] On the other hand, CTT has been proposed to

offer better success rates due to a dual outflow mechanism through Schlemm's canal (trabeculotomy) and the trabeculectomy fistula. [32]

7.8 Other Post-operative Characteristics

Post-operative Snellen VA (or equivalent) was recorded for only 28 eyes. Although majority of eyes developed clear cornea, other qualitative ways of measuring VA were used, possibly due to the age of these patients. VA was not recorded for 10% of the eyes. There appeared to be a general improvement in vision, with more eyes recorded as having a VA of being able to pick up or follow objects and fewer patients recorded as not following light. The difficulties in analyzing VA for PCG patients are well-recognized and are due to age of patients and corneal status. Essuman et al. reported that data on VA and refractive status of their patients was too inadequate for them to analyze statistically.[34] In this study, pre-operative refraction was only done in only 11 eyes whilst post-operative refraction was done in 88 eyes. This may reflect the improvement in corneal status of eyes or older age of patients, which would make refraction more feasible.

The number of eyes with clear corneas increased from 5.7% pre-operatively to 61.5% at final follow-up visit (p=0.01). This value reflects the good IOP control achieved in about 70% of eyes post-surgery. Some eyes with good IOP control remained not clear due to corneal scarring. Essuman et al. similarly reported that although virtually all eyes in their study had clouded corneas before surgery, majority achieved clear corneas at final follow-up visit. [34] Likewise, Bowman et al. reported an increase in the number of eyes with clear corneas from 8.5% pre-operatively to 78% at final follow-up visit. In this study, clouded cornea could have been haze, oedema, scars or striae since it was not always specified in the patients' records. The degree of corneal haze was also not graded for these patients.

There was a significant change in CCT, AL and CDR from pre-operative period to final follow-up period. For CCT and AL, the number of eyes with values were however few (<10) since it was only in 1 out of the 4 institutions where these values routinely recorded during EUA. Median CDR reduced from 1.0 to 0.7 (p=0.00) at final follow-up visit. CDR reversal in children after surgery for PCG is a well-documented phenomenon. Zhang et al. reported reversal of CDR in eyes which were successfully operated for PCG, whilst Wu et al. described a reversal in CDR

in 61.1% of their patients after surgery. [64,67] The mechanism of this reversal is unknown, but may be related to the elasticity of the scleral ring in children and its shrinkage after IOP control.[68]

7.9 Post-operative use of anti-glaucoma drugs

The mean number of drugs is discussed instead of median for comparison with other studies. There was a decrease in mean number of drugs from pre-operative period to post-operative day 1. However after that, there was a gradual increase such that there was no significant difference between mean number of drugs used pre-operatively and that at final follow-up visit. In fact, there was an increase in the number of eyes on drugs from 65.3% before surgery to 70.4% post-operatively. For some patients, it appeared that anti-glaucoma medications were re-started after surgery with no clear indication as to the reason for doing so. For instance, some patients would come for clinic review and have clear corneas and no IOP recorded but are started on drugs during this visit. This may explain the increase in the number of eyes on drugs post-surgery noted in this study.

These findings are very much in contrast to those reported by most other studies on PCG surgery, which have reported a decrease in the number of eyes of drugs post-operatively. [10,69] In Japan, Ikeda et al. looked at 80 eyes of 66 patients undergoing primary trabeculotomy for PCG and reported an increase in the number of eyes on drugs post-operatively.[70] They further explained that this was because most patients had surgery immediately after diagnosis, so there was no need for temporary IOP control with drugs. Therefore, the drugs were started post-operatively when there was need for further IOP lowering. Their study also had a longer follow-up period of up to 10 years, which could explain why drugs were needed later for IOP control, since the surgeries for PCG were more likely to fail with increased follow-up duration.

7.10 Re-operations

The need for additional surgical/laser procedures was lowest for trabeculotomy and similar for TET, CTT and AGV.

In total, 39 re-operations were done in 33 eyes, 16 of which had primary surgeries during this study and 17 which were operated elsewhere or before the study period. Of these, 12 eyes achieved successful IOP control, 5 eyes needed 2 or more re-operations to achieve good IOP control and the rest did not achieve good IOP control even at final follow-up visit. Overall, re-operations had a lower success rate (36.4%) compared to primary surgeries and only achieved a percentage reduction in median IOP from baseline of 21.9%. These findings are similar to those described by Mandal et al. who reported an increased risk of IOP failure in eyes who had a history of prior glaucoma surgery. [10,24] They gave no explanation for this, but it may be related to the scarring that results from the first surgery.

7.11 Complications

Shallow/flat AC and hyphaema were the most common complications, most of which resolved spontaneously. Shallow/flat AC was especially common after TET. The 1 case of endophthalmitis occurred 2 years after CTT and the eye was eviscerated. Endophthalmitis is the most feared complication that can occur after surgery for PCG. Some authors have proposed higher rates in children, especially with the use of anti-fibrotic agents.[43] The complications from this study are similar to those reported by Al Hazmi et al. who assessed 820 eyes undergoing goniotomy, trabeculotomy and CTT. Most of these eyes had moderate and advanced disease, similar to our population of eyes. Similarly, a shallow AC and hyphaema were the most common complications; they also reported 1 eye with endophthalmitis and retinal detachment (RD) each. In this study, the serious complications of RD and suprachoroidal haemorrhage (SCH) each occurred in 2 eyes, also after CTT. One eye had an SCH on post-operative day 1and was managed conservatively. 3 months later, the same eye developed a giant retinal tear with a total RD and was referred to a vitreoretinal unit. The second eye with an SCH developed a partial lens dislocation into the AC, but had no surgical intervention, the reason not being documented. Another eye developed an exudative RD at post-operative month 1, was treated with steroids and by month 6 the RD had resolved.

AGV recorded the highest percentage of complication rates, although the number of eyes was few for this procedure. 3 out of 8 eyes with AGV recorded tube-corneal touch. These findings

correlated well with other studies on AGV implantation for PCG. Ou et al. looked at 30 eyes of 19 patients with refractory PCG who had AGV implanted. [45] They reported that tube migration was the most common complication and lead to tube-corneal touch. Their proposed mechanisms for this were shrinkage of the sclera and globe after IOP reduction, continued growth of the globe and vigorous eye rubbing by the child, all leading to an initially well-positioned tube rotating more anteriorly over time.

7.12 Predictors of IOP Failure

Only pre-operative CDR was a significant predictor of failure to achieve an IOP <21mmHg. Several other demographic and clinical factors have been reported to influence success of PCG surgery from literature, including age at presentation and surgery, sex, pre-operative IOP>35mmHg, severity of disease, buphthalmos etc.[22,24,26,69] According to Al Hazmi et al., pre-operative HCD was directly proportional to severity of disease, and as such risk of surgical failure.[22] This study did not find a link between pre-operative HCD and risk of surgical failure, possibly because not all eyes had pre-operative HCD recorded.

8. STUDY LIMITATIONS

Due to the design of this study, the following limitations were encountered in this study:

- This was a retrospective case series. As such data for some patients was unavailable or incomplete
- Different surgeons and the variations in their techniques and experiences may also have affected the outcomes
- The number of patients presenting for subsequent follow-up visits declined with time, and this may have adversely affected the results
- Due to the age of these patients, most of them required examination under anaesthesia to document the clinical findings. This may have been responsible for delay in the follow-up appointments of some of these patients
- Different methods of IOP readings (Schiotz, tonopen, I care, Perkins) under different conditions (clinic, general anaesthesia) may have influenced outcome measures
- Different examiners with no standardization in VA measurements

9. CONCLUSIONS

1. The most common primary procedures performed were TET and CTT.
2. Surgical intervention for PCG in Kenya was successful up to a period of 2years after surgery.
3. CTT and AGV achieved the highest rates of surgical success.
4. There was an increase in the number of eyes on drugs post-operatively.
5. Re-operations were less successful compared to primary surgeries.
6. A large pre-operative CDR was a risk factor for surgical failure.
7. The follow-up drop-out rate was high for these patients with PCG.

10. RECOMMENDATIONS

1. CTT is an effective and safe option as a primary procedure for PCG.
2. Review of indications for post-operative drug use is important to ensure appropriate use of drugs.
3. Educate parents to ensure good compliance to follow-up appointments.
4. Conduct a prospective study with a longer follow-up period to assess the long-term success rates of these procedures.

11. REFERENCES

1) DeLuise VP, Anderson DR. Primary Infantile Glaucoma (Congenital Glaucoma). Surv Ophthalmol, 1983; 28(1):1-19.

2) Taylor RH, Ainsworth JR, Evans AR, Levin AV. The Epidemiology of Paediatric Glaucoma: the Toronto Experience. J Pediatric Ophthalmol Strabismus, 1999; 3:308-15.

3) Vision 2020: The Right to Sight. Blindness in Childhood. Available at http://89.234.89.107/vision2020/main.cgfm?type=WIBCHILDHOOD . Accessed on 1/2/2015.

4) Gilbert C, Foster A. Childhood Blindness in the Context of VISION 2020: The Right to Sight. Bull World Health Organ, 2001; 79(3):227-32.

5) Fung DS, Roensch MA, Kooner KS, Cavanagh HD, Whitson JT. Epidemiology and Characteristics of Childhood Glaucoma: Results from the Dallas Glaucoma Registry. Clin Ophthalmol, 2013; 7:1739-46.

6) Kanski JJ, Bowling B. Clinical Ophthalmology: A Systematic Approach. 7th Edition.

7) Aponte EP, Diehl N, Mohney BG. Incidence and Clinical Characteristics of Childhood Glaucoma: A Population-based Study. Arch Ophthalmol, 2010; 128:478-82.

8) Dandona L, Williams JD, Williams BC, Rao GN. Population-based Assessment of Childhood Blindness in Southern India. Arch Ophthalmol, 1998; 116:545-46.

9) Mandal AK, Chakrabarti D. Update on Congenital Glaucoma. Indian J Ophthalmol, 2011; 59:148-57.

10) Mandal AK, Matalia JH, Nutheti R, Krishnaiah S. Combined Trabeculotomy and Trabeculectomy in Advanced Primary Developmental Glaucoma with Corneal Diameter of 14mm or more. Eye, 2006; 20-135-43.

11) Melka F, Alemu B. The Pattern of Glaucoma in Menelik II Hospital Addis Ababa, Ethiopia. Ethiop Med J, 2006; 44:159-65.

12) Ellong A, Ebana MC, Nyouma ME, Bella-Hiag A. Juvenile Glaucoma in Cameroon. Bull Soc Belge Ophthalmol, 2007; 305:69-77.

13) Papadopoulos M, Cable N, Rahl J, Khaw PT. The British Infantile and Childhood Glaucoma (BIG) Eye Study. Invest Ophthalmol Vis Sci, 2007; 48(9):4100-06.

14) Qiao CY, Wang LH, Tang X, Wang T, Yang DY, Wang NL. Epidemiology of Hospitalized Paediatric Glaucoma Patients In Beijing Tongren Hospital. Chin Med J, 2009; 122(10):1162-66.

15) Turacli ME, Aktan SG, Sayli BS, Akarsu N. Therapeutic and Genetical Aspects of Congenital Glaucomas. Int. Ophthalmol, 1992; 16:359-62.

16) Safarazi M, Stoilov I. Molecular Genetics of Primary Congenital Glaucoma. Eye, 2000; 14:422-28.

17) Papadopoulos M, Khaw PT. Advances in the Management of Paediatric Glaucoma. Eye, 2007; 21:1319-25.

18) Chen TC, Chen PP, Francis BA, Junk AK, Smith SD, Singh K et al. Paediatric Glaucoma Surgery: A Report by the American Academy of Ophthalmology. Ophthalmology, 2014; 121(11):2107-15.

19) Schaffer RN, Hoskins HD. Montgomery Lecture: Goniotomy in the Treatment of Isolated Trabeculodysgenesis (Primary Congenital [Infantile] Developmental Glaucoma). Trans Ophthalmol Soc UK, 1983; 103:581-85.

20) Haas J. Principles and Problems of Therapy in Congenital Glaucoma. Invest Ophthalmol, 1968; 7:140-46.

21) Song J, Stinnett SS, Whitson JT, Kooner KS. Ten Year Surgical Experience with Childhood Glaucoma. J Pediatric Ophthalmol Strabismus, 2003; 40(1):11-18.

22) Al-Hazmi A, Awad A, Zwaan J, Al-Mesfer SA, Al-Jadaan I, Al-Mohammed A. Correlation between Surgical Success and Severity of Congenital Glaucoma. Br J Ophthalmol, 2005; 89(4):449-53.

23) Ben-Zion I, Bogale A, Moore DB, Helveston EM. Surgical Results in the Management of Advanced Primary Congenital Glaucoma in a Rural Paediatric Population. Ophthalmology, 2011; 118:231-5

24) Mandal AK, Gothwal VK, Nutheti R. Surgical Outcome of Primary Congenital Glaucoma: A Single Surgeon's Long-term Experience from a Tertiary Eye Care Centre in India. Eye (Lond), 2007; 21:764-74.

25) Ho CL, Walton DS. Primary Congenital Glaucoma: 2004 Update. J. Paediatr Ophthalmol Strabismus, 2004; 41:271-88.

26) Bowman RJC, Dickerson M, Mwende J, Khaw PT. Outcomes of Goniotomy for Primary Congenital Glaucoma in East Africa. Ophthalmology, 2011; 118:236-40.

27) Tamcelik N, Atalay E, Bolukbasi S, Capar O, Ozkok A. Demographic Features of Subjects with Congenital Glaucoma. Indian J Ophthalmol, 2014: 62(5): 565-69.

28) Fong D, Seddon J. A Review of Primary Congenital Glaucoma in the Developing World. Surv Ophthalmol, 2013; 58(3):278-85.

29) American Academy of Ophthalmology. Glaucoma: Basic and Clinical Science Course Section 10. American Academy of Ophthalmology; 2011-2012.

30) Gencik A. Epidemiology and Genetics of Primary Congenital Glaucoma in Slovakia: Description of a form of Primary Congenital Glaucoma in Gypsies with Autosomal Recessive Inheritance and Complete Penetrance. Dev Ophthalmol, 1989; 16:76-115.

31) Safarazi M, Akarsu AN, Hossain A, Turacli ME, Aktan SG, Barsoum-Homsy MA et al. Assignment of Locus (GLC3A) for Primary Congenital Glaucoma (Buphthalmos) to 2p21 and Evidence for Genetic Heterogeneity. Genomics, 1995; 30:171-7.

32) Morales J, Shahwan SA, Odhayb SA, Al Jadaan I, Edward DP. Current Surgical Options for the Management of Paediatric Glaucoma. J Ophthalmol, 2013; 1-16.

33) Kulkarni SV, Damji KF, Fournier AV, Pan I, Hodge WG. Endoscopic Goniotomy: Early Clinical Experience in Congenital Glaucoma. J Glaucoma, 2010; 19:264-9.

34) Essuman VA, Brimah IZ, Ndanu TA, Ntim-Amponsah CT. Combined Trabeculotomy and Trabeculectomy: Outcome for Primary Congenital Glaucoma in a West African Population. Eye, 2011; 25:77-83.

35) Onwasigwe EN, Ezegwui IR, Onwasigwe CN, Aghaji AE. Management of Primary Congenital Glaucoma by Trabeculectomy in Nigeria. Ann Trop Paediatr, 2008; 28:49-52.

36) Gramer E, Tausch M, Kraemer C. Time of Diagnosis, Reoperations and Long-term Results of Goniotomy in the Treatment of Primary Congenital Glaucoma: A Clinical Study. Int Ophthalmol, 1996-1997; 20:117-23.

37) Chang TC, Cavuoto KM. Surgical Management in Primary Congenital Glaucoma: Four Debates. J Ophthalmol, 2013. Article ID 612708: 1-7. Hindawi Publishing Cooperation.

38) Meyer G, Schwenn O, Grehn F. Trabeculotomy in Congenital Glaucoma: Comparison to Goniotomy. Ophthalmology, 2000; 239(11):893-899.

39) Anderson DR. Trabeculotomy compared to Goniotomy for Glaucoma in Children. Ophthalmology, 1983; 90(7):805-6.

40) Beck AD, Lynch MG. 360 degrees Trabeculotomy for Primary Congenital Glaucoma. Arch Ophthalmol, 1995; 113:1200-2

41) Girkin CA, Marchase N, Cogen MS. Circumferential Trabeculotomy with an Illuminated Microcatheter in Congenital Glaucomas. J Glaucoma, 2012; 21:160-3.

42) Mandal AK, Bhatia PG, Bhaskar A, Nutheti R. Long-term Surgical and Visual Outcomes in Indian Children with Developmental Glaucoma Operated on within 6 months of Birth. Ophthalmology, 2004; 111:283-90.

43) Sidoti PA, Belmonte SJ, Liebmann JM, Ritch R. Trabeculectomy with Mitomycin-C in the treatment of Paediatric Glaucomas. Ophthalmology, 2000; 107:422-9.

44) Dietlein TS, Jacobi PC & Kriegistein GK. Prognosis of Primary ab Externo Surgery for Primary Congenital Glaucoma. Br J Ophthalmol, 1999; 83(3):317-22.

45) Ou Y, Yu F, Law SK, Coleman AL, Caprioli J. Outcomes of Ahmed Glaucoma Valve Implantation in Children with Primary Congenital Glaucoma. Arch Ophthalmol, 2009; 127(11);1436-41.

46) Barton K, Feuer WJ, Budenz DL, Schiffman J, Costa VP, Godfrey DG et al . Three-Year Treatment Outcomes in the Ahmed Baerveldt Comparison (ABC) Study. Ophthalmology, 2014; 121(8):1547-57.

47) Christakis PG, Tsai JC, Kalenak JW, Zurakowski D, Cantor LB, Kammer JA et al. The Ahmed versus Baerveldt Study: Three-Year Treatment Outcomes. Ophthalomology, 2013; 120: 2232-40.

48) Englert JA, Freedman SF, Cox TA. The Ahmed Valve in Refractory Paediatric Glaucoma. Ophthalmology¸ 1999; 127(1):34-42.

49) Dave P, Senthil S, Choudhari N, Sekhar GC. Outcomes of Ahmed Valve Implant following a Failed Initial Trabeculotomy and Trabeculectomy in Refractory Primary Congenital Glaucoma. Middle East Afr J of Ophthalmol, 2015; 22(1):64-68.

50) Chen TC, Bhatia LS, Walton DS. Ahmed Valve Surgery for Refractory Paediatric Glaucoma: A Report of 52 Eyes. J Paediatr Ophthalmol Strabismus¸2005; 42(5):274-283.

51) Beck AD, Freedman S, Kammer J, Jin J. Aqueous Shunt Devices Compared with Trabeculectomy with Mitomycin-C for Children in the first two years of life. Ophthalmology, 2004; 137(6):1163-4.

52) Gedde SJ, Singh K, Schiffman JC, Feuer WJ. The Tube versus Trabeculectomy Study: Interpretation of Results and Application to Clinical Practice. Curr Opin Ophthalmol, 2012; 23(2):118-26.

53) Kiage DO, Gradin D, Gichui S, Damji KF. Ahmed Glaucoma Valve Implant: Experience in East Africa. Middle East Afri J Ophthalmol, 2009; 16(3):151-5.

54) Biswas J, Fogla R. Sympathetic Ophthalmia Following Cyclocryotherapy with Histopathologic Correlation. Ophthalmic Surg Lasers, 1996; 27(12):1035-38.

55) Aminlari A. Cyclocryotherapy in Congenital Glaucoma. Glaucoma¸1981; 3(6):331-332.

56) Mastrobattista JM, Luntz M. Ciliary Body Ablation: Where are we and how did we get here? Surv Ophthalmol, 1996; 41(3):193-213.

57) Kirwan J, Shah P, Khaw PT. Diode Laser Cyclophotocoagculation: Role in the Management of Refractory Paediatric Glaucoma. Ophthalmology, 2002; 109:316-23.

58) Bock CJ, Freedman SF, Buckley EG, Shields MB. Transcleral Diode Laser Cytophotocoagulation for Refractory Paediatric Glaucoma. J Paediatr Ophthalmol Strabismus, 1997; 34(4):235-9

59) Al-Obeidan SA, Osman EE, Dewedar AS, Kestelyn P, Mousa A. Efficacy and Safety of Deep Sclerectomy in Childhood Glaucoma in Saudi Arabia. Acta Ophthalomol,2014; 92:65-70.

60) Dietlein TS, Jacobi PC, Luke C, Krieglstein. Morphological Variability of the Trabecular Meshwork in Glaucoma Patients: Implications for Non-penetrating Glaucoma Surgery. Br J Ophthalmol, 2000; 84(12):1354-59.

61) Shaaraway M T, Mark B S, Grehn F. Guidelines on Design and Reporting of Glaucoma Surgical Trials. World Glaucoma Association: 79. Amsterdam: Krugler; 2009.

62) Mirakhur RK, Elliot P, Shepherd WF, McGalliard JN. Comparison of the effects of Isoflurane and Halothane on Intraocular Pressure. Acta Anaesthesiol Scandinavia, 1990; 34(4):282-5.

63) S-Katzenschlager S, Deusch E, Dolezal S, Michalek-Sauberer A, Grubmuller R, Heinz G. Sevoflurane and Propofol decrease Intraocular Pressure equally during Non-ophthalmic Surgery and recovery. Br J Anaesth, 2002; 89(5):764-66.

64) Zhang X, Du S, Fan Q, Peng S, Yu M, Ge J. Long-term Surgical Outcomes of Primary Congenital Glaucoma in China. Clinics (Sao Paulo), 2009; 64(6):543-51.

65) Rodrigues AM, Junior AP, Montezano FT, de Arruda Melo PA. Prata J Jr. Comparison between results of Trabeculectomy in Primary Congenital Glaucoma with and without the use of Mitomycin C. J Glaucoma, 2004; 13(3):228-32.

66) Autrata R & Lokaj M. Trabeculotomy versus Trabeculectomy for Primary Congenital Glaucoma. Scr Med (Brno), 2003; 76(2):79-86.

67) Wu SC, Huang SC, Kuo C, Lin K, Lin S. Reversal of Optic Disc Cupping after Trabeculotomy in Primary Congenital Glaucoma. Can J Ophthalmol, 2002; 37(6):337-41.

68) Mochizuki H, Lesley AG & Brandt JD. Shrinkage of Scleral Canal during Cupping Reversal in Children. Ophthalmology, 2011; 118:2008-13.

69) Yalvac IS, Satana B, Suveren A, Eksioglu U, Duman S. Success of Trabeculotomy in Patients with Congenital Glaucoma operated on within 3 months of birth. Eye, 2007; 21:459-64.

70) . Ikeda H, Ishigooka H, Muto T, Nagata M. Long-term Outcome of Trabeculotomy for the Treatment of Developmental Glaucoma. Clin Sci, 2004; 122:1122-28.

12. APPENDICES

12.1 Appendix I: Data collection form

Demographics

Hospital ID/File number:…… Code:……

Hospital:……. Age:…… Sex:……

African (Black) [ ] African (Non-Black) [ ] Non-African [ ]

Residence:……..

History of Consanguinity Yes [ ] No [ ]

Family History: Yes [ ] No [ ]

If yes, specify: ……..

Clinical Presentation:

Eye: Right [ ] Left [ ] Bilateral [ ]

Age at presentation:……. Age at Diagnosis:……..

Presenting symptoms: Tearing [ ] Photophobia [ ] Blepharospasm [ ]

Redness [ ] Buphthalmos [ ] Corneal Clouding [ ]

Poor Vision [ ] Other [ ], Specify:……

Pre-operative data

Examination Findings: VA: OD…….

OS……

IOP:…….. HCD:……

AL:…….... VCDR:……. CCT:…….

Corneal Oedema: Yes [ ] None [ ]

Refractive error (spherical equivalent) ……

Anti-glaucoma medications:

Beta-Blocker …….

PGA …….

Alpha-2 Agonist …….

Pilocarpine ……

CAI (oral) ……

CAI (topical) ……..

Other (specify) ……..

Total number of medications …….

Previous surgical therapy for Glaucoma:

Goniotomy [ ] Trabeculotomy [ ] Trab [ ] Trab plus anti-fibrotics [ ]

CTT [ ] GDD [ ] Cyclocryotherapy [ ] CPC [ ]

Other (specify) ……

Post-Operative Data

Surgery done ……..

Date of Surgery ……../……/……..

Follow-up Period	IOP	HCD	AL	VCDR	CCT	Corneal Oedema‡	Refractive Error*
Day 1							
Month 1							
Month 3							
Month 6							
Year 1							
Year 2							

‡ Recorded as Yes or None

*Measured in spherical equivalent

BCVA: OD…..…….

OS…….…..

Anti-glaucoma medications:

Beta-Blocker …….

PGA …….

Alpha-2 Agonist …….

Pilocarpine ……

CAI (oral) ……

CAI (topical) ……..

Other (specify) ……..

Total number of medications …….

Complications:

Hypotony [ ]	Flat AC [ ]	Suprachoroidal Haemorrhage [ ]
Hyphaema [ ]	Cataract [ ]	Retinal Detachment [ ]

Tube Blockage [ ] Tube Migration [ ] Tube-corneal Touch [ ]

Tube Extrusion [ ] Corneal Decompensation [ ] Phthisis [ ]

Encapsulated Bleb [ ] Endophthalmitis [ ]

Other (specify)…….

Surgical Interventions:

AC Reformation [ ] AC Washout [ ] Needling [ ] Cataract Surgery [ ]

Drainage of Suprachoroidal Haemorrhage [ ] Retinal Detachment Surgery [ ]

Second Valve [ ] Tube Shortening [ ] Tube Reposition [ ]

Other (specify) ……..

12.2 Appendix II: Classification of disease severity according to criteria used by Al Hazmi et al. [22]

Severity	IOP (mmHg)	Corneal diameter (mm)	Corneal clarity
Mild	<25	<13	Good
Moderate	25-35	13-14.5	Fair
Severe	>35	>14.5	Poor

12.3 Appendix III: Budget

Item	Quantity	Unit cost (Kshs)	Total kshs
Proposal			
Printing and Packing	35 pages	10	350
Photocopy of Proposal	70 pages	3	210
Binding Proposal	3 copies	120	360
Proposal Printing 2nd draft	30 pages	10	300
Photocopy of proposal 2nd draft	90 pages	3	270
Binding of proposal 2nd draft	4 copies	120	480
Ethics			2,000
Sub-total			**3,970**
Contracted services			
Statistician	1	50,000	50,0000
Research assistants	3	15,000	45,000
Sub-totals			**95,000**
Data Retrieval			
KNH	All Files (50)	2,500	2,500
KEU	~300	100	30,000
Sub-total			**32,500**
Data Collection			
Printing of questionnaire	4pages	10	40
Photocopy of questionnaire	4 * 350	3	4,200
Subtotal			**4,240**
Communication & Accommodation			
Telephone			3,000
Transport to all hospitals + Lunch			22,000
Accommodation			30,000
Subtotal			**55,000**
Results			
Printing of results (black & white)	3*70 pages	10	2,100

Printing of results (color)	3*20 pages	20	1,200
Copy of final book			
Black and white	70*8 copies	3	1,680
Color copies	20*8 copies	20	3,200
Binding of final paper	8 copies	200	1,600
Subtotal			**12,220**
Grand total			**202,930**

12.4 Appendix IV: PCEA Kikuyu Eye Hospital study approval letter

P.C.E.A Kikuyu Hospital

P.O. Box 45-00902 Kikuyu, Tel: (020) 2044766-68, (020) 2044769-71
Fax: (020)2044765/772 Mobile:0722-207636 / 0733-606133 / 0736-270192

4th May 2015

Dr. Jalikatu Mustapha
UON Department of Ophthalmology
NAIROBI

Dear Madam,

RE: OUTCOME OF SURGERY FOR PRIMARY CONGENITAL GLAUCOMA IN KENYA

Thank you for choosing KEU to conduct a study on the above subject.

We would like to inform you that the request has been approved. You will carry out the study under the supervision of Dr. Mundia.

At the end of the study you are required to furnish the hospital with copy of the research findings.

Yours faithfully,

Dr. Alain N. M'bongo-Zindamoyen
Director of Clinical Services (Eye Unit)

Cc

CEO
Dr. Mundia

12.5 Appendix V: Tenwek Mission Hospital study approval letter

TENWEK EYE UNIT
Sharing the Light, Restoring Vision

PO Box 39
Bomet, 20400
Kenya
EAST AFRICA

M 0787602845
ben.roberts@wgm.org

21 May 2015

Dr. Jalikatu Mustapha
UON Department of Ophthalmology
Nairobi

Re: OUTCOME OF SURGERY FOR PRIMARY CONGENITAL GLAUCOMA IN KENYA

To whom it may concern:

In regards to the above mentioned study, we would like to inform you that your request to carry out this study at Tenwek Hospital is approved under the supervision of Dr. Ben Roberts (Head of Ophthalmology Dept) and in his absence, Dr. Mike Chupp (Medical Superintendent).

Please be aware that all patient information is confidential and names of patients may not be used in your study without the direct permission of the patient. Also, you will not be allowed to look at patient information outside of the scope of this study.

We are happy to include our patients in this study and look forward to the results that you find.

Sincerely,

Benjamin W Roberts, MD
Ophthalmology- Retina Surgeon
Tenwek Mission Hospital
Bomet, Kenya

12.6 Appendix VI: Sabatia Eye Hospital study approval letter

Friends Church - Sabatia Eye Hospital

P.O.Box 214
Wodanga 50311
Vihiga District, Kenya
Chavakali-Kapsabet-Eldoret Rd.
www.sabatiaeyehospital.org

Fax: 020 2393883
Zain: 0733 731013
Safaricom: 0723 721316
Landline: 020 2393883
email: sabeyehosp@gmail.com

22nd May, 2015

Dr. Jalikatu Mustapha,
UON Department of Ophthalmology,
NAIROBI.

Dear Madam,

RE: OUTCOME OF SURGERY FOR PRIMARY CONGENITAL GLAUCOMA IN KENYA.

Thank you for choosing Sabatia Eye Hospital to conduct study on the above subject.

We would like to inform you that the request has been approved. You will carry out the study under the supervision of Dr. Sarah Sitati.

At the end of the study you are required to furnish the hospital with a copy of the research findings.

Yours faithfully,

FRIENDS CHURCH
P. O. BOX 214,
WODANGA.
SABATIA EYE HOSPITAL

for Dr. Ernest Ollando.
Medical Director/Consultant Ophthalmologist

Cc.
Dr. Sarah Sitati / Deputy Medical Director

OUR MOTTO: "WE TREAT, HE HEALS"

12.7 Appendix VII: Kenyatta National Hospital Ethics & Research Committee Study Approval

KENYATTA NATIONAL HOSPITAL APPROVED 24 JUL 2015 KNH/UoN-ERC P.O.Box 20723-00202 NRB.

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
(254-020) 2726300 Ext 44355

KNH/UON-ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/325

24th July 2015

Dr. Jalikatu Mustapha
H58/69441/2013
Dept . of Ophthalmology
School of Medicine
University of Nairobi

Dear Dr. Mustapha

RESEARCH PROPOSAL – OUTCOMES OF SURGERY FOR PRIMARY CONGENITAL GLAUCOMA IN KENYA: A RETROSPECTIVE CASE SERIES (P246/04/2015)

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above proposal. The approval periods are 24th July 2015 – 23rd July 2016.

This approval is subject to compliance with the following requirements:

a) Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b) All changes (amendments, deviations, violations etc) are submitted for review and approval by KNH/UoN ERC before implementation.
c) Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH/UoN ERC within 72 hours of notification.
d) Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH/UoN ERC within 72 hours.
e) Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
f) Clearance for export of biological specimens must be obtained from KNH/UoN-Ethics & Research Committee for each batch of shipment.
g) Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/or plagiarism.

For more details consult the KNH/UoN ERC website **www.erc.uonbi.ac.ke**

Protect to discover

Yours sincerely,

PROF. M. L. CHINDIA
SECRETARY, KNH/UON-ERC

c.c. The Principal, College of Health Sciences, UoN
The Deputy Director CS, KNH
The Chair, KNH/UoN-ERC
The Assistant Director, Health Information, KNH
The Dean, School of Medicine,UoN
the Chairman, Dept. of Ophthalmology, UoN
Supervisors: Prof. Karimurio Jefitha, Dr.Marco Sheila, Dr. Mundia Danie