PENETRATING KERATOPLASTY IN KENYA: A REVIEW OF INDICATIONS AND OUTCOMES OVER A 2-YEAR PERIOD

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By

DR. ABBA HYDARA, MB ChB (UTG)

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DECLARATION

This dissertation is my original work and it has not been presented for a degree at any other University.

SIGNED:.....DATED:...../...../.....

DR. ABBA HYDARA

(Candidate)

APPROVAL

This dissertation has been submitted for examination with our approval as University supervisors.

Professor Dunera Rahel Ilako

MB ChB, M. Med Ophthalmology (Nairobi), MBA-Health, FEACO

Associate Professor, Department of Ophthalmology, University of Nairobi

SIGNED: _____

DATED: ...../...../.....

Dr. Sheila Akinyi Marco

MB ChB, M. Med Ophthalmology (Nairobi), FEACO, Glaucoma (Alberta),

Lecturer, Department of Ophthalmology, University of Nairobi

SIGNED: _____

DATED: ...../...../.....

Professor Daniel Oira Kiage

MB ChB, M. Med Ophthalmology (Nairobi), FEACO, GLAUCOMA SPECIALIST

Assistant Professor and Head of Section of Ophthalmology, Department of Surgery

Aga Khan University Hospital, Nairobi

SIGNED: _____

DATED: ...../...../.....

DEDICATION

To my family for their love, patience, and understanding during my long absence

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LIST OF ABBREVIATIONS

ABK Aphakic bullous keratopathy

ALK Anterior lamellar keratoplasty

BK Bullous keratopathy

BSS Balanced salt solution

CCTS Collaborative corneal transplantation studies

CJD Creutzfeldt-Jakob disease

EK Endothelia keratoplasty

FML Fluorometholone

HLA Human leukocyte antigen

HSK Herpes simplex keratitis

IOP Intraocular pressure

KC Keratoconus

KEH Kikuyu Eye Hospital

KNH Kenyatta National Hospital

LK Lamellar keratoplasty

PBK Pseudophakic bullous keratopathy

PKP Penetrating keratoplasty

SJS Stevens-Johnson syndrome

VAD Vitamin A deficiency

WHO World Health Organization

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ABSTRACT

Introduction: Acquired corneal blindness is the third leading cause of visual loss globally. The greatest proportion of the blindness is either preventable or treatable; most of those due to corneal diseases are amenable to successful prevention or treatment. Penetrating keratoplasty can alleviate selected cases of corneal blindness and is one of the most successful and most frequently performed solid organ transplants world-wide. However, not many centres offer penetrating keratoplasty in Africa; those that do depend on modest amounts of donor corneas from overseas.

Aim: To document the indications for and outcomes of penetrating keratoplasty in Kenya over a 2-year period.

Methods: A retrospective case series of 174 eligible penetrating keratoplasties performed in 6 different facilities in Kenya from January 2001 to December 2011 was undertaken. Univariate and multivariate analyses were done. Corneal graft survival probabilities were determined using the Kaplan-Meier method.

Results: Keratoconus was the commonest indication accounting for 48.8% followed by bullous keratopathy at 18.4%.Pre-operatively, 66.7% of the eyes were blind with visual acuities <3/60.Corneal epithelial defect (43.5%) was the commonest early complication followed by corneal oedema (25.2%); persistent corneal oedema was the commonest late postoperative complication. At 24 months, 82.2% of the grafts remained clear while 17.8% (n=31) were not clear; only 8.24% of keratoconus grafts failed while 26.97% from other indications failed (relative risk=3.2745, [95% CI 1.4895-7.1986], p<0.0012).Postoperatively, 71.82% of all grafts had final uncorrected vision of 6/60 or better, while 16.67% of grafts remained blind. Thirty-one (17.82%) grafts failed, of which 25.8% were due to primary graft failure and 74.2% were due to secondary graft failure. Survival probabilities at 24 months showed 90% of keratoconus grafts survived while 68% for the other indications survived with p< 0.0068. Poor predictors of corneal graft outcome were: bullous keratopathy (p<0.0019), postoperative glaucoma (p<0.0023), infection (p<0.0001), and persistent corneal oedema (p<0.0001).

Conclusions: Keratoconus remains the leading indication for corneal grafts in Kenya and grafts provide meaningful vision for the commonest indications. Corneal graft survival has improved,

especially for corneal dystrophies and keratoconus. These findings are similar to results in industrialised countries. Poor predictors of graft outcome were corneal ulcers, herpes simplex keratitis, corneal graft glaucoma, and corneal graft oedema. Contemporary causes of corneal blindness in Africa such as vitamin A deficiency and trachomatous corneal blindness were not encountered and may be receding in importance. Our findings suggest most corneal grafts in this part of Africa could attain longer graft survivals as well as better visual outcomes.

Key Words: Penetrating Keratoplasty, Indications, Visual Outcome, Survival, Risk Factors, Poor Predictors.

1.0 LITERATURE REVIEW

1.1 INTRODUCTION

Visual impairment is a major global public health problem. The World Health Organization estimates that globally about 314 million people are visually impaired, of whom 45 million are blind. It has been estimated that over 80% of global visual impairment is preventable or treatable. [1] Globally, acquired corneal blindness is the third leading cause of visual loss after cataract and glaucoma respectively, accounting for 8 million blind, including 1.5 million blind children. [2,3] Because the greatest proportion of the blindness is either preventable or treatable, most of those due to corneal diseases are also amenable to successful prevention or treatment interventions. In some parts of Africa, 25% to 90% of all causes of blindness are of corneal origin and corneal blindness ranks second only to cataracts as the leading cause of blindness. [3-8]

1.1.1 Corneal Grafting is a surgical procedure in which abnormal host corneal tissue is replaced by healthy donor cornea. A corneal graft may be of full-thickness, in which case it is known as penetrating keratoplasty, or of partial thickness/lamellar keratoplasty.[9] In this study, unless otherwise stated, corneal grafting or transplantation means Penetrating Keratoplasty (PKP).

PKP can alleviate selected cases of corneal blindness and is one of the most successful and most frequently performed solid organ transplants.[9]Despite variable reports of good success rates for some indications of PKP from industrialized countries, overall success ultimately depends on astute selection of cases (i.e., pre-operative condition of the recipient eye) as well as donor material (notably the age of the donor cornea, the endothelial cell density, duration from death to harvest time, duration from harvest to transplantation, including methods of preservation).[10-14] In short, reasonable successful rates postoperatively are possible when cases are selected appropriately for PKP.[13, 14]

In sub-Saharan Africa, not many centres offer PKP services and those that do depend on donor corneas from overseas that are often only sporadically available. [15, 16]

In Kenya, two reviews were done on the indications for and outcomes of PKP and both studies were conducted at the Kikuyu Eye Hospital (KEH). These were the works of Yorston *et al* in 1996 that reviewed PKPs done over a 5-year period and the M.Med ophthalmology dissertation

of Mboni in 2006 that reviewed PKPs done over a 10-year period. [13, 17] KEH is in the Central County of Kenya and has a broad catchment area, though certainly was not the only facility that performs PKPs in Kenya. Data from the KEH may not be exclusively representative nationally and thus there is need for a more comprehensive review of the indications and outcomes of PKPs in Kenya that takes into account data from different facilities in different locations across the country.

1.2 EPIDEMIOLOGY OF CORNEAL BLINDNESS

1.2.1 GLOBAL PERSPECTIVE

Corneal blindness tends to be more prevalent among the younger age groups as compared to cataracts; hence the total number of blind years among corneal blind is greater. The causes and prevalence of corneal disease varies from region to region and even within regions, from country to country. Within individual countries, the pattern may vary between regional subpopulations and these are highly dependent on both the availability and the standard of eye care in the specific population. In developed countries the main burden of corneal blindness is contributed by non-infectious causes such as keratoconus, corneal dystrophies and pseudophakic bullous keratopathy (PBK). In the developing world it is malnutrition (mainly from Vitamin A Deficiency and measles) and infectious causes of corneal blindness (such as trachoma, and suppurative keratitis) and trauma that predominate. Several population-based studies have documented these issues both in sub-Saharan Africa and India. [1-8, 14]

1.3 PENETRATING KERATOPLASTY

1.3.1 DEFINITION

Penetrating keratoplasty is defined as the *full-thickness* replacement of a diseased host cornea with healthy donor cornea. [18] Full-thickness hereby meaning a corneal button containing all layers of the cornea (epithelium, stroma, and endothelium). The donor cornea if from a human (same species) is called an *allograft* and when the donor tissue is from a non-human species it is called a *xenograft* or xenotransplantation (XG). A corneal graft may also consist of *partial-thickness*, which could be of anterior or posterior lamellar. [18] Anterior Lamella entails corneal epithelium up to anterior part of the superficial stroma. Posterior Lamella entails stroma up to endothelium.

1.3.2 HISTORY OF CORNEAL TRANSPLANTATION

Dr. Eduard Konrad Zirm (1863-1944) an Austrian ophthalmologist from Vienna, performed the very first human (tissue) corneal transplant on 7th December 1905 in the Czech Republic on a labourer named Alois Glogar, who had been blind bilaterally from lime eye injuries. [19]

Over the past decade, lamellar keratoplasty (LK) has gained popularity and success and is almost replacing PKP in some major centres. Varied versions of lamellar keratoplasty such as endothelial keratoplasty (EK) have now been accepted as the procedure of choice for patients with endothelial disease, while anterior lamellar keratoplasty (ALK) becomes the procedure of choice in patients with corneal stromal disease. [20-22] Despite these recent gains for LK, PKP remains the gold standard procedure for the management of corneal diseases affecting clarity and visual function. [9]

1.3.3 GENERAL INDICATIONS OF PENETRATING KERATOPLASTY

The following are the General Indications of PKP. [18, 23-25]

1. **Optical** – for improvement of vision and visual rehabilitation.
2. **Therapeutic** – for tissue substitution for refractory corneal infections.
3. **Tectonic** – for reinforcing altered corneal structure (descemetocele or corneal melting).
4. **Cosmetic** – rarely, a graft may be performed to improve cosmesis

1.3.4 SPECIFIC INDICATIONS

PKP is the definitive treatment for a corneal opacity. However, only 40% of bilateral corneal blindness is treatable. [15] Overall, long-term success for PKP is higher in developed countries at over 75%; it is low in developing countries at 46.5%. [14] Studies from South India [14] showed 69% of grafted corneas were clear two years after surgery and in East Africa 87% of grafts for keratoconus survived at two years, compared to 65% for other indications for surgery. [13]

Yorston *et al* reviewed 216 corneal grafts at the Kikuyu Eye Hospital (KEH) in Kenya and found that keratoconus was the most common indication for corneal graft accounting for 50%. [13]Mboni [17] *et al* found similar indications to Yorston *et al*. Similar preoperative indications were found in Ethiopia in a review by Tilahun and Shimelash but infections were the most predominant indications. [26, 27]

Dandona *et al* in a review of 1725 grafts in India found bullous keratopathy (both aphakic and pseudophakic) to be the leading indication making up 25.5% of the cases while keratoconus was found in only 6.8% of indication for overall. [14]

PKP indications from the Dandona *et al* [14] series were different from the Kenyan experience: while keratoconus made up half of the Kenyan cases, it was a bare 7% in the above South Indian series. The main indications from this South Indian series was in keeping with a high cataract surgical rate in India (more than 3100-4500 cataract surgeries/million/year, which is comparable to rates in developed countries at 4000-5000 cataract surgeries/million/year) as compared to Kenya (of <600 cataract surgeries/million/year).[13-15,17]

In the Kingdom of Saudi Arabia, a similar large series looked at 1721 grafts. Keratoconus was indicated in 50.9%; corneal oedema was the indication in 20.7%, 19.2% was due to stromal scarring and 9.1% was due to stromal dystrophy.[30] Trachoma was responsible for the scars.

Indications from some developed countries was not different: the Italian CORTES Study of 4415 PKPs and 489 LKs performed across Italy found keratoconus to be the major indication, constituting 47% and 66% for PKP and LK respectively. This was followed by regrafts 14% and bullous keratopathy 14% (in the PKP group).[31] In Canada PBK accounted for 42.7%, keratoconus 10.7%, ABK 8.8% and corneal dystrophies 7.7%.[32]

The Australian Corneal Graft Registry Study found the following indications: keratoconus 30%, PBK and ABK 25%, failed previous graft 18%, corneal scars and opacities 11%, and corneal dystrophies 7%.[10]

The common indications for PKP are: keratoconus with apical scarring, with/without rapid progression; aphakic or pseudophakic bullous keratopathy; corneal scarring; Fuch's endothelial dystrophy; failed corneal graft (due to primary graft failure from graft rejection or infection); stromal necrosis from herpes simplex keratitis (HSK); severe anterior segment ocular trauma with a normal posterior segment; congenital corneal opacities (such as Peter's anomaly, or sclerocornea); Stevens-Johnson Syndrome (SJS); corneal dystrophies; chemical burns; and select cases of corneal ulcers with good visual potential (bacterial, fungal, parasitic, or viral). [29, 30]

The second most frequent indication for PKP is for relief from discomfort and pain due to bullous keratopathy from endothelial damage (whether aphakic [ABK]or pseudophakic[PBK]). However, a PKP may not be indicated if the eye is blind. [28]

PKP to eliminate infection is rarely indicated. However, early surgery may be necessary if there is a corneal perforation. PKP is not an early option for amoebic infections since the risk of recurrence and graft rejection is very high. Therapeutic PKP is necessary in most cases of fungal keratitis due to filamentary organisms, as these respond poorly to medical therapy. [28]

A tectonic PKP can be used to reinforce globe support or seal a perforation and this is the most common indication for inflammatory melting that develops as a complication of rheumatoid arthritis with dry eyes. However, an LK is the preferred option if there is active corneal melting. [28]

1.3.5 PREOPERATIVE PATIENT EVALUATION AND POOR PROGNOSTIC FACTORS

A patient is evaluated for any evidence of poor prognostic factors which include: active ocular inflammation, glaucoma, corneal vascularization, ocular surface abnormalities (such as an associated lid abnormality (entropion, ectropion), tear film dysfunction and dry eyes). The recipient is also assessed for any evidence that may militate against an optically successful corneal grafting. [18, 29-34]

Other important factors to consider are corneal hypoesthesia, corneal irregularity, pre-existing cataract (this may require further counselling for consideration of the Triple Procedure) and any evidence of structural changes of the anterior chamber (peripheral anterior synechiae, rubeosis). [18, 29-34]

Topical antibiotics, steroids, and cyclosporine A may be initiated preoperatively to modify some of the ocular surface if necessary. [18, 33, 34]

The Collaborative Corneal Transplantation Studies (CCTS) evaluated the effect of donor-recipient histocompatibility matching and crossmatching on the survival of corneal transplants in high-risk patients. ABO blood type incompatibility was a possible risk factor for rejection. High-risk status for graft failure was indicated by any of the following: vascularization of the cornea in

at least 2 quadrants; history of previous graft rejection; glaucoma; extensive peripheral anterior synechiae; traumatic or hereditary ocular surface disorders. [32]

1.3.6 SOURCING DONOR MATERIAL FOR PENETRATING KERATOPLASTY

Before the year 2007, there was no eye bank for storage of retrieved corneas in Kenya. Donor tissues have been available rather sporadically from overseas, notably the USA and Asia. Other developed countries source their donor tissues mainly locally. Many developing countries source their corneas from facilities in the USA, which have met the Eye Bank Association of America accreditation standards. [13, 16, 26]

The 'National Eye Bank of Kenya', "sited" at the Lions Sight First Eye Hospital at Loresho in the outskirts of the Kenyan capital Nairobi has a programme of retrieving donor corneas from local sources as well as external sources. The amount of tissue sourced locally was said to be limited due to socio-cultural factors, thus limiting the availability of donor corneas despite advocacy to create awareness. The impact of this on locally sourced corneal tissues has yet to be evaluated. The lack of awareness on the need for organ donations is not unique to Kenya alone: a survey among final year medical students in Nigeria on eye donation concluded that medical students lack adequate knowledge about some aspects of eye donation and corneal transplantation, thus by inference, suggesting the low level of awareness in the general population. [43]

1.3.7 PRESERVATION OF DONOR CORNEA

In Yorston *et al*, corneas were sourced from eye banks in the USA and Sri Lanka and tissues were preserved in Optisol with interval from retrieval to transplant time of 2-14 days. [13] Mboni *et al* gave no information on the storage material used but indicated that corneas were preserved for between 1-27 days.[17]In that review, an inverse relationship was clearly demonstrated between donor tissue retrieval time to transplant time with overall graft survival. Those corneas retrieved within one week of the death and preservation of the donor had the greatest chance of survival, with over 73% surviving. [17]

Corneas for PKP can be preserved in one of several ways[31]: (1) Short Term Preservation is achieved in: (a) Moist Chamber with 100% humidity at 4°C could hold the donor cornea viable

for 48 hours; and (b) McCarey-Kaufman Medium (which is a Standard Tissue Culture Medium (TC199) in 5% Dextran with antibiotics and maintained at 4°C could hold donor for 96 hours.[31](2) Intermediate Term Preservation is achieved in: (a) Dexsol, Optisol, Ksol, & Procell media. These are also Standard Tissue Culture Medium (TC199) but with the addition of Chondroitin sulphate, bicarbonate buffer, amino acids and gentamicin, maintained at 4°C. These can preserve donor corneas for up to 2 weeks (336 hours). [31](b) Organ Culture medium is said to decrease corneal graft rejection rate since it is believed that the culture kills the antigen presenting cells.[12] However, there is the fearsome disadvantage of possible increase in infection rate, since the medium is maintained at 37°C with donor tissue preservation of up to 4 weeks (672 hours). [31] (3) Long Term Preservation utilizes cryopreservation with liquid nitrogen at a temperature of -196°C. This method can preserve donor tissue for up to one year. However, the process is expensive and the results have been unpredictable. Cryo-preserved tissue has a favourable preferential role in tectonic indications of PKP. [31]

1.3.8 SURGICAL TECHNIQUE FOR PKP

Detailed description of the surgical technique is beyond the scope of this dissertation. Graft sizes bigger than 8.5mm diameter can lead to peripheral anterior synechiae formations, increased intra-ocular pressure as well as run the risk of attracting limbal blood vessels and rejections and subsequent failure, while smaller diameter <7.25mm corneal buttons lead to high astigmatism as well as having lesser endothelial cell counts, which will ultimately lead to graft failure. [18, 29, 31-34]The donor corneal button is excised via trephine and scissors. However, the trephination technique is now automated using vacuum or the Femtosecond laser method to ensure a uniform and an exact-fit of donor button onto the recipient bed. This prevents wound leak (with associated problems of hypotony, shallow anterior chamber, uveitis and endothelial failure) in the early postoperative period as well as minimises astigmatism in the long-term. [18, 31, 32] The donor corneal button is secured onto the recipient bed via 10/0 nylon sutures in a variety of ways (interrupted, continuous or a combination of these two).[31-33] A review by Williams *et al* [51] found no statistical difference with respect to graft survival between continuous or interrupted sutures for postoperative astigmatism.

1.3.9 POSTOPERATIVE CARE AND FOLLOW-UP

Topical steroids are used frequently initially according to surgeon's preferences. As the inflammation subsides, this is tapered down to lesser frequencies from several weeks to few months, dependent on overall response and level of inflammation. Subsequently, usually, a low dose fluorometholone (FML) eye drops is used since it does not increase the intraocular pressure in topical steroid responders.[18, 31, 33] Newer topical steroid medications such as Rimexolone 1% eye drops can be a substitute in those at risk of developing high IOPs.[62]

Cycloplegic eye drops are used in the first two weeks or longer if there is anterior uveitis. However, in keratoconus the use of cycloplegics may be avoided if the Urrets-Zavalia syndrome is contemplated. It has also been reported to occur even in the absence of use of dilating eye drops and in a variety of other intra-ocular surgeries. [51]

Topical antibiotic eye drops or lubricants may be prescribed until the cornea has re-epithelialized. [29, 33]

If the graft was performed for HSK, oral Acyclovir 400mg twice a day should be given in the immediate postoperative period of lasting not less than 6 months. [18, 29, 31, 33]

High-risk grafts would require use of systemic immunosuppressive agents.[29, 31-34] Oral steroids are effective in controlling acute inflammation, while cyclosporine 4mg/Kg is suitable for long-term maintenance therapy. Cyclosporine has several inherent risks associated with its use over a prolonged period and these include risk of hypertension, potentiating malignancies, and increased risk of lymphoma, which must be discussed with the patient. [18, 29, 33]

Brightbill's Classification is used to describe corneal graft prognosis. (Appendix I, page 57).

Patient reviews are usually conducted weekly for one month then monthly for three months and thereafter at three monthly intervals. However, these visits can be more frequent or less frequent dependent on patient's overall response to therapy and surgery. [29, 33]

At each visit the IOP is measured. The graft is inspected to make sure the suture knots are buried and that there is no vascularization or rejection. Loose sutures should be removed as they are a potential source of infection as well as stimulus for corneal vascularization and rejection. Sutures are usually removed at 12 to 18 months after surgery but they can be left longer. [18, 29]

Visual rehabilitation may require glasses or a contact lens. A rigid gas-permeable contact lens is recommended to reduce the risk of neovascularization. [18, 29, 33]

Patients must be counselled that although the risk of rejection reduces over time, it never disappears entirely. [16] Patient should be reminded of the symptoms of early rejection and the importance of prompt consultation. [29, 33]

1.3.10 OUTCOME MEASURES IN PKP

Outcome measures can be analysed under short-term outcomes and long-term outcomes. Invariably, these would be determined by either visual or corneal graft survival. A number of studies had looked at these two main endpoints as outcome measures in PKP series.

Studies from South India by Dandona *et al* [14] showed that 69% of grafted corneas were clear at two years after surgery. In East Africa by Yorston *et al,* [13] 87% of grafts for keratoconus were clear at two years and 65% for other causes. However, graft clarity does not always guarantee good vision. In the follow-up period, coexisting ocular problems that can reduce vision must be identified and managed appropriately. In both Yorston *et al* [13] and Mboni [17] visual outcomes were better for grafts for keratoconus than for other indications.

Yorston *et al* and Mboni *et al* both demonstrated that a reasonable number of cases of corneal blindness particularly those due to corneal dystrophies, keratoconus and bullous keratopathy in the African setting were amenable to PKP with good outcomes.[13,17] Graft failure occurred in 21.8% with bacterial infections being responsible for 6%.[13]

The Australian Corneal Graft Registry (ACGR) study reviewed grafts at 1 year, 5 years and at 7 years and found that corneal grafts achieved survivals of 91%, 72% and 69% respectively over the stated periods. The common causes of graft failure were immunologic rejection at 34%, infection at 18% and corneal graft glaucoma at 9%. In their series, 52% achieved a Snellen visual acuity of 6/18 or better postoperatively. Poor postoperative visual outcomes (acuity less than 6/60) were attributed to coexisting ocular morbidities in the grafted eye (43%). [10]

The New Zealand National Eye Bank study [53] that looked at PKP survival and visual outcome at one year found the leading cause of failure to be irreversible rejection from one or more episodes of reversible rejection. Their overall graft survival was 87%. This New Zealand study

[53] found no statistically significant difference in the association between donor factors (such as age, donor source, and cause of death, death-to-preservation interval, endothelial cell density, donor lens status, and storage duration) and decreased graft survival.

Despite the above findings for primary PKP, outcomes in regrafts and/or combined procedures have only been modest, ranging from 0-50%.[54] In Southern India, Dandona *et al* found survival among regrafts to be 21.2% at 5 years.[14]

1.3.11 POSTOPERATIVE COMPLICATIONS AND MANAGEMENT

A successful PKP depends largely on good postoperative management. Clinicians should identify and promptly manage any possible early complication such as wound leak from poor graft-host apposition, infection, glaucoma, and graft failure or rejection. Also to monitor graft clarity, endothelial function, status of corneal epithelium, depth and reaction in the anterior chamber, and synechiae. Late problems such as superficial punctuate keratitis either due to dry eyes, irregular graft-host junction, trichiasis, exposure, or due to medication toxicity, epithelial defects, filaments, and loose sutures and/with infection. These problems require careful assessment and appropriate management. Important late postoperative period problems include astigmatism, immunological graft rejection, graft failure, and glaucoma. [18, 32-34]

According to Mboni *et al*, the commonest immediate complications were uveitis, persistent epithelial defects and primary failure. Mboni *et* al also found an overall failure rate of 35.1%, and infection was the main trigger for failure. HSV keratitis was the leading cause of infection. [17]In the study by Yorston *et al*, they found graft opacification in 21.8% and graft failure in 21.3%. Bacterial keratitis was responsible for 15.7% of the failed grafts. However, this particular review 'classified' recurrent HSV keratitis in the graft as a recurrent disease and *not* as infection. [13]

Common postoperative complications following PKP include the following:

1.3.12. a. Wound Leak: presents as a shallow anterior chamber with low IOP on the first postoperative day after PKP. If the primary cause is due to a broken suture or inadequate wound apposition then surgical revision and resuturing is urgently indicated. [18, 33, 34]

1.3.12. b. Flat Anterior Chamber with High IOP: this may result from pupillary block, anterior rotation of the lens-iris diaphragm (from choroidal haemorrhage), choroidal effusion, or malignant glaucoma. Whatever the cause, it must be treated urgently. [18, 33, 34]

1.3.12. c. Endophthalmitis: may result from a variety of factors such as contamination of donor or host tissue or postoperative infection. It requires aggressive management. [18, 33, 34]

1.3.12. d. Persistent Epithelial Defect: Persistent epithelial defects occur in eyes with ocular surface disorders such as dry eyes, blepharitis, exposure keratopathy, and rosacea, or in those with systemic diseases, such as diabetes or rheumatoid arthritis. Frequent topical lubrication is indicated but topical toxicity must be excluded as a cause. Non-resolving cases may require a tarsorrhaphy and/or punctual occlusion. [18, 33, 34]

1.3.12. e. Primary Graft Failure: is recognised when significant oedema of the donor tissue in a non-inflamed eye is present on the first postoperative day and does not clear. It is often due to poor donor endothelial function or surgical damage to donor cornea during PKP. The graft is observed for few weeks to allow the oedema to clear failing which a regraft should be considered. [18, 34, 35]

1.3.12. f. Secondary Graft Failure: an irreversible opacification in a previously clear graft from whatever cause.

1.3.12. g. Suture-Related Problems: such as loose or broken suture must be removed immediately because it can result in vascularization or abscesses. [34, 35] Both these events can lead to a rejection and/or failure. [32-35]

1.3.12. h. Graft Rejection: graft rejection remains the most common cause of corneal graft failure. Alldredge and Krachmer reported a rate of 21%.[32,33] In the Yorston *et al* series, 5.1% of grafts failed permanently due to rejections[13] and in Mboni's review, 14.3% grafts failed due to rejection.[17] Rejection is a type IV hypersensitivity immunologic event that is observed after two weeks. [34, 36]

Graft rejection may be divided anatomically into three categories: epithelial rejection, subepithelial rejection, and endothelial rejection. [34, 36]

Treatment of graft rejection consists primarily of intensive topical corticosteroids. For epithelial graft rejection, the frequency of topical steroids is increased to hourly; endothelial graft rejection warrants hourly or more often topical steroids until the rejection process is reversed. Subconjunctival steroid injections as well as systemic steroids may be utilized in severe cases but are often not necessary.[33-36] In the Yorston *et al* series, they had 54 episodes of rejection in 46 grafts, wherein 11 grafts ultimately failed (5.1%).[13]

1.3.12. i. Astigmatism: adequate control of postoperative astigmatism is vital to achieve the best visual acuity possible. Selective removal of interrupted sutures can be initiated as early as 6-8 weeks post PKP. Continuous sutures can be adjusted on the slit lamp based on serial corneal topography images. [37] Astigmatic keratotomies may be performed late if a significant amount of residual astigmatism remains after all sutures has been removed and the patient is intolerant of contact lenses. [36]

1.3.12. j. Corneal Ulcers: patients who have had PKP are more susceptible to infectious keratitis. Factors such as suture abscess and persistent epithelial defect may contribute to the development of corneal ulcers. [33-36]

1.3.12. k. Recurrence of Diseases: various corneal dystrophies and infections may recur in grafts. Among the three stromal corneal dystrophies (macular, granular, and lattice), lattice corneal dystrophy has the highest recurrence rate, and herpes simplex keratitis can recur. [33-36]

2.0 JUSTIFICATION

For more than three decades, ophthalmologists in Kenya have been performing PKP. However, there is a mismatch in terms of the demand for corneas on the one hand and the availability of donor corneas on the other. Locally acquired corneas are hard to get, possibly pointing to the fact that the level of awareness on the importance of organ donations is low (anecdotal reports).

Previous studies by Yorston *et al* and Mboni *et al* looked at corneal grafts done in a single facility at the Kikuyu Eye Hospital. Those reviews looked at data accrued over a 5-year to a 10-year period and those were nearly two decades ago. [13, 17]

To the best of our knowledge, there has been no national review of indications and outcomes of corneal grafts in the Republic of Kenya.

It is our hope that the results of such a review will help to serve as a guide for clinicians in making best case selection decisions as well as use the evidence in patient counselling in order to maximize the best outcomes for PKP.

3.0 BROAD OBJECTIVE

To document the indications and outcomes of PKP in Kenya over a 2-year period

4.0 SPECIFIC OBJECTIVES

1. To document the main indications for PKP in Kenya
2. To determine the outcomes of PKP in Kenya (in terms of corneal clarity, visual acuity, and complications)
3. To determine the corneal graft survival rates
4. To determine the factors that influence poor outcome following PKP in Kenya

5.0 METHODOLOGY

5.1 STUDY DESIGN

A retrospective case series (a Medical Record Review study)

5.2 STUDY PERIOD

July to August 2012

5.3 STUDY LOCATION– Treatment Facilities in Kenya with dedicated eye units that perform PKPs. KNH is the only government treatment facility; the rest are private.

- Lighthouse For Christ Eye Centre, located in Mombasa, Coast Province
- Tenwek Mission Hospital, located in the Rift Valley Province
- Upper Hill Medical Centre, situated in the city of Nairobi, Central Province
- Upper Hill Eye and Laser Centre, situated in the city of Nairobi, Central Province
- Kenyatta National Hospital, situated in the city of Nairobi, Central Province
- Aga Khan University Hospital, situated in suburban Nairobi, Central Province

5.4 SAMPLE SIZE

All consecutive cases within the given time frame were selected [54, 55] for PKP surgeries that met our inclusion criteria.

5.5 INCLUSION CRITERIA

Recorded cases of PKP performed between and inclusive of the period from 1st January 2001 to 31st December 2011 in the study locations were reviewed and analyzed.

5.6 CASE DEFINITION

A patient who underwent PKP in any of the study locations in the period under review is a case.

5.6.1 A case must have completed a minimum follow-up of 3 months

5.6.2 The maximum follow-up end-point was 2-completed years from date of surgery [10, 13, 14, 25-27, 38, 39]

5.7 EXCLUSION

5.7.1 Keratoprosthesis.

5.7.2 Non-optical and non-therapeutic indications: tectonic or cosmetic.

5.7.3 Descemet Stripping Endothelial Keratoplasty (DSEK), Descemet Stripping Automated Endothelial Keratoplasty (DSAEK), Deep Lamellar Endothelial Keratoplasty (DLEK), and Deep Anterior Lamellar Keratoplasty (DALK).

5.7.4 The triple procedure (combined corneal graft, cataract extraction and intraocular lens implantation).

5.8 RESOURCE PERSONNEL

5.8.1 Administrative and records personnel services was obtained for case file extraction

5.8.2 Services of an epidemiologist were utilized for data organization and analysis

5.9 ETHICAL CONSIDERATION

5.9.1 Ethical approval was obtained from the Kenyatta National Hospital/University of Nairobi Ethics and Research Committee. See appendix VI.

5.9.2 Approval was obtained from the respective consultants in the study centres.

5.9.3 This retrospective case series was conducted within the framework of the principles of the Helsinki Declaration (Helsinki Principles of Research).

5.10 MATERIALS AND METHODS

5.10.1 Coded structured Excel™ worksheets for data collection was used (see Appendix II)

5.10.2 Primary identification of PKP procedures from the theatre registers and collection of registration (IP) numbers of cases was undertaken.

5.10.3 Extraction of case files from the records office was done through the assistance of the respective records officers in each of the centres.

5.11 PROCEDURE AND DATA ANALYSIS

5.11.1 The coded structured Excel™ worksheets were used to manually transcribe data from individual case files.

5.11.2 Data was inputted using Microsoft® Excel™ (Windows 7) and exported to Epi Info™ (Centers for Disease Control and Prevention, USA; version 3.4.3) for statistical analysis. Data consistency was ensured by 'reviewing' randomly selected case files against entries.

5.11.3 Descriptive statistic was used to describe demographic characteristics such as age, sex, and preoperative diagnosis into means and percentages for categorical variables. Cox

univariate regression analysis was used to select variables with p-values of 0.25 or less for further selection into a forward multivariate analysis. The Cox proportional hazards regression was used to determine associations between possible risk factors and graft failure in the final multivariate analysis model. P-values of less than 0.05 are considered statistically significant. Kaplan-Meier method was used to determine PKP survival probability for indications and outcomes of PKP as well as gender, age group and postoperative complications. Odds Ratios or Risk Ratios were determined where appropriate for risk estimation.

5.12 OUTCOME MEASURES

5.12.1 Primary Outcome Measure determined was the proportion of corneal grafts that remained clear at the end of the 24-month follow-up period.

5.12.2 Secondary Outcome Measures determined were:

(a): final visual acuity at the end of the 24-month follow-up or last visit, if this was less than 24 months;

(b): C**omplications** of PKP. These can be: in the *"early postoperative period"* (events occurring within the first 2 months postoperatively); and the *"late postoperative period"* (events continuing from or occurring after the "early post-operative period" and up to the end of the 24-month follow-up period).

5.12.3 Primary Graft Failure: Corneal graft opacity noted on the first postoperative day [13] – synonym is Early Endothelial Failure.

5.12.4 Time of Graft Failure: the first postoperative examination of which the patient was seen with a failed graft. This also marks the end-point for the inclusion of such an eye in the outcome analysis; it will be censored in the survival analysis. [52]

5.12.5 Secondary Graft Failure: An irreversible change in a graft preventing recovery of useful vision after the graft had been initially clear 2 weeks after PKP [52] – synonym is Late Endothelial Failure.

6.0 RESULTS – DEMOGRAPHIC CHARACTERISTICS

6.1 A total of 240 records were identified from theatre registers. Of these, 174 PKPs were analysed. Figure 1 below shows the flow chart of study patients' records utilised.

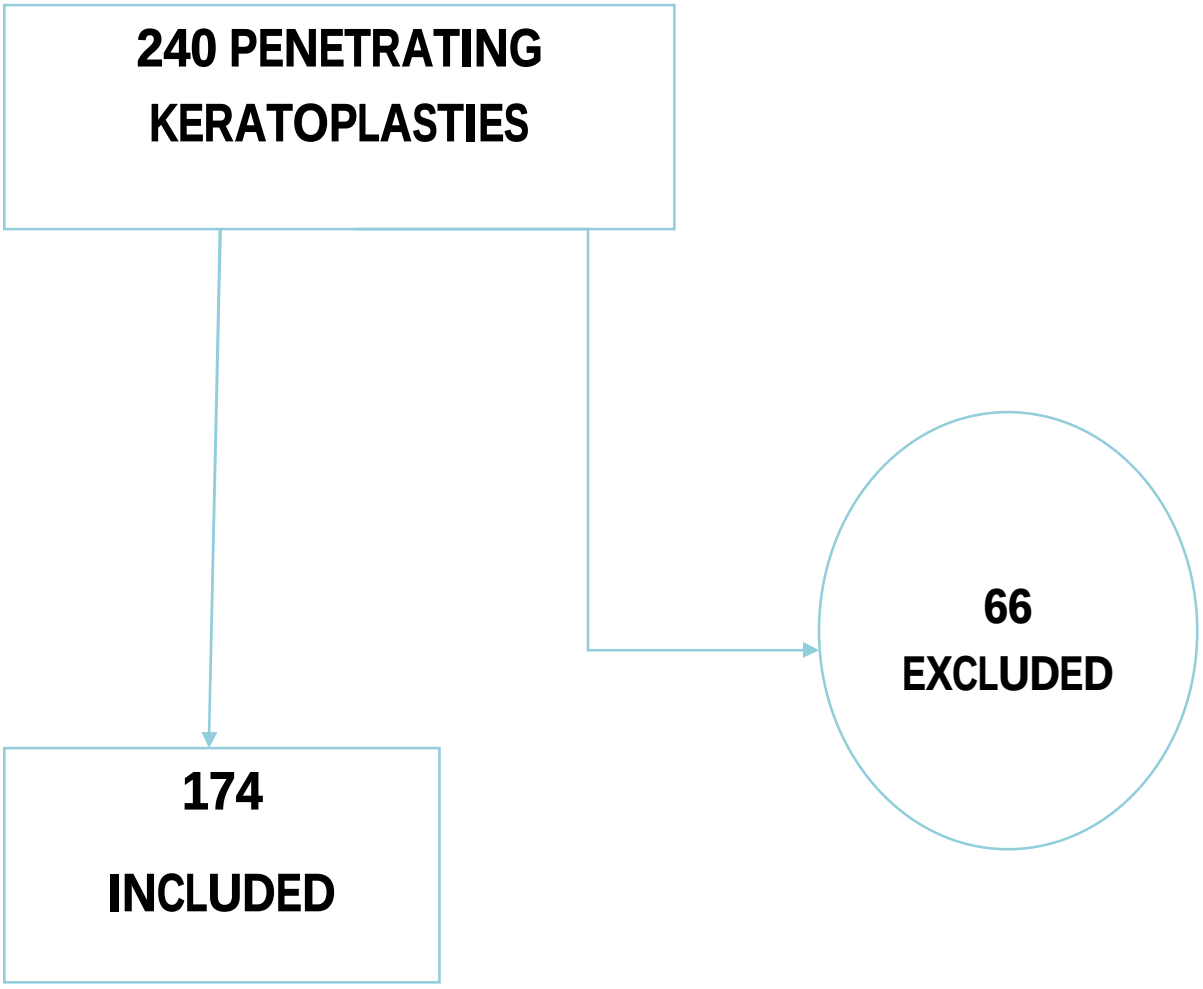

Figure 1: Flow chart of study

6.2 Treatment Facilities– Six eye hospital facilities participated in our review. These were found in three main counties: Nairobi, Mombasa and Bomet counties respectively.

Table 1: Number of PKPs by Facility, N=174

Facility	Number of PKPs	Percentage
LHFCEC	80	46
TENWEK	36	20.7
UHEAL	24	13.8
AKUH	15	8.6
KNH	13	7.5
UHMC	6	3.4
TOTAL	**174**	**100**

 Of 174 PKPs, 19 (10.92%) were bilateral grafts and 4 (2.3%) were regrafts. Recipients of bilateral grafts were analysed as individual cases.

6.3 Trend – The trend of annual PKPs over the review period showed an increase overall.

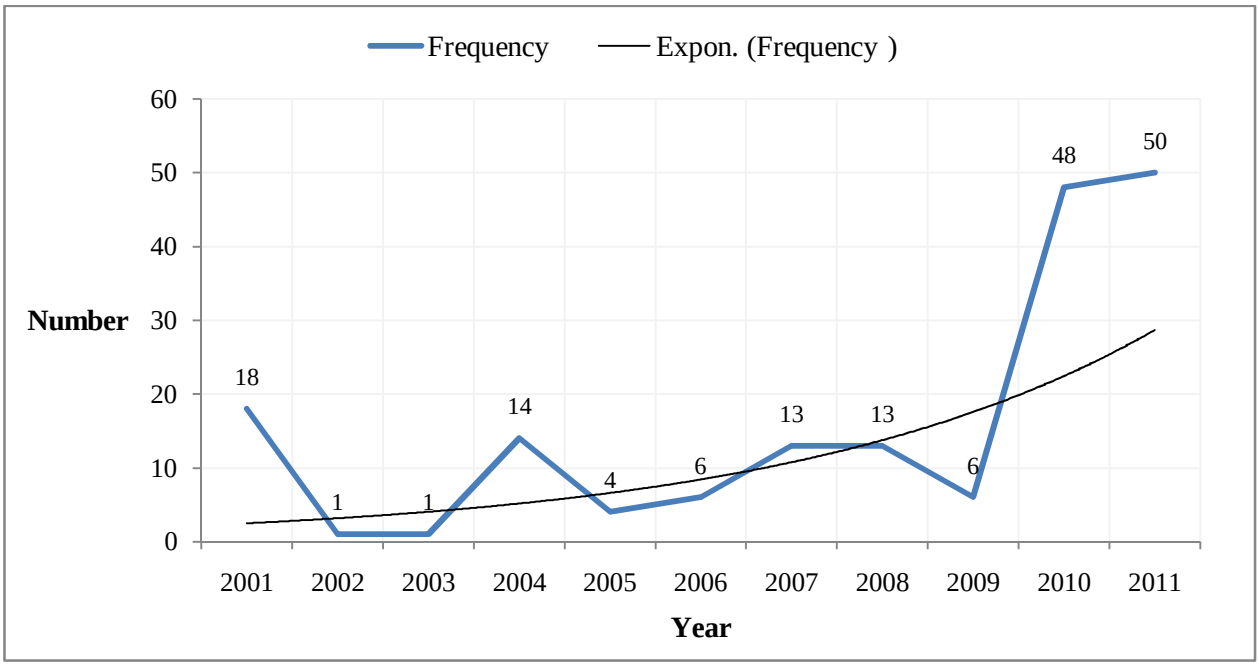

Figure 2: Trend of PKPs in Kenya 2001-2011.

6.4 **There were** 117 males and 57females, giving a male/female ratio 2.3:1.

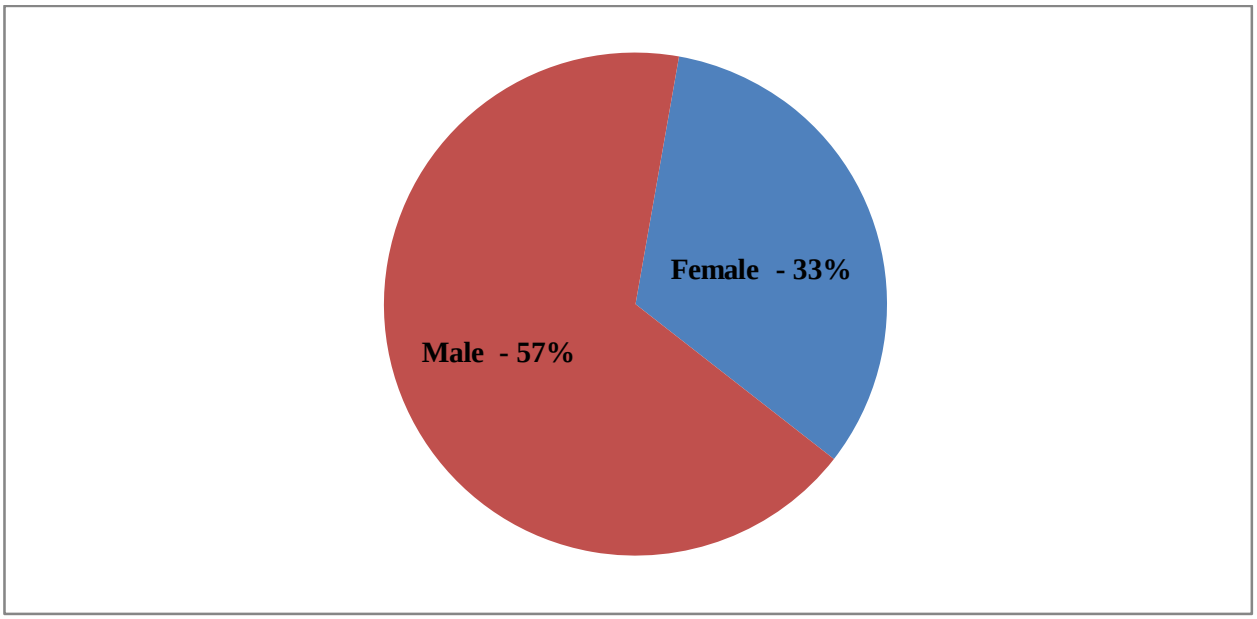

Figure 3: Gender of PKP Recipients, N =174

6.5 **Age Distribution –**The age range was 9 months to 88 years; the median age was 26 years; and the mode was 16 years. More than half of the recipients were less than 30 years (57.5%).

Table2: Age Groups of PKP recipients, N=174

Age Group of Recipient	Frequency	Percent
0-9	11	6.3
10-19	48	27.6
20-29	41	23.6
30-39	17	9.8
40-49	13	7.5
50-59	11	6.3
60-69	18	10.3
70-79	10	5.7
80-89	5	2.9
TOTAL	**174**	**100**

6.6 PREOPERATIVE CHARACTERISTICS

6.6.1 Main Indications: keratoconus was the commonest, accounting for 48.8% (n=85).

Table3: Preoperative diagnoses/indications for PKP, N=174

Diagnosis	Frequency	Percentage
Keratoconus	85	48.8
Bullous Keratopathy	32	18.4
Corneal Scars	29	16.6
HSK	11	6.3
Dystrophies	11	6.3
Failed PKP	4	2.3
Buphthalmos	1	0.6
Ulcer	1	0.6
TOTAL	**174**	**100**

6.6.2 Preoperative Vision: About two-thirds (64.4%) of the eyes were blind at presentation (visual acuity of <3/60 - PL).

Table 4: Preoperative Visual Acuity, N=174

Category of Baseline VA	Frequency	Percentage
6/6-6/18	1	0.6
<6/18-6/60	26	14.9
<6/60-3/60	35	20.1
<3/60-1/60	60	34.5
<1/60-LP	52	29.9
Total	**174**	**100**

6.6.3 Preoperative visual acuity by recipient age group: Majority of those in all categories of visual impairment are in the age brackets 10-19 years and 20-29 years respectively. Figure 4 shows the burden of visual impairment by age group preoperatively.

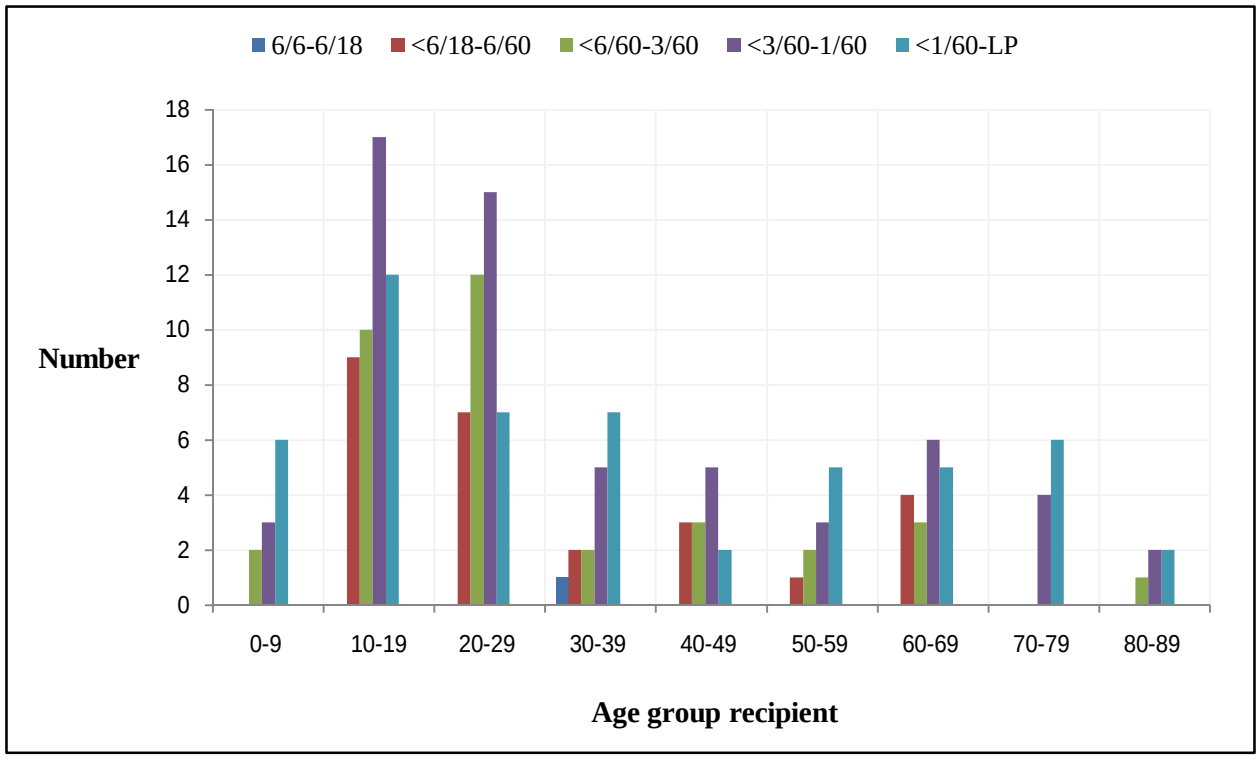

Figure 4: Preoperative visual acuity categories by age group of recipients.

6.7 POSTOPERATIVE CHARACTERISTICS - OUTCOME MEASURES

6.7.1 Corneal Clarity – Overall, 82.2% of the grafts remained clear and 17.8% were unclear. See table 5 below. Keratoconus was the most frequent indication among those with clear grafts and bullous keratopathy among those with unclear grafts: see tables 6 and 7 below.

Table 5: Corneal clarity general characteristics, n=174

Characteristic	Clear Grafts	Unclear Grafts	
Median Age	24	48	
Mode Age	16	72	
Primary Graft Failure		8	
Secondary Graft Failure		23	
Total	**143**	**31**	***p*< 0.0032**

Table 6: Proportion of **clear** grafts by indication at 24 months, n=174

DIAGNOSIS	Total Patients	Clear grafts	Percentage	95% CI
Keratoconus	85	78	54.5	46.0 - 62.9
Scar	29	23	16.1	10.5 - 23.1
Bullous keratopathy	32	18	12.6	7.6 - 19.2
Herpes simplex keratitis	11	10	7.0	3.4 - 12.5
Dystrophies	11	9	6.3	2.9 - 11.6
Failed PKP	4	3	2.1	0.4 - 6.0
Buphthalmos	1	1	0.7	0.0 - 3.8
Ulcer	1	1	0.7	0.0 - 3.8
Total	**174**	**143**	**82.2**	**0.77-0.87**

Table 7: Proportion of **unclear** grafts by indication, n=174

DIAGNOSIS	Total Grafts	Unclear Grafts	Percentage	95% CI
Bullous keratopathy	32	11	35.5	19.2 – 54.6
Scar	29	8	25.8	11.9 – 44.6
Keratoconus	85	7	22.6	9.6 – 41.1
Dystrophies	11	2	6.5	0.8 – 21.4
Failed PKP	4	1	3.2	0.1 – 16.7
Herpes simplex keratitis	11	1	3.2	0.1 – 16.7
Ulcer	1	1	3.2	0.1 – 16.7
TOTAL	**174**	**31**	**100**	

6.7.2 Visual Outcome –Overall, more than a third (36.2%) achieved final uncorrected normal vision of **6/6-6/18.**

Table8: Final visual outcome, N=174

Final VA	Frequency	Percentage
6/6-6/18	63	36.2
<6/18-6/60	64	36.8
<6/60-3/60	15	8.6
<3/60-1/60	14	8.0
<1/60 – LP	15	8.6
NPL	3	1.7
Total	**174**	**100**

6.7.3 Visual outcome by recipient age group – Majority of eyes that achieved **normal vision** were in the age bracket 10-29 years; of those eyes that were **blind,** a third were in the age bracket 10-29 years.

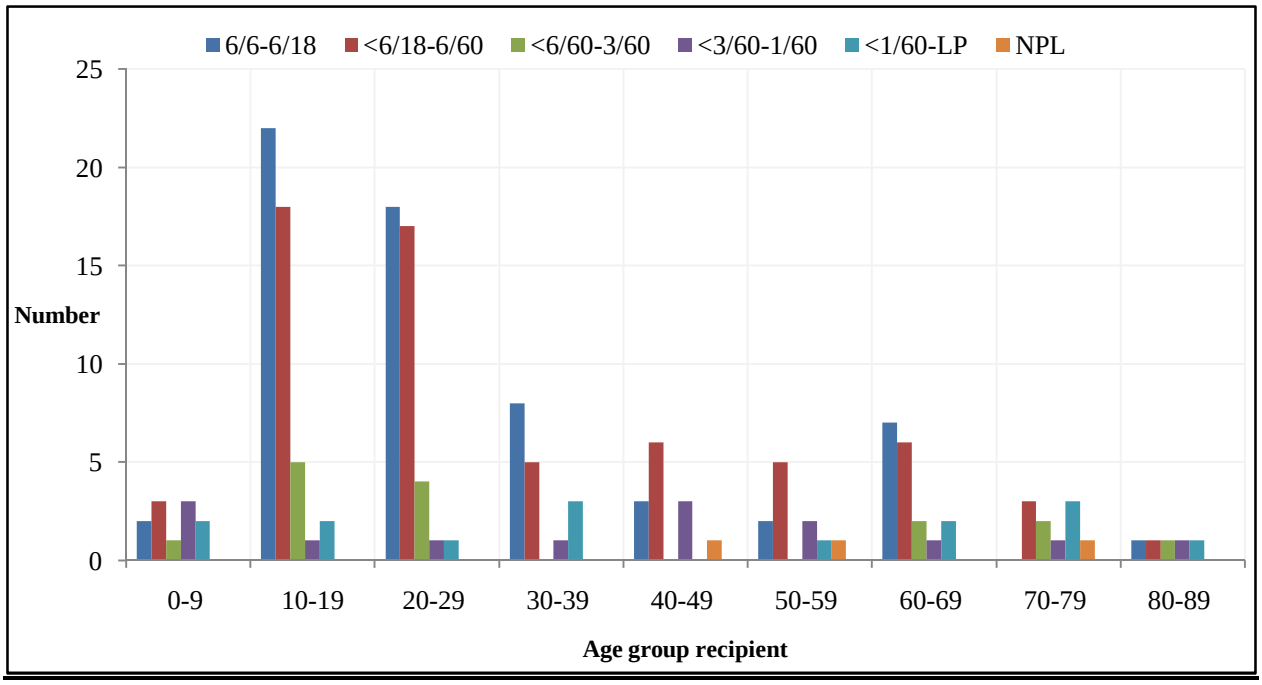

Figure 5: Final visual acuity by recipient age group, N=174

6.7.4 Final Visual Acuity by Indication – Two-thirds of eyes that achieved **normal vision** had keratoconus. Three-quarters of eyes that were **blind** had bullous keratopathy.

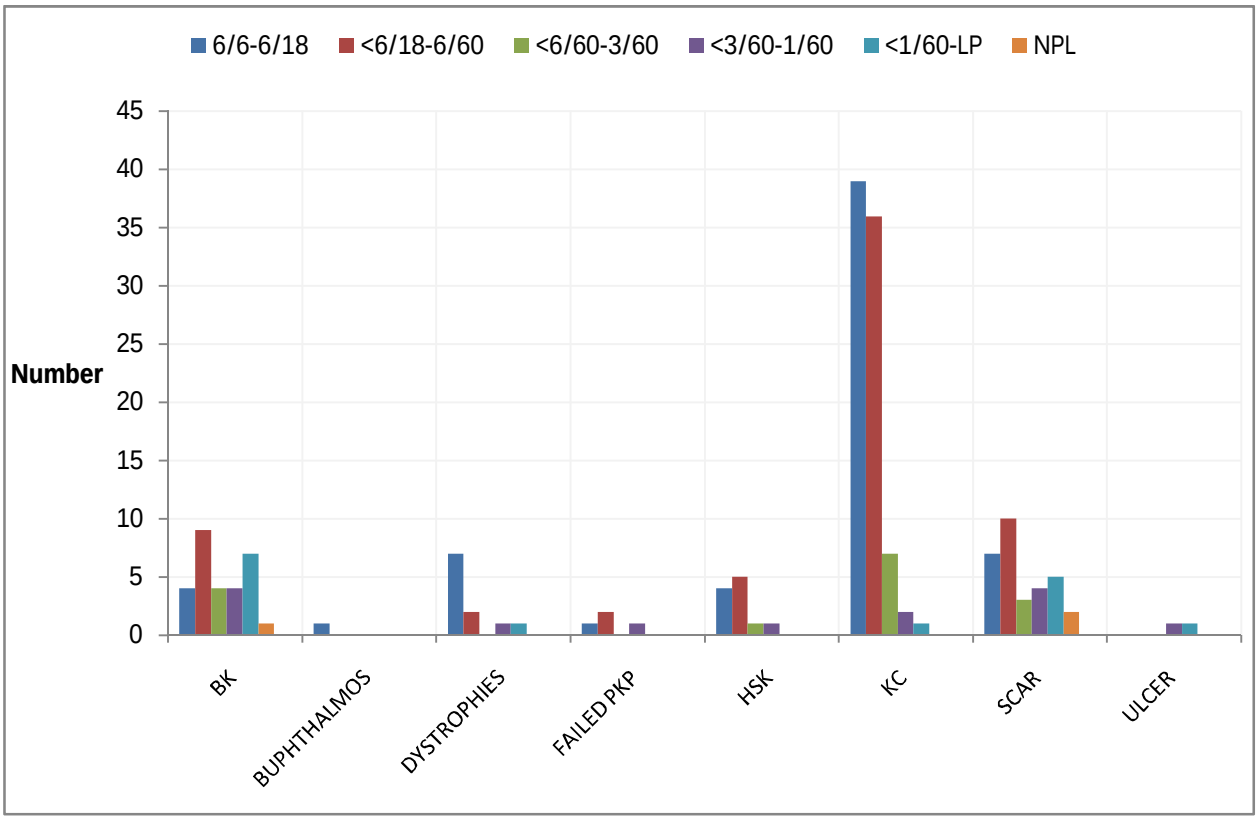

Figure 6: Final Visual Acuity by indication, N=174

6.7.5 Complications: Early Postoperative Complications – A total of 115 events were recorded, mainly epithelial defects. Majority of the events occurred in the first 2 weeks.

Table 9: Early Complications, N=174

Early Complication	Frequency	Percentage
No Complication	59	33.9
Epithelial defect	50	28.7
Stromal oedema	29	17.0
Uveitis	7	4.0
High IOP	5	2.8
Loose stitch	4	2.3
Infection	4	2.3
Shallow anterior chamber	3	1.7
Traumatic dehiscence	3	1.7
Immune rejection	3	1.7
Hyphaema	2	1.1
Others‡	5	2.8
Total	**174**	**100**

‡Others = Blunt trauma, Iris sutured to graft, Peripheral Anterior Synechiae, Retinal Detachment, Urrets-Zavalia Syndrome

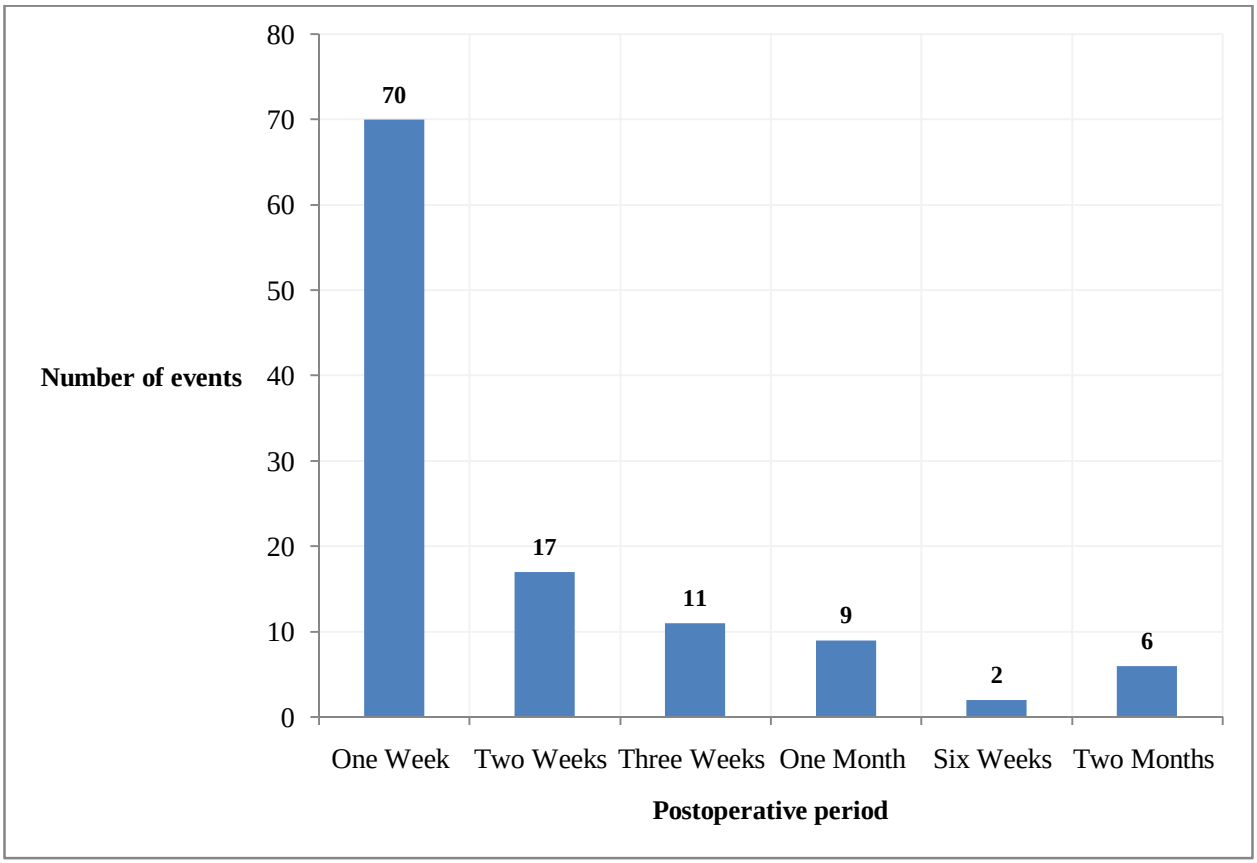

Figure 7: Timing of early complications, n=115

6.7.6 Complications: Late Postoperative Complications – A total of 66 events were recorded, mainly persistent stromal oedema and high intraocular pressure. Most of these (73%) occurred in the first 6 months (>2 months to ≤6 months).

Table 10: Late Postoperative Complications, n=66

Late Complication	Number of events	Percentage
Stromal oedema	19	28.78
High IOP/glaucoma	11	16.67
Bacterial infections¶	6	9.10
Severe astigmatism	5	7.57
Vascularised graft	4	6.06
Peripheral anterior synechiae	4	6.06
Recurrent herpes simplex keratitis	3	4.55
Traumatic dehiscence	2	3.03
Others‡	12	18.18
TOTAL	**66**	**100**

¶Bacterial infections = corneal ulceration x4 & endophthalmitis x2.
‡Others = retinal detachment, vitreous haemorrhage, severe dry eyes, immune rejection, uveitis, corneal melting, iris prolapse.

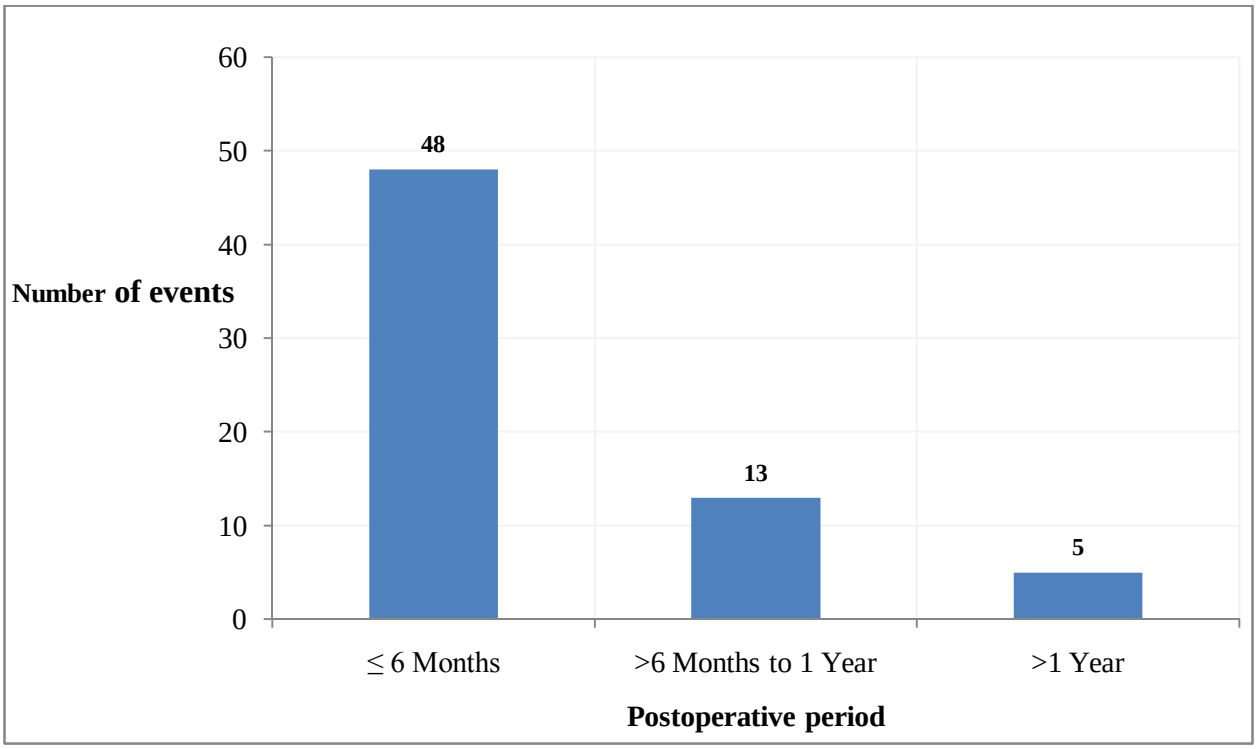

Figure 8: Timing of late complications, n=66

6.7.7 Corneal Graft Survival Rate –The two-year survival probability for corneal dystrophies and keratoconus were100% and 90% respectively. Repeat PKPs and corneal ulcers had the shortest survival rates at 75% and 50% respectively in 12 months; bullous keratopathy had the least two-year graft survival at47%. These differences were statistically significant at p=0.0191. Figures 9 – 11 below show the Kaplan Meier survival probabilities for various indications for PKPs.

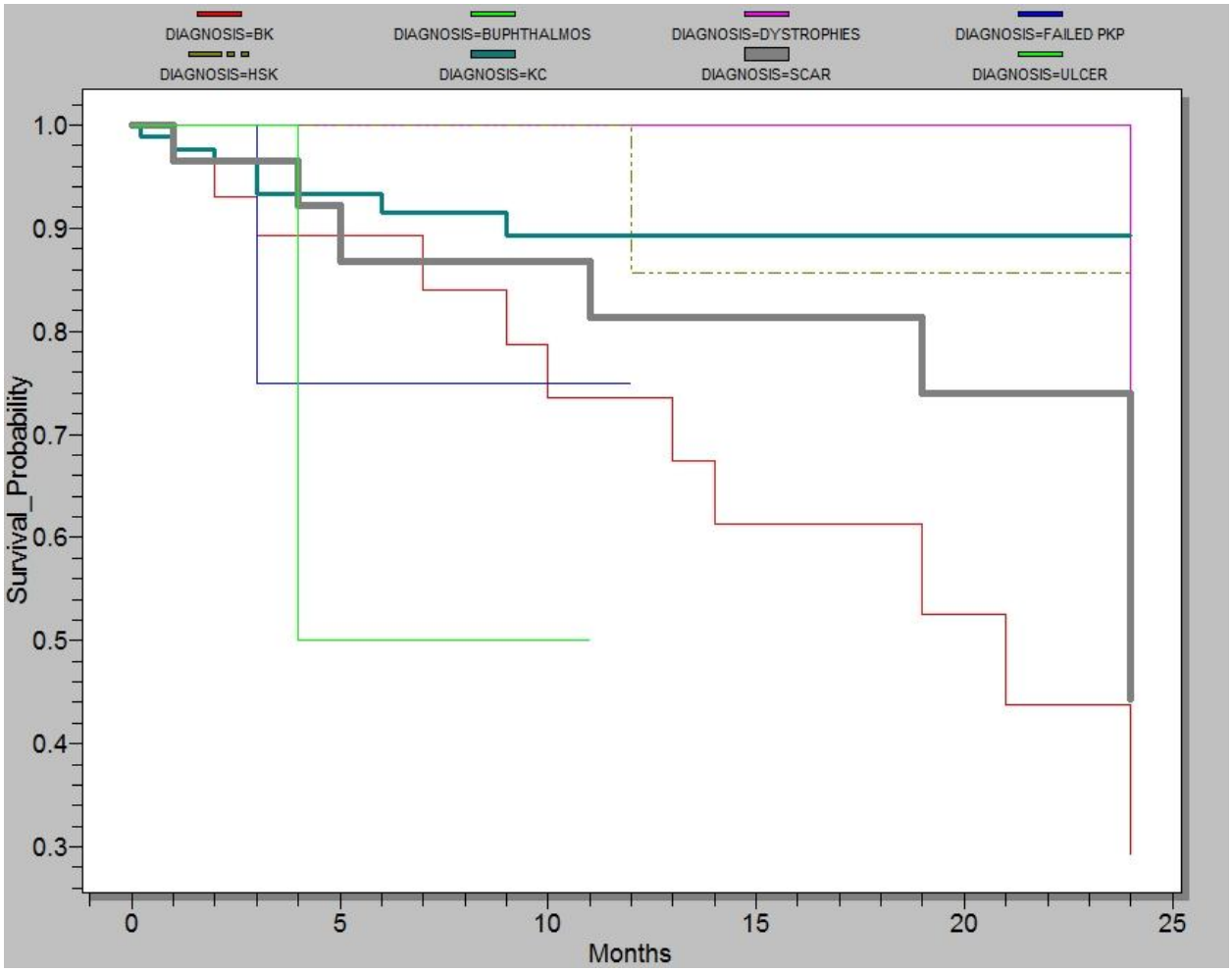

Figure 9: Kaplan Meier survival probability by PKP indication, N=174, p=0-0191

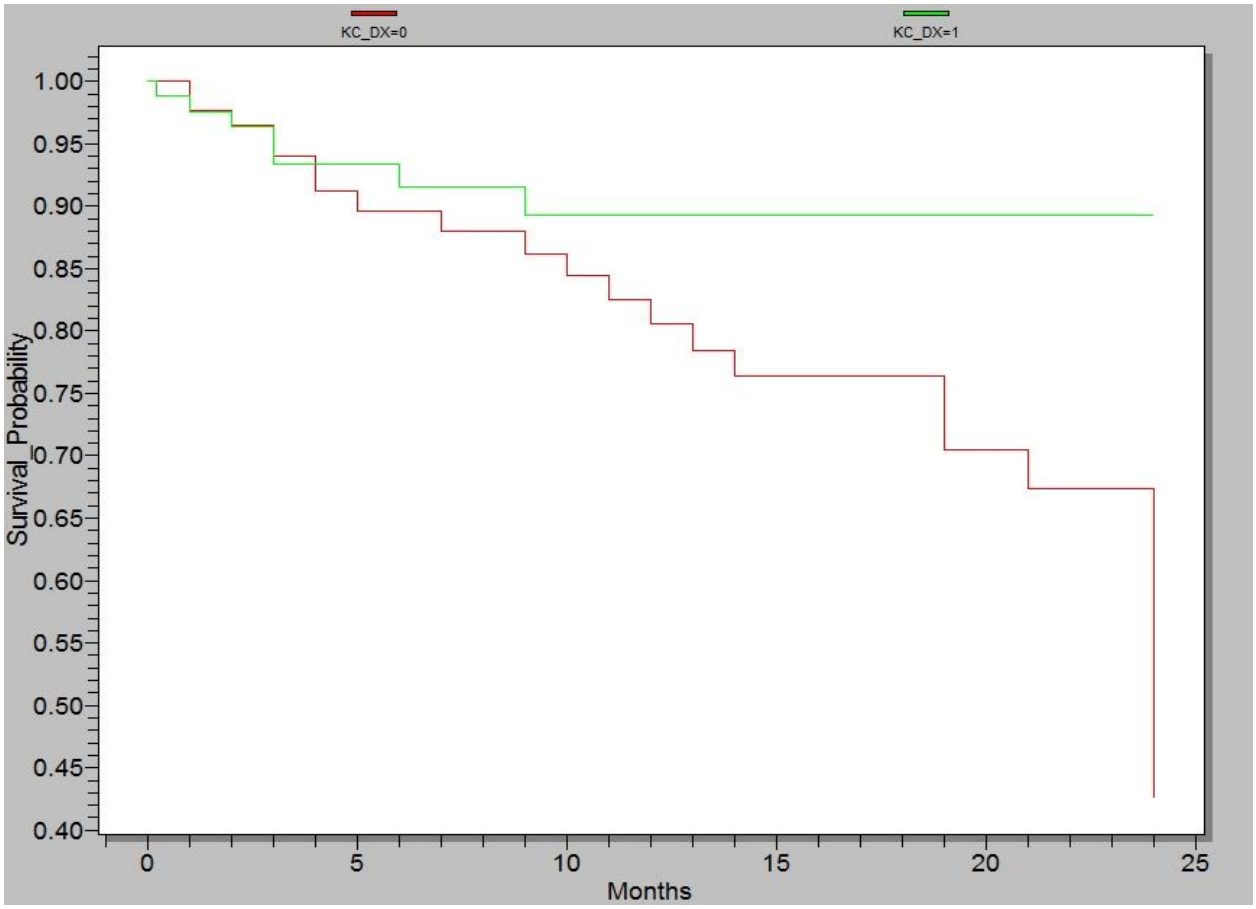

Figure 10: Kaplan Meier survival probability for keratoconus versus other indications

Key: keratoconus = [→], survival of 90%; other indications = [→], survival of 68%, p<0.0068.

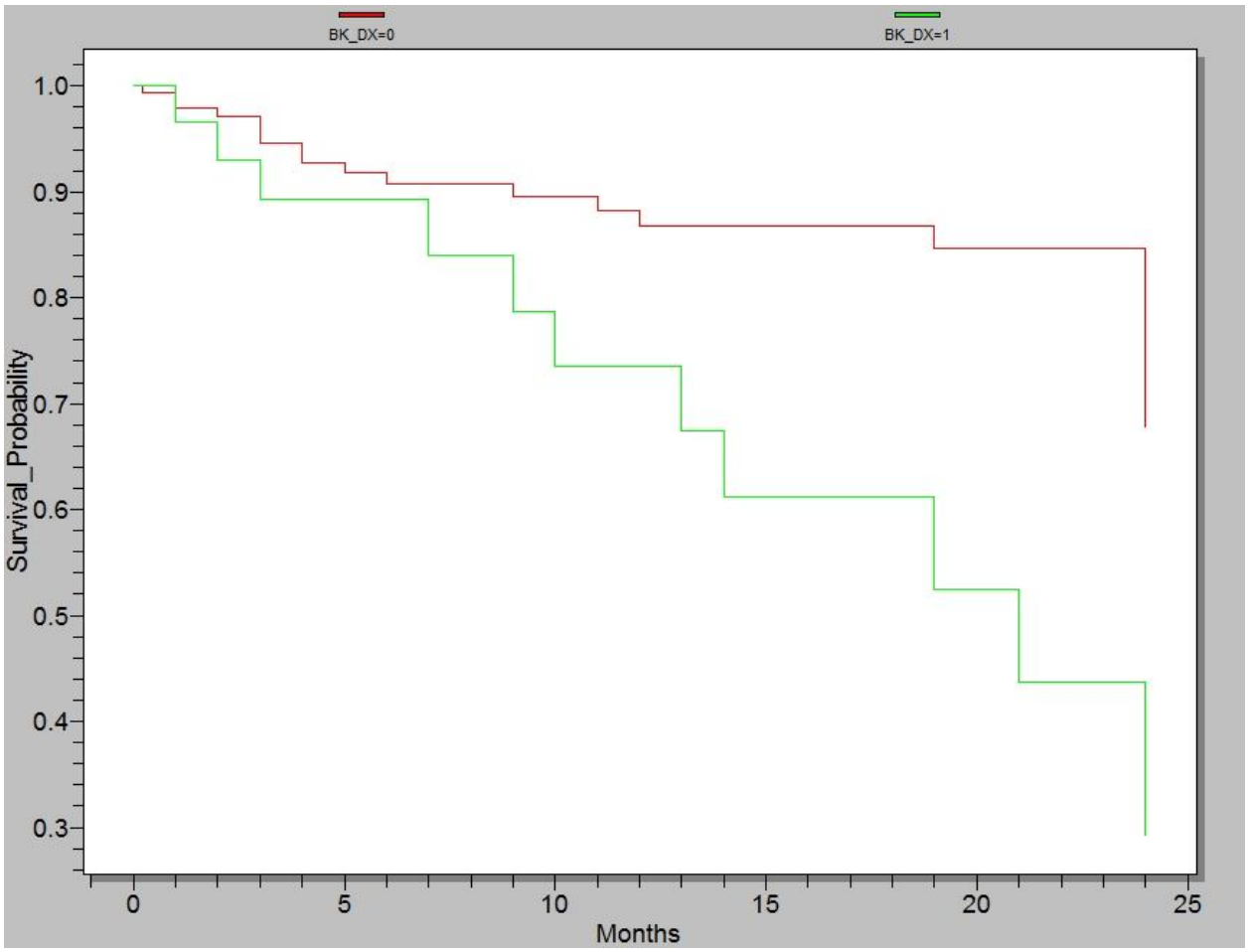

Figure 11: Kaplan-Meier survival probability for bullous keratopathy versus other indications

Key: bullous keratopathy = [→], survival of 47%; other indications = [→] survival of 85%, p<0.0022

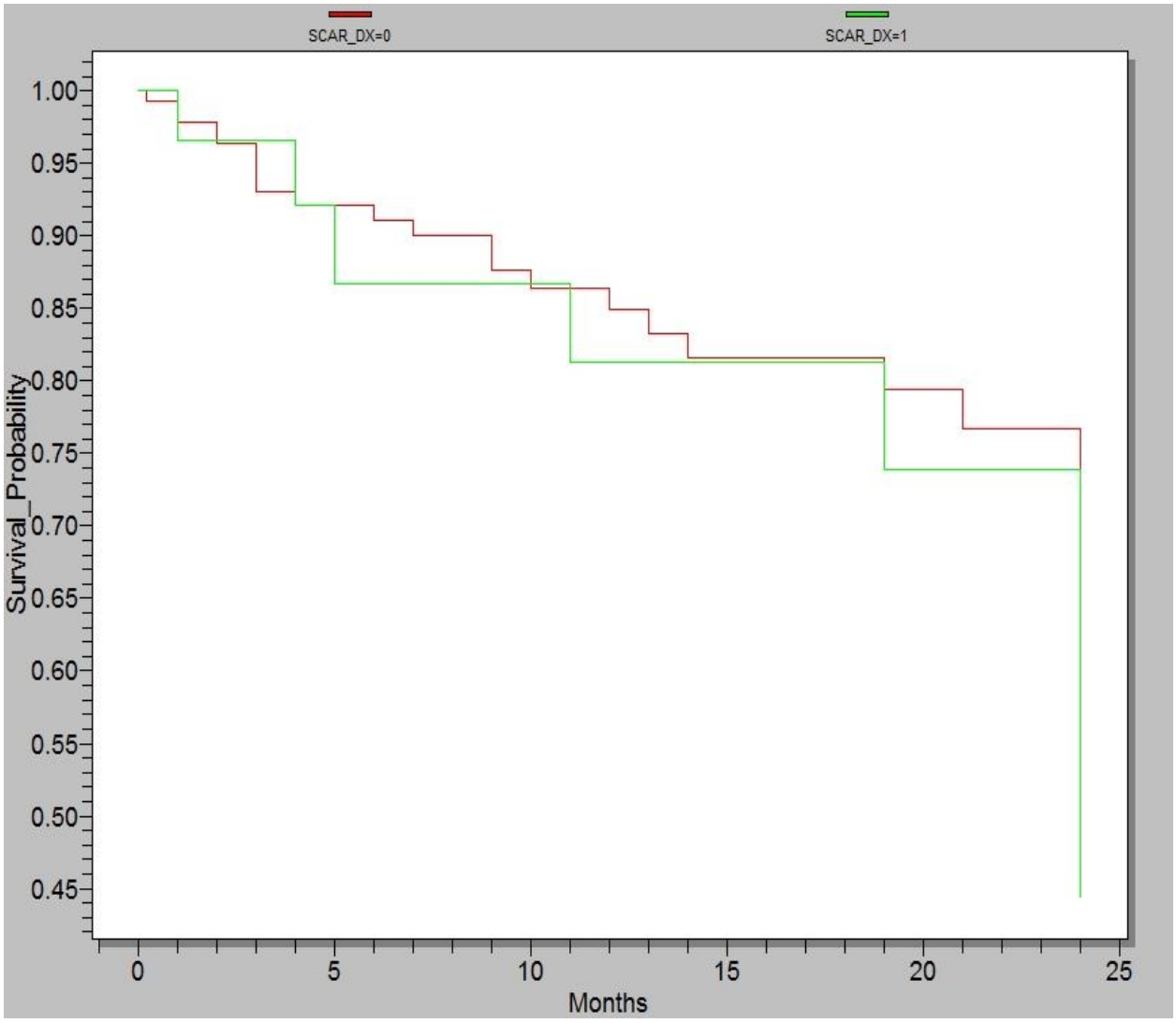

Figure 12: Kaplan-Meier survival probability for corneal scars versus other indications

Key: corneal scars = [→], survival of 74%; other indications = [→], survival of 77%, p=0.3339

6.7.8 Factors that influence poor graft outcome– Univariate Analysis. More than 91% of keratoconus grafts were clear compared to73% for other indications: the risk ratio was 3.27 and this difference was significant at p<0.0012.

Table 11: Factors that influence poor graft outcome: univariate analysis, N=174

DIAGNOSIS	Clear	Unclear	Odds Ratio	Relative Risk
Keratoconus	78	7	4.1143	3.2745
Bullous keratopathy	18	11	3.8194	2.75
Dystrophies	9	2	1.0268	1.0219
Failed PKP	3	1	1.5556	1.4167
Herpes simplex keratitis	10	1	0.4433	0.4939
Corneal Scar	23	8	1.8147	1.6045
Ulcer	1	1	4.7333	2.8667
Astigmatism	3	1	1.5556	1.4167
Glaucoma	0	3	8.7826	5.931
High IOP	7	2	1.3399	1.2644
Infection	1	5	27.3077	5.3846
Oedema	7	13	14.0317	5.5611
PAS	4	1	1.1573	1.1267
Recurrent HSK	2	1	2.3500	1.9
Other Late Complications	10	5	2.5577	2.0385
Age Group <19	51	8	0.6275	0.678
Age Group 20-39	53	5	0.3266	0.3846
Age Group 40-59	16	8	2.7609	2.1739
Age Group 60-79	20	8	2.1391	1.8137
Age Group >79	3	2	3.2184	2.331
Gender Female	49	8	0.6673	0.714
Gender Male	94	23		

6.7.9 Factors that influence poor graft outcome - Multivariate analysis. Risk factors identified from the univariate analyses were subjected to multivariate logistic regression analysis to determine the strength and consistency of the association. Factors that independently confer poor corneal graft outcome were identified: infection, prolonged corneal graft oedema, and other causes of late complication. Increasing recipient age (>60 years) may confer poor graft outcome.

Table 12: Factors that influence poor graft outcome: multivariate analysis, N=174

Risk Factor	Odds Ratio	95% C.I.		p-value
Age Group (>60-79/<=19)	5.2326	1.2267	22.3211	0.0254
Infection (Late Complication)	201.6549	14.8347	2741.1789	0.0001
Oedema (Late Complication)	40.2338	10.2874	157.3529	0.0001
Glaucoma	8.7826	1.5160	50.8809	0.0153
Other Late Complications	9.6642	2.2638	41.2558	0.0022

6.7.10 Factors that influence poor graft outcome: Synthesis of Univariate & Multivariate. Glaucoma occurred in 3 PKPs and was found to be associated with an 8-fold risk of graft failure, p=0.0153. High IOP per se occurred in 9 eyes (including two PKPs that failed) but the p value was 0.7235, which was not significant.

Infections, such as bacterial corneal ulcer and endophthalmitis, occurred in 6 PKPs, of which 5 grafts failed: 4 from bacterial corneal ulcers and an endophthalmitis. The relative risk was 5.3846 (95% CI 3.2564-8.9038) and p value of <0.0001.

Persistent corneal oedema occurred in 20 grafts, 13 of which failed; the relative risk was 5.5611 (95% CI 3.2398-9.5456) and the p-value was <0.0001.

Peripheral anterior synechiae occurred in 5 grafts; only one failed; the p= 0.8972.

Recurrent herpes simplex keratitis occurred in 3 grafts; only one failed; p= 0.4798.

Traumatic dehiscence of graft occurred in 2 patients; only one failed. Three cases of total retinal detachment were identified, of which one had vitreous haemorrhage: all three grafts failed.

6.8 Donor Characteristics

6.8.1 All the donor corneas identified in this review came from North America. Median donor age was 68 years with age range 3-80 years. About 5% of donors were younger than 39 years. Mean cadaveric time was 7.2 days for those with clear grafts and 7.6 days for those with unclear grafts; time range 2-15 days, p=0.6504. There was no significant statistical relationship between donor characteristics and recipient graft outcome.

Table 13: Age distribution of donors, n=98

Age Group Donor	Frequency	Percentage
<=39	5	5.1
>39-54	17	17.4
>54-69	54	55.0
>70	22	22.5
Total	**98**	**100**

Table 14: Corneal Tissue Donor Characteristics

Donor Characteristic	Measure
Source of corneas	**USA (n=109), Canada (n=1)**
Mean Cadaveric Time	7.2 days (clear), 7.6 days (unclear), range: 2-15 days (p=0.6504)
Preservation	Optisol - GS (n=107), Eusol – C (1)
Mean Age	60.6 years
Median Age	68 years
Age Range	3 years to 80 years
Corneal button size – Mean, Median & Mode	7.96mm, 8.00mm & 7.75mm
Corneal button size – Range	7.00mm to 9.00mm

6.8.2 Donor Endothelial Cell Density: Data was available for 80 donor corneas. Endothelial cell density range was1589 cells/mm^2 to 3924 cells/mm^2; mean cell density was 2520 cells/mm^2.

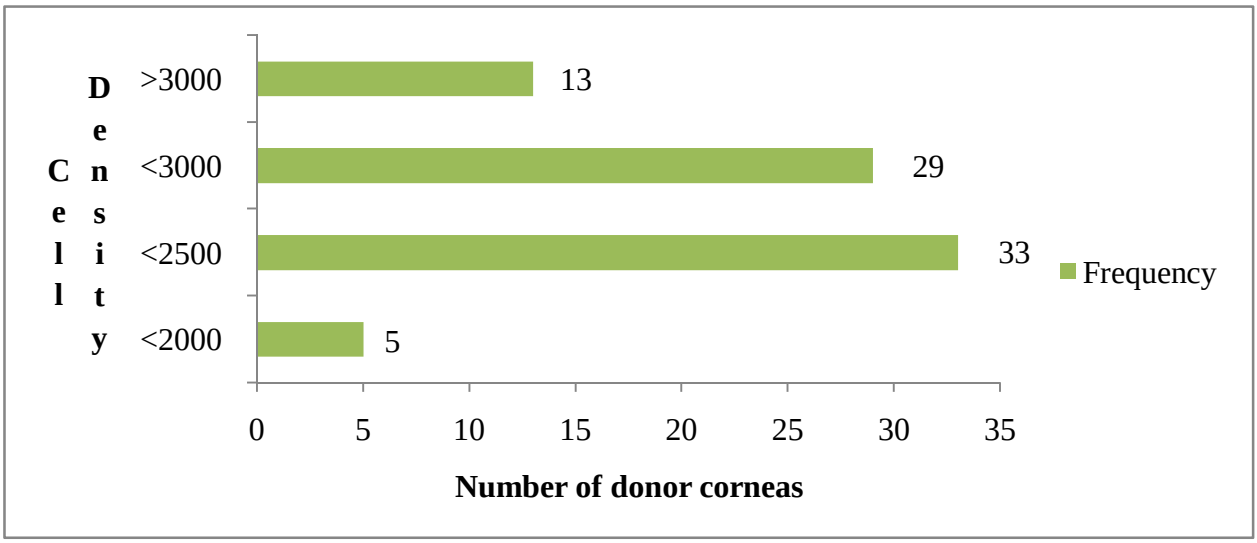

Figure 13: Endothelial cell density, n=80

7.0 DISCUSSION

DEMOGRAPHIC CHARACTERISTICS

Regions/Counties: Previously, there were seven administrative regions in Kenya but these have been superseded by the Counties as defined by the Independent Electoral and Boundaries Commission and the new constitution of the Republic of Kenya 2011. Currently there are 47 counties in Kenya. At the time of collecting data the transition to devolve regional and state authorities to the counties was ongoing. (see Appendix VII: Administrative map of Kenya showing the Counties according to the new Kenya Constitution).[56] Treatment facilities that we visited in this study were found in Central, Coast and Rift Valley Provinces that constitute present day Nairobi, Mombasa, and Bomet Counties respectively. Of the treatment facilities that offered PKP, none was found in the other regions/counties.

In Nairobi, we visited KNH, UHMC, UHEAL and AKUH. The Tenwek Mission Hospital is located in Bomet County in the former Rift Valley Province and Lighthouse for Christ Eye Centre in Mombasa County in the former Coast Province. Road networks in Kenya are comparatively good and patients from any part of Kenya can choose to receive treatment anywhere. Thus, recipients came from virtually all parts of Kenya. In terms of addresses of the recipients, 38.5% of all PKP recipients were from Mombasa County, 33.3% from Nairobi County, 16.1% from Bomet County, and 10.4% from the remaining counties. Three recipients were non-Kenyans: a South Sudanese, a Tanzanian, and a Cameroonian respectively. The earlier reviews in KEH did not identify the addresses of the recipients. [13, 17]

Treatment Facilities: KNH is a tertiary national referral hospital and the only government facility in this review while the rest of the facilities are private. The private treatment facilities were responsible for more than 90% of all PKPs in Kenya. The public facility (KNH) does not have a dedicated cornea clinic and equipment was sparse even though it conducts a twice-weekly anterior segment consultant clinic in Clinic #35. The private facilities have anterior segment-cum-cornea specialists. This study did not look at user fees/cost in any of the facilities. In addition, admission facilities were not available in the UHMC and UHEAL. A study on user fees between government and private (faith-based and private-private) facilities might shed some light on issues of barriers and service uptake preferences.

National Trend: This review has demonstrated a pattern of steady increase in numbers of PKPs performed nationally in Kenya. This trend is in keeping with global trend of increased PKPs. Our data did not include recipients from KEH as well as those who had undergone the triple procedure as well as other forms of keratoplasty other than our inclusion criteria.

Gender: We found a female/male ratio of 1:2.3. The review by Mboni *et al* found a lower female/male ratio of 1:1.2. [17] Both the youngest as well as the oldest recipients were females. The significance of these gender differences with regards to PKP may need further investigation.

Age: Mean recipient age was 33.45 years and mode was 16 years. Almost 60% of all PKP recipients were less than 30 years of age and one-quarter were 50 years and older. The recipients in our series were younger than was found in earlier works by Yorston *et al* with modal age of 17.8 years as well as Mboni *et al* with modal age of 17 years.[13, 17] The recipients in our series were generally younger than reported in similar, larger series in India, New Zealand and Australia.[14, 10, 53]The younger recipient age is in keeping with the high prevalence of allergic conjunctivitis in our population as well as the paucity of facilities for fitting hard contact lenses that may delay the decision to operate on a keratoconus eye, a scenario that has not changed over the past two decades. [13]

PREOPERATIVE CHARACTERISTICS

Main Indications: Keratoconus still remains the commonest indication for PKP in Kenya. This was similar to the earlier findings of Yorston *et al* [13] wherein keratoconus was responsible for one-half of indications but it was even higher in the Mboni *et al* [17] series, wherein keratoconus was responsible for 60.8% of all indications. Bullous keratopathy has become the second commonest indication for PKP in Kenya. Earlier, bullous keratopathy was thrice lower in the Yorston *et al* [13] series and more than twice in the Mboni series.[17] This increase in the proportion of bullous keratopathy could be attributed to the widespread availability of cataract surgery, notably phacoemulsification as well as the implantation of AC IOLs for unplanned and/or secondary ECCEs.[57] Places that perform high volume cataract surgeries tended to have more bullous keratopathies and this is also in keeping with our earlier assertion on the widespread availability of cataract surgical services.[57] Corneal scarring was the third commonest indications and was higher than was found in the Yorston *et al* series of 11% and the Mboni *et al* series of 1.3% but excluding trachomatous corneal opacification of 3.5% and

vitamin A deficiency 2.6%. [13, 17]The combination of the latter causes of corneal opacification in the Mboni *et al* series accounted for 7.4% of the indications and was less than one-half in our finding. [13, 17]These diagnosis/indication changes, though small in proportions, could be pointers toward improvements in the socio-economic status of the recipient population. Herpes simplex keratitis still remains an important indication for PKPs but our figures were lower than earlier reports by Yorston *et al*. [13] The decline in the number of indications due to herpes simplex keratitis may also point to better case management by ophthalmologists, wherein prophylactic Acyclovir has been used for all herpetic cases. Corneal dystrophies though small are also important in our setting. Repeat (failed) PKP was responsible for 2.3% of indications and this was a third of what was found in the Yorston *et al* series. Most of the repeat PKPs in the Yorston *et al* series were for failed KC. Could it mean that overall, outcomes are better today than a decade ago? At this juncture we may be permitted to speculate but cautiously. However, in one USA study that reviewed PKPs performed by resident surgeons, repeat PKP was found to be the commonest indication and that was a decade ago. [57]

Rare indications (Brightbill's Grades III-V, see appendix I) [36] for buphthalmos and corneal ulcer were responsible for 1.2% of PKPs. However, in the Yorston *et al* series they found indications for trachomatous corneal opacification and measles. [13] Mboni *et al* did not find any case of measles or bacterial keratitis as indications for PKP but found other indications such as vitamin A deficiency and infections such as fungal keratitis and herpes simplex keratitis, which contributed a significant proportion of all indications in their series. Mboni *et al* also found Mooren's ulcer as one of the indications for PKP. [17] Cases of vitamin A deficiency and measles were not encountered in our review and our findings are in agreement with the Kenya Ocular Status Survey by Whitfield *et al*. [5] Again, these may be pointers to overall improvements in the socio-economic status of the corneal graft recipient population.

In neighbouring Ethiopia, a review by Tilahun *et al* found a pattern of indications similar to the Kenya series, which suggests similarities in local corneal disease pattern. [26, 27]

In the Middle East notably Saudi Arabia, Israel and Iran, keratoconus was the leading indication for PKP, responsible for more than 40% of annual PKPs in Saudi Arabia [30], and 40.8% in Iran. [56] The indications in the Middle East were similar to indications in Kenya.

In a Singapore series, bullous keratopathy was the leading indication for PKP. The trend in Singapore two decades earlier saw declining indications for herpes simplex keratitis and increasing indications for PBK. [51] Apparently, this trend may be similar to what is being observed in Kenya with increasing proportions of bullous keratopathy. In India, bullous keratopathy was the leading indication and it could be understood from the very high cataract surgical rate of 4,500 cataract surgeries per million per year.[14] As Kenya's cataract surgical rate improves, we should witness a further increase in the proportion of indications for PKP due to bullous keratopathy to levels similar to the Indian experience.

In Italy, keratoconus was the main indication for PKPs and LKs. Regrafts and bullous keratopathy were the second and third most frequent indications. [31] These findings were similar to our results even though in Kenya LK may not be readily available as in Italy.

In Australia, keratoconus was the commonest indication followed by bullous keratopathy. [10] These indications are similar to current indications for PKP in Kenya. However, in most other industrialised countries, the commonest indications were BK (North America) and regrafts (Europe). Regrafts, though important, they remain marginally so in Kenya.

Preoperative Vision: Almost all eyes had visual impairment (see appendix IV on the WHO categories of visual impairment) at presentation. Only one eye had normal vision; the reason for this single case was unknown. A third had severe visual impairment; Mboni *et al* found 13.22% at presentation with severe visual impairment. Two-thirds of eyes (64.4%) were blind at presentation. However, in the Mboni *et al* series three-quarters of all eyes were blind. [17]

Majority of eyes with visual impairment were from recipients younger than 30 years. This pattern of visual impairment may be related to the high prevalence of severe chronic allergic keratoconjunctivitis among the same age groups as has been described in East Africa and the Middle East. [13, 17, 26, 27, 30, 50] The high prevalence of severe visual impairment in this age group may also be related to the frequency and severity of repeated exacerbations of the keratoconjunctivitis and concomitant tear film disturbances.

POSTOPERATIVE CHARACTERISTICS - OUTCOME MEASURES

Corneal Clarity, Graft Outcome and Graft Survival Rates: Overall, more than 80% of all PKPs remained clear at 2 years. The median age for those with clear grafts was 24years, which

was a half of the median age for those with unclear grafts at 48 years. This finding was similar to findings by Mboni *et al.*[17] Corneal graft survival rates for corneal dystrophies was 100% at 2 years and for keratoconus it was 90% at 2 years compared to 68% for other indications ($p<0.0068$). These rates appear to be improving since first reported by Yorston *et al*, who found 87% for keratoconus and Mboni *et al* found 81.2% for keratoconus. [13, 17]Two-thirds of the other indications in our series survivedat2 years and this was better than reported in Yorston *et al*.[13] A quarter of all failed grafts occurred in recipients aged less than 20 years. Less than a tenth of keratoconus grafts failed while thrice that figure for other indications failed with a relative risk (RR) of 3.2745. This means non-keratoconus grafts were more than three times likely to fail than keratoconus indicated grafts. Herpes simplex keratitis grafts had 88% survival at 2 years and this high success rate could be attributed to active preoperative and early postoperative herpes simplex prophylaxis with high-dose oral Acyclovir. These indicated an improvement from earlier results from Yorston *et* al and Mboni *et al.* [13, 17] Three-thirds of corneal scars survived at 2 years and this decrease was attributed to the preoperative recipient corneal vascularization. Bullous keratopathy had the least 2-year survival rate at 47% ($p=0.0191$). Corneal graft outcomes were not reported to be good for indications such as corneal ulcers, and in our series, only a half survived within the first 12 months. It is risky to undertake PKP for a bacterial/fungal infection. There was no record of use of systemic immunosuppressive agents in our series, even though justification for their use has been well documented. [29, 31-34]

In India, the overall corneal graft survival at 2 years was 68.7% but 95.1% of all keratoconus grafts remained clear at 5 years.[14] The reduced overall survival rate was due to the inclusion of high-risk cases in that series. Regrafts did not do well with less than 25% surviving at 3 years. [14] In New Zealand, 87% of all grafts survived at the end of the first year.[53] About 7% of grafts in the New Zealand series failed as a result of immunologic rejection, and this was the leading cause of failure.[53] In Australia, 91% of grafts survived at 1 year and this declined to 79% at 3 years.[10]

In summary, the overall 2-year survival rate of 82% in our study is acceptable and is comparable to earlier reports in the literature, wherein survival range from 80% to 91%.[53] These outcomes are encouragingly good for the commonest indications for corneal grafts especially in our setting.

Visual Outcome: Almost three-quarters of recipient eyes achieved **≥6/60** vision postoperatively; of these, more than a third achieved normal vision. However, 16.6% remained blind and 1.7% was blind to light. In the Mboni *et al* series, twice as many eyes as we found were blind postoperatively.[17] In that series, there was no distinction between the visual impairment categories of "<3/60-1/60", "<1/60-LP", and "NPL". As a result, it could not be known the proportion of patients who were "blind to light" postoperatively, thus making a fairer comparison difficult.

Two-thirds of grafts that achieved normal vision were in the age bracket 10-29 years. These findings are similar to results from other major studies found in the literature. [13, 17, 27, 30]

More than 88% of keratoconus eyes attained vision of 6/60 or better, of which 45.9% had normal vision even though 3.5% keratoconus eyes remained blind. This may be a result of better case selection since keratoconus eyes tend to achieve better visual and better overall graft outcomes.[10, 13] In Yorston *et al*, 73% of keratoconus and 35% of non-keratoconus eyes attained visual acuity of 6/18 and better.[13] These imply PKP can improve vision from blindness and severe visual impairment to normal vision.

In Australia, more than half of PKP recipients achieved normal vision and this was slightly better than in our series.[10] However, these Australian patients had access to early contact lens fitting that minimised postoperative astigmatism and thus may explain the good visual outcome.[10, 13]

The above results could have been better if each centre determined and documented the **best corrected visual acuities**, taking into consideration that uncorrected astigmatism is a major cause of decreased vision after PKP.

Complications: Early and Late Postoperative Complications: The commonest early complications were epithelial defects and corneal stromal oedema. Three-quarters of these early complications occurred in the first two weeks postoperatively. In Mboni *et al* the earliest complications were uveitis, persistent epithelial defects and primary graft failure. [17] This has implication for monitoring and targeted postoperative visits in order not to miss cases that may subsequently fail if not managed promptly.

The commonest late postoperative complications were persistent corneal stromal oedema and high IOP/glaucoma. Graft stromal oedema implies endothelial dysfunction and most of these

grafts ultimately fail. In our series almost one half of grafts failed due to endothelial failure. Other late complications that require prompt attention are graft infections such as bacterial corneal ulcers and endophthalmitis. One-sixth of grafts that failed were due to infections. In the Mboni *et al* series, infection was responsible for most of the 35.1% of grafts that failed and more than 15% in the Yorston *et al* series. [13, 17]

Factors that predict poor corneal graft outcome: A synthesis of the univariate and the multivariate analyses has demonstrated poor predictors of graft survival. These findings were similar to results from the Yorston *et al* and Mboni *et al* series and are consistent with known predictors of poor corneal graft outcome. [13, 17]

Persistent corneal oedema was found to be a poor predictor of graft survival and carried a 5-fold risk of failure at $p<0.0001$ and was responsible for 13 of the failed grafts. Persistent corneal stromal oedema is a direct pointer to ongoing endothelial dysfunction, which tends to be more noticeable in a corneal graft.

Glaucoma was six times more likely to be associated with corneal graft failure in the univariate analysis ($p<0.0023$), however, this was not confirmed at the multivariate regression analysis. High intraocular pressure was known to compromise host endothelial function (mainly corneal deturgescence) and this is more important in a corneal graft. Corneal Graft Glaucoma has been known to be a postoperative challenge for ophthalmologists. It is not known exactly the proportion of corneal graft recipients that were corticosteroid responders. Some clinicians have advocated the use of Rimexolone to reduce the risk. [54, 55]

Infection such as bacterial corneal ulcer and endophthalmitis carry a 5-fold risk of graft failure ($p<0.0001$) and was responsible for 5 of 6 infected grafts that failed. Recurrent herpes simplex disease was associated with one failed graft but this was not significant statistically. A graft is prone to infections due to a variety of factors foremost amongst which is the lack of neuronal support to the new graft as well as graft epithelial defects. Host ocular and personal factors are equally important in the development of graft infection.

Severe astigmatism was encountered in 4 grafts but only one failed. There was no significant association between astigmatism and graft survival but severe uncorrected astigmatism is inherently associated with poor visual outcome. [17]

Peripheral anterior synechiae was associated with one failed graft. Synechia formation would incite immunologic response that can cause graft failure. An important donor factor that can trigger such is a donor corneal button size that exceeds 8.50mm. [18, 29, 31-34]

Traumatic dehiscence led to one failed graft. Corneal grafts are particularly at risk of dehiscing due to delayed wound appositional forces. The dehiscence can happen even several years after a successful PKP. The commonest method of corneal graft closure was the interrupted type with 10/0 nylon but this bore no consequence to final graft outcome and there was no statistically significant association between style of closure and final graft outcome. [52]

OTHER CHARACTERISTICS OF INTEREST: Donor and Recipient Factors

All the corneal tissues utilised came from North America, notably USA and Canada. Each supplying eye bank was an accredited member of the Eye Bank Association of America and this was verified from the accompanying tissue utility form. Almost all tissues were stored using intermediate term preservation in Optisol-GS whereas in earlier reviews of Yorston *et al* and Mboni *et al* tissues were stored in Optisol. [13, 17] It took 4 days to 15 days from retrieving donor cornea to transplantation and this was similar to what was found in the Yorston *et al* series while in the Mboni *et al* series it ranged from 1 day to 27 days. Endothelial cell densities had a range of 1589 cells/mm^2 to 3924 cells/mm^2. All the donor corneal buttons were in excellent or very good conditions and none was rejected prior to transplantation, which also points to very high eye banking standards maintained by the supplying centres. The mean donor age was 60.6 years with a range 3 to 80 years. We did not find these donor characteristics to be of any statistical significance in terms of ultimate graft clarity or outcome.

Developed countries source all their corneas locally.[33] There was no significant association between donor factors and decreased graft survival and this was demonstrated in earlier series in the New Zealand study.[53] Of the 174 PKPs, 31 grafts failed, 8 of which were due to primary failure. The smaller number of primary failures meant donor materials could be transported over vast distances to be used elsewhere with little fear for failure. [13] Ideally, locally sourced donors would be the best option given that such tissues can be retrieved in the shortest possible time and utilised within 24 hours. [15]

Inasmuch as donor corneal tissues were not always available, improvements in current diagnostic capabilities and surgical procedures have encouraged some clinicians to advocate for the utilization of one corneal tissue for two recipients based on the fact that some patients present with a purely anterior corneal lamellar opacification while others present with only posterior lamellar problems and a single healthy donor tissue can be efficiently utilized to serve these disparate conditions in two different patients. [52]

All grafts were sutured with nylon sutures 10/0 utilising mainly the interrupted technique with 16 stitches. There was no association between suturing technique and corneal graft outcome. The mean donor corneal button size was 7.96mm. The donor trephine sizes range from 7.00mm to 9.00mm with a median size of 8.00mm and the mode was 7.75mm. We did not find any significant association between trephine size and corneal graft outcome and this was similarly demonstrated by earlier works elsewhere. [17, 36, 40]

Few patients had been on topical as well as systemic treatment for ocular co-morbid illnesses. There was no significant association between these treatments and overall graft outcome.

8.0 CONCLUSIONS

1. Keratoconus was the leading indication for corneal grafts in Kenya

2. Grafts provide meaningful visual benefit for commonest indications

3. Corneal dystrophies and keratoconus have the best graft outcome and should be selectively prioritized over other indications.

4. Compared to earlier similar studies in Kenya, our results showed that graft survival has improved, especially for corneal dystrophies & keratoconus.

5. Poor Predictors of corneal graft outcome: Infections, Glaucoma, Graft Oedema, & Older Recipient Age >60 years

9.0 RECOMMENDATIONS

1. Every attempt should be made to determine the best corrected visual acuity after PKP through refraction.

2. Most complications occurred in the first 6 months: close follow-up visits are encouraged within the first 6 months in order to catch most cases.

3. Our study looked at PKP-only cases: a review is recommended to look at all forms of corneal grafts (lamellar and combined procedures) in order to evaluate if the outcomes in those cases would yield any new information.

4. There is no known national incidence data on indications such as keratoconus and bullous keratopathy. A longitudinal study is recommended to address this information gap.

5. All donor corneas came from North America; there is need for a National Eye Bank.

10. LIMITATIONS

1. Our information may not have been complete by virtue of it being retrospective.
2. The uncorrected Final Visual Acuity may not be a true reflection of the best possible vision
3. Some centres declined participation in our study: their series might have added a different perspective to our analysis.
4. This review looked at only PKPs but not combined or other similar procedures and we may not know if those other procedures conferred any added advantage or otherwise for final graft state and visual outcome.

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12.0 APPENDIX I: BRIGHTBILL'S CLASSIFICATION FOR CORNEAL GRAFT PROGNOSIS

Those in bold are the commonest and most important prognosticating diseases. [23-25, 36, 37]

GRADE I (Excellent)

- **Keratoconus**
- **Lattice** and **Granular Dystrophy**
- Traumatic Leukoma
- Superficial Stromal Scars

GRADE II (Good)

- **Bullous Keratopathy**
- **Fuch's Dystrophy**
- **Macular Dystrophy**
- Small Vascularized Scars
- Interstitial Keratitis
- Failed Grade I PKP
- Combined PKP and Cataract Operation

GRADE III (Fair)

- **Active Bacterial Keratitis**
- **Vascularized Cornea**
- Active HSV Keratitis
- Congenital Hereditary Endothelial Dystrophy
- Failed Grade II PKP

GRADE IV (Guarded)

- **Active Fungal Keratitis**
- **Congenital Glaucoma**
- **Paediatric Grafts**
- Mild Keratoconjunctivitis Sicca
- Mild Chemical Burns
- Corneal Blood Staining
- Corneal Staphyloma
- Failed Grade III PKP

GRADE V (Poor)

- Severe Keratoconjunctivitis Sicca (SJS, Ocular Cicatricial Pemphigoid, Chemical and Thermal Burns)

13.0 APPENDIX II: DEFINITION OF TERMS

The following will be our operational definitions for some of the terms used for some outcome measures in this study:

12.1 Primary Graft Failure: Corneal graft opacity noted on the first postoperative day [13] – synonym is Early Endothelial Failure.

12.2 Secondary Graft Failure: An irreversible change in a graft preventing recovery of useful vision after the graft had been initially clear 2 weeks after PKP [52] – synonym is Late Endothelial Failure. Causes include: irreversible loss of graft clarity, astigmatism, central corneal scarring, and end-stage glaucomatous loss of the eye. [52]

12.3 Time of Graft Failure: the first postoperative examination of which the patient was seen with a failed graft. This also marks the end-point for the inclusion of such an eye in the outcome analysis; it will be censored in the survival analysis. [52]

12.4 Stromal Vascularization: Vascularization of the middle or deep stroma, which extended into the area of trephination at the time of surgery. The total number of clock hours affected will be noted where possible. [52]

12.5 Lost to Follow-up: An eye will be considered lost to follow-up when the patient had not been examined for more than one year from the first missed postoperative examination period. [52]

12.6 Graft Survival: Graft clarity as found and documented on each follow-up visit.

12.7 Long-Term Survival of Corneal Graft: Clear graft for the maximum end-point of this review, i.e., at 2 years postoperatively.

12.8 Visual Acuity: Ideally, this would refer to the recorded best corrected visual acuity for the graft recipient eye. Visual acuity will be classified according to the WHO categories of visual impairment. [1] See Appendix IV. In this review VA was uncorrected.

14.0 APPENDIX III: DATA COLLECTION QUESTIONNAIRE

SECTION A: DEMOGRAPHIC DATA

IP #	FULL NAMES	AGE	SEX	ADDRESS/DISTRICT/COUNTY

CENTRE=CODE KNH =1 TENWEK=2 AGA KHAN=3 LIGHT HOUSE=4 UPPER HILL=5 UHEAL=6 OTHER=99	INDICATION / PREOPERATIVE DIAGNOSIS	DATE DIAGNOSIS MADE	DATE OF SURGERY	EYE OPERATED RE/LE

SECTION B: PATIENT'S PREOPERATIVE DETAILS

VISUAL ACUITY	RE	LE
VISUAL STATUS		

SECTION C: PREOPERATIVE OCULAR MORBIDITY AND TREATMENT SURVEY

OCULAR STATE	RE	LE	OCULAR MEDICATION X DURATION OR PRIOR SURGERY
NORMAL			
TBUT/TEAR FILM			
CONJUNCTIVITIS			
BLEPHARITIS			
KERATITIS			
ENTROPION			
TRICHIASIS			
PANNUS			
SYMBLEPHARON			
ECTROPION			
GLAUCOMA			
CATARACT			
APHAKIA			
PSEUDOPHAKIA			
IOP			
FUNDUSCOPY			
ULTRASOUND			
FAILED GRAFT			
OTHERS			

SECTION D: SYSTEMIC DISEASE

SYSTEMIC ILLNESS	DURATION	MEDICATION/TREATMENT

SECTION E: INTRAOPERATIVE INFORMATION

DONOR CORNEAL SIZE	
RECIPIENT SIZE	
ANAESTHESIA GA / LA	
ADDITIONAL PROCEDURE	
SUTURING TECHNIQUE	
SUTURE MATERIAL	
PEROPERATIVE PROBLEMS	
OTHERS	

SECTION F: POSTOPERATIVE PERIOD – FIRST 2 WEEKS, 1 MONTH, 3 MONTHS, 6 MONTHS, 12 MONTHS AND 24 MONTHS

COMPLICATION	TIMING
WOUND LEAK	
SHALLOW OR FLAT A/C	
LOOSE SUTURES	
HYPHAEMA	
UVEITIS	
GRAFT OEDEMA OR OPACIFICATION	
HIGH IOP	
INFECTION	
EPITHELIAL DEFECT	
OTHERS:EXCESSIVE TEARINGPAIN	

SECTION G: POSTOPERATIVE PERIOD – ONE MONTH, 3 MONTHS, 1 YEAR & 2 YEARS

REVIEW DATE	GRAFT STATE	SUTURES REMOVED	COMPLICATIONS	GRAFT VISUAL ACUITY

SECTION H: FINAL REFRACTION AFTER REMOVAL OF SUTURES – BEST CORRECTED VISION

EYE	SPHERE	CYLINDER
RE		
LE		

SECTION I: BEST CORRECTED VISION (3 MONTHS, 1 YEAR AND 2 YEARS POSTOPERATIVELY)

RE	LE

SECTION J: CATEGORY OF GRAFT FAILURE& DATE RECOGNISED

PRIMARY GRAFT FAILURE	
SECONDARY GRAFT FAILURE	

SECTION K: CLINICAL CAUSE OF GRAFT FAILURE

SECTION L: DONOR TISSUE CHARACTERISTICS

SOURCE		**DONOR AGE**	
STORAGE MEDIA		**CADAVERIC TIME**	
STORAGE TIME		**ENDOTHELIAL COUNT**	

15.0 APPENDIX IV: W.H.O CATEGORIES OF VISUAL IMPAIRMENT [1]

CATEGORY	BEST CORRECTED VISUAL ACUITY	DEGREE OF VISUAL IMPAIRMENT
0	6/6 – 6/18	NORMAL
1	<6/18 – 6/60	VISUAL IMPAIRMENT
2	<6/60 – 3/60	SEVERE VISUAL IMPAIRMENT
3	<3/60 – 1/60	BLIND
4	<1/60 – LIGHT PERCEPTION	BLIND
5	NO LIGHT PERCEPTION	BLIND TO LIGHT
6	UNDETERMINED OR UNSPECIFIED	

16.0 APPENDIX V: BUDGET ESTIMATE

1.	STATIONERY FOR PROPOSAL & FINAL COPY OF BOUND BOOK	KSh20, 000. 00
2.	HONORARIUM FOR DATA ENTRY CLERK & STATISTICIAN	KSh25, 000. 00
3.	TRANSPORT FARES FOR DATA COLLECTION	KSh20, 000. 00
4.	MAINTENANCE& FOOD ALLOWANCE FOR FOUR WEEKS	KSh30, 000. 00
5.	KNH/UoN ETHICS AND RESEARCH COMMITTEE FEE	KSh1, 500. 00
6.	INCIDENTAL COVER – 10%	KSh9, 650. 00
TOTAL		**KSh106, 150. 00**

{One hundred and six thousand, one hundred and fifty Shillings only}

SOURCE OF FUNDS: to be sourced from personal monthly maintenance stipend.

17. 0 APPENDIX VI: STUDY APPROVAL LETTER FROM THE KNH/UoN ERC

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: www.uonbi.ac.ke
Link:www.uonbi.ac.ke/activities/KNHUoN

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

Ref: KNH-ERC/A/217

30th July 2012

Dr. Abba Hydara
Dept.of Ophthalmology
School of Medicine
University of Nairobi

Dear Dr. Abba

RESEARCH PROPOSAL: "PENETRATING KERATOPLASTY IN KENYA: A REVIEW OF INDICATIONS AND OUTCOME OVER A 10-YEAR PERIOD" **(P160/03/2012)**

This is to inform you that the KNH/UoN-Ethics & Research Committee (KNH/UoN-ERC) has reviewed and **approved** your above revised research proposal. The approval periods are 30th July 2012 to 29th July 2013.

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 severe 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.uonbi.ac.ke/activities/KNHUoN**

"Protect to Discover"

Yours sincerely

PROF. A.N. GUANTAI
SECRETARY, KNH/UON-ERC

c.c.

The Deputy Director CS, KNH
The Principal, College of Health Sciences, UoN
The Dean, School of Medicine, UoN
The Chairman, Dept. of Ophthalmolgy, UoN
The HOD, Records, KNH
Supervisors: Prof. Dunera R. Ilako, Dept.of OPhthalmolgy, UoN
Dr. Sheila A. Marco, Dept.of Ophthalmology, UoN
Dr. Daniel o. O. Kiage, Dept. of Surgery, Aga Khan University, Nairobi

3rd Resub P160/3/2012

PENETRATING KERATOPLASTY IN KENYA: A REVIEW OF INDICATIONS AND OUTCOMES OVER A 10-YEAR PERIOD

A RESEARCH PROPOSAL BY

DR. ABBA HYDARA, *MB ChB (UTG)*

SUPERVISORS:

PROFESSOR DUNERA R. ILAKO, *MB ChB, M Med Ophthalmology (Nairobi), MBA-Health, FEACO*

CHAIRMAN – DEPARTMENT OF OPHTHALMOLOGY

UNIVERSITY OF NAIROBI

DR. SHEILA A. MARCO, *MB ChB, M Med (Ophthalmology), GLAUCOMA SPECIALIST, FEACO*

LECTURER - DEPARTMENT OF OPHTHALMOLOGY

UNIVERSITY OF NAIROBI

DR. DANIEL O. KIAGE, *MB ChB, M Med (Ophthalmology), GLAUCOMA SPECIALIST, FEACO*

ASSISTANT PROFESSOR AND HEAD OF SECTION OF OPHTHALMOLOGY

DEPARTMENT OF SURGERY

AGA KHAN UNIVERSITY HOSPITAL, NAIROBI

KENYATTA NATIONAL HOSPITAL RESEARCH SECRETARIAT
RECEIVED
Date 30/7/12
Time

KENYATTA NATIONAL HOSPITAL
APPROVED
30 JUL 2012
ETHICS & RESEARCH COMMITTEE

0

18.0 APPENDIX VII: ADMINISTRATIVE MAP OF KENYA SHOWING THE COUNTIES