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Editorial: The role of research in advancing quality eye care

The aim of this editorial is to highlight a few examples of research in the East African region that has made a positive contribution to the quality of eye care in the different fields of clinical and public eye health. Finally, it points out areas that still need exploration and hopefully provoke deep thought and action.

Research is defined as a systematic investigation. The prefix *re-* is an interesting one to consider. It often means to repeat or do again, for instance to review is to view again, to revitalize is to vitalize again and thus to research is to search again. Even when we think we know something from long experience, we should keep the wonder of inquiry alive by continuously checking whether what we know still holds true in the same way it did before. The famous philosopher, Socrates, advocated for this continuous sense of wonder and inquiry.

The unexamined life is not worth living - Socrates

We must keep investigating again and again in order for things to improve. Those who keep inquiring are more likely to improve than those who do not stop to ask questions. Auditing our work has been shown to improve outcomes[1].

Quality of care, like beauty, lies in the eyes of the beholder. We all have perceptions of what pleases us and when we receive a service that meets it, we say that it was high quality and vice versa. We need to have an agreed criteria for measuring and comparing quality[2]. Health practitioners are often guilty of measuring quality from the provider perspective when what really matters is the perspective of the recipients of our services. We tend to measure clinical outcomes but not patient-centered outcomes. An eye hospital in Nairobi reported that asking patients for their feedback is very important for cataract services and that the interventions to improve that patients requested are not expensive[3]. Most patients were very satisfied with the clinical services but were unsatisfied with lack of provision of information brochures before surgery for a family member to read, pain management, long queuing time and lack of phone access to staff after surgery. This is an example of inquiry about the patients' perspectives. Beyond clinical outcomes, we should also include effectiveness, efficiency, equity, integration, people-centredness, safety and timeliness[4]. We in low- and middle-income countries do not often evaluate quality. In 2021 we conducted a global scoping review on how to improve the quality of cataract services for all[5]. Out of 143 studies, 65% were from high income countries. Most studies evaluated efficiency while integration and timeliness were the least studied domains. Timeliness is very important to patients, yet it is the least studied aspect of quality. The quality of eye care services offered is the end-product of a value-chain that begins in the training programs for eye health workers. Health care training was built on a history of apprenticeship where the trainee lived with the teacher and observed daily the goings-on of diagnosis and treatment. This style still prevails today. Like everything, it has its strengths and weaknesses. Strengths in the respect and strong bonds created between the teacher and the trainee and lifelong mentorship that continued after formal training but weakness in knowing only what the teacher knew and not what others you were not exposed to knew. To know beyond what you saw, you had to read journals and that depended on whether others wrote. This has not changed much today. If we keep researching and sharing our experiences in writing and speech, others will get to know.

The era of evidence-based medicine saw a transformation in the way information was assimilated. A more formal systematic examination or critique of written material and its application in clinical care began. The term evidence-based raises a question. What was medicine based on before? The answer lies in the history of apprenticeship training. For years medicine was taught in a hierarchical authoritative and sometimes dogmatic fashion. The consultant knew everything. Trainees towed the line just to graduate. The anecdotes from single patient encounters written in case reports and case series dominated old medical literature before study designs like case-control studies, cohort studies, randomized controlled trials and systematic reviews emerged. The first clinical trial was done by James Lind in 1747 using citrus fruits for scurvy[6] and it was not until 1948 when the first drug treatment randomized controlled trial was conducted testing streptomycin for pulmonary tuberculosis[7]. The ethical basis of a clinical trial is equipoise, the admission that we do not know. A healthy skepticism that continuously asks questions about the results of treatment would reveal this and help us conduct trials to test new methods or systematic reviews of existing trials. A recent trial in India demonstrated that square edge IOLs gave better visual outcomes and less risk of requiring YAG posterior capsulotomy than non-square edge IOLs[8]. Trials from low and middle income countries are not always received with open arms. When we conducted the first ever randomized controlled trial of 5FU for Ocular Surface Squamous Neoplasia (OSSN), a reviewer of the manuscript commented that there were numerous studies that showed the efficacy of 5FU so there was nothing new derived from our study. However, we had conducted a Cochrane systematic review which showed that this knowledge we claimed to have was actually based on numerous small case series and case reports[9,10]. From the preceding examples, if the quality of care of cataract or OSSN is to improve, we must be willing to change and apply research results. This latter phase is now the realm of the rapidly emerging field of implementation research.

Beyond the clinical setting, our eyecare programs can also benefit from the use of research. For many years, trachoma programs required large sample sizes to map Trachomatous Trichiasis (TT) in populations ≥ 15 years old because the prevalence is generally low (< 5%) in most endemic areas. A study by Jefitha *et al*[11] in Kenya found that examining those aged ≥ 40 years instead of the whole spectrum of ≥ 15 years yielded good results with a lower sample size. This example shows how improving the efficiency of survey methods can make it easier for national programs to obtain required data. Unfortunately, the indexing of this study in Pubmed lists the lead author as Jefitha K and not Karimurio J as would be expected making it difficult to find if one searched for studies using his surname.

At health system level there are examples of research studies locally that examined referral pathways and pointed out areas that need improvement. A study in Tanzania examined the delays in accessing emergency care for eye trauma and found that injury on weekends, using topical drops and visiting other health facilities before the center that could offer definitive treatment were major causes of delay[12]. In Uganda, a study looking at patients with microbial keratitis found that visiting another facility before an eye hospital and use of traditional eye medicine increased delay[13]. In Kenya, a similar study of patients with OSSN found that females and those who visited more than one health facility before going to one that could offer surgery experienced significant delay[14]. To further address the referral system problem, Rono *et al*[15] conducted a cluster randomized trial to test the use of a mobile phone based application called Portable Eye Examination Kit (PEEK) for vision screening in schools. Participants were connected to health facilities via reminders sent through a text message (SMS) to monitor attendance to the referral centers. This innovative approach increased attendance.

Research here should not mean only quantitative methods. We need to venture more into qualitative research and also collaborate with experts in other areas such as health economics, engineering and agriculture. One area that needs evaluation and implementation research is the way care delivery is organized for instance conducting outreach for cataract surgery. This is sometimes an emotive subject which makes it difficult to study or even discuss. For a long time now, ophthalmology in East Africa has run on an aid model giving free services. The motivations for donating towards or getting involved vary and are not always congruent to the needs of the actual providers or recipients of the service. There are issues of effectiveness, efficiency, cost, sustainability, and safety among others that need to be explored. There is a complex relationship that seems to have developed between poverty and eyecare here that has locked us in a poverty mentality. If someone else always pays the bill, the local governments have no incentive to budget and apply the taxes that citizens pay towards funding these services. There is no dignity in begging, and no one begs their way out of poverty. The logistical constraints in our eye care services have remained the same for decades. The livelihoods of professionals in such a setting are adversely affected making it difficult to attract talent. What can we cross-learn from other specialties in health? There is a gaping lack of knowledge that needs to be filled.

Lastly, we should not shy away from conducting world-class research. We can teach the world as we also learn. Our hands are able, our heads can learn and create, but perhaps our hearts are challenged. If we don't know ourselves and believe in ourselves and the potential we have, then it becomes easy to subjugate ourselves to others. We allow ourselves to be referred to using names that we don't call ourselves. There is no third-world. God created one world. Even the term, low- and middle-income countries which I am guilty of using in this editorial implies a hierarchy based on income, yet we know that the abundance of money does not equate to a happy life or quality of life. The argument about whether research and clinical practice are separate is obsolete. It leads to division. Clinicians practice what research produces and research studies what clinicians do, and we should not forget that there are those who are good researchers and good clinicians as well.

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Late presentation of advanced glaucoma patients; missed opportunities for diagnosis

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ABSTRACT

Objective: This study aimed to determine the proportion of late glaucoma presenting patients who have had previous contact with a primary eye health worker prior to presentation.
Methods: A systematic review and analysis was performed on ten studies with a total of 47,367 study participants identified meeting the inclusion and exclusion criteria. A meta- analysis of proportions was conducted on the late presenting glaucoma patients as well as the proportion of those that had previous contact with a primary eye care worker prior to diagnosis. We combined a narrative synthesis and quantitative (statistical pooling) approach for the synthesis of the extracted studies' information.
Results: The pooled proportion of late presenting glaucoma patients was 0.325 (95% CI 0.178 -0.493). Out of all the late presenting glaucoma patients, n=2967, 96% (CI 0.85- 1.00) had previous contact with a primary eye health worker. The commonest type of primary eye health care workers identified were optometrists, general practitioners, ophthalmic nurses and technicians.
Conclusion: Out of all the late presenting glaucoma patients, a high number have previously been referred by a primary eye care worker. This represents a huge opportunity for directing effort at primary eye care level to identify and appropriately refer glaucoma patients for timely and definitive care.

Key words: Advanced glaucoma, Late presentation, Refer, Optometrist, Screen

INTRODUCTION

Glaucoma is a group of eye diseases which is characterised by progressive optic nerve damage and visual field loss. It is the leading cause of irreversible blindness worldwide and has highest prevalence in low income regions[1].The number of people with glaucoma worldwide is projected to increase to 111.8 million in 2040, and affecting more people in Africa and Asia[2]. Currently, in Africa, glaucoma contributes to 13.47% of all causes of blindness in Sub Saharan Africa[3], and with a prevalence of 4% in people aged above 40 years[4].

This disease can be screened early on in its asymptomatic stage and therefore avert irreversible blindness. The fact that glaucoma is typically asymptomatic, patients are usually unaware of the continuing damage, and most especially unaware too of the irreversible nature of the disease.

There has been evidence that unfortunately, most of the glaucoma patients are first diagnosed with advanced disease, more so in sub-Saharan Africa[4] and factors such as limited access to facilities, cost of care, lack of awareness have been attributed[5,6]. As much as late glaucoma presentation is a worldwide concern, African nations have been noted to have more patients presenting with advanced glaucoma as opposed to patients in developed countries[5].

Classification of glaucoma in research largely depends on the level of peripheral vision dysfunction as assessed by automated visual field assessment. This is referred to as functional damage assessment. Additionally, optic disc structural damage assessment is also done as part of the triad of glaucoma diagnosis[7]. However, either of the two assessments in isolation can also be used to grade glaucoma[4,7]. For the purposes of this study, either of the grading system, functional or structural, was used for advanced glaucoma case definition as well as staging.

Late presentation is described where patients present for the first time with advanced glaucoma features at the diagnosis centre[6,9,10].

Primary eye care workers are trained to offer eye health promotion, prevention, treatment and rehabilitation. This as in primary examination, diagnosis and eye health education to patients at the primary health facilities as well as in the community. In most countries, they include optometrists, opticians, ophthalmic technicians, ophthalmic nurses, ophthalmic clinical officers, assistant medical officers and general practitioners[11]. Their

distribution and particular job description varies from country to country depending on development status as well as policy pattern[12].

MATERIALS AND METHODS

The objective of this review was to analyse the proportion of late glaucoma presenting patients who have had previous contact with a primary eye health worker prior to presentation.

This review tested the hypothesis that patients with advanced glaucoma at initial presentation usually have had previous contact with a primary eye health care worker.

Eligibility criteria: All studies with advanced primary glaucomas in adults, who are presenting late at initial presentation as defined by either structural disc damage and/or functional visual field damage described in either eye[7].

The study population was the patients identified in the study as having advanced glaucoma as defined by the extent of visual field loss through perimetry testing using a 24-2 or 30-2 strategy. This extent uses the the Hodapp–Parrish–Anderson (HPA) Glaucoma classification[10].

The studies would include observational, case control, cross- sectional, cohort and randomised control trials. Record of previous contact with the eye health worker had to be present, as in optometrist visit, prior referral, or previous screening depending on the particular study in either hospital or community setting.

Exclusion criteria: Included case reports, studies with patients already on glaucoma treatment, or glaucoma suspects.

Search strategy: We followed the PRISMA-S: An Extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews (Last updated February 27, 2020) statement for guiding our reporting of methods[13].The search schema was designed consultatively by the two main reviewers. Various databases were searched by using the key words of the concept areas. These databases include Medline, Web of Science, Pubmed and Embase using the Ovid platform. Other search methods included citation tracking of the identified papers by browsing reference lists. All searches were done without date, language or study design restrictions. The search yielded published papers, reviews and conference abstracts. Last search date was June 2022. No search filters were employed. No additional data was sought from the authors of the studies reviewed as it was not required. The full search strategy and history is summarised below in Appendix 1.

Appendix 1: Database specific search strategy

Database searched Through Ovid Interface	Search strategy/ History
	Database: Ovid MEDLINE(R) <1946 to March Week 3 2022> Search Strategy: ----------
	1 exp Glaucoma, Open-Angle/ or Glaucoma/ or exp Low Tension Glaucoma/ (53367)
	2 exp Visual Fields/ (31912)
	3 exp Optic Disk/ab, an, dg, pa, ul [Abnormalities, Analysis, Diagnostic Imaging, Pathology, Ultrastructure] (7134)
	4 exp Late Onset Disorders/di, pa, pc, th [Diagnosis, Pathology, Prevention & Control, Therapy] (109)
	5 exp Time-to-Treatment/cl [Classification] (2)
	6 exp Optometrists/ (169)
	7 screen*.mp. (827404)
	8 reffer*.mp. (126)
	9 community.mp. or Residence Characteristics/ (584460)
	10 ophthalmic* nurse.mp. (76)
	11 clinical officer.mp. (80)
	12 optician.mp. (119)
	13 optician.mp. or Vision Screening/ (2489)
	14 first.mp. (2358291)
	15 initial.mp. (727400)
	16 1 or 2 or 3 (81472)
	17 4 or 5 (111)
	18 7 or 8 or 9 or 10 or 11 or 12 or 13 (1377074)
	19 14 or 15 (2954509)
	20 16 and 17 (1)
	21 16 and 18 (3386)
	22 16 and 17 and 18 (0)
	23 16 and 17 and 18 and 19 (0)

Database searched Through Ovid Interface	Search strategy/ History

#	Query	Results from 26 Mar 2022
1	exp Glaucoma, Open-Angle/ or Glaucoma/ or exp Low Tension Glaucoma/	53,367
2	exp Visual Fields/	31,912
3	exp Optic Disk/ab, an, dg, pa, ul [Abnormalities, Analysis, Diagnostic Imaging, Pathology, Ultrastructure]	7,134
4	exp Late Onset Disorders/di, pa, pc, th [Diagnosis, Pathology, Prevention & Control, Therapy]	109
5	exp Time-to-Treatment/cl [Classification]	2
6	exp Optometrists/	169
7	screen*.mp.	827,404
8	reffer*.mp.	126
9	community.mp. or Residence Characteristics/	584,460
10	ophthalmic* nurse.mp.	76
11	clinical officer.mp.	80
12	optician.mp.	119
13	optician.mp. or Vision Screening/	2,489
14	first.mp.	2,358,291
15	initial.mp.	727,400
16	1 or 2 or 3	81,472
17	4 or 5	111
18	7 or 8 or 9 or 10 or 11 or 12 or 13	1,377,074
19	14 or 15	2,954,509
20	16 and 17	1
21	16 and 18	3,386
22	16 and 17 and 18	0
23	16 and 17 and 18 and 19	0

exp Glaucoma, Open-Angle/ or Glaucoma/ or exp Low Tension Glaucoma/
exp Visual Fields/
exp Optic Disk/ab, an, dg, pa, ul [Abnormalities, Analysis, Diagnostic Imaging, Pathology, Ultrastructure]
exp Late Onset Disorders/di, pa, pc, th [Diagnosis, Pathology, Prevention & Control, Therapy]
exp Time-to-Treatment/cl [Classification]
exp Optometrists/
screen*.mp.
reffer*.mp.
community.mp. or Residence Characteristics/
ophthalmic* nurse.mp.
clinical officer.mp.
optician.mp.
optician.mp. or Vision Screening/
first.mp.
initial.mp.
1 or 2 or 3
4 or 5

7 or 8 or 9 or 10 or 11 or 12 or 13
14 or 15
16 and 17
16 and 18
16 and 17 and 18
16 and 17 and 18 and 19

Database:
Ovid MEDLINE(R) <1946 to March Week 3 2022>

Database searched Through Ovid Interface	Search strategy/ History

#	Query	Results from 26 Mar 2022
1	late presentation.mp.	2,351
2	exp Optometrists/ed [Education]	8
3	initial diagnosis.mp.	15,464
4	exp Glaucoma, Open-Angle/ or advanced glaucoma.mp.	16,084
5	1 and 2 and 3 and 4	0

late presentation.mp.
exp Optometrists/ed [Education]
initial diagnosis.mp.
exp Glaucoma, Open-Angle/ or advanced glaucoma.mp.
1 and 2 and 3 and 4

Database:
Ovid MEDLINE(R) <1946 to November Week 1 2021>

#	Query	Results from 14 Nov 2021
1	exp Glaucoma/ or advanced glaucoma.mp.	55,967
2	late presentation.mp.	2,279
3	Glaucoma/ep and Glaucoma/pc and Glaucoma/sn and Glaucoma/su and Glaucoma/th [Epidemiology,Prevention&Control,Statistics& Numerical Data,Surgery,Therapy]	0
4	exp Glaucoma/	55,925
5	1 and 2	31

exp Glaucoma/ or advanced glaucoma.mp.
late presentation.mp.
Glaucoma/ep and Glaucoma/pc and Glaucoma/sn and Glaucoma/su and Glaucoma/th [Epidemiology,Prevention&Control,Statistics& Numerical Data,Surgery,Therapy]
exp Glaucoma/
1 and 2

Database:
Embase<1980 to 2022 Week 13>

#	Query	Results from 8 Apr 2022
1	detect*.mp.	3,353,377
2	glaucoma/ or glaucoma.mp.	94,845
3	reffer*.mp.	857
4	1 and 2 and 3	0
5	optic disc change*.mp.	224
6	3 and 5	0
7	1 and 5	59
8	community/ or community.mp.	786,108
9	screen*.mp.	1,488,348
10	2 or 5	94,896
11	8 and 9 and 10	298

Database searched Through Ovid Interface	Search strategy/ History
	detect*.mp. glaucoma/ or glaucoma.mp. reffer*.mp. 1 and 2 and 3 optic disc change*.mp. 3 and 5 1 and 5 community/ or community.mp. screen*.mp. 2 or 5 8 and 9 and 10
	Database: Ovid MEDLINE(R) <1946 to April Week 2 2022>

#	Query	Results from 15 Apr 2022
1	Advanced glaucoma.mp.	736
2	blind*.mp.	366,411
3	refer*.mp.	1,009,361
4	primary eye.mp.	409
5	optometr*.mp.	7,858
6	3 or 4 or 5	1,016,518
7	1 and 2	61
8	6 and 7	9
9	late detection.mp.	466
10	nurs*.mp.	733,096
11	3 or 4 or 5 or 10	1,721,130
12	8 and 11	9

Advanced glaucoma.mp.
blind*.mp.
refer*.mp.
primary eye.mp.
optometr*.mp.
3 or 4 or 5
1 and 2
6 and 7
late detection.mp.
nurs*.mp.
3 or 4 or 5 or 10
8 and 11

Manual search using the Schema was done in Pubmed, and Web of Science up to May 2022 but no additional studies were identified. Citation tracking was done to add 3 studies to the screening

Data extraction: Total number of records identified were 683. The records searched were then exported to Covidence software for screening and data extraction, where one hundred and two duplicates were removed.

Each study abstract was screened independently by the two main reviewers. Any outstanding disagreements were arbitrated by a third reviewer. The identified articles subsequently underwent full text review similarly using the inclusion and exclusion criteria. The flowchart is provided in Figure 1.

Ten studies were finally arrived at for data extraction after agreement by the reviewers. All the ten studies had been independently assessed by the two main reviewers.

Quality assessment: We conducted a quality assessment of the included studies using the Strengthening The Reporting of Observational Studies in Epidemiology (STROBE) guidelines[14], as the included studies were largely observational. The two primary areas that were of importance were; adequately described study participants with population identification, as well as outcome data as in appropriate methods of arriving at study findings. This is elaborated in Appendix 2. The risk of bias was graded as low, moderate and high risk of bias.

Appendix 2: Guidelines used for assessing risk of bias as derived from the STROBE guidelines

Potential Bias	Items to be Considered	Risk ratings
Study Participants (STROBE Item 6) Does the study have the population of interest?	There is adequate description of the study population of interest Description of the extent of which identification of advanced glaucoma patients is considered Is Humphrey Visual field (HVF) used? Is median deviation highlighted? Is optic disc assessment done? Have the study participants been previously managed for glaucoma?	**High risk of bias** No grading classification is mentioned **Moderate risk of bias** Only one criteria are used, as in either optic disc criteria or median deviation (MD) **Low risk of bias** Both perimeter with Humphrey visual field analyser testing as well as optic disc assessment
Descriptive data (Item 14a) Are characteristics of study participants adequately detailed? Is geographical, clinical, and demographic information detailed?	Well detailed description of the study clinical setting and context	**High risk of bias** Study setting not well described **Moderate risk of bias** Study setting described but not to detail on geographical zone or clinical setting **Low risk of bias** Clinical and geographical context well outlined
Outcome data (Item 15) Is the description of the participating primary eye care workers adequately done? Is there adequate demonstration of the referral of an unconfirmed glaucoma participant	Number of advanced glaucoma patients who are referred is clearly arrived at to allow for reproducible extraction Tertiary eye hospital or ophthalmologist arrival at a definite diagnosis is demonstrated Is the role of the primary eye care worker in patient identification clearly explained? Detailed demonstration that referral pathway is present	**High risk of bias** No primary eye care worker identified, nor their role in referring an advanced glaucoma patient **Moderate risk of bias** Referral pattern or primary eye care worker role not adequately demonstrated **Low risk of bias** Role of Primary eye care workers clearly demonstrated as well as their contact with advanced glaucoma patient referral

Data synthesis: The extracted data was put up in a table of included studies. Proportional meta-analysis was undertaken with the statistical software R for the main outcome of interest. All meta - analysis used the random effects model that considers both between studies and within studies variances into account. We did not use the fixed effect model as differences among observed effect sizes were not solely due to within-study variance, but as a result of studies performed in different settings which caused the true effect sizes to vary[15].

A point estimate was arrived at with 95% confidence interval. In testing for heterogeneity, and inconsistencies, tau- squared test, and I2 were used.

Subgroup analysis was also undertaken to determine whether the observed heterogeneity was due to a particular effect. Similarly, tau- squared test, Q test and I^2 were used. For the subgroup analysis the on meta-analytical methods used were:

- Inverse variance method
- DerSimonian-Laird estimator for tau^2
- Jackson method for confidence interval of tau^2 and tau
- Freeman-Tukey double arcsine transformation
- Clopper-Pearson confidence interval for individual studies

We combined a narrative synthesis and quantitative (statistical pooling) approach for the synthesis of the extracted studies' information. This was done according to the guidance approach provided[16]. This approach was arrived at as the heterogeneity of the studies included was large, that is, greater than 75%.

A stratified narrative sub analysis was done on how the late presenting patients vary by geographic region, study design, diagnostic criteria for determining late stage of glaucoma (HVF vs disc only), and type of primary referring eye care worker.

RESULTS

Ten studies were recruited from the search. The screening process is shown in Figure 1.These studies[5,17-25] yielded a cumulative total of 47,367 study participants. Study participants ranged from 32,918 to 84 patients per study. The characteristics of the selected papers are shown in

Table 1. The studies cut across various countries. Four studies had participants from United Kingdom, three from across Africa, and one from Australia, Canada, India, and Sweden each.All of the studies were observational.

Table 1: Description of included studies

Study ID	Country	Study design	Investigation	Participants	Glaucoma patients	Late presenters	Referred
Verma 2014	Canada	Cohort study	Optic disc	247	77	16	16
Fraser 2001	UK	Case control study	HVF, optic disc	220	220	110	110
Olawoye 2013	Nigeria	Cross sectional study	HVF	653	653	370	370
Jeganathan 2015	UK	Retrospective	HVF	84	84	23	23
Azuara-Blanco 2016	UK	Comparative diagnostic evaluation	HVF	943	158	28	28
Green 2018	Australia	Retrospective	HVF	188	188	4	4
Jones 2020	Tanzania, UK	Retrospective extraction from medical records	HVF	10766	10766	2,166	2166
Marco 2021	Kenya	Cohort study	Optic nerve criteria	1187	42	23	23
Heijl 2013	Sweden	Cross sectional study	HVF, optic disc assesment	32,918	406	163	134
Odayappan 2021	India	Cross sectional study	Optic disc criteria	161	161	64	9

Table 2: Table showing outcome of quality assessment and justification for rating

Study	Risk of participants bias	Risk of descriptive data bias	Risk of outcome data bias
Azuara-Blanco 2016	Low risk Detailed description of imaging devices that were used Assessment using Humphrey Visual Field, 24-2 SITA strategy and classification by median deviation Optic disc assessment by using Optical Coherence Topography (OCT)	Low risk Study setting adequately described; Five NHS hospitals Participant recruitment process well demonstrated Comparative diagnostic evaluation	Low risk Confirmation of advanced glaucoma patients who are presenting late is adequately done
Fraser 2001	Moderate risk Fist presentation mentioned Eligibility criteria well outlined with detail of Humphrey visual field used as well as optic disc assessment The late presenters, described by visual field loss from fixation (this being a field loss within five degrees of fixation and greater than thirty degrees in one or both eyes. Participants excluded who had difficulty performing visual field test and therefore considered as moderate risk of bias	Low risk Study setting well described as three independent eye departments Participant recruitment process well demonstrated Case control	Low risk Principle referring primary eye workers mentioned Late presenters can be arrived at
Green 2018	Visual field and optic disc assessment done Classification of advanced glaucoma done by assessing median deviation (MD) Study had only initial presenting patients at the hospital and eye centre Some participants however is mentioned had previously been managed by another practitioner	Moderate r isk Study setting in hospital as part of a new model of care	Low risk Referring primary care worked mentioned Late presenters are identifiable

Study	Risk of participants bias	Risk of descriptive data bias	Risk of outcome data bias
Heijl 2013	Low risk Recruitment of participants well described Perimetry done as well as optic disc assessment Median deviation (MD) used for classification of glaucoma	Low risk Population based screening with diagnosis at a tertiary eye centre Referral system clearly outlined	Low risk Primary eye care worker in Early Manifest Glaucoma Trial secondary paper; ophthalmic technicians Late presenters well identified
Jeganathan 2015	Low risk Participants well described as first hospital visit Perimetry done as well as optic disc assessment Median deviation (MD) used for classification of glaucoma Advanced glaucoma patients well described	Low risk Hospital based with referral pattern/ process well outlined	Low risk Primary referring eye workers mentioned distinctly Late presenters well outlined
Jones 2020	Low risk Participants well described at the very first appointment Perimetry done as well as optic disc assessment Median deviation (MD) used for classification of glaucoma Advanced glaucoma patients well described	Moderate risk Study setting adequately described in two distinct geographical zones therefore considered as moderate risk of bias	Moderate risk Late presenters well outlined Referral by ophthalmic technician Referral strategy not elaborately outlined and therefore considered as moderate risk of bias
Marco 2021	Moderate risk Participants well described as first presentation Optic nerve criteria is only used for classification of glaucoma and therefore considered as moderate risk	Low risk Study setting adequately described	Low risk Detailed demonstration that referral pathway is present up to the tertiary eye centre Role of primary eye care worker outlined
Odayappan 2021	Moderate risk Participants well described as first presentation Perimetry done, but not for all patients, using a Humphrey Field Analyser as well as optic disc assessment Optic nerve criteria used for classification of glaucoma Advanced glaucoma patients are well derived	Low risk Study setting well described as clinic patients	Low risk Referral pathway clearly described, done by various primary eye care centres in the referring centre Advanced glaucoma patient number clearly identified
Olawoye 2013	Low risk Participants well described as first presentation Perimetry done as well as optic disc assessment Median deviation (MD) used for classification of glaucoma severity Advanced glaucoma patients well described	Low risk Study setting well outlined from referral centre to the base hospital	Low risk Referral pathway clearly outlined as well as the referring team
Verma 2014	High risk Exclusion criteria was patients with already advanced glaucoma as at the screening site Perimetry done as well as optic disc assessment	Low risk Study design as collaborative tele glaucoma programme Clinical setting well outlined	Low risk Clinical referral pathways were well outlined

Figure 1: Flowchart of records search process

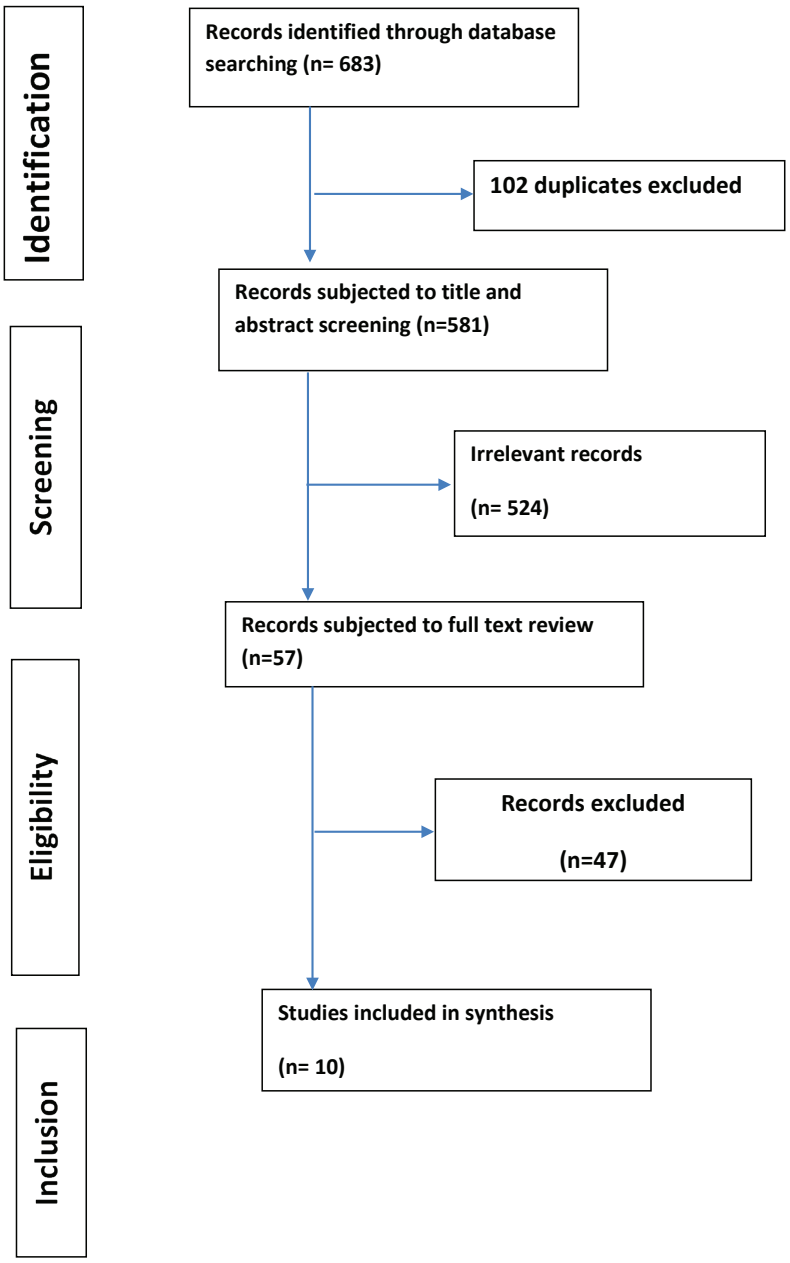
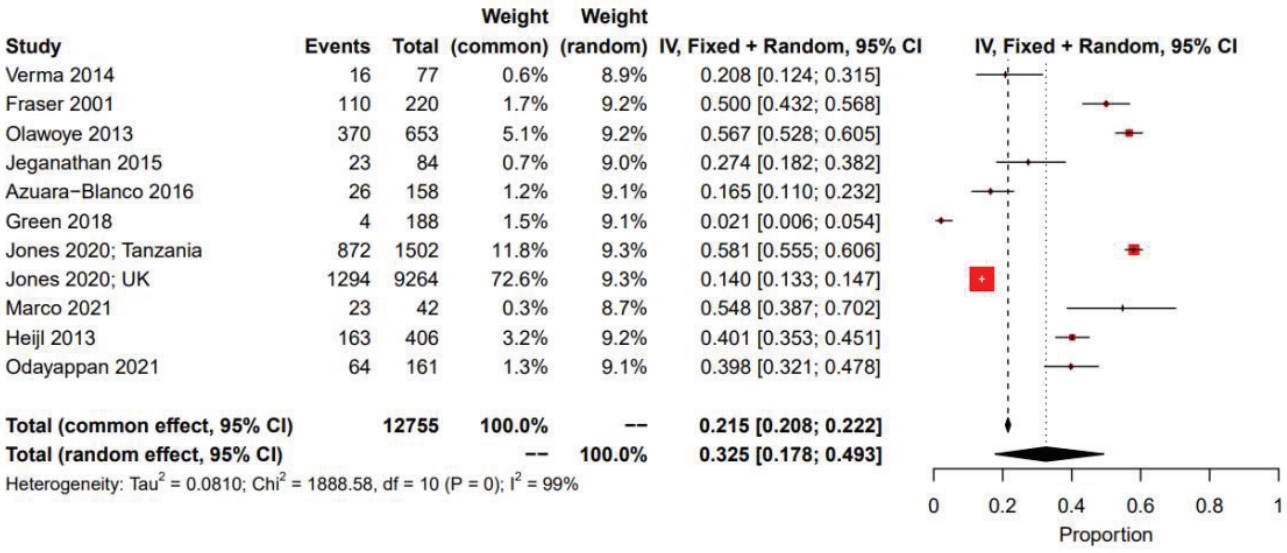


Figure 2: Forest plot of meta- analysis of proportion of late presenting glaucoma patients



The pooled proportion of late presenting glaucoma patients was 0.325 (95% CI 0.178 -0.493) (Figure 1). However due to the large statistical heterogeneity identified, this value should be interpreted with caution. Total heterogeneity, as estimated by tau^2, was 0.0810. The late presenting glaucoma patients from the included studies, ranged from to 2.1% to 58.06%. Out of all the late presenting glaucoma patients (n=2967), 96% (CI 0.85- 1.00) had previous contact with a primary eye health worker. The pooled proportion was 0.96 (0.85-1) (Figure 2). From the weighted proportion of each study, the proportion of advanced glaucoma patients who were referred did not vary significantly between the countries represented in the summary. There was significant heterogeneity of the included studies as in the I^2 greater than 95% in the proportion meta- analyses. A narrative synthesis was therefore employed to allow investigation of the observed heterogeneity. The primary eye health care workers identified were mostly optometrists in seven studies, general practitioners in four studies, ophthalmic technician and ophthalmic nurse in three studies each. Two studies reported screening as done by a team of primary eye care workers in the community and therefore referral was evaluated as from 'other' source.

We categorised and analysed the study in subgroups. The subgroups were based on geographical location of the study, type of study design used, and the method of classification of advanced glaucoma (Humphrey Visual Field vs optic disc criteria). All the subgroups analysed showed over 90% heterogeneity. The I^2 test was preferred as the one to quantify heterogeneity as is the most reliable in meta-analysis of less than ten studies[26]. The number of studies done in each subgroup analysis, pooled proportion of advanced glaucoma with its accompanying confidence interval is shown in Figures 5- 7. There was no observed effect when we analysed effect of the geographical region where the studies were carried out (Figure 5).

Figure 3: Forest plot of meta- analysis of proportion of patients who were referred by a primary eye care worker

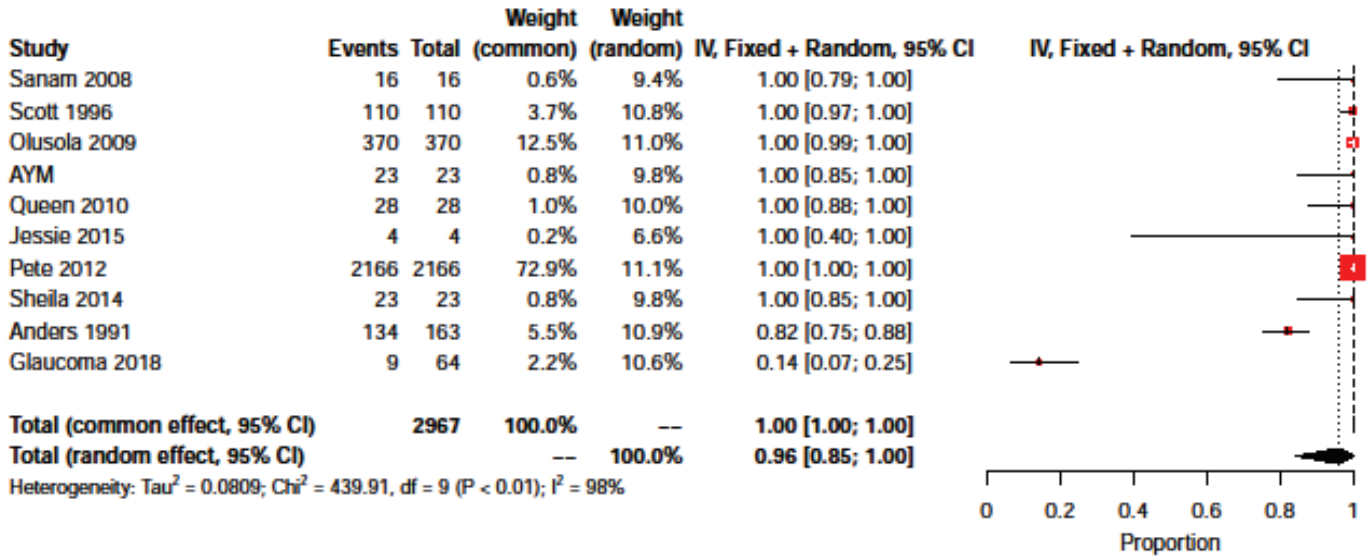


Figure 4: Frequency bar chart showing type of primary eye care worker that referred advanced glaucoma patients

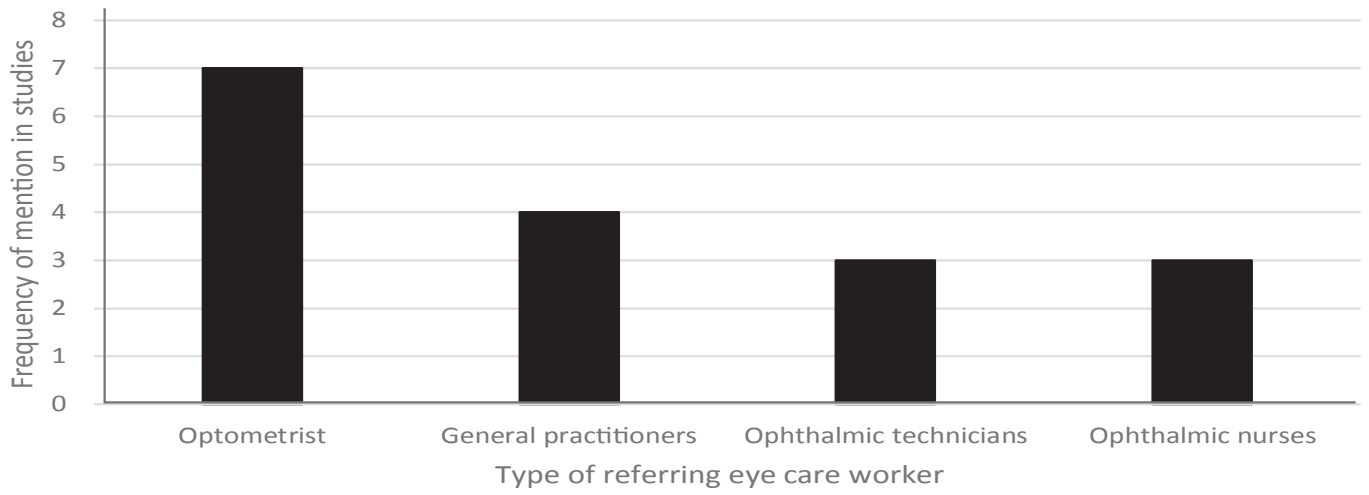


Figure 5: Results of subgroup analyses based on geographical location

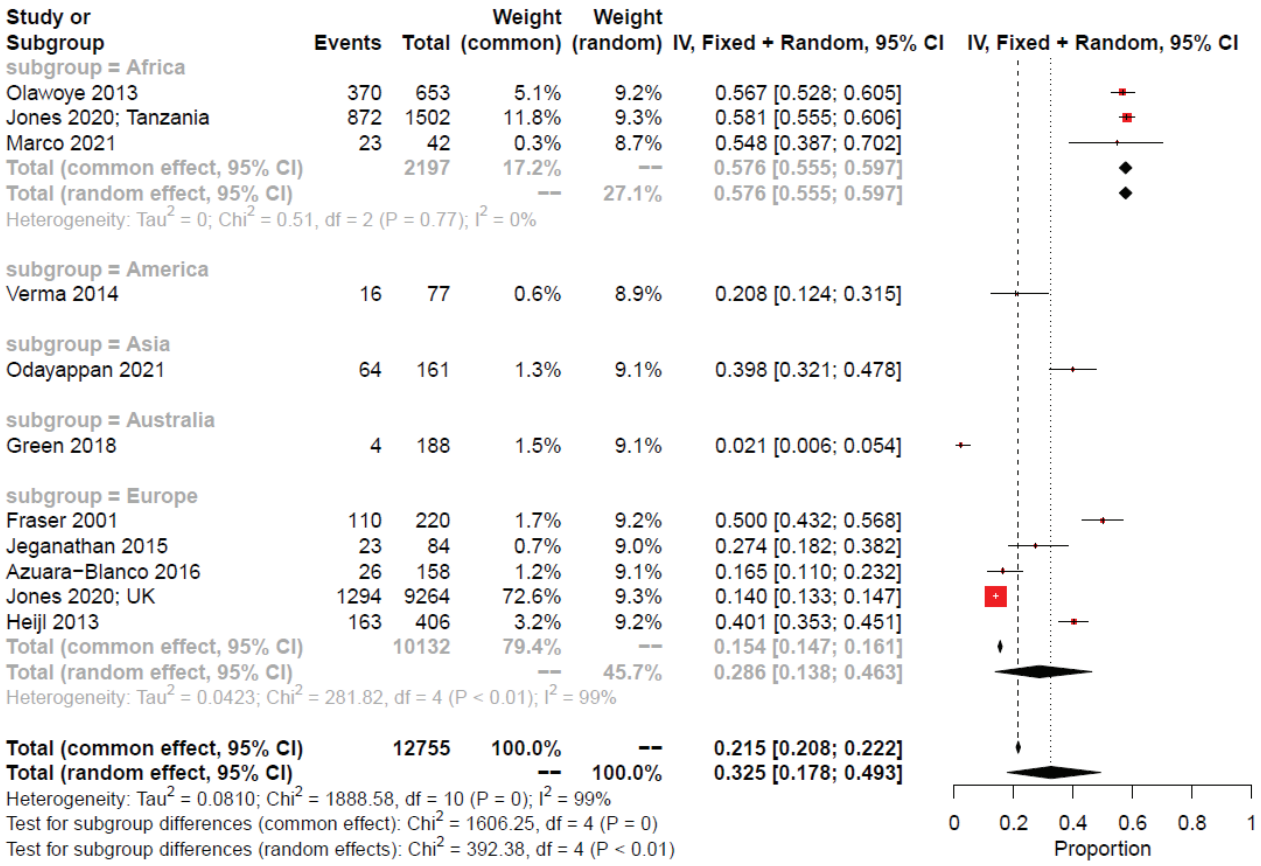


Figure 6: Results of subgroup analyses based on method of classification of advanced glaucoma (Humphrey Visual Field vs optic disc criteria)

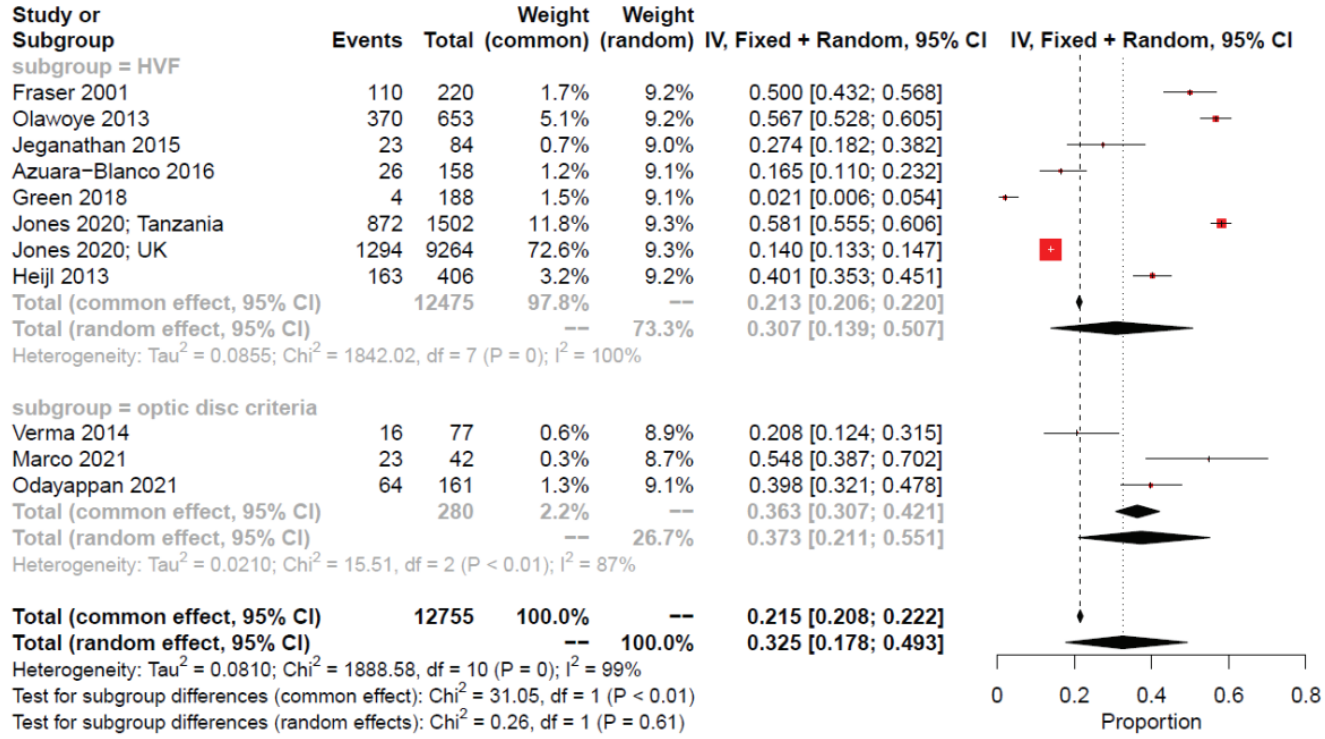
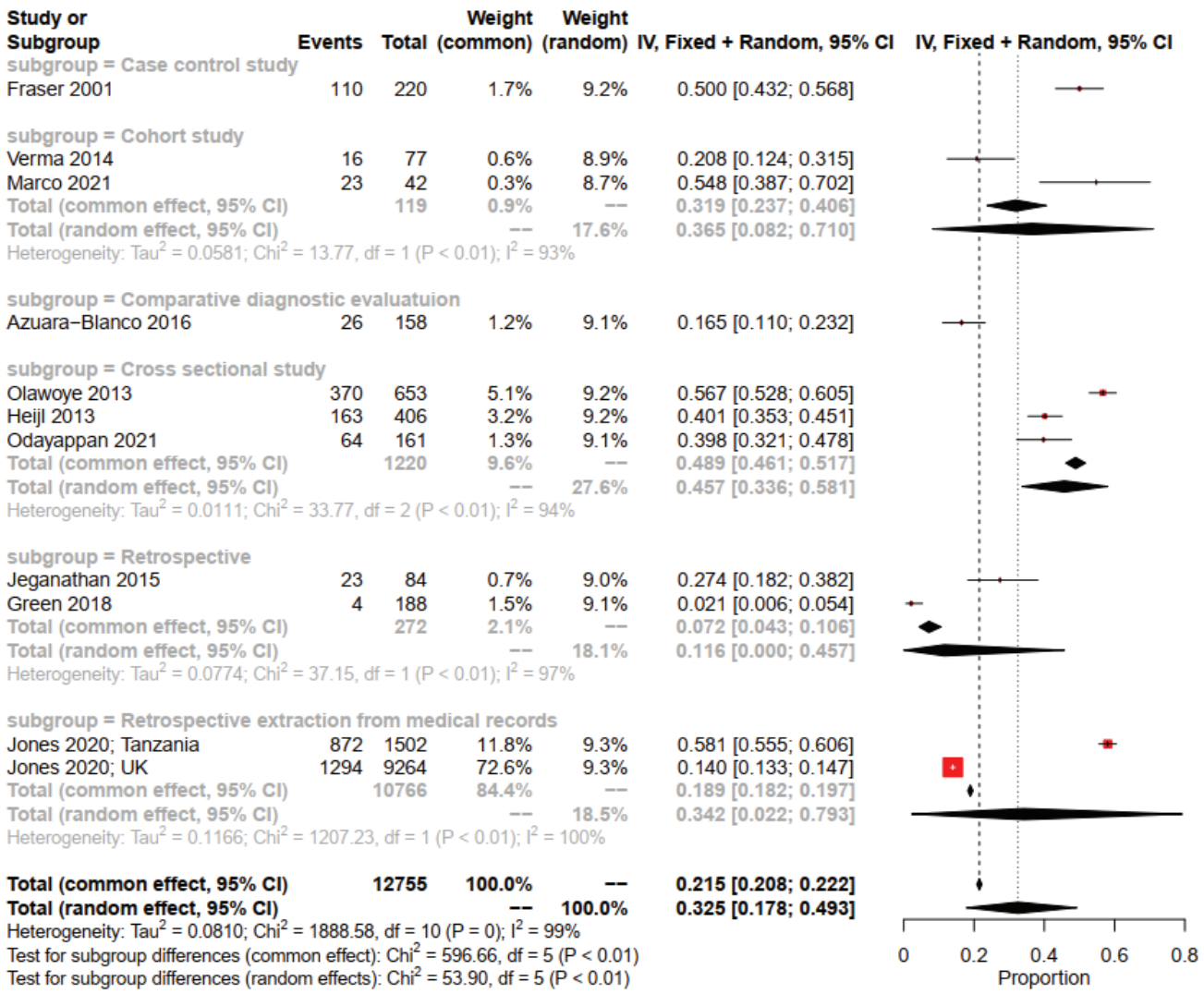


Figure 7: Results of subgroup analyses based on study design used



We performed a qualitative assessment of studies' quality. All studies were assigned quality of reporting as per the quality assessment tool used. However, no study was disqualified due to the technical quality.

DISCUSSION

The pooled proportion of late presenting glaucoma patients was 0.325 (95% confidence interval 0.178-0.4931). From this study finding, this indicates that 32% of all referred newly diagnosed glaucoma patients are late presenters.

In our study we demonstrated equally a varied range of proportion of advanced glaucoma patients, from 2% to 58% as demonstrated earlier in the results. We however were interested in those patients having advanced glaucoma and presenting for the first time at the initial diagnosis centre, whom we referred to as late presenting patients. These patients had been referred to a tertiary eye centre for a definitive diagnosis and management.

Advanced glaucoma has been a topic of interest and various studies have estimated the incidence of advanced glaucoma. This varies from 10% to 61% depending on study location, study design and study participants[5,19,27]. Our study findings also fall within this range, but on the higher side since it indicates over three in ten glaucoma patients present late.

In the included studies, out of the late presenting patients, (n= 2,967), 2,883 of them had previous contact with a primary eye health worker. The proportion did not vary significantly among studies that were analysed. This indicates that usually an advanced glaucoma patient will have sought medical help upon noticing vision problems even prior to getting a definitive diagnosis.

Referral by primary eye care workers: Optometrists were noted as the primary eye health workers who had the most contact with the advanced glaucoma patients. This finding reflects that in most of the included studies, optometrists are the first point of contact with glaucoma patients.

The type of primary eye health worker who serves as the first contact for an advanced glaucoma patient varies from country to country or region to region depending on various health system unique set up. In England and most other western countries, most referrals to the hospital eye service originate from community optometrists, who have been demonstrated to have a particularly low threshold for glaucoma diagnosis[28,29]. This study finding could also be interpreted that patients usually interpret their visual problem as needing refractive attention rather than medical treatment.

The first point of contact for a patient largely determines the disease outcome. In African countries, and most other developing countries, patient referrals to a tertiary eye unit are done by a varied range of primary eye care workers.This varies from private facilities, government owned primary care facilities, traditional healers as well as local pharmacies[30,31]. The choice of facility to visit has been shown to largely depend on proximity and cost, with the low income group preferring the less costly primary health facilities. All these stakeholders should be sensitised and integrated to establish protocol and referral pathways for eye patients. From our included studies in developing countries, primary contact area was at a primary health facility.

Geographical region: When we analyse for geographical region, studies carried out in Africa had a higher percentage of late presenters as compared to the European population (57.6% in Africa vs 28.6% in European subgroup). The heterogeneity also dropped in the analysis of the African subgroup. This was however from only three studies. These findings could be due to the more streamlined health care system in developed countries that allows for early detection of glaucoma as well as timely referral of patients.

We compared two sets of similar studies conducted with reproducible methods, one retrospective study in Tanzania and UK done from data collected between 2009 to 2017 with 10,766 study participants while the other being cohort studies in Canada vs Kenya. Both demonstrate a higher incidence of late presenters in the less developed countries. The Tanzanian subset showed a proportion of 58.1 (55.6, 60.6) percent of late presenters, while in comparison a lower proportion in England of 14.0% (CI, 95%: 13.3, 14.7). Among other factors, the study identified fewer community based optometrist as a barrier for access to regular eye examinations in a vast and underserved geographical region. In addition, another challenge identified, despite presence of community optometrists was lacking engagement of the community to take up the existing eye services seeing as there was a significant proportion of glaucoma patients in UK still presenting late (14.7%).

Two cohort studies had a similar study design but in different geographical locations[20,23]. The Kenyan study[20], also showed a higher proportion of late presenters as compared to the Canadian group[23]. The Kenyan group showed 54.76% (23/42) of all glaucoma patients as late presenters as opposed to the Canadian group who had 20.78% (16/77) of all glaucoma patients being late presenters.

Africa has been shown to carry the most burden of disease from glaucoma in terms of visual disability as well as economic burden[32]. Residing far away from hospital has been demonstrated as a barrier to access of glaucoma services[6]. As much as primary eye care workers are needed in the low resource countries, their distribution should be equally proportionate in all regions to allow access by eye patients. All these efforts should be therefore directed toward reducing the number of late presenters in this region.

Future studies should consider comparing the characteristics of late presenting patients in the various macro-geographic continental regions, as in, Asia, Africa, Europe, north America, Latin America and the Caribbean, and Oceania in greater depth. Only one study was carried out in Asia[17].

Classification of advanced glaucoma: When we analysed for effect of studies that utilised Humphrey perimetry versus those that used optic disc signs only, we found that the latter group had a higher proportion of late presenters (37.3%), but with a lower heterogeneity.Three studies used the optic disc criteria for classification of advanced glaucoma.

Most of the studies that used perimetry had the same criteria for diagnosing advanced glaucoma by using the median deviation. Fraser[18] described late presenters, by visual field loss from fixation, this being a field loss within five degrees of fixation and greater than thirty degrees in one or both eyes. All these are however acceptable in the Hodapp, Parrish and Anderson's classification described earlier. This allowed for comparison of data between the study participants. Use of perimetry however could potentially have locked out from the study those subjects who could not be in a position to undertake or successfully complete the test.

Study design: Despite the study design employed, there was a high heterogeneity observed between the studies. This heterogeneity dropped, insignificantly, in the subgroup of cohort studies.

The quality of all studies was generally high, demonstrated low risk of bias, and satisfied the majority of the risk of bias and applicability criteria. The risk of bias from these studies was mostly from participant bias, which reflects the diversity in the methods of recruitment of patients to a particular study.

Limitations

This systematic review as described by the included studies, doesn't accurately capture time before presentation. Glaucoma is a chronic progressive disease

and it would be helpful to know how far in the disease progression that most patients present so as to know when to intensify screening efforts. Additionally, Humphrey visual field testing is a subjective psychophysical testing method. It is therefore never completely accurate nor reproducible.

CONCLUSIONS

We reviewed ten studies that reported the prevalence of late presenting glaucoma patients which was found to be 32.5% (95% CI 0.178 -0.493). Out of these patients, we found a large proportion of them, 96% (95% CI 0.85-1.00), had previous contact with a primary eye health worker before getting a definite diagnosis in a tertiary eye hospital.

This study demonstrates the value of primary eye care workers bridging the gap between glaucoma patients and prevention of blindness from glaucoma. This finding therefore demonstrates a huge opportunity to channel efforts and resources toward investing in primary eye health workforce for referral of glaucoma patients and subsequently preventing irreversible blindness.

Consent for publication: All authors have given consent to the submission of this manuscript. This research was undertaken as part of the final year of the ChM in Clinical Ophthalmology (University of Edinburgh, Edinburgh Surgery Online).

Availability of data and materials: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Details of the protocol for this systematic review were registered on PROSPERO and can be accessed at www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42022324514.

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Causes of childhood blindness: Results from Sebeta School for the Blind, Oromia Region, Ethiopia

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ABSTRACT

Background: Childhood blindness is a widespread problem in developing countries such as Ethiopia, so it's crucial to identify region-specific causes to combat visual impairment.
Objective: To determine the causes of blindness in school children attending the Sebeta School for the Blind in the Oromia region.
Design: Cross-sectional descriptive study.
Subjects: All children attending the school during the study period were included, and those willing to participate were the study subjects.
Methods: The study involved all school children who volunteered, with some excluded: those who declined to participate, were 18 years or older, absent, or uncommunicative. The researchers collected data through a questionnaire based on the WHO/PBL format for children with blindness and low vision, modified as appropriate, and eye exams administered by the principal investigator and an ophthalmic nurse. Key informants (e.g., teachers) were also interviewed. They also used secondary data from students' files to supplement and verify primary data. The data quality was ensured, and it was analyzed using SPSS version 23. Descriptive analysis was used to determine variable means, frequencies, and proportions.
Results: One hundred and fifty five students aged 7-17 years were examined. Childhood blindness affected 148 of them (95.5%). The most common anatomical cause of blindness was the whole globe (37.8%). The cause of blindness was unknown in over two-thirds of cases, with abnormalities since birth and cataracts responsible for 14.9% and 13.5%, respectively. Childhood factors accounted for most of the known causes of SVI/BL (15.5%), with trauma (7.4%) being the most common. Forty-two percent of the causes were avoidable, 14.2% preventable, and 27.7% treatable.
Conclusion: Trauma, a preventable cause, is recognized as a cause of avoidable blindness in these children. Cataract and glaucoma, treatable causes of childhood blindness, have become major causes in blind school children in Central Ethiopia, displacing corneal blindness.
Recommendations: Policymakers should consider these findings when designing health service frameworks. Primary health workers should receive training to refer children early for treatable childhood blindness causes. Increasing the number of specialist paediatric ophthalmic services is crucial for cataract and glaucoma treatment. Preventing trauma involves strict adult supervision and creating a safe domestic environment for children.

Key words: Blind school, Childhood blindness, Ethiopia

INTRODUCTION

Childhood blindness or severe visual impairment is caused by diseases and conditions in childhood or early adolescence, which, if left untreated, can lead to permanent blindness later in life. The causes of childhood blindness vary depending on socio-economic development and access to primary health and eye care services[1].

Preventable causes are responsible for a high percentage of childhood blindness in low-income countries, and community-based interventions are needed to address this. While treatable diseases like cataracts can restore vision in children across all regions, specialized expertise and equipment are necessary as children's eyes differ from adults[1].

In 2010, the estimated number of blind children worldwide was 1.26 million, a decrease from the previous estimate of 1.4 million in 1999. However, in sub-Saharan Africa, there was a 31% increase in blind children to 419,000[2].

The causes of childhood blindness are evolving. In many developing countries, integrated management of childhood illness programs has reduced corneal scarring due to measles and vitamin A deficiency. Therefore, the proportion of blindness caused by cataracts is growing. Retinopathy of prematurity is becoming a significant

cause in middle-income countries, and the prevalence of refractive errors, particularly myopia, is rising in school-age children[1].

Approximately 1.4 million children worldwide are blind, accounting for 3.9% of general blindness globally. Seventy five percent of these children live in the poorest regions of Africa and Asia, primarily due to social and economic disparities and inadequate access to primary health care and eye care services[1]. This is also true for Ethiopia, where primary health care and eye care services are poor.

A global update on childhood blindness and its causes highlights that in countries like Ethiopia, 7-31% of childhood blindness and visual impairment can be avoided, 10-58% can be treated, and 3-28% can be prevented[4].

Blind children face lifelong visual impairment, resulting in emotional, social, and economic costs for them, their families, and society[5]. In countries like Ethiopia, where there is little awareness of childhood blindness, it becomes more challenging for affected children to integrate into society.

Significance of the study: Childhood blindness is a major public health issue, and it is crucial to identify region-specific causes to aid nations in preventing and treating childhood blindness and visual impairment[1]. The findings of this study can aid in understanding region-specific causes and guide appropriate resource allocation for the prevention and treatment of childhood blindness.

"Vision 2020," the global initiative against avoidable visual impairment led by the WHO and the International Agency for Prevention of Blindness, prioritizes children. Country-specific programs are developed and implemented based on specific priorities for prevention, treatment, and rehabilitation, given the varying causes of visual loss. This study is of immense importance in identifying such causes of visual loss in children, serving as a reference for such programs[1].

In 2001, a study on the causes of childhood blindness was conducted at the Sebeta School for the Blind[5]. Since the study was conducted, there have been changes in the community's knowledge, attitude, and practice and improvements in health facilities and services. These factors impact childhood blindness. The present study was, therefore, aimed to identify the causes of childhood blindness at the same school, including determining anatomical sources of visual impairment, uncovering underlying causes for severe visual loss, and identifying preventable or treatable factors contributing to blindness in children.The results will help identify changes and guide further public health interventions for children with treatable eye conditions.

MATERIALS AND METHODS

Study setting: The study was conducted at Sebeta School for the Blind, a boarding school that houses around 256 blind or visually impaired children aged 7-23 years. Some students have other physical or learning disabilities. Most are from Ethiopia's Oromia region and live on the school premises up to the age of 14 years or grade 6, after which they move to town lodgings. The curriculum is taught in Braille in the local language (Afaan Oromo).

Study design, study period and population: A blind school-based cross-sectional descriptive study was conducted from October 2019 to January 2020. All students attending Sebeta School for the Blind during the study period were taken as the source population. The study subjects were those willing to participate.

Inclusion/exclusion criteria: All children attending the school and present during the study period were included. Excluded from the study were students who refused participation, were aged 18 years or older, were absent from school three times, or couldn'tprovide the necessary history due to communication barriers.

Sampling: Children aged 7-17 years among the 256 students were invited to participate. Those who agreed were included as study subjects.

Data collection procedure and instruments: Data was collected through a structured questionnaire, including personal details, history of eye surgery, and accompanying disabilities. An eye examination was also performed to identify the anatomical site and possible cause of visual impairment, and key informants (e.g., teachers) were also interviewed.

The questionnaire was based on the WHO/PBL format for children with blindness and low vision, modified as appropriate. The WHO Program for the Prevention of Blindness developed the Eye Examination Record for Children with Blindness and Low Vision (ERCB) to record causes of visual loss among children in blind schools, hospitals, and population-based surveys.

Visual acuity levels were measured using a Snellen "illiterate" E optotype. If a child could not see the 3/60 optotype, their perception of light was checked. Distance visual acuity was measured for each eye and both eyes separately. A pinhole was used to assess visual acuity improvement. Students whose visual acuity improved with a pinhole were referred for further refraction. Anterior segment examination was done using a portable slit lamp. Posterior segment evaluation was performed

using a direct ophthalmoscope after pupil dilation with one drop of 1% tropicamide eye drop, with a 30-minute wait for it to work.

Data were collected by the principal investigator, and an ophthalmic nurse familiarized with the questionnaire and objectives of the study. Secondary data from the students' files complemented the information and/or validated the primary data collected directly. Students who needed further workup and intervention were referred to Saint Paul's Hospital Millennium Medical College (SPHMMC).

Data quality assurance: Structured data collection forms were used to gather all relevant study data. Data were collected by an ophthalmic nurse, with regular supervision by the principal investigator. The principal investigator checked all data for completeness and resolved any identified issues.

Data processing and analysis: Data were entered into SPSS version 23. Descriptive analysis was used to determine means, frequencies, and proportions. Cross-tabulations were also performed, and tables were used to present the findings as appropriate.

Operational definitions

- *Child:* A human being below the age of 18 years[14].
- *Visual Impairment (VI):* Visual acuity worse than 6/18 up to 6/60 in the better eye[15].
- *Severe visual impairment:* Visual acuity worse than 6/60 up to 3/60 in the better eye[15].
- *Blindness:* Visual acuity of <3/60 in the eye with better vision[15].
- *Childhood blindness:* An eye condition that results in blindness or severe visual impairment[1].
- *Avoidable blindness:* Results from conditions that could have been prevented or controlled if the available knowledge and interventions had been timely applied[1].
- *Uncommunicative:* Not disposed to talk or impart information[16].

Ethical considerations: The SPHMMC review board approved the research proposal, and permission was obtained from the Sebeta School director. Informed written consent was also obtained from each participant's parent or guardian. If not available, the teachers signed the consent form, which was attached to each questionnaire. Patient confidentiality was maintained using initials instead of full names on the questionnaires. Children with treatable eye conditions were identified and referred to SPHMMC for further assessment and treatment.

RESULTS

Demographic background: One hundred and fifty-five students (63.2% male, 36.8% female) aged 7-17 years (mean age: 13.0) were examined. Most (62%) were aged 7-14 years, and 37.5% were over 14 years. Two students (1.2%) had additional impairments (mental retardation and hearing loss). Seventeen students (11.%) had a family history of similar conditions. Visual loss began between ages 1-14 years for most students (54.8%), followed by birth (36.1%) and the first year of life (7.7%). The onset age was unknown for 1.3% of students.

Out of 155 students, 148 (95.5%) had childhood blindness per WHO category: Seven (4.5%) had visual impairment, and 15 (9.7%) had severe visual impairment. Three students (1.9%) showed improvement with a pinhole for the right eye and one (0.6%) for the left eye (Table 1).

Regarding functional vision, 61(39.4%) had no residual vision, 35(22.6%) had useful residual vision, 31(20%) could see to walk, 9(5.8%) could recognize faces, and 19(12.3%) could see print. Twelve (7.7%) had previous surgery: 7(58.3%) cataract surgery, 2(16.7%) eye removal, and 3(25%) unknown. Sixteen (10.3%) had previous trauma, 135(87.1%) had no history of trauma, and 4(2.6%) were unsure.

Regarding anatomical causes of SVI/BL in 148 students, the globe was the most common site (37.8%), with phthisis being the most common lesion (21.6%). Optic nerve pathologies accounted for 21.0%, corneal

Table 1: Presenting visual status of students attending Sebeta School for the Blind by sex and age, August 2019

	Sex		Age (years)		
WHO category of visual loss	M	F	7-14	15-17	Total (N%)
Visual impairment (6/18-6/60)	6	1	4	3	7 (4.5)
Severe visual impairment (6/60-3/60)	10	5	11	4	15 (9.7)
Blindness (<3/60)	47	29	42	34	76 (49)
Blindness (NLP)	35	22	39	18	57 (36.8)
Total					155(100)

pathology, mainly corneal scar, for 16.2%, and cataract for 14.2%. The retina and uvea were the least common sites, accounting for 5.4% and 3.4%, respectively (Table 2).

Aetiological causes of SVI/BL: For more than two-thirds of the students, the aetiology was unknown. Abnormalities since birth and cataract accounted for 14.9% and 13.5% of the unknown aetiology group, respectively. Childhood factors were responsible for most of the known causes of SVI/BL (15.5%). Among childhood factors, trauma was the most common cause (7.4%), followed by hereditary eye disease as the second most common cause. Heredity was autosomal dominant in 4(2.7%) students, unspecified in 6(4.1%), while toxoplasmosis causing macular scar was found in 1(0.7%) student. Additionally, two students had childhood neoplasm, one with brain tumour with compressive optic neuropathy and the other with retinoblastoma.

Table 2: Anatomical site of abnormality in 148 students with SVI/BL in SebetaSchool for the Blind, August 2019, based on WHO/PBL classification

Anatomical site	Total (N%)
Globe	56 (37.8)
Phthitic	32 (21.6)
Anophthalmos	3 (2.0)
Microphthalmos	1 (0.7)
Buphthalmos	17 (11.5)
Removed	1 (0.7)
Disorganized	2 (1.4)
Cornea	24 (16.2)
Scar	20 (13.5)
Staphyloma	4 (2.7)
Lens	21 (14.2)
Cataract	21 (14.2)
Uvea	5 (3.4)
Aniridia	1(0.7)
Coloboma	2 (1.4)
Uveitis	2 (1.4)
Retina	8 (5.4)
Dystrophy	5 (3.4)
Retinoblastoma	1 (0.7)
Toxoplasma scar	1 (0.7)
Coloboma	1 (0.7)
Optic nerve	31 (21)
Atrophy	26 (17.6)
Hypoplasia	4 (2.7)
Coloboma	1 (0.7)
Globe appears normal	3 (2.0)
Cortical blindness	3 (2.0)
Grand Total	148 (100)

Table 3: Aetiologic category of visual loss in 148 students with SVI/BL in Sebeta School for the Blind, August 2019, based on WHO/PBL classification

Aetiology	Total (N%)
Hereditary	10 (6.8)
Autosomal dominant	4 (2.7)
Unspecified	6 (4.1)
Intrauterine factor	1 (0.7)
Toxoplasmosis	1 (0.7)
Childhood factors	23 (15.5)
Vitamin A deficiency	4 (2.7)
Measles	6 (4.1)
Neoplasm	2 (1.4)
Trauma	11 (7.4)
Unknown aetiology	114 (77.0)
Cataract	20 (13.5)
Glaucoma/Buphthalmos	17 (11.5)
Abnormality since birth	22 (14.9)
Other	55 (37.2)
Grand Total	148 (100)

Avoidable causes of SVI/BL: Forty-two percent of the students had avoidable causes of childhood blindness. Fourteen percent were preventable, and 28% were treatable. Trauma (7.4%) was the most common preventable cause of SVI/BL, while cataract (13.5%) was the most common treatable cause (Table 4).

Table 4: Avoidable causes of visual loss in 148 students with SVI/BL in Sebeta School for the Blind, August 2019, based on WHO/PBL classification

Aetiology	Total (N%)
Preventable	21 (14.2)
Trauma	11 (7.4)
Measles	6 (4.1)
Vitamin A deficiency	4 (2.7)
Treatable	41 (27.7)
Glaucoma	17 (11.5)
Uveitis	2 (1.4)
Cataract	20 (13.5)
Neoplasm	2 (1.4)
Total avoidable	62 (41.9)

Eight students had the potential for improved visual acuity with intervention. Two had pseudophakia, one improved with pinhole, and the other had dense posterior capsular opacity. Four had dense cataracts and light perception acuity, and two had refractive errors. The students were referred to SPHMMC for further attention. The school director was also informedfor follow-up.

DISCUSSION

Ninety-five-point five percent of the examined blind students at the Sebeta School for the Blind had SVI/BL, comparable to 93% reported in 2015 and 94.5% in 2001 in Amhara regional state, Northwest Ethiopia[2] and children in schools for the blind in Ethiopia(Bako, Shashemene, and Sebeta)[5], respectively.

Sixty percent of the students in the school were included in the study, indicating that many elementary school students were over 18 years old. This delay could be due to a lack of Braille educational support materials and late school start-ups for blind children. Also, their parents or guardians may abandon children with SVI/BL.

This study found that the lesion of the whole globe was the most common cause of SVI/BL. Similar results were reported in the People's Republic of China, where the whole globe was also the most typical anatomical site of visual loss (25.5%)[12]. A 2015 research report from Northwest Ethiopia found that corneal pathologies were the most frequent causes of SVI/BL, which contrasts with the results of this study[2]. Measles immunization coverage differed between Oromia (38.8%) and Amhara (33.3%)[17], regions according to the 2005 Ethiopian Demographic and Health Survey (DHS) which may have contributed to the difference in the causes of SVI/BL in these regions. Similar findings were reported in a study conducted in Eritrea, where corneal pathologies accounted for the highest proportion of SVI/BL (16.9%)[7]. Corneal pathologies were also the most common causes of SVI/BL in East and southeastern African countries, such as Malawi, Kenya, and Uganda, with a prevalence of 35.2%[9].

It was also found that corneal scar/phthisis accounted for 35.1% of SVI/BL cases, with measles and vitamin A deficiency contributing to only 6.8%. Measles immunization coverage has improved in Ethiopia over the years, which may explain the low number of affected children. However, measles and vitamin A deficiency may have contributed to corneal scar/phthisis cases where the causes were unclear. The prevalence of Bitot's spots in Ethiopia was 1.7% among children aged 6-71 months, and 47% of children aged 6-35 months received vitamin A supplements, according to the DHS 2019[8]. The results may appear low, but the problem remains significant.

Reviewed literature has conflicting classifications for phthisis bulbi, with the majority considering it caused by childhood factors in developing countries. The current study found that corneal scarring and phthisis accounted for 35.1% of cases, which is lower than a study from 19 years ago in Ethiopian schools for the blind, where it accounted for 62.4%[5]. Similar findings were reported in other countries, including Chile (35.9%) and South India (38.4%)[10].

In the study, 21 (14.2%) students with SVI/BL had cataracts, and 7 (33.3%) had cataract surgery on at least one eye. Compared to the four East African countries, where 18% of children attending schools for the blind had cataracts as the primary cause of visual impairment, and 83% had undergone cataract surgery on at least one eye[19]. The number of children in this study who had undergone cataract surgery was much lower.

Of the subjects in this study, 41.9% had avoidable causes of SVI/BL, with treatable causes accounting for the majority (27.7%). In contrast, a 2015 study in Northwest Ethiopia reported over 80% of the causes were avoidable, with potentially preventable causes accounting for 65%[2]. The proximity of the school to Addis Ababa, where healthcare is easily accessible, and prior visits by governmental and non-governmental organizations to the Sebeta school may explain the lower percentage (41.9%) of avoidable causes of SVI/BL found in this study. This result is similar to findings in Eritrea, where avoidable causes of childhood blindness were reported at 47.9%[7]. In contrast, the percentage of avoidable causes of SVI/BL found in this study (41.9%) was higher than the results of a study conducted in China, which reported 37.5% of avoidable causes (15% potentially preventable and 22.5% potentially treatable)[11].

The WHO/PBL eye examination form for children with blindness and low vision was used. Many of the research results consulted used the same document for comparison, ensuring a reliable and consistent benchmark for comparison.

In this study, most students with SVI/BL (77.0%), most of whom had phthisis bulbi, had an unknown cause. This may be due to the prolonged presence of the ocular problem and delayed consultation with health professionals.

Some students involved in this research might not know the probable cause and the age of onset of their blindness, and some were also not cooperative during physical examination.

Children from remote and underserved parts of the country may not attend a special school. Therefore, there may be under-representation of these children.

CONCLUSION

(i) Trauma, a preventable cause of blindness, has become a recognized cause of avoidable blindness in blind school children.
(ii) Cataract and glaucoma, both treatable causes of childhood blindness, have become major causes of blindness in blind school children in Central Ethiopia. This is a notable shift from the commonly reported corneal blindness.
(iii) Regarding the anatomic site, lesion of the whole globe was the most common cause of SVI/BL.

Eight students in this study had visual acuity that could be improved with further workup and intervention, indicating a lack of screening before entering school.

RECOMMENDATIONS

A low percentage of students in this study had undergone cataract surgery. Many factors could be considered as causes, but the limited number of centers in Ethiopia that provide such services and the low health-seeking behavior of the community may be the major ones. We recommend training primary health workers to refer children diagnosed with treatable causes of childhood

blindness early and increasing the number of specialist paediatric ophthalmic services to address paediatric cataracts and glaucoma. Community awareness creation could also contribute a lot.

Ensuring strict adult supervision of children and creating a safe domestic environment can help prevent trauma. Furthermore, community education on the importance of seeking immediate professional medical attention after an injury is crucial. We recommend providing low-vision aids for the children. An ophthalmic exam should be mandatory for registering students in special needs schools.

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Surgical induced astigmatism and associated factors in manual small incision cataract surgeries done at the Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

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ABSTRACT

Background: Cataract surgery is a popular ophthalmic procedure with a high success rate for restoring vision. Its goal is to minimize astigmatism after surgery and achieve desired refractive outcomes. This study examines Surgically Induced Astigmatism (SIA) at Saint Paul's Hospital Millennium Medical College (SPHMMC), providing valuable insights for developing practical cataract surgery guidelines.
Objective: The objective of the study was to determine the level of post-operation astigmatism and its associated factors in manual small incision cataract surgery (MSICS) at Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia.
Design: A prospective analytical study was conducted at SPHMMC, Addis Ababa, Ethiopia.
Setting: The study included all patients who underwent MSICS cataract surgery in the SPHMMC eye clinic during the study period and agreed to participate.
Methods: The hospital-based prospective study analyzed MSICS patients at SPHMMC hospital in Ethiopia for ten months (2019/2020), excluding those with previous intraocular surgery or complications. Using convenience non-probability sampling, a structured questionnaire collected data on independent variables like age, sex, and incision details. SPSS version 23 was used to analyze the data, focusing on the dependent variable, surgically induced astigmatism. Descriptive and logistic regression analyses were performed to determine the association between factors.
Results: A total of 240 subjects aged 40-85 years with a mean age of 63.1 (SD±9.89) years and pre-operative visual acuity ranging from 6/60-LP were studied. Clinically significant surgically induced astigmatism ranged from 0 to 5.62D, with a mean SIA of 1.38D (SD±0.92D) and axis of 88.12 (SD±56.74). Multivariable logistic regression showed significant associations between surgically induced astigmatism and tunnel size (P=0.000) and suture presence (P=0.005).
Conclusion: Scleral tunnel size and wound sutures are critical factors associated with significant SIA. Whenever it is necessary to put a suture at the end of the surgery, removing it at the third postoperative visit is always important.
Recommendation: It is recommended to measure tunnel size with a caliper, especially during the beginning periods of doing MSICS, and to minimize it.

Key words: Astigmatism, Cataract, Manual small incision cataract surgery

INTRODUCTION

A cataract is a vision impairment caused by the opacity of the lens or its capsule. Age-related cataract is the leading cause of blindness for approximately 20 million people worldwide. In countries with insufficient surgical services, cataract remains the primary cause of blindness. Manual Small Incision Cataract Surgery (MSICS) is commonly used in developing nations like Ethiopia. However, it has several postoperative complications, with postoperative astigmatism being a significant concern[1].

Astigmatism is an eye condition where the curvature of the cornea or lens varies at different meridians, causing light rays from an object to not focus on a single point. Instead, it results in two focal lines[2].

Regular astigmatism is a refractive condition where the principal corneal or lenticular meridians have a constant orientation across the pupil, and the amount of astigmatism is equal at every point. Correcting it is possible through cylindrical spectacle lenses[2].

Regular astigmatism can be classified as with-the-rule or against-the-rule astigmatism. With-the-rule

astigmatism has the steepest vertical corneal meridian, requiring a correcting plus cylinder axis near 90°. Against-the-rule astigmatism has the steepest horizontal meridian, needing a correcting plus cylinder axis near 180°. Oblique astigmatism is when the principal meridians are not near 90° or 180° but are close to 45° or 135°[2]. In irregular astigmatism, the orientation of the principal meridians or the amount of astigmatism changes from point to point across the pupil[2].

Statement of the problem: The surgical technique used for cataract extraction impacts the occurrence of SIA, ultimately affecting the visual outcome[3]. A 2011 study in Nigeria revealed that surgically induced astigmatism affected almost 75% of the reviewed patients, with clinically significant astigmatism as high as 25-30%[4]. Similarities in surgical setup and techniques suggest that Ethiopia may face a similar issue[4]. Currently, cataract surgery is considered a type of refractive surgery, and reduction of refractive defects to the lowest level is possible, leading to increased expectations of patients[5].

Significance of the study: Previous research has examined the occurrence of post-cataract surgery astigmatism in Western settings, but no similar studies have been published for Ethiopia. Establishing baseline data is crucial, making this study important. This study provides insight into the prevalence of Surgically Induced Astigmatism (SIA) in Saint Paul's Hospital Millennium Medical College (SPHMMC) and can aid in developing practical cataract surgery management guidelines. The study also identifies contributing factors and proposes corrective measures.

Objectives

General objective: The general objective of this study was to determine the amount and associated factors of surgically induced astigmatism after MSICS performed at the SPHMMC from April 2019 to February 2020.

Specific objectives

(i) To determine the amount of SIA after MSICS done at SPHMMC from April 2019 to February 2020.
(ii) To identify the associated factors of SIA after MSICS done at SPHMMC from April 2019 to February 2020.
(iii) To determine the pre-operative and postoperative keratometric astigmatism after MSICS done at SPHMMC from April 2019 to February 2020.

MATERIALS AND METHODS

Study setting: The study was conducted at SPHMMC's Ophthalmology Department, part of a teaching hospital in Ethiopia. SPHMMC provides eye care services for individuals with various eye diseases and has a team of ophthalmic professionals, including nurses, optometrists, residents, and consultants. Additionally, SPHMMC has an operating room designed explicitly for ocular surgeries.

Study design, study period, and population: A prospective longitudinal analytical study was conducted at SPHMMC from April 2019 to February 2020. The source population comprised all patients who visited the eye clinic during the study period. The study population consisted of all patients who had cataract surgery at the hospital. The study subjects were those who volunteered to participate.

Inclusion/Exclusion criteria: All patients who underwent MSICS in the study period were included. The following category of patients was excluded from the study:
(i) Subjects with previous intraocular surgery, e.g., keratoplasty, glaucoma, combined surgeries
(ii) Surgical techniques other than MSICS
(iii) Complicated cataract (with posterior synachae, with corneal opacity)
(iv) Patients aged less than 18 years
(v) Corneal ectasias (e.g., Keratoconus)
(vi) corneal opacity (pre-existing)
(vii) Pterygium
(viii) Surgeries with late postoperative complications (e.g., late endophthalmitis, CO, PBK, corneal ulcer)

Sampling technique: The sample size was calculated using the single proportion formula:

$$\text{Sample size } n_f = \frac{N\left(Z_{\alpha/2}\right)^2 p(1-p)}{d^2(N-1)+\left(Z_{\alpha/2}\right)^2 p(1-p)}$$

Z α/2 at 95% confidence Interval from Z table= 1.96

p = 45% Taken from previous studies done in Togo

d = absolute precision (0.05)

N = population size (800)

The sample size was found to be 283 after using a non-response rate of 10%.

A convenience non-probability sampling technique was used, and consecutive patients who have undergone MSICS in the study period and were not in the exclusion criteria were taken as study subjects.

Data collection procedure and instruments: A structured questionnaire was used to collect data during the pre-operative, intraoperative, and postoperative periods. Informed consent was obtained from all study participants before the surgery. Demographic data was collected through face-to-face interviews and medical records before the operation, while visual acuity was assessed using a Snellen "E" chart. Patients who did not meet the inclusion criteria were identified using slit-lamp biomicroscopy. Biometry was conducted using a keratometer (Carl Zeis) and an A-scan ultrasound (Compact Touch), and the SRK formula was used to calculate the power of the intraocular lens (IOL).

On the first postoperative day, the Snellen E chart was used for uncorrected visual acuity, and slit-lamp biomicroscopy was performed to detect early complications. In the 6th week, best-corrected visual acuity, keratometry, and slit-lamp biomicroscopy were conducted. A study subject underwent biometry twice - preoperatively and six weeks postoperatively - to calculate keratometric astigmatism using K-horizontal, K-vertical, and axis. SIA was calculated using SIA calculator software based on pre-operative and postoperative data[6].

Data was collected with the assistance of ophthalmic residents and an optometrist. The questionnaires were attached to the cards of the patients. Post-MSICS visual outcome was measured using the World Health Organization (WHO) post-cataract surgery visual outcome category as good (6/6-6/18), borderline (<6/18-6/60), or poor (<6/60 – LP)[7].

Data quality assurance: The questionnaire was pretested at SPHMMC's Department of Ophthalmology for adequacy and validity. Data collection was performed with the help of familiarized ophthalmic residents and an optometrist, and regular supervision was carried out to ensure the accuracy and completeness of the data.

Dependent variables: The dependent variable was surgically induced astigmatism.

Independent variables: The independent variables include age, sex, size of the incision, location of the incision, the configuration of the scleral incision, presence of side port, presence of sutures, and pre-operative VA.

Data processing and analysis: Data were analyzed using SPSS version 23, with descriptive analysis used to determine means, frequencies, and proportions of variables. Logistic univariate and multivariate regression analyses were used to determine factors associated with a confidence level of 95% ($p<0.05$), with a calculated p-value for clinically significant SIA. SIA was calculated using SIA calculator software version 2.1 by Dr. Saurabh Sawhney and Dr. Aashima Aggarwal[6].

Operational definitions

(i) *Surgically induced astigmatism:* Astigmatism caused by some degree of flattening of the corneal meridian at a right angle to the direction of the incision
(ii) *Clinically significant astigmatism:* Astigmatism, which is higher than 2D.
(iii) *Regular astigmatism:* Refractive power changes uniformly from one meridian to another[2].
(iv) *Irregular astigmatism:* When the two principal meridians are not perpendicular to each other[2].
(v) *With-The-Rule Astigmatism:* The vertical corneal meridian is steepest, and a correcting plus cylinder axis should be used at or near 90[2].
(vi) *Against-The-Rule astigmatism:* The horizontal meridian is steepest, and a correcting plus cylinder axis should be used at ornear 180[8].
(vii) *Oblique astigmatism:* Regular astigmatism in which the principal meridians do not lie at, or close to, 90° or 180° but instead lie near 45° or 1350[8].
(viii) *Postoperative complication:* Any complication identified after surgery and notified as immediate if within the 1st day or one week after surgery, early within 2-3 weeks after surgery, and late after one month.
(ix) *Keratometry:* The technique of measuring the radius of curvature of a small portion of the central cornea (3mm) using a keratometer[9].
(x) *Biometry:* Measurement of the size and lens power of the eye using ultrasound measurements and formulas[9].

Ethical considerations: The study obtained ethical clearance from the Institutional Ethical Review Board of SPHMMC and informed written consent was obtained from each participant. The data collector read the written consent to the patients, and those who gave consent were included. Only medical record numbers - not full names - were used to maintain confidentiality when completing the questionnaires.

RESULTS

Demographic background: This study included 240 subjects aged 40-85 years, with a mean age of 63.1 (SD±9.89). Of the subjects, 139 (57.9%) were female, and 101 (42.1%) were male. The majority were retired (22.5%) or housewives (36.7%) and could read and write (56.7%). Most subjects resided in Addis (52.5%), followed by the Oromia region. The uncorrected pre-operative visual acuity ranged from 6/60-LP. Five percent had 6/60, 45.9% had in the range of CF 3m to CF in front, 36.7% had HM, and 12.5% had LP.

The mean preoperative keratometric (k) readings were: K1 (42.89D±1.69D), K2 (43.99D±1.68D), and axis (86.33±44.2). Most surgeries were performed by consultant ophthalmic surgeons (72.9%), with the remaining 27.1% by ophthalmology residents. The tunnel site was superior in 93.8% of surgeries and temporal in 6.2%. The tunnel configuration was a frown shape in 65.4% of surgeries and straight in 34.6%. The mean tunnel size was 6.43 (SD±0.41mm), ranging from 5-8mm, with 74.17% of surgeries having tunnel sizes between 5-6.5mm and 25.83% between 6.6-8mm. Side ports were present in 34.6% of surgeries, with the side port site 90 degrees from the tunnel site in 92.8%, less than 90 degrees in 6.0%, and greater than 90 degrees in 1.2%.

Some 13.8% of surgeries used Nylon sutures, with 90.9% interrupted and 9.1% continuous. The PMMA posterior capsular lens was used in all surgeries except

one which used AC IOL. The IOL power ranged from 7-27D (mean=21.29D, SD±2.44D).

Some 21.7% of subjects had intraoperative complications, with posterior capsular tear being the most common (10%), followed by posterior capsular tear with vitreous loss (5.4%). Premature entry, descemet strip, and iris damage were also observed during the surgeries. A total of 76.3% of the study subjects had good Best Corrected Visual Acuity (BCVA) after six weeks post-operation, while 22.5% had a borderline outcome, and only 1.3% had a poor outcome (Table 1).

Table 1: Postoperative BCVA at 6th-week post-op of 240 MSICS done at the SPHMMC, 2019/20

Visual outcome	SIA		Total (N%)
	≤ 2D	>2D	
Good (6/6-6/18)	156	27	183 (76.3)
Borderline (<6/18-6/60)	35	19	54 (22.5)
Poor (<6/60 – LP)	2	1	3 (1.3)
Grand Total	193	47	240 (100)

Preoperatively, 91.3% of subjects had With The Rule (WTR) astigmatism, 1.3% had Against The Rule (ATR) astigmatism, 3.3% had oblique astigmatism, and 4.2% had no astigmatism. Post-surgery, 71.7% had WTR astigmatism, 21.3% had ATR astigmatism, 5.8% had Oblique Astigmatism (OA), and 1.3% had no astigmatism.

Table 2: Pre-operative and postoperative keratometric astigmatism of 240 MSICS done at the SPHMMC, 2019/20

Keratometric astigmatism	Pre-operative (N%)	Postoperative (N%)
WTR	219 (91.3)	172 (71.7)
ATR	3 (1.3)	51 (21.3)
OA	10 (4.2)	14 (5.8)
No	10 (4.2)	3 (1.3)

Clinically significant SIA was 19.6%. Surgically induced astigmatism ranged from 0 - 5.62D. The mean SIA was 1.38D (SD±0.92D) with an axis of 88.12(SD±56.74).

Significant associations with surgically induced

Table 3: Factors associated with surgically induced astigmatism among 240 MSICS done at the SPHMMC, 2019/2020

Variables	SIA		COR (95% CI)	P-value	AOR (95%CI)	P-value
	Clinically Significant	Clinically Insignificant	Univariate Logistic Regression		Multivariate Logistic Regression	
Age (years)						
40-60	23	80	1			
61-80	23	112	0.29(0.02-4.78)	0.39		
80-85	1	1	0.21(0.01-3.40)	0.27		
Sex						
Male	17	84	1			
Female	30	109	0.74(0.38-1.42)	0.36		
Tunnel size						
5-6.5mm	0	2	1			
6.6-8mm	47	191	0.02(0.01-0.08)	0.000	0.02(0.003-0.09)	0.000*
Scleral tunnel site						
Superior	39	186	1			
Temporal	8	7	0.18(0.06-0.54)	0.002	0.87(0.12-6.29)	0.89
Scleral tunnel configuration						
Frown	26	131	1			
Straight	21	62	0.59(0.31-1.12)	0.11	0.77(0.29-2.03)	0.60

Variables	SIA		COR (95% CI)	P-value	AOR (95%CI)	P-value
	Clinically Significant	Clinically Insignificant	Univariate Logistic Regression		Multivariate Logistic Regression	
Presence of sutures						
No	25	182	1			
Yes	22	11	0.07(0.03-0.16)	0.00	0.07(0.01-0.45)	0.005*
Presence of a side port						
No	39	123	1			
Yes	8	70	2.63(1.20-5.74)	0.02	2.49(0.91-6.83)	0.08
Pre-op VA						
6/60	2	9	1			
<6/60-LP	45	184	0.91(0.19-4.35)	0.91		
Intraoperative complications	23	80				
No	1	1	1			
Yes	23	112	0.20(0.1-0.4)	0.000	1.03(0.20-5.25)	0.98

*Statistically significant

astigmatism were found for tunnel size and the presence of suture, as determined through univariate and multivariate logistic regression analyses. Other variables, including tunnel site, side port, tunnel configuration, and intraoperative complications, were also significant in univariate analysis but did not remain significant in multivariate analysis.

DISCUSSION

The study found that 76.3% of subjects had 'good,' 22.5% had 'borderline' and 1.3% had 'poor' best-corrected visual acuity six weeks after surgery, below the WHO target outcome for cataract surgery of 80% for visual acuity under the 'good' category[10].

Mean corneal SIA was higher in the current study (1.38±0.92D) compared to a study in Nepal published in 2017 (0.84±0.80D). The clinically significant SIA in the present study was 19.6%, slightly higher than the 17.8% reported in the Nepal study for SIA >1.5D[11]. The figures were also higher when compared to a study on the prevalence of corneal astigmatism in Northern Ireland published in 2016. The mean corneal astigmatism in the study was 1.09 ± 0.83D, and the prevalence of SIA >2D was 11.6%[12]. This can be due to the difference in the intraoperative techniques during MSICS in the different setups, which could be related to the surgeon factor or the instruments used.

Postoperative against the rule astigmatism significantly increased from 1.3% to 21.3% in the present study due to the flattening effect of the superior incision site. A similar study in Ghana published in 2016 also showed a statistically significant increase in postoperative corneal astigmatism compared to pre-operative astigmatism in patients with pre-operative Against-The-Rule astigmatism who underwent superior approach MSICS[13].

A 2020 Indian study found that larger incisions induced more astigmatism in tunnel construction during small incision cataract surgery. This is similar to the current study's finding that clinically significant SIA was associated with a large tunnel size[14].

In a Nigerian study, ECCE with PC-IOL and sutures had the highest surgically induced corneal astigmatism. Similarly, the current study found a significant association between the presence of sutures and clinically significant SIA[4].

The tunnel configuration was not associated with clinically significant SIA in this study. However, a study conducted in India on surgically induced astigmatism in various incisions in manual small incision cataract surgery found that the mean SIA was minimal with the Inverted V incision, which was statistically significant[1]. This difference may be due to the limited types of tunnel configurations used in the current study compared to the varied incisions in the Indian study.

This study found no significant association between the site of the scleral tunnel and clinically significant SIA. However, a study conducted in India and published in 2019 found that the temporal scleral incision group had less SIA compared to the superotemporal scleral incision group, which was statistically significant with $P < 0.001$[15]. The difference in the pre-operative keratometric astigmatism of the subjects in the two studies might have contributed to the dissimilarity in the induced astigmatism by the incision site. Also, the small number of temporal incisions performed in this study could have played a role.

CONCLUSIONS

(i) Scleral tunnel size and the presence of scleral wound sutures were found to be critical associated factors with clinically significant SIA.
(ii) Knowing pre-operative astigmatism and practicing the propermanual small incision cataract surgery technique can improve the postoperative visual acuity and reduce the spectacle burden on patients.

RECOMMENDATIONS

(i) Whenever it is required to put a suture at the end of surgery as part of the management of intraoperative complications, it is always important to remove the suture at the third postoperative visit before sending patients for refraction. Refraction of all postoperative patients at the third visit should also be mandatory.
(ii) We recommend that the scleral tunnel size be measured by a caliper, especially during the beginning periods of doing MSICS, and minimizing the tunnel size is always important.
(iii) There will be a flattening effect of the incision site to the meridian perpendicular to it. Therefore, considering pre-operative astigmatism and placing incisions on the steeper corneal meridian is recommended.

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Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests: The authors declare that they have no competing interests.

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Prevalence, clinical profile, and factors associated with diabetic retinopathy in south-Western Uganda: a population-based study

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ABSTRACT

Background: Diabetic Retinopathy (DR) is one of the most common complications of Diabetes Mellitus (DM), and it is a leading cause of vision loss in the working-age population globally.
Objective: This study aimed to determine the prevalence of DR at a population level, the clinical profile, and the factors associated with DR in Southwestern Uganda.
Methods: This was a secondary analysis of data generated by a large-scale four-year community screening program through the "Lions Diabetic Retinopathy Screening and Treatment Project for Southwestern Uganda." Patients with known DM underwent DR screening, and fundus photography was performed on all patients. An ophthalmologist subsequently graded these photographs. Patients with gradable fundus images were included for analysis.
Results: Of the 1,515 diabetic patients who were screened, 1,120 were considered for analysis. The majority were female and had a family history of DM. The overall prevalence of DR was 15.1% (95% CI, 11.9 - 18.9), of which 63% had referable DR and 20.2% had sight-threatening DR. Factors associated with any DR were: duration of DM (AOR 2.1 [95% CI 1.3- 3.5]), poor glycemic control (AOR 1.9 [95% CI 1.2 - 3.0]), and hypertension (AOR 2.0 [95% CI 1.3-3.4]).
Conclusion: This study has provided the baseline prevalence of DR in Southwestern Uganda and the proportion of sight-threatening DR that can be used for planning service delivery in the region.

Key words: Diabetic retinopathy, Prevalence, Clinical profile, Southwestern Uganda

INTRODUCTION

Diabetic Retinopathy (DR) is one of the most common complications of Diabetes Mellitus (DM) and the leading cause of vision loss in the working-age population worldwide[1,2]. Uncontrolled longstanding hyperglycemia generates advanced glycation end products, leading to retinal ischemia, microvascular damage, haemorrhage, and fluid leakage in the retinal tissue, which can progress and cause vision loss if left untreated[3,4]. DR is broadly classified into Non-Proliferative Diabetic Retinopathy (NPDR)(with three stages of severity), Proliferative Diabetic Retinopathy (PDR), and Diabetic Macular Edema (DME)[5].

The global prevalence of DR is estimated at 22.27% for any DR, 6.17% for visual-threatening DR, and 4.07% for DME[6]. A systematic review of population-based studies from countries in Africa showed the prevalence of DR, PDR, and any diabetic maculopathy in patients with diabetes was 30.2 to 31.6%, 0.9 to 1.3%, and 1.2 to 4.5%, respectively[7]. These estimates are expected to rise, considering the rapidly increasing prevalence of DM in Africa and the increasing life expectancy of DM patients. The International Diabetes Federation has estimated that 24 million adults live with DM; this number is predicted to increase by 129% to 55 million people by 2045[8]. In Uganda, about 1.4% of the total population has DM, according to 2014 data[9]. However, the prevalence of DR is not known. Our previous hospital-based work among DM patients found that among established DM clinic patients, 12.5% had any DR[10]. Therefore, this study aimed to determine the prevalence of DR, the clinical profile, and factors associated with DR at the population level.

MATERIALS AND METHODS

Ethics: Institutional review board approval was granted by the Mbarara University of Science and Technology (MUST) Research and Ethics Committee (ref: MUST-2021-224). This study adhered to the strictest data security and privacy standards and the general principles of the Declaration of Helsinki.

Design: This was a secondary analysis of data generated through the "Lions Diabetic Retinopathy Screening and Treatment Project for Southwestern Uganda," a large-scale four-year community screening program that was funded by the Lions Clubs International Foundation (LCIF, Oak Brook, United States) and the Latter-day Saints Charities (LDS, Salt Lake City, United States). This project aimed to raise awareness about DM and DR, offer screening for DM and DR, and provide appropriate referrals for patients with referable DR to receive care. Referable diabetic retinopathy was defined as any NPDR more severe than mild NPDR, which necessarily includes PDR and DME[11]. A detailed protocol for this project was recently published by Arunga *et al*[12]. Through mass media campaigns and the existing high-volume DM clinics, DM patients were invited to a designated screening site for an eye examination, including fundus photography, by well-trained Fundus Camera Technicians (FCT).The technicians were trained to identify any DR and could provide immediate feedback to the patients when they were found to have any DR. Appropriate counseling and referral to Mbarara University and Referral Hospital Eye Centre (MUHREC) were done by a health worker if a patient had changes of moderate NPDR or worse.

Data collection procedure: Data on demographics, family history of DM, duration of DM, height, weight, blood sugar level, blood pressure, visual acuity, and spot diagnosis at the site were collected during screening. Fundus photography was then captured using a 3nethra Classic fundus camera (Forus Health Pvt Ltd, Bengaluru, India). The screening team consisted of a registration clerk; a nurse to measure anthropometry, blood sugar, and other vitals; an experienced Ophthalmic Clinical Officer (OCO) to perform rapid eye examinations, offer counseling and referral; and an FCT to capture 40° fundus photos. Participants underwent fast eye examination consisting of visual acuity testing using the Snellen chart, anterior segment examination with a penlight, and non-dilated fundoscopy with the direct ophthalmoscope conducted by an OCO. Patients without media opacity underwent fundus photography. At the end of the screening day, the technicians would return with the cameras to the base hospital MUHREC and upload images to the database. The principal investigator later examined all images for DR grading. From July 2019 to January 2021, 1,710 diabetic patients were screened for DR, and completed data from this period were used for analysis.

Case definition: For purposes of this analysis, any DR had retinal changes such as microaneurysms, dot-blot haemorrhages, cotton wool spots, hard exudates, venous beading, Intraretinal Microvascular Anomalies (IRMA), Neovascularization of the Disc (NVD) or Neovascularization Elsewhere (NVE), sub-hyaloid haemorrhage, vitreous haemorrhage, and macular edema[5].

Inclusion and exclusion criteria: Any adult aged 18 years and older with DM who was screened at one of the screening sites during the screening period with a gradable screening fundus photo was included for analysis.

Variables: The primary outcome measure was any DR as determined by the grade of DR from fundus photography: mild, moderate, and severe NPDR, PDR, and DME, according to the International Council of Ophthalmology (ICO) classification[5]. The independent variables included age, sex, family history of DM, duration of DM, treatment of DM, Body Mass Index (BMI), blood sugar control (random and fasting blood glucose level), hypertension, and Vertical Cup-to-Disc Ratio (VCDR). VCDR was established by Forus Health's built-in measurement tool, where trained photographers marked the area considered the optic nerve head.

Data analysis: The unit of analysis was each individual. For grading and case definition, the more severely affected eye was considered for patients with bilateral DR. Better eye and worse eye Visual Acuity (VA) was classified into mild, moderate, severe visual impairment, and blind according to WHO classification[13]. Glycemic control was deemed suitable if random blood glucose < 11.1 mmol/L or fasting blood glucose < 7.8 mmol/L[14]. Hypertension was defined as systolic and diastolic blood pressure > 140/90. The VCDR was further characterized as normal (VCDR < 0.5), borderline (VCDR 0.50 – 0.59), and glaucoma suspect (VCDR > 0.6). Methods used include summary descriptive statistics, prevalence proportions by stratified sampling design and age-standardization, and multivariable logistic regression using stepwise forward elimination of variables chosen by crude univariate analysis to retain value with $p < 0.1$ with significance deemed as associations with $p < 0.05$. The statistical software package for these analyses was STATA 17.0 (Stata Corp, College Station, United States).

RESULTS

There were 1,515 DM patients eligible, with 414 patients excluded due to missing fundus images (278 individuals) and ungradable images (117); thus, 1,120 individuals with 2,240 eyes were available for analysis. The baseline characteristics are presented in Table 1. The mean age was 56.1 (standard deviation 12.5) years with a female-to-male ratio of 4:1. About 60% of participants had a family history of DM. The median duration of the disease was 4 years (interquartile range of 2-10, full range of 1- 42). Almost half of the participants had good glucose control (58%). About 80% of patients had normal vision in the better-seeing eye.

Among adults with DM, the prevalence of any DR, as determined by fundus photography, was 15.1% (95% CI, 11.9 - 18.9). Table 2 displays the prevalence proportions

Table 1: Baseline characteristics of individuals included for analysis (n = 1120)

	Female n (weighted %) (n = 855 individuals)	Male n (weighted %) (n = 265 individuals)
Age (years)		
18 - 49	233 (27.2)	77 (29.1)
50 - 59	264 (30.9)	82 (30.9)
60 - 69	234 (27.4)	62 (23.4)
> 70	124 (14.5)	44 (16.6)
Occupation		
None	18 (8.6)	95 (14.8)
Peasant	107 (50.9)	443 (68.9)
Small business owner	24 (11.4)	54 (8.4)
Professional	61 (29.1)	51 (7.9)
Family history of diabetes mellitus	132 (50.4)	513 (60.8)
Duration of diabetes mellitus (years)		
0 - 5	149 (56.2)	470 (55.0)
6 - 10	60 (22.7)	194 (22.7)
> 10	56 (21.1)	191 (22.3)
Treatment for diabetes mellitus		
No pharmacotherapy	28 (10.6)	98 (10.5)
Oral anti-hyperglycemic	189 (71.3)	667 (78.0)
Insulin	38 (14.3)	67 (7.8)
Orals and insulin	10 (3.8)	23 (2.7)
Body mass index (kg/m^2) (n = 333 individuals)		
Normal (< 24.9)	81 (30.8)	29 (43.3)
Overweight (25 - 29.9)	95 (36.1)	24 (35.8)
Obese (> 30)	87 (33.1)	14 (20.9)
Glycemic control by blood glucose (mmol/L) (n = 808 individuals)		
Good (< 11.1 random, < 7.8 fasting)	329 (54.6)	120 (58.2)
Poor (> 11.1 random, > 7.8 fasting)	273 (44.4)	86 (41.8)
Hypertension (blood pressure > 140/90)		
(n = 888 individuals)	114 (43.0)	381 (44.6)
Visual acuity of the better eye		
Normal (> 6/12)	184 (70.8)	582 (68.1)
Mild visual impairment (6/12 - > 6/18)	28 (10.8)	102 (11.9)
Moderate visual impairment (6/18 - > 6/60)	46 (17.7)	147 (17.2)
Severe visual impairment (6/60 - > 3/60)	2 (0.8)	22 (2.6)
Blind (< 3/60)	0 (0.0)	2 (0.2)
Vertical cup-to-disc ratio (n = 985 individuals)		
Normal (< 0.50)	215 (90.3)	692 (92.6)
Borderline (0.50 - 0.59)	10 (4.2)	34 (4.6)
Large/glaucoma suspect (> 0.60)	13 (5.5)	21 (2.8)

among different stratifications. There was no significant difference in the prevalence of any DR between males and females ($\rho = 0.586$) or sight-threatening DR ($\rho = 0.605$), as defined by severe NPDR and DME. Mbarara District had the lowest prevalence of any DR at 12.3% (9.7 - 15.4) ($\rho < 0.001$). Of individuals with DR, 63% had referable retinopathy (moderate NPDR [36.7%], severe NPDR [5.9%], PDR [11.3%], and DME [8.9%]. Sight-threatening DR represented 20.2% of any DR. There was no significant difference in DR severity when stratifying between male and female sex ($\rho = 0.869$).

Figure 1: Representative fundus photographs of the severity of DR

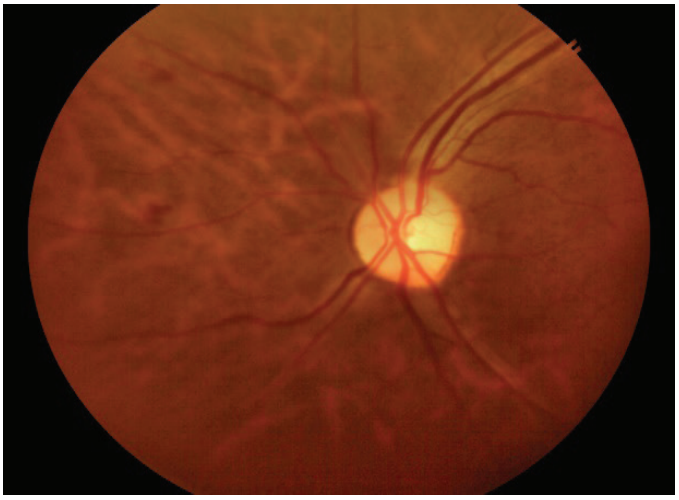

Figure 1.1: Mild NPDR: microaneurisms

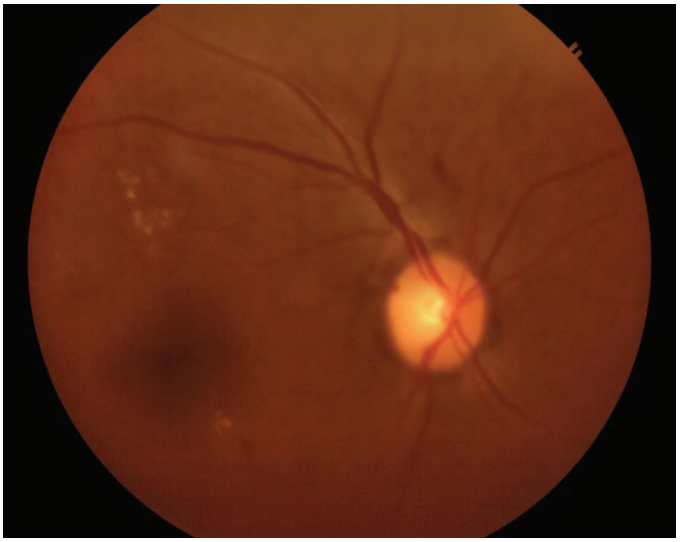

Figure 1.2: Moderate NPDR: exudates, MA, IR haemorrhage

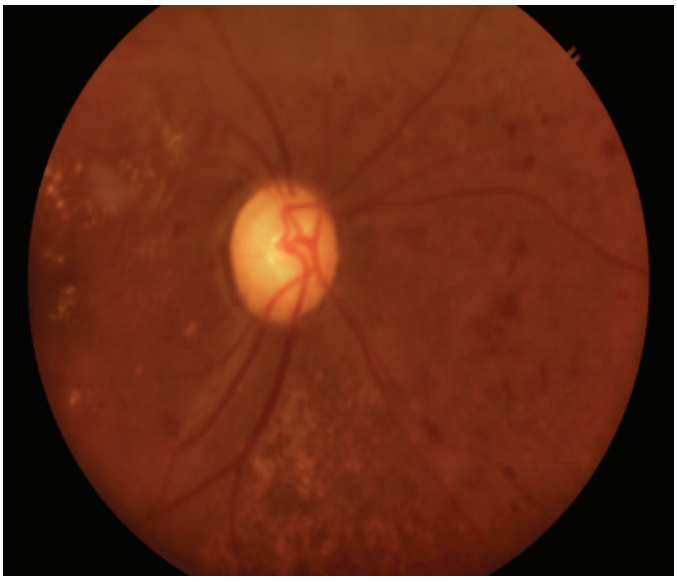

Figure 1.3: Severe NPDR: Venous beading

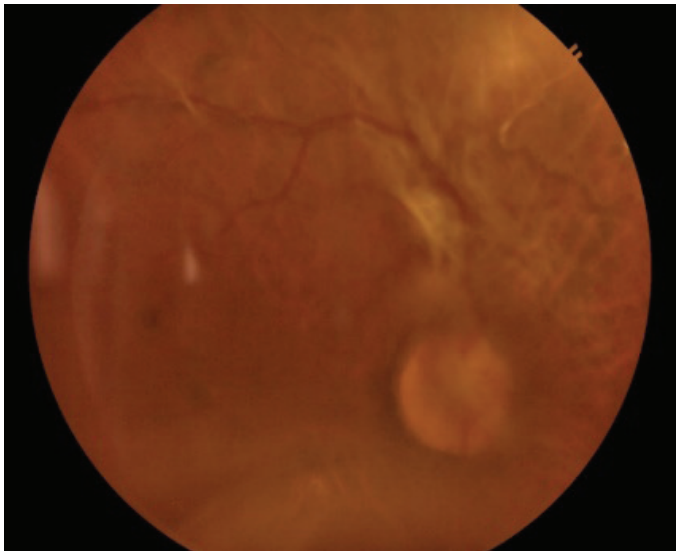

Figure 1.4: PDR: fibrovascular membranes

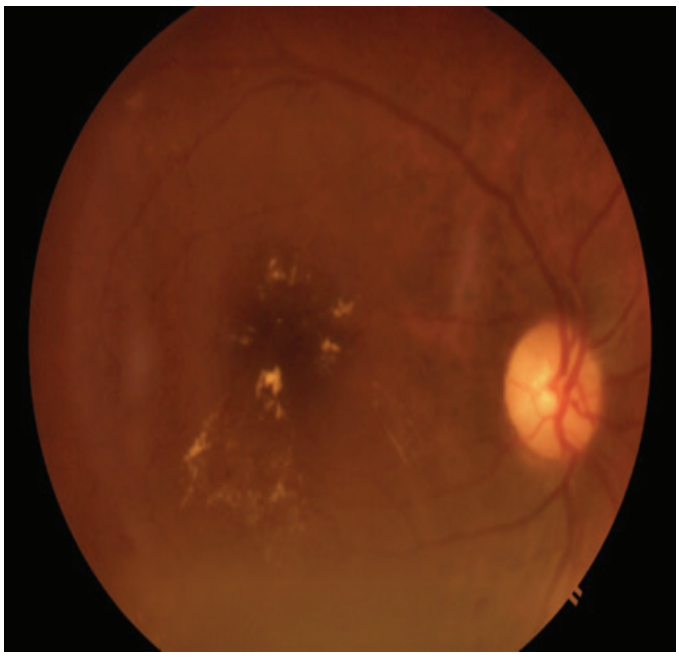

Figure 1.5: DME

Table 2: Prevalence of diabetic retinopathy, age-adjusted (N = 1120 individuals)

	Prevalence proportion (95% CI)	Estimated individuals in 2020 (95% CI)
Any DR: general adult population	15.1% (11.9 - 18.9)	41,872 (33,092 - 52,479)
Vision threatening DR: general adult population	3.0% (2.0 - 4.6)	8424 (5541 - 12,737)
Any DR: female	14.7% (11.8 - 18.3)	21,648 (17,306 - 26,852)
Any DR: male	16.2% (10.7 - 23.9)	21,180 (13,921 - 31,209)
Any DR: Bushenyi District	24.2% (12.3 - 42.3)	401 (203 - 700)
Any DR: Kabale, Ntungamo, Rukungiri Districts	15.0% (10.2 - 21.5)	1123 (766 - 1607)
Any DR: Kabarole District	13.1% (9.6 - 17.5)	294 (216 - 395)
Any DR: Masaka District	27.5% (20.7 - 35.6)	616 (463 - 798)
Any DR: Mbarara District	12.3% (9.7 - 15.4)	320 (252 - 402)

CI: confidence interval, DR: diabetic retinopathy

Figure 2: Displays the breakdown of DR severity in this study

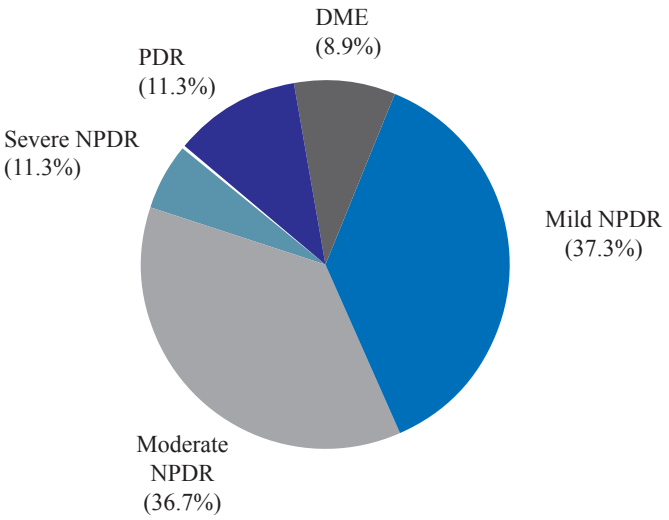

Table 3 shows factors associated with DR among DM patients. The multivariate model shows the main factors associated with any DR were: duration of DM with an Adjusted Odds Ratio (AOR) of 2.1 (95% CI 1.3 -3.5), poor glycemic control (AOR 1.9, 95% CI 1.2 - 3.0) and hypertension AOR 2.0 (95% CI 1.3 -3.4).

Table 3: Factors associated with any diabetic retinopathy (N = 1120 individuals)

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI)	P value
Age	0.99 (0.98, 1.10)	0.98		
Female sex	0.92 (0.63, 1.35)	0.70		
Occupation				
None	Base	0.64		
Peasant	0.75 (0.44, 1.27)			
Small business owner	0.65 (0.28, 1.46)			
Professional	0.89 (0.45, 1.77)			
Family history of diabetes mellitus	1.00 (0.71, 1.40)	0.98		
Duration of diabetes mellitus (years)				
0 - 5	Base	0.0068		0.010
6 - 10	1.04 (0.63, 1.72)		1.37 (0.71, 2.63)	
> 10	1.80 (1.24, 2.60)		2.15 (1.30, 3.55)	

Variable	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P value	Adjusted odds ratio (95% CI)	P value
Treatment for diabetes mellitus				
None	Base	0.32		0.80
Oral anti-hyperglycemic	1.56 (0.20, 12.31)		2.62 (0.29, 23.78)	
Insulin	1.97 (0.23, 16.47)		2.58 (0.26, 25.79)	
Orals and insulin	3.20 (0.35, 29.00)		2.90 (0.26, 32.60)	
Body mass index (kg/m^2)				
Normal (< 24.9)	Base	0.79		
Overweight (25 - 29.9)	0.78 (0.39, 1.58)			
Obese (> 30)	0.86 (0.42, 1.76)			
+Poor glucose control	1.62 (1.10, 2.38)	0.014	1.96 (1.25, 3.04)	0.0030
Hypertension				
(blood pressure > 140/90)	1.50 (1.03, 2.17)	0.031	2.08 (1.28, 3.37)	0.0030
Vertical cup-to-disc ratio				
Normal (< 0.50)	Base	0.98		
Borderline (0.50 - 0.59)	0.90 (0.37, 2.18)			
Large/glaucoma suspect (> 0.60)	0.98 (0.37, 2.60)			

+Poor glucose control was defined as random blood glucose level > 11.1 mmol/L or fasting blood glucose level > 7.8 mmol/L

DISCUSSION

This is the first population-based study on DR conducted in Uganda. It showed the prevalence of any DR among patients with DM was 15.1%, among whom 20.2% had sight-threatening DR. Using the most recent national population estimates from the Uganda Bureau of Statistics[15] and the 1.4% as mentioned above prevalence of DM among adults, these proportions extrapolate to approximately 41,872 individuals (95% CI, 33,092 - 52,479) with DR and 8,424 individuals (95% CI, 5541 - 12,737) with sight-threatening DR.

The 15.1% proportion is likely a more conservative estimate considering that we only used gradable fundus photographs to define DR. Other population-based studies from sub-Saharan Africa have reported higher proportions. For example, one population-based study conducted in Tanzania reported a prevalence of 27.9% for any DR and 16.1 for any maculopathy among those with established DM[16]. Another population-based study conducted in Zambia reported the prevalence of high as three times our finding (52%)[17]. Variations among different types of surveys, diverse severity among different settings, and lack of uniform case definitions contribute to such broad ranges for prevalence. A systematic review of studies on the prevalence of DR in sub-Saharan Africa reported high variability of results ranging from 30.2 - 31.6% in population-based studies and 7.0 - 62.4% in hospital-based screening[7]. As predicted, these prevalence proportions were highly heterogeneous, but they provide the context for the prevalence proportion determined by this study. Our finding may also underestimate the prevalence as these patients were accumulated among different geographic locations through one-time screening, compared with most reported studies using longitudinal data from well-established DR screening programs. Another factor is individuals with severe visual impairment were likely not to access the screening site due to their disability and inability of social support to help mobilize them. Moving forward, as this project established screening programs in the communities throughout southwestern Uganda, those with severe VI will eventually be captured and represented. Between the previous hospital-based study in Mbarara and this community-based study, the prevalence of any DR remained static at 12.5% versus 12.3% in this study, which included people with previously undiagnosed DM. Mbarara is the most developed District in this region, with a significantly higher density of healthcare providers and health units. These factors certainly contribute to better DM control at the population level, leading to a lower prevalence of DR.

In this study, the overall proportion of sight-threatening DR was 20.2%. Although our finding seems to be lower than other published studies in sub-Saharan Africa, this suggests a modest estimate of nearly 19,000 people who require Pan-Retinal Photocoagulation (PRP), multiple serial anti-VEGF injections, and pars plana vitrectomy for non-clearing vitreous haemorrhage and tractional retinal detachment. In most cases, these interventions are not easily accessible and not affordable. Access to appropriate DR treatment remains the most significant challenge within the region. Distance from the specialized eye care facility, cost of the treatment, and resources limited facilities render access to eye care more complicated. Therefore, emphasis should be made on strengthening screening programs in the community, which will allow early detection of DR, timely referral, and capacity building of treatment centers to provide procedural and surgical interventions, especially PRP and anti-VEGF.

In our study, we found that the duration of DM (>10 years), poor glycemic control, and hypertension were significantly associated with DR among DM patients in Southwestern Uganda. Although these are not revelations, they reaffirmed what has been reported in other major landmark population-based studies[17-19]. This reaffirms the importance of primary care and access to essential medications when pharmacotherapy is indicated. The patients not on treatment for DM were not due to lack of treatment indication, but they either did not know they had DM or could not access pharmacotherapy. Collaboration among clinicians managing highly prevalent conditions, such as DM and hypertension, and eye health providers will be vital to meeting timely referral goals and sustainable long-term DR screening programs.

The limitations of this study included a lack of optical coherence tomography imaging to identify clinically undetectable macular edema, inability to grade DR among those with media opacities, and inability to mobilize individuals with severe visual impairment given the short-term and those with severe illness, and the one-time screening nature of this project. These limitations likely lead to an underestimation of the prevalence. Nevertheless, this is the first population-based study on DR in Uganda and provides estimates that show the magnitude of the disease burden and potential unmet needs. These results ought to allow the patients, government, non-governmental organizations, academia, and relevant stakeholders to set goals for the prevention of DR, treatment of early stages of DR, and we would argue treatment of the advanced complications of DR as well to restore sight and provide some quality of life.

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Reliability of clinical signs in diagnosis of fungal keratitis

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ABSTRACT

Objective: To determine clinical signs predictive of fungal Keratitis (MK) in Uganda.
Methods: We prospectively recruited patients presenting with MK at two main eye units in Southern Uganda between December 2016 and March 2018. We collected information on clinical history and presentation and microbiology. Clinical signs predictive of a positive microbiological diagnosis of fungal keratitis were analyzed in a multi variable logistic regression model.
Results: Three hundred and thirteen individuals were enrolled. Median age was 47 years (range 18-96 years) and 174 (56%) were male. Trauma was reported by 29% and use of traditional eye medicine by 60%. Majority presented with severe infections (median infiltrate size 5.2 mm); 47% were blind in the affected eye (vision <3/60). Microbiology results were available in 265/313 (84.7%) participants. Overall, most infections were fungal (49%), 10% were bacterial and 4% were mixed (fungal and bacterial). Ninety-seven (37%) of the corneal scrapping samples were negative on both microscopy and culture. Presence of a slough (aOR 3.58, 95% CI [1.60-8.04], p=0.002), a serrated infiltrate margin (aOR 1.58, 95% CI [1.00-2.51], p=0.051), satellite lesions (aOR 2.90, 95% CI [1.65-5.11], p<0.0001) and a hypopyon (aOR 3.24, 95% CI [1.78-5.90], p<0.0001) were associated with a positive microbiology result for fungal keratitis.
Conclusion: This study conducted in a predominantly African population provided clues to support clinicians in making a diagnosis of fungal keratitis in settings where there is no microbiology support.

Key words: Microbial keratitis, Fungal keratitis, Clinical diagnosis, Microbiology

INTRODUCTION

Microbial Keratitis (MK) can be caused by a range of pathogens including; bacteria, viruses, protozoa, and fungi. It is characterized by acute or sub-acute onset of pain, conjunctival hyperemia and corneal ulceration with a stromal inflammatory cell infiltrate[1].

MK has been described as a "silent epidemic", which leads to substantial morbidity, related to blindness, pain and stigma[2]. It is the leading cause of unilateral blindness after cataract in tropical regions estimated at 2 million cases of monocular blindness per year[3]. MK frequently leads to sight-loss from dense corneal scarring, or even loss of the eye, especially when the infection is severe and/or appropriate treatment is delayed.

Our previous work in Uganda showed that the majority of MK is caused by filamentous fungi[4]. Compared to other infections, patients with Fungal Keratitis (FK) were more likely to have a worse outcome[4]. A good outcome depends on early identification of the causative organism so that appropriate treatment can be initiated[5,6]. However, in many Low and Middle-Income Countries (LMIC), good microbiology diagnostic support is not readily available[7]. Even in good "Centres of excellence", a microbiology diagnosis is negative in about 1/3 of the patients[4,8,9].

In many settings therefore, clinicians need to rely on clinical signs to confidently make a diagnosis. Reports from India and Ghana have described clinical signs that are predictive of fungal/bacterial keratitis with variable rates of reliability[9–11]. In this report, we describe the clinical signs that were predictive of a microbiology diagnosis of fungal keratitis in a cohort in Uganda.

MATERIALS AND METHODS

Ethical statement: This study followed the tenets of the Declaration of Helsinki. It was approved by the London School of Hygiene & Tropical Medicine Ethics Committee (Ref 10647), Mbarara University Research Ethics Committee (Ref 10/04-16) and Uganda National Council for Science and Technology (Ref HS-2303). Written, informed consent in the local language, was obtained before enrolment. If the patient was unable to read, the information was read to them, and they were asked to indicate their consent by application of their thumbprint, which was independently witnessed.

Study design and setting: In this cohort, we prospectively enrolled patients with MK that presented to Ruharo Eye Centre (REC) and Mbarara University and Referral Hospital Eye Centre (MURHEC) from December 2016 to March 2018. These are the two tertiary eye hospitals in Mbarara, Uganda.

Study participants: MK was defined as loss of corneal epithelium (of at least 1mm diameter) with underlying stromal infiltrate, associated with any or all signs of inflammation (conjunctival hyperemia, anterior chamber inflammatory cells, +/- hypopyon)[12]. We excluded those not willing to participate, those not willing to return for follow-up, pregnant women, lactating mothers, and those aged below 18 years.

Assessment: We documented demographic information and ophthalmic history, presenting Log MAR (Logarithm of Minimum Angle of Resolution) visual acuity at 2 meters in a dark room was measured using Peek Acuity software[13]. Participants were examined with a slit lamp to assess the anterior segment using a structured protocol, including eyelid assessment, corneal ulcer features, anterior chamber (flare, cells, hypopyon shape and size) and perforation status. Infiltrate size was determined from the greatest diameter of the infiltrate (major axis) and the widest perpendicular diameter (minor axis)[12]. The final infiltrate size was then derived as the geometric mean of these two diameters[12]. The same was repeated after fluorescein staining of the ulcer to determine epithelial defect sizes. High-resolution digital photographs with and without fluorescein staining were taken with a Nikon SLR 7200 digital camera with Macro lens.

Corneal scrape specimens were collected from the ulcer at a slit lamp or an operating microscope, using 21G needles after application of a proxymetacaine (minims) anaesthetic eye drops. Samples underwent processing for the Gram stain, Potassium Hydroxide [KOH] stain, Calcofluor White [CFW] stain and direct inoculation on culture media (Sheep's Blood Agar [BA], Chocolate Agar [HBA], Potato Dextrose Agar [PDA] and Brain Heart Infusion broth [BHI]).The choice of microbiological investigations and culture media used was to maximise isolation of fungus and bacteria.

Two sterile corneal swab samples were taken for pan fungal gene sequencing at a reference laboratory at Kilimanjaro Christian Medical Centre, Moshi, Tanzania. The number of corneal samples were dependent on how much material could be safely scraped from the cornea. The order was samples for microscopy, agar, broth and finally corneal swabs.

Microscopy, culture and antimicrobial sensitivity work was done at the Mbarara University Department of Microbiology. The technician underwent initial training in ocular microbiology at the Aravind Eye Hospital System, Department of Ocular Microbiology in Madurai, India and had a site supervision visit by a mycologist from the London School of Hygiene & Tropical Medicine. Immediate CFW staining was also done in the side lab at MURHEC on a fluorescein microscope (Zeiss Primostar ILED) by the attending ophthalmologist. Agar plates and broths were incubated and read daily at 35-37°C for bacteria for up to 7 days and at 25°C for up to 21 days for fungi. Organism identification and sensitivity testing (MIC/zone of inhibition) were performed using standard microbiological techniques. We followed a previously described approach for reporting positive microbiology results[8]. Briefly, bacteria were identified using routine biochemical identification tests. Identification of fungi was according to the macroscopic appearance of cultures on potato dextrose and microscopic appearance of conidia and spore bearing structures. Positive culture was growth at the site of inoculation or growth on one solid medium consistent with microscopy; or semiconfluent growth at the site of inoculation on one solid medium (if bacteria); or growth of the same organism on repeated scraping. If, by microscopy, hyphae were observed in corneal tissue, but failed to grow in culture, the causative organism was reported as fungal.

Analysis: Data were analyzed in STATA v14.The outcome of interest in this analysis was a positive microbiology result of fungal keratitis. A logistic regression modelling was done for baseline clinical features associated with a positive microbiology result for fungal keratitis. Variables with a p-value less than 0.05 were initially included in the multivariable model. A backward stepwise approach was then used until only the variables with a p-value of less than 0.05 were retained. Adjusted ORs were reported for the final model.

RESULTS

Participants: The baseline characteristics of the patients have been previously presented[14]. Briefly, the median age was 47 years (IQR 35-60, total range 18-96 years), and the majority (56%) were male. The main occupation was farming (70%).

Clinical features: Table 1 shows the clinical features at presentation, including detailed characteristics of the ulcers and microbiology results. Specimen for microbiology was collected in 265 patients. Due to limited amounts of sample material, it was not possible to perform all tests on all those sampled. Almost half of the participants (47%) had a visual acuity of less than 3/60 (blind) in the affected eye at presentation.

Table 1: Clinical features and diagnosis at presentation (n=313)

Variable	Median	(IQR [Total Range])
Infiltrate size (mm)*	5.2	(3.3-7.7 [0.5-13])
Epithelial defect size (mm)*	3.9	(2.4-6.5 [0-14])
Variable	n/313	(%)
Snellen Visual Acuity in affected eye (n=312)		
6/5-6/18	102	(33%)
6/24-6/60	42	(12%)
5/60-3/60	24	(8%)
2/60-1/60	33	(11%)
Counting fingers-light perception	103	(33%)
No Light Perception	9	(3%)
Snellen visual acuity in non-affected eye (n=313)		
6/5-6/18	278	(89%)
6/24-6/60	16	(5%)
5/60-3/60	2	(0.6%)
2/60-1/60	4	(1.3%)
Counting fingers-light perception	6	(1.9%)
No light perception	6	(1.9%)
Missing	1	(0.3%)
Slough (n=313) ┼		
No slough	62	(19.8%)
Flat	124	(39.6%)
Raised	126	(40.2%)
Missing Infiltrate edge (n=313)	1	(0.4%)
Defined	35	(12%)
Serrated	258	(82%)
Not visible	20	(6%)
Satellite lesions present (n=313)		
Yes	178	(57%)
No	126	(40%)
Missing	9	(3%)
Infiltrate colour (n=288)		
White	148	(47%)
Cream	106	(34%)
Other colour	34	(11%)
Missing	25	(8%)
Hypopyon (median height 1.3mm IQR 0.9-2.9, n=313)		
Yes	94	(30%)
No	217	(69%)
Missing	2	(1%)
Site of ulcer (n=313)≠		
Peripheral	27	(9%)
Paracentral	64	(20%)
Central	219	(70%)
Missing	3	(1%)

Variable	Median	(IQR [Total Range])
Perforation status (n=313)		
Not perforated	237	(76%)
Impending	31	(10%)
Perforated	38	(12%)
Perforated and sealed	7	(2%)

*These were calculated as thegeometrical means using the MUTT protocol. The upper limits exceeded normal corneal diameter for some lesions, which extended up to the sclera.
┼ Raised slough was when the corneal infiltrate profile was raised, flat slough was when the profile was flat while no slough is when there was no debris noted.
┼ Site of ulcer was peripheral when the ulcer was marginal, paracentral was when the ulcer was not marginal but not within 4mm of the center of the cornea, central was when the ulcer was within the central 4mm of the cornea.
Impending perforation is when the clinicians felt the ulcer would perforate in the next 48hours.

Microbiology: Microbiology results were available in 265/313 (86.3%) participants (Table 2). Corneal scrapping was not performed on participants who either did not consent, had deep seated infiltrates or small infiltrates (less than 0.5mm). Overall, most infections were fungal (49%),10% were bacterial and 4% were mixed (fungal and bacterial). Ninety-seven (37%) of the corneal scrapping samples were negative on both microscopy and culture.

Table 2: Microbiology of MK (n=265)

Variable	Category	Count	(%)
Gram microscopy	Unknown	139	56 %
	Bacteria	31	13 %
	Fungal	79	31 %
KOH	Unknown	154	65 %
	Fungal	83	35 %
Calcofluor White-KOH ┼	Unknown	32	30 %
	Fungal	75	70 %
BHI culture	Unknown	115	53 %
	Bacteria	23	11 %
	Fungal	78	36 %
Blood agar culture	Unknown	111	51 %
	Bacteria	21	10 %
	Fungal	81	39 %
Chocolate agar culture	Unknown	97	50 %
	Bacteria	20	10 %
	Fungal	79	40 %
Potato dextrose agar culture	Unknown	128	57 %
	Fungal	95	43 %
Fungal PCR	Fungal positive	159	74 %
	Fungal negative	56	26 %
Overall laboratory diagnosis ┼	Unknown	97	37 %
	Bacterial	27	10 %
	Fungal	131	49 %
	Mixed (Bacteria/Fungal)	10	4 %
Cultured organisms	*Staph Aureus* (2 mixed)	8	3 %
	Strep Pneumonae	8	3 %
	Pseudomonas	6	2.5 %
	Klebsiella	4	2 %
	Norcadia	1	0.5 %
	Fusarium (2 mixed)	48	19 %

Variable	Category	Count	(%)
	Aspegillus	19	8 %
	Acremonium	13	6 %
	Bipolaris	6	2.5 %
	Scedospovium	1	0.5 %
	Candida	3	1.5 %
	Lasiodiplodia	2	1 %
	Unidentified fungi	9	3.5 %
	No growth	112	47 %
Yield rates	Gram	112/247	43 %
	KOH	83/249	33 %
	Calcofluor-KOH	72/103	70 %
	BHI culture	101/223	45 %
	Blood agar	102/213	49 %
	Chocolate agar	99/203	48 %
	Potato dextrose agar	97/233	41 %

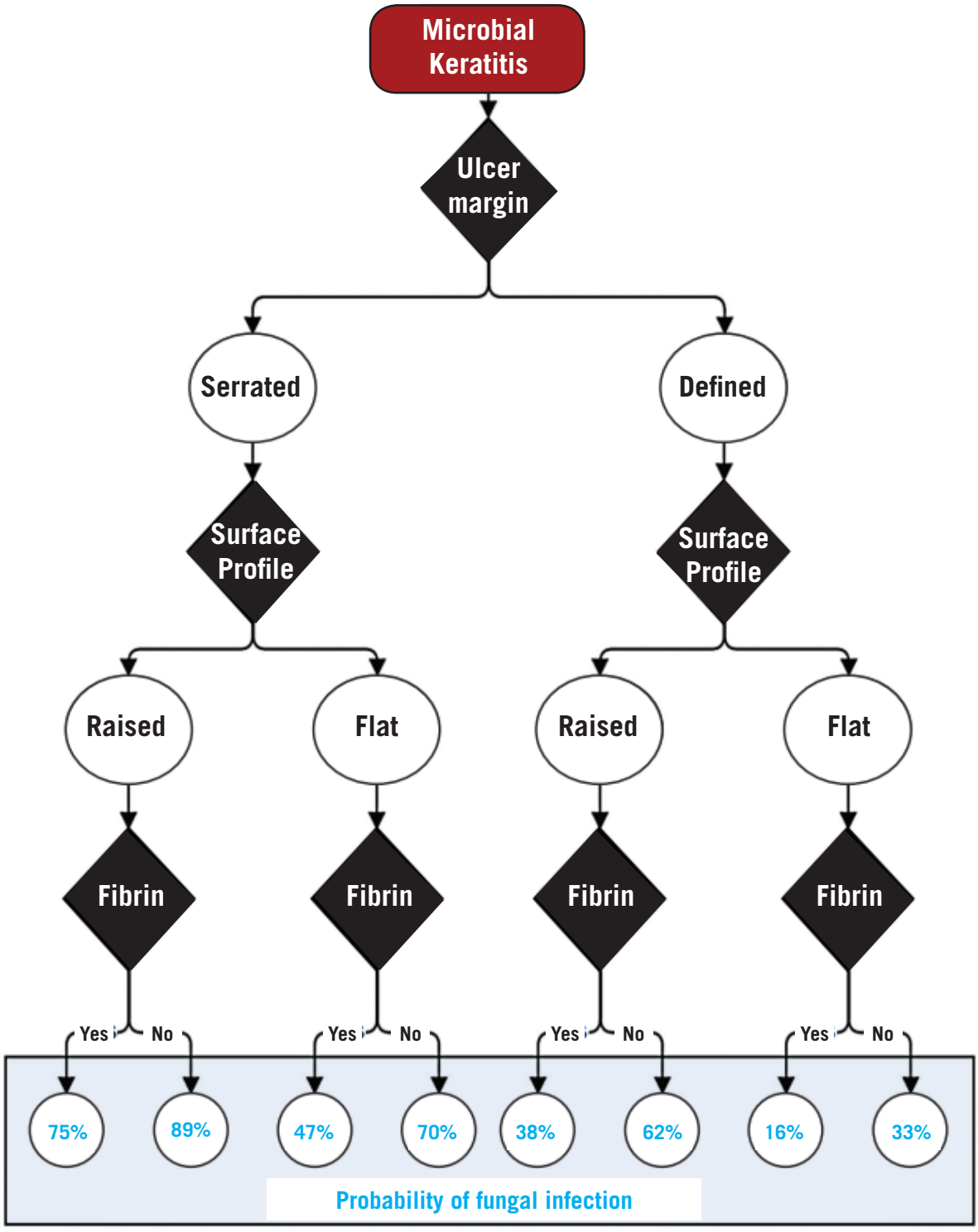
Specimen for microbiology was collected in 265 patients. Due to limited amounts of sample material, it was not possible to perform all tests on all those sampled. The order of material collection was 3 slide smears (gram, KOH, CFW), 3 agar inoculations (blood, chocolate, PDA) and 1 broth (BHI) depending on available material. ǂ Calcofluor stain has less numbers because it was introduced mid-way into the study. ᶜ Fungal PCR results were not included in the overall laboratory diagnosis.

Clinical signs predictive of fungal keratitis: In the final multivariable model, presence of a slough (aOR 3.58, 95% CI [1.60-8.04], p=0.002), a serrated infiltrate margin (aOR 1.58, 95% CI [1.00-2.51], p=0.051), satellite lesions (aOR 2.90, 95% CI [1.65-5.11], p<0.0001) and a hypopyon (aOR 3.24, 95% CI [1.78-5.90], p<0.0001) were associated with a positive microbiology result for fungal keratitis (Table 3).

Table 3: Clinical features associated with fungal keratitis (n=265)

Variable	Univariate analysis			Multivariable analysis		
	Crude OR*	(95% CI)	P-value	Adjusted OR+	(95% CI)	P-value
Slough	3.30	(1.60-6.79)	0.001	3.58	(1.60-8.04)	0.002
Serrated infiltrate edge	1.79	(1.16-2.75)	0.008	1.58	(1.00-2.51)	0.051
Satellite lesions	3.12	(1.86-5.25)	<0.0001	2.90	(1.65-5.11)	<0.0001
Infiltrate color						
White	1		0.102			
Cream	1.74	(1.01-2.99)				
Colored	1.67	(0.76-3.67)				
Immune ring	1.30	(0.48-3.54)	0.601			
Hypopyon	3.55	(2.05-6.15)	<0.0001	3.24	(1.78-5.90)	<0.0001
Perineural infiltrate	2.04	(0.99-4.22)	0.054			
Fibrin	2.24	(0.87-5.79)	0.096			
Flare	2.41	(1.39-4.20)	0.002			
Endothelial plaque	2.50	(1.50-4.13)	0.001			
Solid inflammatory mass in AC	2.50	(1.33-4.59)	0.004			

Figure 1: Algorithm for determining the probability of fungal keratitis[10]



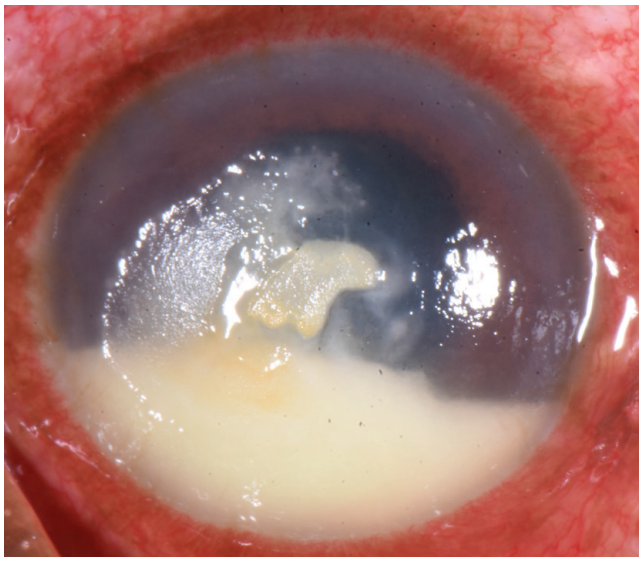
DISCUSSION

This study describes the clinical signs that were associated with a microbiological diagnosis of Fungal Keratitis (FK) in a cohort in Uganda. Some of these features have been highlighted in Figure 2.

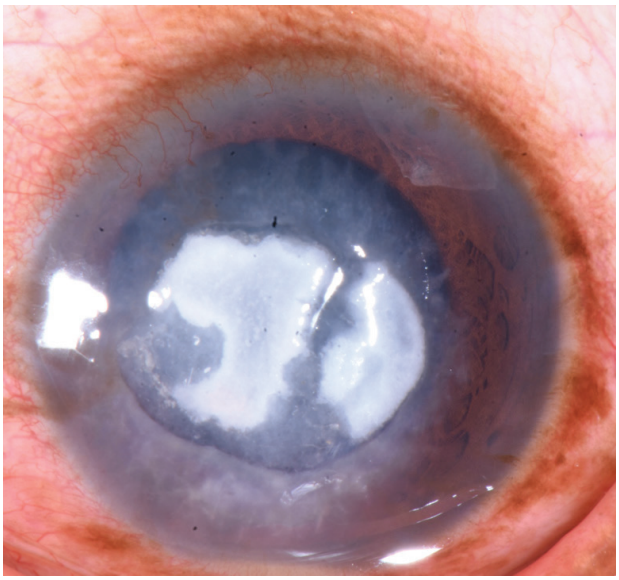
The overall microbiology yield was 80%. This was a composite of all the microscopy and culture results. Overall culture positive results were 55% like the expected yield reported in literature[8,15]. Maximum microscopic yield for fungal keratitis was achieved when we introduced the calcofluor white combined with Potassium Hydroxide staining (CFW + KOH). CFW is a non-specific fluorochrome dye that fluoresces when illuminated by light of a particular wave length making visualisation of fungal elements under a fluorescence easy[16,17]. In this study, we were also able to do PCR pan fungal testing for fungal DNA from corneal swabs. Although this showed the highest yield, it is a technology that is not readily available in most settings and was purely used for research purposes in our cohort.

We found that the clinical signs predictive for FK were presence of a slough, a serrated infiltrate margin, satellite lesions and hypopyon. These features seem to have been consistently reported in other settings of variable designs and size. Some of these include a study done by our colleague in India that analyzed data of 191 patients with confirmed FK; fungal ulcers were more likely to have feathery margins/serrated margins ($p< 0.001$) with ulcers caused by *Fusarium sp* four times more likely to have feathery margins as compared to those caused by *Aspergilus sp* (OR: 4.55, 95% CI: 1.92 – 10.75, $p = 0.001$). The study also reported that a raised profile/slough ($p = 0.039$) and dry texture of a surface slough ($p = 0.007$) was significantly associated with FK. However, this particular study noted that bacterial ulcers are more likely to have a hypopyon ($p = 0.02$) as compared to FK[18]. Another study by our group in Nepal found that serrated

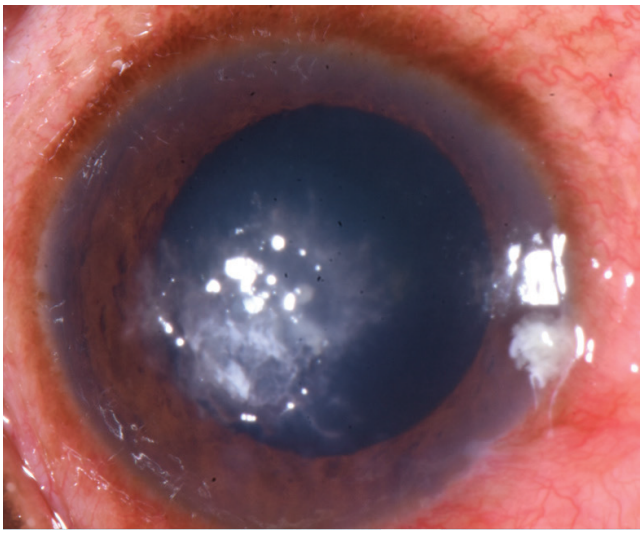
Figure 2: Pictures showing some of the clinical signs associated with microbial keratitis in our cohort



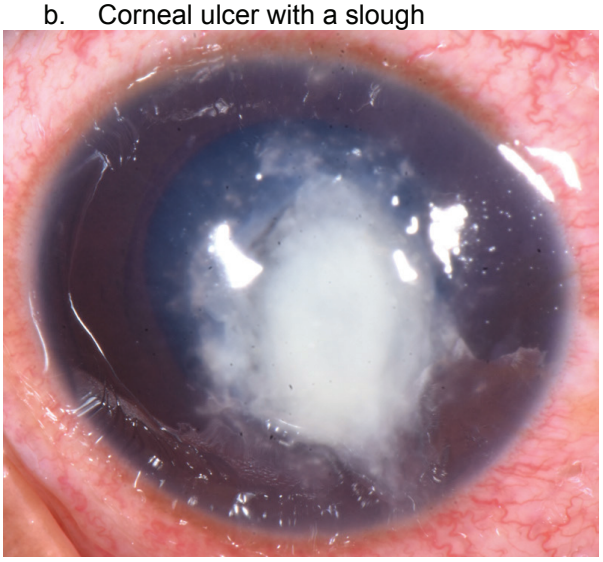
a. Corneal ulcer with a hypopyon



b. Corneal ulcer with a slough



c. Corneal ulcer with serrated margins/Feathery margins



d. Corneal ulcer with satellite lesions

margins (OR: 7.5, 95% CI: 4.09 – 13.78, p < 0.01) and a raised slough (OR: 4.27, 95% CI: 2.51 – 7.24, p < 0.001) are predictive of FK. However unlike in our study that found that satellite lesions are associated with FK, the study in Nepal noted that despite satellite lesions being more common in patients with FK, it was not a significant predictor for FK[19].

In summary most of the findings from these studies show that the key predictive clinical features for FK are a serrated margin, satellite lesions and the presence of a slough. It should be noted that these clinical features (serrated margins, slough and satellite lesions are also found in some patients with BK[8,19].

Basing on the above clinical signs, scientists have tried to devise a scoring system to aid in the diagnosis of FK. One such study was a large multicentre prospective study that created a clinical scoring system to aid in the diagnosis of microbial keratitis, with ability to calculate the probability of the causative infection[10,20]. In the study, the clinical data of 360 patients with FK and 132 patients with BK was analysed. The clinical signs that were significantly indicative of fungal keratitis as opposed to bacterial were serrated margins, raised slough, dry textured slough, satellite lesions and colouration other than yellow ($p<0.05$)[20]. Conversely, bacterial infections were associated with a hypopyon and fibrinous exudate ($p<0.05$). Hence the three clinical signs were used to create a score for diagnosing MK. Based on this model, Leck *et al*[10] developed an algorithm for determining the probability of FK. This algorithm uses the clinical signs: nature of ulcer margins, nature of the surface profile and presence of fibrin to calculate the probability of fungal infection[21]. The algorithm has been added as Figure 1 with permission and can be useful in settings where there is no microbiology support.

The recent study in Nepal has also created a scoring system for predicting patients with FK. The scoring system however uses four clinical features (serrated margins, raised slough, a nasolacrimal obstruction and trauma with vegetative objects) to predict whether the patient has FK[19].

Knowledge of the causative organism in patients with MK can help aid healing by reducing the drug toxicity associated with polypharmacy, facilitate informed disease monitoring for appropriate intervention, allow rationale use of antifungals, reduce the risk of developing drug resistance and reduce the cost of treatment. It should be noted that the use of clinical diagnosis is not completely reliable and can have variable conclusions even among corneal specialists. In one study that presented corneal photographs with a confirmed microbiology diagnosis to corneal specialists, only 66% could correctly differentiate between bacterial and fungal keratitis[21]. However, in the absence of a reliable microbiology support, these clinical signs could be useful to help clinicians make a rational clinical judgment.

Strengths and limitations

This is the first large prospective cohort study in SSA to describe the predictive signs of FK. The large number of patients gave sufficient power to analyze the clinical signs associated with MK. However, there was a sizable proportion of patients with whom a microbiology diagnosis could not be made and were subsequently dropped from the analysis. Ocular microbiology is not performed in many settings in SSA. As part of this study, we undertook to build the capacity of the hospital to provide this service as the first ocular microbiology laboratory in Uganda.

CONCLUSION

This study conducted in a predominantly African population provided clues to support clinicians in making a diagnosis of fungal keratitis in settings where there is no microbiology support. The main clinical signs that are predictive for FK are presence of a slough, serrated infiltrate margins, satellite lesions and hypopyon.

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The 2024 COECSA Exams Calendar is as Follows;

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Month	Type of Exam
JANUARY, 19th 2024	Written Part 1A: Basic Sciences
(Written Exams 1st Session)	Written Part 1B: Optics, Refraction & Instruments
	Written Part 2: Clinical Ophthalmology
JUNE, 19th 2024	Written Part 1A: Basic Sciences
(Written Exams 2nd Session)	Written Part 1B: Optics, Refraction & Instruments
	Written Part 2: Clinical Ophthalmology
AUGUST, 18 - 19th 2024	Clinical Fellowship Exams 1: OSCE
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Exam Name	Exam Time	Total Scheduled	Total Present	Absent
Basic Opthalmic Sciences	09:00 AM - 11:30 AM (EAT)	52	50	2
Clinical Ophthalmology	09:00 AM - 12:30 PM (EAT)	25	22	3
Optics, Refraction and Instruments	14:00 PM - 15:30 PM (EAT)	63	59	4
Total		**140**	**131**	**9**

The exams were held at various centres in Ethiopia 🇪🇹, Malawi 🇲🇼, Tanzania 🇹🇿, Uganda 🇺🇬, Zimbabwe 🇿🇼and Rwanda 🇷🇼!

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