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Editorial: Integrating artificial intelligence for better eye health in Africa: Potential challenges

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Artificial Intelligence (AI) is the ability of a computer system to mimic the cognitive functions of the human brain[1]. This emerging technology has rapidly expanded, and it is being applied in various fields, such as speech recognition, image, and video processing even in health systems assisting clinicians in decision-making for diagnosing and treating a wide range of diseases[1,2]. In eye health, AI is mainly applied in the diagnosis and classification of the common diseases of the back of the eye, such as Diabetic Retinopathy (DR)[3], Age-Related Macular Degeneration (ARMD)[4], and glaucoma[5]. Studies have reported the use of AI in detecting other eye diseases such as cataracts, keratoconus, and others. For the past decades, efforts have been made at the global scale to develop AI algorithms that could effectively diagnose DR. As of now, more than 400 AI-based DR screening algorithms exist, yet only a few are currently used in the clinical practice[6-9].

In the resource-limited context of most African countries, health systems face challenges in delivering appropriate health care to patients with multisystemic chronic diseases such as DM, hypertension, and cancers. In eye care, DR screening and treatment services are poorly organized, and the scarcity of specific skills and resources needed to manage DR remains the biggest challenge.

In the era of digital innovations and AI technology, AI has an important role in supporting clinicians and healthcare systems to streamline care pathways and provide timely and high-quality care for patients. In eyecare, AI is an effective tool that can potentially lower the burden of screening DR and vision loss. This tool is a potential solution to overcome manpower scarcity in resource-limited settings. Recently, AI DR screening has been adopted and successfully implemented in most high-resource settings to screen for DR in primary care. For example, the IDX-DR system, the first FDA-approved AI-based DR screening system, is used in primary care in the USA[10]; EyeART DR in the UK, Netherlands, and USA[11-13], and SELENA Plus System in Singapore[14] to mention a few.

With the currently available knowledge about AI DR screening systems, it is well established that this tool can effectively detect DR and outperform human graders: it is faster, accurate, with a very short learning curve, and does not need specifically a specialized health worker to produce an accurate result. However, challenges related to its application and integration in clinical practice remain the major problem that scientists have yet to find a solution to. The major concerns include ethics, technical, liability, and regulatory issues, workforce, social and patient safety[15]. These concerns are real in both, resource-limited and high-resource settings. However, it weighs more in resource-limited countries.

In Africa, besides the ethics, liability, and regulatory concerns, the technical capacity and workforce are the most critical concerns for integrating AI DR screening in Africa:

(1) From the development to clinical validation
   (i) The development of an AI Diagnostic Retinal (DR) algorithm necessitates considerable resources, including specialized skills in data science, retinal imaging, image grading, image labeling, and computing. It also requires substantial financial support to cover all associated activities and significant time for data collection and preparation for algorithm training.
   (ii) The developed algorithms must undergo both internal validation and external clinical validation testing to assess their performance. This process is essential for obtaining regulatory approval. However, it is time-consuming and requires substantial funding, which many African countries are often unable to secure.

(2) *The origin of the AI DR screening algorithm*: Current knowledge shows that the same AI-based Diabetic Retinopathy (DR) screening algorithm can perform differently in various settings[9,10,15,16]. The origin of the algorithm is not the primary concern anymore. Each AI algorithm needs to undergo local clinical validation in the specific setting or population where it will be used to evaluate its performance. Even when African countries decide to implement a foreign AI tool, local clinical validation is necessary in that specific context. This process allows for adjustments and adaptations of the algorithm to better fit the local environment.

(3) *Infrastructure*: Besides the infrastructure required to develop an AI DR screening tool, there are other "hidden" factors that need to be considered while

planning to integrate an AI-based DR screening in Africa.

(i) While internet connectivity may not be a concern in high-resource settings, this is a serious fact in most African countries, specifically in rural areas. Most AI DR tools are cloud-based software, the server is usually located in the country of origin. For an AI screening to take place, high-speed internet is required for uploading the image in the system, and processing and interpreting the findings. Offline versions of these AI systems would be ideal for Africa.

(ii) Electricity is another hidden fact that is to be considered. A stable power supply throughout the screening process. Another source of energy such as solar systems must be considered in Africa.

(iii) The quality of the fundus camera to use must be taken into consideration. Image quality is one of the most important determinants of an accurate AI screening. A poor retina image quality may not be processed by the AI system or may result in inaccurate reading. Higher-quality cameras would require significant financial investment which may be challenging to acquire in the African context.

(4) *Organization of health system:* Most African countries have not managed to incorporate a systematic screening of DR using traditional methods, that is fundus examination or fundus photography. Most patients are screened opportunistically when they present to an eye clinic for visual issues. Integrating an AI screening method would help overcome manpower shortages, but if health systems are not strengthened to coordinate referrals and if there is no infrastructure and skilled retina specialists who will treat these patients, we will be creating more problems than solving them. For AI screening to revolutionize eye health in Africa, there should be an established workforce to coordinate and establish a systematic DR screening program in each country. The health systems must be strengthened at all levels, local, district, and national levels to coordinate DR screening activities. There should be mechanisms for planning consecutive visits after the initial screening; the referral pathways must be well established; treatment centers must be created, equipped, and accessible to the rural population.

CONCLUSION

AI technology has the potential to enhance eye health service delivery in Africa. While there are significant challenges related to its application and integration into clinical practices, these can be managed through collective efforts aimed at improving eye health in the region. As a starting point, DR screening programs across African countries must be supported to establish a robust screening framework equipped with reliable, up-to-date technology that produces high-quality images and is accessible to all. The data collected from these screenings can serve as a foundation for creating a well-curated database of retinal images at the country level. Through data-sharing agreements, these databases can be utilized to develop algorithms that detect retinal diseases across Africa.

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Retinal photographic screening in a diabetic clinic versus ophthalmologist screening in an eye clinic; Task-sharing to increase diabetic retinopathy screening in Tanzania

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ABSTRACT

Background: We compared two methods of screening for diabetic retinopathy in a diabetic clinic by a technician using a digital retinal camera, and in an eye clinic by an ophthalmologist.
Objective: To find out if task-sharing might result in more screening uptake.
Methods: The study site was a tertiary referral hospital in North Tanzania. All patients aged 18 years and above attending the adult diabetic clinic during this period, living in Kilimanjaro Region and diagnosed with type-2 diabetes were invited to participate. After attending their regular diabetes check-ups, the participants in the study either remained in the diabetic clinic to be screened by a technician using the retinal camera or moved through a fast-track system and were screened for diabetic retinopathy in the eye clinic by an ophthalmologist. One hundred and thirty six participants were screened in the diabetic clinic group and 137 in the eye clinic group.
Results: Diabetic retinopathy was detected at 52.4% in the diabetic clinic, with 3.2% requiring treatment. In the eye clinic detection was 36.9% with 4.1% requiring treatment.
Conclusion: Diabetic retinopathy screening with a retinal camera operated by a trained technician is an effective and efficient method of diabetic retinopathy screening, to detect diabetic retinopathy and maculopathy, and a good use of task-sharing. This research suggests the implementation of comprehensive community-based programmes with the aim of providing knowledge-based teaching, clinical support, resources and action plans that health care workers can use to empower people with diabetes to be healthy living with diabetes and be proactive in preventing the complications of diabetes.

Key words: Retinal photographic screening, Task-sharing, Diabetic retinopathy

INTRODUCTION

Diabetic Retinopathy (DR) is the most common microvascular complication and the leading cause of preventable adult blindness[1,2]. When the capillaries of the retina are exposed to high and sustained glucose levels, they become damaged. Subsequent leaking and closure of these capillaries causes retinal oedema and ischaemia with loss of function, especially with central retinal or macular involvement[3]. Ischaemia causes production of vascular endothelial growth factor stimulating production of new blood vessels leading to proliferative diabetic retinopathy[1].

Worldwide the number of People with Diabetes (PWD) is increasing[2-4]. There are 19 million people in Africa (20-79 years) with diabetes, more than half undiagnosed[5]. In sub-Saharan Africa; the number of adults living with the disease will be 23.9 million by 2030[2,5,6], with an increase amongst poorer rural populations[7]. Diabetic Retinopathy (DR) is a microvascular complication[3], and if left untreated may lead to irreversible loss of vision, frequently among those of working age[4]. Vision Threatening Diabetic Retinopathy (VTDR) can significantly affect a person's psychosocial functioning and ability to manage their diabetes[5-7].

DR-screening meets the WHO-criteria for screening and blindness prevention[8]. Early diagnosis and treatment are both effective and efficient in preventing vision loss and blindness[9]. DR-screening should be initiated at diagnosis for people with type-2 diabetes, and in certain contexts repeated annually even when the person remains asymptomatic so that if VTDR is detected it can be successfully treated[9].

In resource-poor areas of sub-Saharan Africa access to care is difficult, and socioeconomic factors hinder optimal prevention of visual loss from DR[10]. Despite eye care services supporting diabetic clinics, late presentation for screening and treatment are common[11-13]. Task-sharing has been highlighted as an important strategy in the management of care in understaffed and resource-poor health systems[14]. A previous study in Kilimanjaro demonstrated that free referral for DR-screening from the diabetic clinic to the eye clinic (<100 meters away) only increased uptake by 36%; 71% had not had a dilated eye examination in the past year[13].

Knowledge that diabetes damages the eyes and the need for screening, do not translate into action[15-17]. Additional efforts are needed[18,19]. Poor health literacy is a worldwide issue facing health educators and carers[20]. The International Council of Ophthalmology emphasises the need that PWD are well informed by HCWs about their diabetes condition, self-care, how diabetes affects their eyesight and the need to receive prompt treatment before loss of vison[21].

The rational for this study was to establish if the target population would accept screening by a technician versus an ophthalmologist to promote task sharing prior to the roll out of the rural screening program, and the efficacy of Diabetic Retinopathy (DR)-screening using the digital diabetic retinopathy screening and grading of the images. We compared two methods of DR-screening: (i) in a diabetic clinic by a technician using a digital retinal camera, and (ii) in an eye clinic by an ophthalmologist; to find out if task-sharing might result in more screening uptake. The Intervention Mapping (IM) protocol was the basis of the intervention program[16,22]. IM is comprised of six iterative steps with discrete tasks, supported with theoretical and empirical evidence[16].

This study built on a previous tertiary hospital study, to test more pro-active ways to encourage utilization of free DR-screening services at the hospital by task-sharing[13], using IM to determine if DR-screening in the diabetic clinic with a digital retinal camera operated by a technician, would lead to higher uptake of screening compared to screening in the eye clinic by an ophthalmologist[23,24]. The comparison also aimed to identify if task-sharing, i.e., DR-screening with a technician, was as effective and efficient in detecting diabetic retinopathy; measured by recording the findings on the dilated eye screening form and comparing the findings of patients screening by the technician or by the ophthalmologist.

MATERIALS AND METHODS

Study design: A randomised prospective comparison of two screening methods.

Study setting: The study site was a tertiary referral hospital in the Northern Region of Tanzania. The Eye Department provides a full range of ophthalmic services, while the diabetic clinic (headed by a specialist endocrinologist) holds clinics twice a week for People with Diabetes (PWD). The uptake of screening compared (i) DR-screening in the diabetic clinic with a digital retinal camera (TOPCON-NW8) operated by a technician and (ii) DR-screening in the eye clinic <100 metres away by an ophthalmologist, who was a registrar-in-training. A four-day pilot was followed by the comparison, which ran for a two-month period (16 days).

Participants: The sample size was calculated based on the estimated difference in proportion between P1 (current use of service = 30%) and P2 (anticipated use of service after intervention = 50%) as 20 with a significance level of $\alpha = 0.05$ (two-sided) and power of $1-\beta = 0.2$. To detect a difference, 103 patients were needed in each group. In the final analysis n=124 in the diabetic clinic and n=122 in the eye clinic, were adequate numbers of participants to be analysed for the study.

Inclusion criteria and consent: All patients aged over 18 years attending the adult diabetic clinic during this period, living in Kilimanjaro Region and diagnosed with type-2 diabetes were invited to participate in the comparison by a research assistant. Patients who did not meet these criteria were excluded, but still received free DR-screening. Reasons for non-inclusion in the comparison: being too ill (having a blood sugar level requiring urgent hospital admission), having type-1 diabetes, and living outside of Kilimanjaro Region. Consenting participants had a leaflet explaining the study read to them. Each participant gave written consent before participation. Confidentiality and continued quality of care were assured, and participants were informed they could withdraw from the study at any time. The study adhered to the World Medical Association Guidelines for Screenings outlined at the 1964 Declaration of Helsinki[25]. A questionnaire regarding participants' eye health behaviour in terms of knowledge of DR and previous screening for DR was completed with assistance of diabetic clinic staff.

Randomisation and masking: On entry participants were given an envelope by the primary investigator allocating them to the eye clinic or the diabetic clinic from a random numbers table. Once the participants had been reviewed by the diabetic clinic doctors and nurses, they were moved on to where they had been allocated for DR-screening. Not all participants chose to be screened on the same day; some chose to come back on another day.

Procedure: In the eye clinic a fast-track system enabled PWD presenting for DR-screening to bypass waiting lines for general ophthalmology patients. In the diabetic clinic PWD were screened consecutively as they presented to the technician. Participants were administered pupil-dilating eye drops before DR-

screening was conducted by the technician who used a TOPCON-NW8 camera to take retinal photographs and entered data onto the Dilated Eye Screening Form (Figure 1). The demographic data, images and results of DR-screening where later entered onto the program's database and participants were appropriately informed of the results, either by short messaging service (SMS/ text) or phone call.

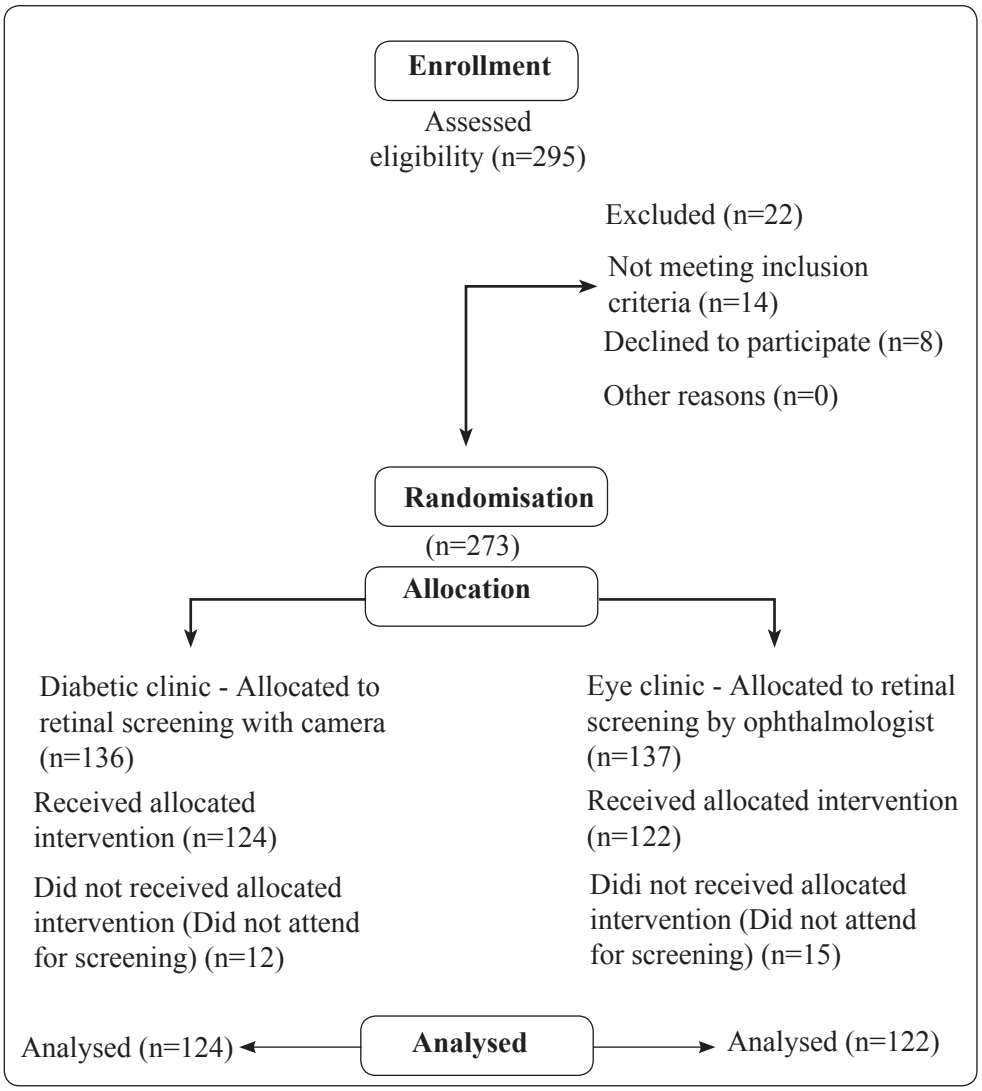
Figure 1: Diabetic retinopathy screening

The standard criteria for detection of DR were developed in 1991 by the Early Treatment Diabetic Retinopathy Study, with classification of DR and capture of fundus images using 30-degree stereoscopic photographs with 7 standard fields on colour slide film[13]. These guidelines require the support of trained graders with costly equipment and is both labour intensive and time consuming[14].

In the United Kingdom national screening programs have been adopted using digital photography with central reading centres[15], whereas elsewhere digital fundus photography is becoming more common if the guidelines set out in 2013 by the International Council of Ophthalmology (ICO) are followed[14,16]. The most important being that any DR-screening program is coupled with timely and adequate referral and access to ophthalmic consultation for care to ensure that the screening is beneficial.

Various studies of digital photography validation have shown it as an effective and efficient method to accurately identify and appropriately determine the severity of DR, compared to slit lamp biomicroscopic examination by a trained ophthalmologist[12,14]. Digital fundus photography has several notable advantages; it is less distressing to the patient, less time consuming, can be performed by trained technicians (as opposed to ophthalmologists) and taken into areas where access to eye health is limited, and allows for storage of retinal images for analysis, review, and epidemiological study[17]. Mydriasis (pupil dilation) for photography increases specificity and sensitivity of screening[18,19,] whilst a collateral benefit of digital screening is the high detection of other eye conditions[20].

Figure 2: Flow of participants through the trial consort diagram



On completion of the DR-screening the technician gave the participant written information on how they would be informed of the outcome of the findings. Grading of photographs was done by the consultant ophthalmologists; results were entered onto the Dilated Eye Screening Form and then entered with the digital fundus photographs into the program's database for future follow-up or treatment. We based our grading on the international classification of diabetic retinopathy and diabetic macular oedema. Diabetic macular oedema was graded as: M0 no macular findings, M1 hard exudates within one to 2 disc diameters of the fovea and M2 haemorrhage or exudates within one disk diameter of the fovea. If no VTDR was detected, participants were informed by SMS/text message and would receive a further SMS reminder for repeat DR-screening in one year. If VTDR was detected for participants attending the diabetic clinic, they were phoned with a date for follow-up assessment at the hospital's eye clinic. If VTDR was detected in participants attending the eye clinic, they were offered treatment on the same day. Results from both clinics were entered onto the program's electronic database and into the participants' diabetic diary.

In the Eye Clinic, participants were registered at a special (fast-track) counter. There was no charge for registering at the eye clinic or for DR retinopathy screening. Pupil-dilating eye drops were administered, and a dilated fundus examination was conducted using an indirect ophthalmoscope and slit lamp biomicroscopy by an attending ophthalmologist. The fundus findings were recorded on the Dilated Eye Screening Form (Figure 3) and the participant was immediately informed of the results.

Figure 3: Dilated eye screening form (for completion by the technician)

Diabetic No: ..... Mobile No: .....

Hospital No: ..... E/Clinic No: ..... Age Sex: Male ☐ Female ☐

Name of patient: .....

From patient's KDP diabetic diary: Date ..... R/E: ☐ L/E: ☐

Blood pressure: ☐ RBS: ☐ PH R/E ☐ PH L/E ☐

Digital fundus photograph taken: Y/N patient informed they will be contacted with results: Y/N

Name of photographer : ..... Duration of diabetes .....

Outcomes: The outcome of interest was attendance or non-attendance for screening for DR. Odds Ratios (OR) and 95% Confidence Intervals (CI) were calculated to test associations with screening acceptance. The standard intervention of screening with ophthalmologists was compared with the new intervention of screening with retinal imaging.

The screening was conducted by ophthalmologists working in the eye clinic, replicating real life working conditions. As the primary goal was not to establish presence of diabetic retinopathy but to compare the two interventions, the interobserver variability in grading of diabetic retinopathy is irrelevant. The technician was highly trained in taking retinal photographs.

Ethics approval was granted by Tumaini University Ethics committee, Clearance Certificate Number 241, Research Proposal Number 273. The hospital administration approved the study.

RESULTS

Of the 295 people assessed for eligibility, 22 did not meet the enrolment criteria and 8 declined to take part in the study. Among the 273 patients enrolled, 80 females and 44 males were randomized to the diabetic clinic group. Average ages were 57.02 years and 60.63 years respectively. There were 74 females and 48 males to the eye clinic group. Average ages were 56.72 years and 67.75 years respectively. There were no major differences in demographic or clinical factors between the sexes. Female participants were slightly younger. Females were 2.42 times (95%CI 1.47-3.98) more likely to have no or primary education. Female participants were 9.3 times (95% CI 2.8-31.2) more likely to be unmarried. In the diabetic clinic the mean duration of diabetes for males was 10.9 years, for females 9.5 years. In the eye clinic the mean duration of diabetes for males was 9.51 years, for females was 6.86 years. The Eye-Health Questionnaire results are presented in Table 1.

Table 1: Eye health questionnaire results

Variable	Diabetic clinic		Eye clinic	
Gender	Male (n=49) No. (%)	Female (n=87) No. (%)	Male (n=57) No. (%)	Female (n=80) No. (%)
Knowledge that diabetes damages the eye				
Yes				
No	38 (77.6)	70 (80.5)	41 (71.9)	53 (66.3)
	11 (22.4)	17 (19.5)	16 (28.1)	27 (33.7)
Previous dilated eye examination for DR*				
Yes				
No	30 (61.2)	43 (49.4)	29 (50.9)	37 (46.3)
	19 (38.8)	44 (50.6)	28 (49.1)	43 (53.7)
Knowledge that dilated eye examination should be yearly				
Yes	19 (38.8)	40 (46.0)	16 (28.1)	29 (36.3)
No	30 (61.2)	47 (54.0)	41 (71.9)	51 (63.7)

Of the participants 54% had not previously had a dilated eye examination for DR. The reasons included having no problem with their eyes (n=51), being unaware of the need (n= 14), and difficult access to a clinic (n=24). Only one participant mentioned cost.

The outcomes of the study's Diabetic Retinopathy Screening are presented in Table 2. There was no difference between the two allocation groups in uptake of screening; 124 (91.1%) patients were screened in the diabetic clinic and 122 (89.1%) in the eye clinic (Figure 4). In the diabetic clinic findings for any diabetic retinopathy (R1-R3) were 70 (52.4%), in the eye clinic 35 (36.9%) (Table 2). Diabetic retinopathy requiring treatment were 4 (3.2%) and 5 (4.1%). The most significant difference was between levels of referable maculopathy (M1) detected in the diabetic clinic 31 (25.0%) versus in the eye clinic 16 (13.11) (Table 3).

Table 2: Clinical trial diabetic retinopathy screening results

Variable	Diabetic clinic (n= 124) No. (%)	Eye clinic (n=122) No. (%)
No diabetic eye disease (either eye)	54 (43.5%)	72 (59.0%)
Background DR (R1)	49 (39.5%)	29 (23.8%)
Pre-proliferative DR (R2)	12 (9.7%)	11 (9.0%)
Proliferative DR (R3)	4 (3.2%)	5 (4.1%)
No maculopathy (M0)	89 (71.8%)	90 (73.8%)
Maculopathy Not Referable (MNR)	3 (2.4%)	12 (9.8%)
Referable maculopathy (M1)	31 (25.0%)	16 (13.1%)

Figure 4: Dilated Eye Screening Form (for completion by ophthalmologist)

Diabetic No: ..... Mobile No: .....

Hospital No: ..... E/Clinic No: ..... Age Sex: Male ☐ Female ☐

Name of patient: .....

From patient's KDP diabetic diary: Date ..... R/E: ☐ L/E: ☐

Blood pressure: ☐ RBS: ☐ PH R/E ☐ PH L/E ☐

Digital fundus photograph taken: Y/N Patient informed they will be contacted with results: Y/N

Name of photographer : ..... Duration of diabetes .....

Lens Opacity R/E: No Lens opacity interfering with photo Yes ☐ Referred to KCMC E/Dept ☐

L/E: No ☐ Lens opacity interfering with photograph Yes ☐

Diabetic Retinopathy R/E: R0 = No DR ☐ M0 = No Mac ☐

R1 = DBR ☐ MNR = Mac not referable ☐

R2 = Pre=proliferative DR ☐ M1 = referable maculopathy ☐

R3 = Proliferative DR ☐

P= Photocoagulation ☐ OL/UG = other lesion/ ungradable ☐

L/E: R0 = No DR ☐ M0 = No Mac ☐

L/E: R0 = No DR ☐ M0 = No Mac ☐

R1 = BDR ☐ MNR = Mac not referable ☐

R2 = Pre=proliferative DR ☐ M1 = referable maculopathy ☐

DISCUSSION

The researchers had anticipated that if participants accepted screening with the retinal camera there would be a greater uptake of participants in the diabetic clinic over the eye clinic. The equal uptake of screening in both clinics was a surprise finding. The fast-track service in the eye clinic is thought to have removed the barrier of waiting for screening in this clinic.

There was good detection of diabetic retinopathy in both clinics. The difference in the detection of significant maculopathy in the diabetic clinic can be explained by the fact that the reading and grading of retinal photographs was supervised by the senior (consultant) ophthalmologists with a final grading decision approved by a consultant. The DR-screening in the eye clinic was conducted by a registrar who was not as experienced as the ophthalmologists. This demonstrates the value of retinal photography and task-sharing in DR-screening by technicians.

The study found no difference in screening uptake between the diabetic clinic and the eye clinic. The high level of participation by both groups made it impossible to assess factors associated with DR-screening uptake. Findings of the earlier hospital study suggested that fewer patients would attend the eye clinic due to longer waiting times[26]: Eighteen percent of patients left while their eyes were dilating, and before the fundus examination was completed[26]. The high uptake in both groups was likely due to a motivated team in the diabetic clinic, who provided education on the need for DR-screening, and that the fast-track systems reduced waiting times. Unlike the previous study no patients were observed leaving either clinic whilst waiting for their eyes to dilate prior to DR-screening[13]. The task-sharing undertaken by the staff involved educating the participants about the need for

DR-screening, handing out the DR-information leaflets (comic strips)[20]. The fast-track services in both clinics appear to have removed a key barrier to uptake of DR-screening.

The advantage of digital fundus photography is that each participant had their fundus photographs stored on the program's database for future reference. With task-sharing a technician can conduct a significant number of DR-screenings with a digital fundus camera freeing up the ophthalmologist for clinical work. Another advantage is that a technician can conduct screening in remote locations[26,27]. This task-sharing reduces the need for lengthy, remote travel by trained ophthalmologists. Uptake of DR-screening depends on knowledge that DM damages the eye, need for DR-screening, knowledge of options and the benefits of screening, and access to ophthalmic services. In this population, although females had lower levels of education and were more likely to be unmarried, their level of knowledge regarding DR-screening and the possibility of vision loss due to DR were similar to the levels reported by males. The most common reason for not attending for screening was not perceiving a problem with the eyes. This suggests the need for PWD to understand that routine DR-screening is important in diagnosing sight threating DR that can be effectively treated before visual symptoms occur[21,24,26]. Other researchers support these findings[28,29].

CONCLUSION

DR-screening with a retinal camera operated by a trained technician is an effective and efficient method of DR-screening, to detect diabetic retinopathy and maculopathy, and a good use of task-sharing. Retinal fundus screening was acceptable to the target audience.

Strengths and limitations of the study

The study showed that both modes were an effective and efficient method of DR-screening. Firstly, indicated by high uptake with those accepting free screening with the technician in the diabetic clinic and those accepting free screening with an ophthalmologist using the fast track in the eye clinic. Secondly, by the acceptance of DR-screening using a retinal camera with a technician, and the great value of task-sharing in the context of the target audience. The researchers had been unsure if this method would be acceptable to participants. Thirdly, the use of the retinal camera allowed the researcher to trial the program's database to store demographic data and digital fundal images prior to the roll-out of the proposed regional rural DR-screening program.

Selection bias was a major limitation of the study as the participants were regular attenders of the hospital's diabetic clinic. An attempt was made to interview those who agreed to take part and then failed to attend for screening; an inadequate number agreed to be interviewed.

Relevance of the study for clinicians and policy makers

The study shows that with a motivated team providing clear explanations of the need for and access to DR-screening, uptake can be increased. By providing PWD with information about DR that explains the condition, the rational of screening and why early intervention while asymptomatic is important to preserve sight, it is possible to prevent avoidable blindness from diabetic retinopathy by early diagnosis.

Further research

Researchers should pay careful attention to the barriers identified for DR-screening uptake and treatment[26,28]. PWD need to understand how to access eye health services, the hidden and transparent costs, treatment options and outcome expectations. PWD must understand what being screened for DR means and the disease process. The greatest challenge to researchers is to address the social and cultural barriers to uptake of screening for DR and treatment. Ultimately, we must understand the individual's concerns and fears and personalise care[22,26,29,35,36].

CONCLUSION

The comparison of uptake of DR-screening in the diabetic clinic using a digital retinal camera versus screening in an eye clinic by ophthalmologists demonstrated no significant difference in uptake between the two methods. This unexpected finding was likely influenced by the introduction of a DR-screening service that provided good advice and information about the need for screening, a personal diabetic diary, and the support of a motivated team during the duration of the study. At the same time, the previous barriers to uptake of screening were removed and participants were fast-tracked through the DR-screening service.

The introduction of fast-track systems and DR-screening options in the diabetic clinic and eye clinics which remained after the completion of the study were instrumental in allowing better allocation of ophthalmologist resources. This shows the success of task-sharing which is essential where time and resources are limited. The success of technician operated digital fundus cameras as a method of DR-screening assisted in providing an evidence base for the development of transportable diabetic eye services, to provide care for rurally remote communities. Most importantly the future would be a comprehensive community-based approach with the aim of providing knowledge-based teaching,

clinical support, resources and action plans that HCWs could use to empower PWD to be healthy living with diabetes and avoid the complications of diabetes[22].

Declaration

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Authors' contributions: CH designed the Training Workshop. CH and AH planned the execution and the evaluation study. JM contributed to the implementation. GK helped supervise the project and CH took the lead in writing the manuscript. All authors discussed the results and contributed to the final manuscript.

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Changes in intraocular pressure after phacoemulsification: A pilot study in Uganda

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ABSTRACT

Objective: To determine the changes in intraocular pressure after phacoemulsification surgery among patients with cataracts in Southwestern Uganda.
Methods: This was a retrospective audit of the Intraocular Pressures (IOP) of patients who underwent a routine clear corneal phacoemulsification surgery for cataracts at Dr. Arunga's Eye Hospital between December 2020 and December 2023. The IOPs were measured using i-care rebound tonometer at admission, 2 weeks postoperatively, 6 weeks postoperatively, and at discharge from the clinic. Eyes with glaucoma, complicated cataracts, or post-operative complications were not included. The data was analyzed using STATA 17. The mean difference between the admission and discharge IOPs was tested for significance using the Wilcoxon signed-rank test and a relative difference between the mean IOPs at admission and discharge was calculated.
Results: A total of 78 eyes from 59 patients were included. The majority of patients, 57.7%, were female. The mean age of the patients was 70.0 years. Best corrected visual acuity of 6/12 or better was achieved in 91% eyes at discharge with a median discharge time of 3 months, and IQR of 2-5 months. The mean intraocular pressures were 14.5 mmHg at admission, 13.3 mmHg at two weeks post-operatively, 12.9 mmHg at 6 weeks, and 11.8 mmHg at discharge. The mean reduction in IOP was 1.6 mmHg between admission and at 6 weeks (p=0.001) and 2.7 mmHg between admission and discharge (p=0.001). IOP reduction 3 months post phacoemulsification showed a 17.9% reduction in IOP compared to baseline. The findings of this study are similar to findings in various studies globally that have reported a decrease in IOP post phacoemulsification.
Conclusions: There was a significant reduction in mean intraocular pressure following phacoemulsification. This is the first study assessing changes in intraocular pressure post phacoemulsification in a Ugandan population however the study is limited by a small sample size.

Key words: Intraocular pressure, Phacoemulsification, Cataract, Uganda

INTRODUCTION

A cataract -the clouding of the natural lens in the eye[1]. Cataract is the leading cause of blindness worldwide accounting for 17.1 million blind people[2]. In sub-Saharan Africa, the prevalence varies among countries affecting 3.9–62.5%[3]. In Uganda, cataract is the most common condition among adults aged 60+ years presenting at eye hospitals accounting for over 50%[4]. It is commonly associated with aging though it can be congenital or secondary to trauma. Cataract treatment is surgical with extracapsular cataract surgery (small incision cataract surgery and phacoemulsification) or intracapsular cataract surgery.

Although small incision cataract surgery is the most commonly used surgery around Uganda and many parts of Africa, phacoemulsification is being adapted to different facilities around the country due to its advantages such as being minimally invasive, quick recovery time, reduced risk of complications, minimal discomfort and its high success rate in restoring vision[5].

Intraocular Pressure (IOP) is the fluid pressure of the eye[6]. It can be affected by many factors such as inflammation in the eye, cataracts, surgery, and age. Persistently raised intraocular pressure by any cause can lead to optic nerve damage and hence blindness, a condition commonly known as glaucoma. Studies done in different places have shown a decrease in intraocular pressures post-phacoemulsification[7] and others have proposed this as a reliable option for IOP control among those with high preoperative IOPs[8].

As a relatively newer technology in Uganda, the changes that occur in intraocular pressures after phacoemulsification had not been previously described in a Ugandan population. With other studies reporting a lowering effect of phacoemulsification on IOPs, assessing if the findings are similar would guide in choosing the type of surgery in patients with borderline IOPs as lowering IOPs has been reported to delay or prevent the onset of glaucoma[9]. A pubmed search also indicates no published data about IOP changes post-phacoemulsification in East Africa.

This pilot study therefore was to provide baseline data of changes in intraocular pressures post clear cornea phacoemulsification in a purely Ugandan adult population at Dr. Arunga's Eye Hospital in Mbarara City in Southwestern Uganda and fill the existing knowledge gap in the region.

MATERIALS AND METHODS

This was a retrospective audit of data of patients who underwent clear cornea phacoemulsification at Dr. Arunga's Eye Hospital, a private hospital in Mbarara, City, Uganda that provides services to people from South Western Uganda and other parts of the country.

Data of all patients who underwent a routine phacoemulsification surgery between December 2020 and December 2023 was included with recorded intraocular pressures at the selected visits. Permission was obtained from the hospital administration to conduct this anonymized audit. Glaucomatous eyes, complicated cataracts, and eyes with postoperative complications were excluded. Data from hospital records was extracted. Data extracted included demographics, IOP and VA before the operation, date of admission and discharge, VA at discharge, IOP at 2 weeks, 6 weeks, and at discharge. The main variable for this study was the IOPs at the various visits.

The IOP had been measured by icare tonometer as part of routine practice and recorded as mmHg. The icare tonometer takes five IOP readings and gives an average which is recorded as the final IOP reading for that eye.

Data was entered in Excel and analyzed using STATA 17. Data was tested for normality and different findings were analyzed for significance using the Wilcoxon signed-rank test. A relative difference between the mean IOPs at admission and 6 weeks post-operative and discharge was calculated.

RESULTS

A total of 78 eyes from 59 patients were included. The majority of patients, 57.7%, were female. The mean age of the patients was 70.0 years. The majority of patients, 91% had the best corrected visual acuity of 6/12 or better at discharge. Median discharge time was 3 months, IQR was 2-5months.

Table 1: The baseline characteristics of participants (n=78)

Variable	Frequency (n)	(%)
Sex		
Male	33	42.3
Female	45	57.7
Age group (years)		
30-70	34	43.6
Older than 70	44	56.4
Final BCVA		
6/5-6/12	71	91.0
6/18-6/60	7	9.0
<6/60	0	0.0

Figure 1: The number of patients in different categories of visual acuity preoperative and at discharge

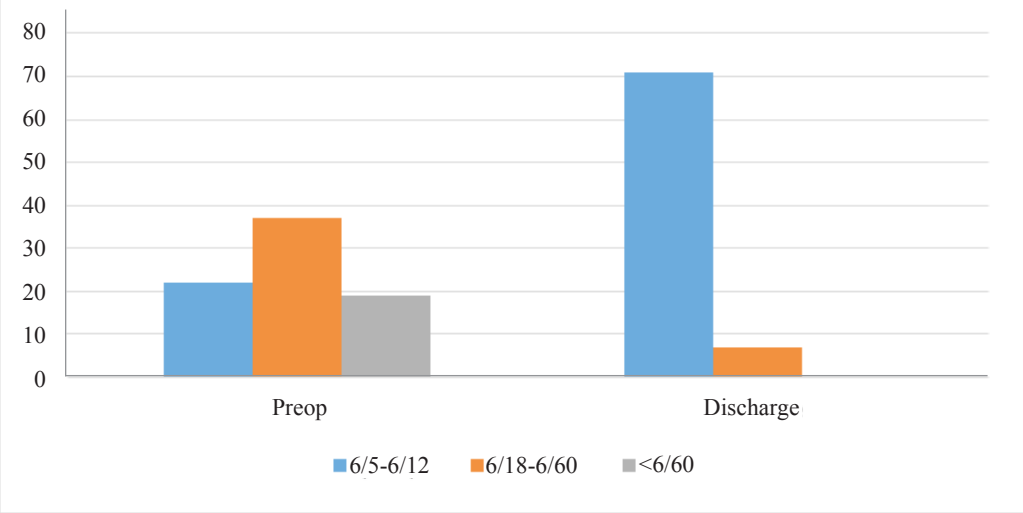
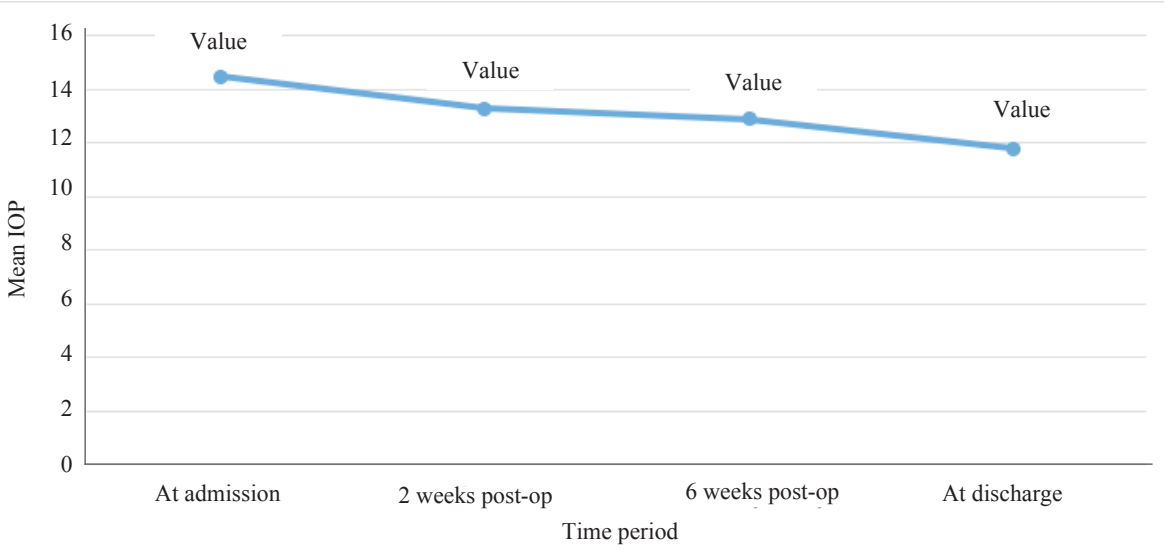


Table 2 shows the summary IOP readings at different time points and serial reductions are graphically illustrated in Figure 2. The mean intraocular pressures were 14.5 mmHg at admission, 13.3 mmHg at two weeks post-operatively, 12.9 mmHg at 6 weeks, and 11.8 mmHg at discharge. The mean reduction in IOP was 1.6 mmHg between admission and at 6 weeks (p=0.001) and 2.7 mmHg between admission and discharge (p=0.001).

Table 2: The mean intraocular pressures and medians at admission, 2 weeks, and 6 weeks and at discharge

	Median	IQR	Range	Mean	SD
At admission	13	11-17	8-29	14.5	4.5
2 weeks post-op	13	10-15	7-25	13.3	4.3
6 weeks post-op	13	10-15.75	6-22	12.9	3.4
At discharge	11	10-14	5-23	11.8	3.2

Figure 2: The mean reductions in Intraocular pressures at the subsequent visits



This is a figure plot showing the reduction trend in mean IOP at subsequent visits after phacoemulsification surgery. The relative differences in mean IOP at subsequent visits postoperative compared to admission IOP were 8.3% at 2 weeks postoperative, 11.1% at 6 weeks post-operative and 17.9% at discharge.

DISCUSSION

In this pilot study, we aimed to describe the trends in IOP changes after phacoemulsification among a purely Ugandan population. Our study found a significant decrease in the mean IOPs post phacoemulsification at 6 weeks and at discharge from the hospital.

Although our study only included patients with a normal pre-operative IOP, other studies have presented evidence that the post-operative IOP reduction is more in people with a higher baseline such as glaucoma patients[8]. One study from Iran evaluated IOP changes in different baseline IOP categories post-phacoemulsification. They included 129 eyes that were grouped into three according to preoperative IOPs with Group 1-IOP<15, Group 2-IOP = 16-20 and Group 3-IOP =21-30. The IOPs at 1 and 6 weeks post-operative were analyzed compared to admission IOPs. The study noted a significant mean and percentage decrease in IOPs at week 6 postoperative as G1-(1.8±1.7 mmHg), 13.5%±12.7, G2-(4.3±2.9 mmHg), 24.5%±11.7 and G3-(9.3±4.1 mmHg), 38.3%±16.2, respectively for the different groups[10]. Similar findings have been reported in other studies between a lower baseline IOP (normal) group and a higher baseline IOP (pseudoexfoliation) group. In a comparison study from Iran, the mean reduction in the pseudoexfoliation group was higher at 4.5 mmHg compared to 2.7 mmHg in the normal eyes group, P<0.0[11].

A similar study in Cairo evaluated the changes in IOP and anterior chamber depth after phacoemulsification of non-glaucomatous eyes. This study looked at 100 eyes that underwent routine surgery for which they noted a significant reduction in IOPs at 1 week, 1 month, and 3 months postoperatively which can be explained by the increase in anterior chamber depth following surgery that was found in this study[12].

Our study reported IOP at discharge which ranged from 2-5 months. Longer cohorts have shown that IOP reduction is steeper in the first weeks and then gently rises to a sub-pre-operative peak by one year. One such fairly large cohort in Korea investigated the long-term effect of phacoemulsification on IOPs among healthy individuals (648 eyes) and those with glaucoma (106 eyes). In this study, the relative reduction was higher at one month with a 13% relative difference compared to 8% at one year. Even then, the IOP in both normal and glaucoma groups remained lower than the pre-operative readings. This

almost permanent reduction in IOP has supported the notion that phacoemulsification might be a reliable option for IOP control among patients with high pre-operative IOP[8].

Strengths

This was the first study of IOP changes post-phacoemulsification in a Ugandan population. The findings thereof were similar to what has been reported in literature and provide an important baseline for our population.

Weaknesses

This was a small hospital audit that included only normal routine patients. Although the practice of phacoemulsification is growing in Uganda, the bulk of cataract care is Small Incision Cataract Surgery (SICS). This study did not explore the IOP changes among patients who underwent SICS.

CONCLUSION

Our pilot study showed an important reduction in IOP after phacoemulsification in a Ugandan population. This finding suggests an additional benefit of phacoemulsification in the surgical management of cataract. Additional information on IOP changes after phacoemulsification cataract surgery in patients with glaucoma might be of clinical importance in our setting where this procedure is becoming more common.

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Availability of data and material: The anonymized data sets used and analyzed for this study are available from the corresponding author on request.

Conflict of interest: None to declare.

Authors' contributions: ZT, OM, RK, NVA, and SA-made the study design, ZT, SA- collected data, and ZT, OM, and SA-analyzed the data, all authors reviewed and approved the final manuscript.

Declaration: The research was presented at the 11th COECSA congress however it has not been submitted to any other journal

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Factors affecting diabetic retinopathy screening uptake among adult patients attending diabetic clinic in a tertiary hospital in Tanzania

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ABSTRACT

Objective: To determine the factors affecting diabetic retinopathy screening uptake among adult patients attending diabetic clinic in a tertiary hospital in Tanzania.

Methods: This study was a hospital based analytical cross-sectional study which was conducted at the diabetic clinic of Muhimbili National Hospital from June to July 2021. All adult patients with diabetes mellitus who met inclusion criteria were enrolled in the study. A stratified random sampling method was used to recruit participants. Data was collected using a structured questionnaire and analysed by using Statistical Package for Social Sciences (SPSS) version 26.

Results: A total of 322 participants were enrolled in this study. Median age was 58 years with a range of 18 to 83 years. Less than half (43.8%) of participants were screened for diabetic retinopathy within 12 months. Physician recommendation had influence on diabetic retinopathy screening uptake (63.6%). Awareness of diabetic retinopathy screening and tolerability of mydriatic eye drops were significantly associated with screening for diabetic retinopathy within 12 months ($p<0.001$)**.**

Conclusion: Improving health education on diabetic retinopathy and diabetic retinopathy screening as well as ensuring comfortability during and after pupillary dilatation is necessary to enhance diabetic retinopathy screening uptake.

Key words: Diabetic retinopathy, Diabetic retinopathy screening, Eye-care Tanzania

INTRODUCTION

Diabetic Retinopathy (DR) is a vascular disease of the retina caused by long standing Diabetes Mellitus (DM). It is among the commonest complication of DM, which accounted for the global prevalence of 35.4% in 2010. According to the World Health Organization (WHO), DR is the fifth chief cause of blindness worldwide and the foremost cause of blindness in working age population, accounting for the overall prevalence of blindness and visual impairment of 2.6% and 1.9% respectively in 2019 [1–3].

Diabetic Retinopathy Screening (DRS) refers to detection of retinal changes by fundus examination or imaging of patients with DM. DRS is of importance as DR may be asymptomatic, and this may lead to patients reporting late with complications. Early diagnosis through screening and timely treatment can prevent more than 90% of DR related visual impairment and blindness[4]. Unfortunately, regardless of good control of blood sugar, more than 90% of patients with type 1 DM and about 60% of patients with type 2 DM will get some form of DR over 20 years. Some of these patients will end up with blindness if not detected early through screening and treated on time, exerting a significant public health problem[5]. The International Diabetes Federation guideline recommends annual screenings for DR to all patients with DM and every 3 months to pregnant women. For patients with type 1 DM screening starts 5 years after diagnosis and for patients with type 2 DM screening starts at the time of diagnosis[3-8].

The rate of DRS uptake varies from place to place and there is a wide range, making difficulties in estimating global screening rates. Despite the availability of screening programs, the rate of screening for DR within 12 months is below the required standard especially in developing countries ranging from 7.4% to 33%, where 75% is considered as minimum acceptable and 85% as achievable[9-12].

Efficacious uptake of screening for DR depends on a number of factors, ranging from health care related factors, disease (DM) related factors and patients related factors. Physician recommendation to screen for DR, longer duration of DM and presence of comorbidities has shown to increase DRS uptake while lack of awareness and knowledge on DR and DRS decreases screening uptake[11,13-16].

Despite having established DR screening services at the DM clinic at Muhimbili National Hospital (MNH), it was noted that a good number of DM patients with good

attendance at the DM clinic still comes to eye clinic with some form of advanced DR. Little was known on the factors affecting DRS uptake. Therefore, this study aimed to provide an updated information on the proportion of DRS uptake within 12 months as well as the factors affecting DRS uptake at MNH.

MATERIALS AND METHODS

Study design: This was a hospital based analytical cross-sectional study conducted for one month from June to July 2021.

Study setting: The study was conducted at the diabetic clinic of MNH in Dar es salaam,Tanzania.

Study population: All patients attending diabetic clinic during the study period.

Inclusion criteria: All adult patients attending diabetic clinic during the study period.

Exlusion criteria: All patients who were on treatment for DR, patients with type 1 DM with duration of disease of less than 5 years and patients with mental or physical conditions that prevented them from participating in the study.

Sample size detarmination: Minimum sample size was estimated using Kish and Leslie formula for proportion in cross-sectional studies ($N= Z^2 p(1-p)/ e^2$). Where N=minimum sample size, Z= standard normal deviation corresponding to 95% confidence level (1.96), e= marginal error (5%) and p= 28.8% a proportion of DR screening uptake in a study done at KCMC, Tanzania[17]. Therefore from the above formula the minimum sample size calculated was 315 participants. In this study a total of 322 participants were enrolled.

Sampling procedure: The study employed stratified random sampling technique, where the participants were divided into two strata as there are two special DM clinics. Stratum one included those aged 18-25 years old, who attend clinic on Mondays. Stratum two were those above 25 years of age who attend clinic on Tuesdays, Wednesdays and Thursdays. A predetermined sample size in each group was calculated in percentage based on clinic attendance register per week. In stratum one 12 participants (7.4%) attend per week and 150 participants (92.6%) in stratum two attend per week. Systematic random sampling was used to recruit participants from each stratum, where every 2nd patient was interviewed from each stratum until the sample size was reached.

Data collection: Data was collected by using researcher administered structured questionnaire. Prior to data collection, the questionnaire was reviewed by two senior ophthalmologists and one statistician. The questionnaire was in Swahili language. Knowledge on DRS was assessed using questions adopted from a study done by Almalki *et al*[18], which was also used in previous studies and its reliability was checked. Permission of using the tool was obtained from the author and translated to Swahili language. The questions consisted of 10 items aiming at assessing knowledge on DRS. Those participants who scored 60% and above were regarded as knowledgeable and those who scored below 60% were regarded as not having knowledge on DRS.

Data analysis: Data were analyzed using IBM SPSS version 26 software. In the bivariate analysis, significant difference between variables was tested using Pearson's chi-square test. For values with p-value of less than 0.2 from bivariate analysis were entered into multivariate regression model. A p-value of less than 0.05 was considered to be statistically significant.

Ethical consideration: Ethical clearance was obtained from MUHAS Institution review board. Permission to conduct the study was obtained from MNH research committee. Written informed consent from all participants was taken after fully explaining the purpose of the study. There was no risk associated with participating in this study.

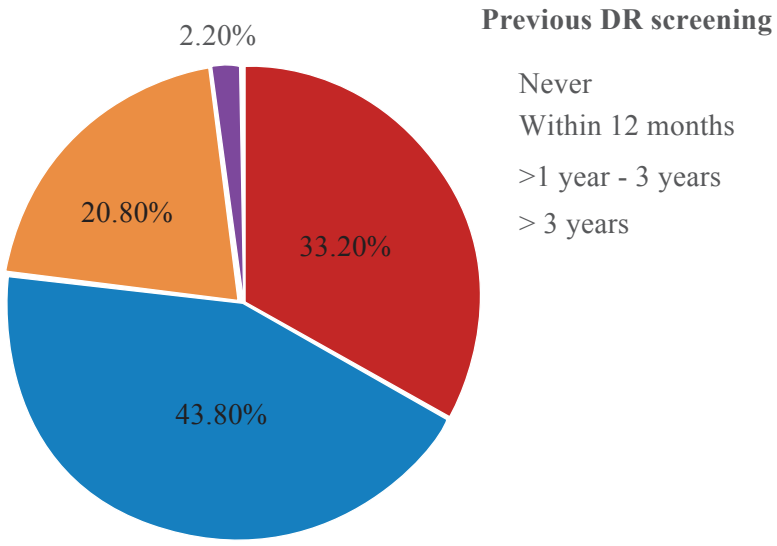
RESULTS

Three hundred and twenty-two participants were recruited and all were included in the analysis. The median age was 58 years with a range of 18-83 years and most participants were females (58.4%). (Table 1). Among the participants 33.2% were recommended to screen for DR.

Table 1: Socio-demographic characteristics of the study participants (n=322)

Characteristic	Frequency		P - value
	No.	(%)	
Age group (years)			
18 - 35	41	12.7	< 0.001
36 - 60	141	43.8	
>60	140	43.5	
Median age in years (range)	58 (18, 83)		
Sex			
Male	134	41.6	0.003
Female	188	58.4	
Marital status			
Single	43	13.4	< 0.001
Married	218	67.7	
Divorced	12	3.7	
Widow	49	15.2	
Residence			
Dar es salaam	272	84.5	< 0.001
Other regions	50	15.5	
Level of education			
No formal education	12	3.7	< 0.001
Primary education	130	40.4	
Secondary education	115	35.7	
College	65	20.2	
Occupation			
Employed	169	52.5	< 0.001
Unemployed	83	25.8	
Retired	70	21.7	
Income status (USD)			
< 124	224	69.6	< 0.001
124 - 506	85	26.4	
>506	13	4.0	
Health insurance coverage			
Insurance	217	67.4	< 0.001
No insurance	105	32.6	

Figure 1: Proportion of diabetic retinopathy screening uptake among study participants (n=322)



Less than half of the participants had screened for diabetic retinopathy within 12 months (43.8%) (Figure 1). Disease related factors (treatment regimen, duration of DM and comorbidities) did not show statistical significant difference in screening for DR within 12 months (Table 2).

Table 2: The relationship between patient related factors and DRS uptake

Patient related factor	Diabetic retinopathy screening within 12 months		
	Yes	No	P - value
	No. (%)	No. (%)	
Age group (years)			
18 - 35	20 (48.8)	21 (51.2)	0.307
36 - 60	55 (39.0)	86 (61.0)	
>60	66 (47.1)	74 (52.9)	
Sex			
Male	57 (42.5)	77 (57.5)	0.702
Female	84 (44.7)	104 (55.3)	
Residence			
Dar es salaam	116 (42.6)	156 (57.4)	0.335
Other regions	25 (50.0)	25 (50.0)	
Level of education			
No formal education	4 (33.3)	8 (66.7)	0.541
Primary education	53 (40.8)	77 (59.2)	
Secondary education	56 (48.7)	59 (51.3)	
College	28 (43.1)	37 (56.9)	
Income status (USD)			
< 124	104 (46.4)	120 (53.6)	0.183
124 - 506	34 (40.0)	51 (60.0)	
>506	3 (23.1)	10 (76.9)	

Awareness of DR			
Yes	131 (58.5)	93 (41.5)	< 0.001
No	10 (10.2)	88 (89.8)	
Awareness of DRS			
Yes	132 (61.7)	82 (38.3)	< 0.001
No	9 (8.3)	99 (91.7)	
Knowledge on DRS			
Knowledgeable (score ≥ 60%)	91 (61.5)	57 (38.5)	< 0.001
Unknowledgeable (score < 60%)	50 (28.7)	124 (71.3)	
History of decreased vision			
Yes	97 (53.6)	84 (46.4)	< 0.001
No	44 (31.2)	97 (68.8)	
Fear of results			
Yes	10 (66.7)	5 (33.3)	0.067
No	131 (42.7)	176 (57.3)	

Majority of those who were not aware of DR (89.85%) and DRS (91.7%) and most of those who were unknowledgeable about DRS (71.3%), did not screen for DR. Additionally, 68.8% of those who had no history of decreased vision did not screen for DR (Table 2).

Table 3: The relationship between healthcare related factors and DRS uptake

Healthcare related factors	Diabetic retinopathy screening within 12 months		
	Yes	No	P - value
	No. (%)	No. (%)	
Physician recommended to screen for DR			
Yes	68 (63.6)	39 (36.4)	**< 0.001**
No	73 (34.0)	142 (66.0)	
Waiting time for screening*			
0 – 15 minutes	15 (88.2)	2 (11.8)	0.052
16 – 30 minutes	81 (65.9)	42 (34.1)	
31 – 60 minutes	44 (56.4)	34 (43.6)	
>1 hour	1 (50.0)	1 (50.0)	
Number of clinic visit			
One visit	0 (0.0)	17 (100.0)	**< 0.001**
Two to three visits	16 (57.1)	12 (42.9)	
More than three visits	125 (45.1)	152 (54.9)	

Cost interfering with screening			
Yes	27 (39.1)	42 (60.9)	0.379
No	114 (45.1)	139 (54.9)	
Tolerability of mydriatic eye drops			
Yes	91 (53.2)	80 (46.8)	**< 0.001**
No	50 (33.1)	101 (66.9)	
Health financing			
Insurance	90 (41.5)	127 (58.5)	0.229
Non insured	51 (48.6)	54 (51.4)	

Key: *Variable with less than total (n < N) due to analysis of subtotal.

All participants with one clinic visit had not screened for DR. Most of those whom DR screening was not recommended by their physician (66%) and those who thought/heard that mydriatic eye drop was not tolerable (66.9%), had not screened for DR (Table 3).

Table 4: Univariate and multivariate analysis of the factors associated with DRS uptake

	Univariate analysis			Multivariate analysis		
Factors	cOR	95% CI	P-value	aOR	95% CI	P-value
Income (USD)						
< 124	2.89	0.77 – 10.78	0.114	3.20	0.65 – 15.70	0.152
124 - 506	2.22	0.57 – 8.67	0.250	1.67	0.32 – 8.61	0.539
> 506	Ref					
Awareness of DR						
Yes	12.40	6.12 – 25.11	< 0.001	1.37	0.37 – 5.16	0.638
No	Ref					
Knowledge on DRS						
Knowledgeable	3.96	2.48 – 6.31	< 0.001	1.38	0.73 – 2.59	0.319
Unknowledgeable	Ref					
History of decreased vision						
Yes	2.55	1.61 – 4.04	< 0.001	1.26	0.65 – 2.45	0.490
No	Ref					
Fear of results						
Yes	2.69	0.90 – 8.05	0.077	2.15	0.53 – 8.72	0.286
No	Ref					
Duration of diabetic mellitus (years)						
>20	2.21	0.91 – 5.40	0.082	0.45	0.13 – 1.54	0.203
11 - 20	1.96	0.92 – 4.18	0.083	0.72	0.24 – 2.13	0.550
1 - 10	1.38	0.67 – 2.84	0.382	0.58	0.21 – 1.66	0.314
< 1	Ref					

Physician recommended to screen for DR						
Yes	3.39	2.09 – 5.51	< 0.001	1.83	0.94 – 3.54	0.074
No	Ref					
Tolerability of mydriatic eye drop						
Yes	2.30	1.46 – 3.61	< 0.001	2.89	1.64 – 5.09	<0.001
No	Ref					
Awareness of DRS						
Yes	17.71	8.48 – 36.96	< 0.001	12.47	3.28 – 47.37	<0.001
No	Ref					

Key: cOR: crude Odds Ratio, aOR: adjusted Odds Ratio, Ref: Reference category

Awareness of DRS and the belief of mydriatic eye drop tolerability were the only factors that remained significantly associated with screening for DR within 12 months. (Table 4).

DISCUSSION

Diabetic Retinopathy (DR) is a potentially blinding disease, early diagnosis through screening and timely treatment can prevent more than 90% of DR related visual impairment and blindness[4]. In this study annual screening uptake for DR was found to be 43.8%, which is low. Our findings were higher than those reported in Tanzania by Mumba *et al*[17], 14 years ago 28.8%, and a multicenter study including MNH by Mafwiri *et al*[19], 6 years ago 29.8%. This difference is due to the fact that currently at MNH, DRS services have been incorporated within the diabetic clinic and patients are no longer required to go to the Ophthalmology Department for screening. Additionally, there is an increase of awareness on diabetic retinopathy screening from 5.8% 6 years ago to 61.7%. These findings imply that more interventions are still needed to raise screening uptake.

In this study it was found that 89.8% of participants who were not aware of DR and 91.7% who were not aware of DRS did not screen for DR. This signifies that lack of awareness on DR and DRS is a potential barrier to DRS uptake. Similar findings have been reported in a study done in Kenya by Mwangi *et al*[11], and in northern Tanzania by Mumba *et al*[17].

Physicians play a key role in initiating and monitoring their patient's diabetic retinopathy screening to reduce preventable blindness. In this study it was found that 63.6% of those who were recommended to screen for DR by their physicians screened for DR. These findings were similar to a study done in Netherland by Van Eijk *et al*[16] and in India by Manu *et al*[14]. Although this study pointed out the influence of physician recommendation in DRS uptake, only 33.2% of participants were told by their physicians to go for DRS. Therefore, further studies are needed to establish the reasons why there is less referral for DR screening by physicians at the diabetic clinic.

Mydriatic eye drop has a stingy irritation on instillation and causes temporary blurring of vision as a result of pupillary dilatation. In this study it was observed that those who thought mydriatic eye drop was not tolerable were more likely not to screen for DR within 12 months. Similar results were reported in Sri Lanka by Piyasena *et al*[13] and in Ireland in a study by Dervan *et al*[12]. The Influence from other patients who have been previously dilated has an impact on the turn up of other patients to screen for DR.

CONCLUSION

The proportion of diabetic retinopathy screening at MNH was low. Lack of awareness on diabetic retinopathy screening was a barrier to DRS uptake and the belief that mydriatic eye drop was intolerable discouraged patients to undergo screening for DR.

RECOMMENDATIONS

All diabetic educators should be trained and sensitized to put more emphasis on DR and DRS when providing health education to patients with DM during conduction of the diabetic clinic. Topical anaesthesia should be used before administering mydriatic eye drop to ensure comfort and the use of miotics after examination so as to relieve photophobia. Patients should be informed and reassured on what will happen after pupillary dilatation and they need to be educated on the importance of pupillary dilatation for the detection of the disease.

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Authors' contributions: Denis MN designed the study, collected data, entered data in SPSS for analysis, interpreted the results and prepared the manuscript. Mosenene S, Mhina C, and Mafwiri MM participated in designing the study and revising the manuscript critically for important intellectual content.

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Pharmacological prophylaxis for endophthalmitis following cataract surgery: Practice pattern in training centres in Nigeria

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ABSTRACT

Background: Post-operative infective endophthalmitis is often caused by normal ocular flora. This informed the practice of pharmacological and non-pharmacological preventive measures such as using ocular sterilising agents and antibiotics.

Objective: This study aimed to determine the practice pattern for pharmacological prophylaxis against post-cataract surgery endophthalmitis in postgraduate ophthalmology training centres in Nigeria.

Methods: An online self-administered questionnaire was sent to consenting ophthalmologists who were key informants purposively selected from accredited ophthalmology training centres across Nigeria. Data was analysed using the IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). Information obtained included perioperative antibiotic use, intraoperative antibiotic use, and povidone-iodine use at surgery.

Results: A total of 39 training centres were recruited, of which 35 responded. Only one (2.9%) centre had a written endophthalmitis prophylaxis protocol. Fifteen (42.9%) respondents reported the routine use of preoperative topical antibiotics by all surgeons in their centres, while preoperative use of topical antibiotics was surgeon-dependent in the remaining 20 (57.1%) centres. The most common class of preoperative antibiotics in use was fourth-generation quinolones (46.7%). Intraoperative antibiotics routinely used were subconjunctival gentamicin in 34 (97.1%), intracameral antibiotics in 9 (25.7%), and 5% povidone-iodine in 30 (85.7%) centres. Postoperative use of topical antibiotics was routine in all centres.

Conclusion: Pharmacological endophthalmitis prophylaxis in Nigerian training institutions commonly involves the intraoperative use of 5% povidone-iodine and intraoperative antibiotics, in keeping with literature. The use of preoperative and postoperative topical antibiotics, though not strongly backed by evidence, is also common in many centres.

Key words: Pharmacological prophylaxis, Endophthalmitis, Cataract surgery, Practice pattern, Nigeria

INTRODUCTION

Endophthalmitis is a severe sight-threatening intraocular inflammation, often caused by the invasion of harmful organisms into the ocular tissues, resulting in tissue damage[1,2]. These microorganisms are usually from exogenous sources following intraocular surgery, or trauma and occasionally may be from a systemic infectious focus[1,3,4]. Endophthalmitis often results in severe and permanent vision loss if prompt and appropriate treatment is not administered[2]. Hence, clinicians often take active measures to prevent endophthalmitis when planning intraocular procedures. Cataract surgery, one of the most frequently performed intraocular procedures, is commonly taught and performed in all postgraduate ophthalmology training centres in Nigeria. It is expected that such training centres should have standard operating procedures for endophthalmitis prophylaxis before, during and after cataract surgery.

Vision loss from endophthalmitis may be potentiated by late presentation, lack of equipment for vitrectomy, virulence of the causative organism, or a combination of these factors[5]. This has potential socio-economic implications as vision-impaired individuals might experience a decline in their quality of life and productivity[6]. This adversely affects, not only their income-earning potentials but also their dependants and the larger society, all of which may contribute to impoverishment and impede the attainment of certain sustainable development goals[6,7]. This impact of endophthalmitis after cataract surgery necessitated several prophylactic practices as prevention is cheaper.

Pharmacological prophylaxis of endophthalmitis has been practised for many decades. The use of different concentrations of povidone-iodine, routes of antibiotic administration, and non-pharmacological approaches have been improved upon over the years. Management of endophthalmitis however remains challenging in Nigeria, hence it is more prudent to prevent than cure[8].

As more ophthalmologists are trained in Nigeria, a corresponding increase in cataract surgical coverage is expected under ideal situations. Likewise, the number of postoperative endophthalmitis cases may increase as cataract surgery rates increase. The prevention of

endophthalmitis is thus a critical aspect of ophthalmic care which every facility offering cataract care expectedly pays attention to[2]. However, there is a need for auditing and standardisation of practice as more evidence emerges in the literature. Studies have shown various effective pharmacological prophylactic approaches to post-operative endophthalmitis, including the use of 5% povidone iodine to disinfect the conjunctival sac, the use of intracameral quinolones and preservative-free cephalosporins[2]. Perioperative instillation of topical antibiotics appears controversial due to the reported insignificant lowering of post-operative endophthalmitis rates, compared to povidone iodine alone[9,10]. It is however reported to be widely used in Nigeria[11].

Guidelines and protocols in medical practice evolve as new evidence emerges in literature through research. Training centres are the hub of knowledge and skill improvement; hence they largely influence the prevalent practices in their locations or regions. In Nigeria, anecdotal reports from centres suggest variations in practice. Furthermore, different practices were found in a recent study among ophthalmologists surveyed at a national conference[11].

This study therefore sought to determine what pharmacological practices predominate in training centres in Nigeria in comparison to current evidence in the literature. The findings from this study will help individual trainers and trainees audit their practice and strengthen areas of weaknesses. This could pave the way for more efficient use of resources and further standardisation of clinical care.

MATERIALS AND METHODS

Study design: A web-based cross-sectional survey of ophthalmology training centres, using Google forms to collect information from one key informant per centre. Data was collected over four weeks with repeated reminder text messages and calls put through to the key informants during this period.

Study population: All ophthalmology residency training centres in Nigeria. For the purpose of this study, training centres were defined as all hospitals with partial or full accreditation of the West African College of Surgeons (WACS) or the National Postgraduate Medical College of Nigeria (NPMCN) to train ophthalmologists. There were 39 training centres with accreditation from one or both colleges. One consultant ophthalmologist having verbally reported high cataract surgery load was recruited per training centre as a key informant. Resident doctors in training and centres where two consecutive consultants declined participation were excluded from the study.

Sampling technique and procedure: A list of accredited training facilities was obtained from the Faculty Chairman and Secretary of WACS and NPMCN. A consultant ophthalmologist practising full-time in each centre was purposively identified and contacted for information on any anterior segment specialist in the centre or in the absence of that, a specialist with the highest cataract surgical volume in that centre. The individual identified as the key informant was contacted by a phone call for verbal consent and the study questionnaire was shared with them once consent was given. Two of the 39 key informants initially contacted declined participation and were replaced by contacting another person in the centre that routinely performs cataract surgery. Four key informants who had consented to participate did not fill out the survey form before the end of the study period, despite several reminders.

Ethical approval and consent: Ethical approval for the study was obtained from the University of Ibadan/ University College Hospital Ethical Review Committee (UI/EC/24/0295).

Data management and analysis: Data from filled forms was downloaded into a Microsoft Excel spreadsheet, cleaned, and then imported into the IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA) for analysis. Data was stored in a password-secured laptop belonging to the Principal Investigator and in a password-protected external hard drive afterwards. Data was made available to all the co-investigators during and after the study. Participants' general characteristics are presented using frequencies and percentages.

RESULTS

The key informants of 35 of 39 eligible centres filled out the forms giving a response rate of 89.7%. All the centres were located in urban areas, 33 (94.3%) were government-owned, while two (5.7%) were missionary centres. There were 12 (34.3%) in the South- West and only one (2.9%) in the North-East. Table 1 details the distribution of the responding centres across the various geopolitical zones. Only one (2.9%) of the 35 facilities had a written endophthalmitis prophylaxis protocol.

Table 1: Proportion of respondents in each geopolitical region of Nigeria (n = 35)

Geopolitical zones	Frequency (n)	(%)
South-west	12	34.3
North-central	7	20.0
South-east	6	17.1
South-south	5	14.3
North-west	4	11.4
North-east	1	2.9
Total	35	100

Preoperative topical antibiotic use: Fifteen (42.9%) facilities use preoperative antibiotics routinely and the usual practice is to start instilling them 24 hours before surgery in all 15 facilities. Antibiotics used included fourth-generation fluoroquinolones (seven centres; 46.7%), cephalosporins (3; 20.0%), and chloramphenicol (2; 13.3%). Other preoperative antibiotics reported were aminoglycosides (1; 6.7%), penicillin (1; 6.7%), and "any broad-spectrum antibiotics" (1; 6.7%). The preoperative use of topical antibiotics was surgeon-dependent in the other 20 centres.

Intraoperative antibiotic use: Intraoperatively, nine centres (25.7%) use intracameral antibiotics with moxifloxacin routinely used by five (55.6%), cefuroxime by three (33.3%), and ceftriaxone by one (11.1%) of the facilities. Subconjunctival antibiotics are routinely used in 34 (97.1%) of the 35 facilities. Gentamicin is the most common antibiotic, used by 33 (97.1%) centres, while one (2.9%) centre routinely uses ceftazidime.

Postoperative antibiotic use: All 35 facilities use topical antibiotics postoperatively. Twenty-nine (82.9%) routinely use fluoroquinolones. Details of postoperative topical antibiotics use is displayed in Table 2.

Table 2: Postoperative antibiotics use across the training institutions (n = 35)

Variable	Frequency (n)	(100%)
Postoperative antibiotics use		
Yes	35	100.0
No	0	0.0
Type of antibiotics used		
Fluoroquinolones	29	82.9
Cephalosporins	5	14.3
Any broad-spectrum antibiotic	1	2.8
Duration of antibiotics use		
Four weeks	11	31.4
Six weeks	17	48.6
Eight weeks	5	14.3
Twelve weeks	2	5.7

Use of povidone iodine: Before the commencement of surgery, 5% povidone-iodine is routinely instilled into the conjunctival sac in 30 (85.7%) centres, while five (14.3%) centres do not use povidone-iodine. The duration of instillation (before rinsing with normal saline) varies from one minute in one (3.3%) centre to three minutes in 14 (46.7%), and five minutes in six (20%) centres. Nine (30%) centres have no standardized duration for povidone instillation as it was reported to be dependent on individual surgeons' preference.

DISCUSSION

This cross-sectional survey presents a snapshot of the pharmacological endophthalmitis prophylaxis practice pattern for cataract surgery in ophthalmology residency training centres in Nigeria. We had a response rate of about 90% from the training centres in the country. This survey reveals that the vast majority use 5% povidone-iodine on the conjunctival sac before surgery commences and use subconjunctival antibiotic injection at the end of surgery. In addition, the use of topical antibiotics post-operatively, for endophthalmitis prophylaxis, is routine in all centres.

Preoperative topical antibiotics use: Slightly less than half (43%) of the responding training institutions use preoperative topical antibiotics, mostly fluoroquinolones. A study by Garg *et al*[12] revealed that, across Asian institutions, preoperative prophylaxis antibiotics use was more common than in this study. In their study, the rate of use was 61.5% and 69.5% for low-risk and high-risk cataract cases, respectively. They had surveyed 26 eye institutions from 13 Asian countries with regard to perioperative, intraoperative, and postoperative antibiotic prophylaxis in cataract surgery. However, a study by Silas *et al*[11] here in Nigeria had a similar rate of preoperative prophylaxis antibiotics use as ours. They reported a 42.7% usage among the responding ophthalmologists. Their study was conducted among ophthalmologists attending the Ophthalmological Society of Nigeria conference; hence it was an individual practice survey and not institution practice as is ours, yet the results were similar. In these two studies, fluoroquinolones were the commonly used preoperative prophylactic antibiotics. It is noteworthy that current literature suggests that preoperative topical antibiotics do not reduce either intraoperative ocular surface bacterial count[13] or the risk of endophthalmitis[14,15]. The continuous use of preoperative antibiotics despite current evidence may not be unconnected to reluctance to a change of practice pattern by the surgeons, or the need for more published evidence to reaffirm its lack of benefits in endophthalmitis prevention.

Intraoperative antibiotics use: Two different meta-analyses on the safety and efficacy of intracameral antibiotics revealed that it was a safe and efficacious means of reducing the risk of postoperative endophthalmitis[16,17]. The meta-analysis by Kato *et al*[17], which included 51 eligible articles and over 6.8 million eyes reported that intracameral injection of vancomycin had the best preventive effect (odds ratio 0.03, 99.6% confidence interval 0.00–0.53) followed by intracameral injection of cefazoline, cefuroxime, and moxifloxacin. Both meta-analyses cited above concluded that a single agent intracameral injection of the studied antibiotics

prevented postoperative endophthalmitis. A study by Herrinton *et al*[15], comparing intracameral antibiotic injection with topical antibiotics only, revealed that intracameral antibiotic was more effective, with an odds ratio of 0.58, (CI: 0.38 – 0.91). In our survey, only a quarter of the institutions used intracameral antibiotics routinely, of which the most common antibiotic used was preservative-free moxifloxacin. Concerning subconjunctival antibiotics, however, all but one of the responding institutions do this routinely, with the most common antibiotic being gentamicin.

Postoperative antibiotics use: All our surveyed institutions use topical antibiotics postoperatively, with more than three-quarters of them routinely using topical fluoroquinolones. Even though postoperative topical antibiotics are routine following cataract surgeries, it has been suggested that with intracameral injection of antibiotics following phacoemulsification, topical antibiotics may not confer additional protection from postoperative endophthalmitis[13]. This practice needs further microbiological evaluation to justify its utility, especially with increasing antibiotic resistance[18]. A randomised clinical trial may shed more light on the need for topical postoperative antibiotics after intracameral injection of antibiotics. Also observed in this study is the varying duration of prophylactic use of antibiotics with some prescribing up to 12 weeks postoperatively. This points to a lack of standardisation and a need to develop written protocols for endophthalmitis prophylaxis across training centres in Nigeria.

Use of povidone iodine: The recommended guideline for povidone-iodine use in ophthalmic surgery includes the application of 10% povidone-iodine over periocular skin before draping and the instillation of 5% povidone-iodine into the conjunctival sac for at least 3 minutes before rinsing off[19]. Halachmi-Eyal *et al*[19] reported that the preoperative instillation of 5% povidone-iodine alone into the conjunctival sac had significant bactericidal effect. There was no significant additive effect by combining preoperative topical moxifloxacin 0.5% with 5% povidone iodine. The American Academy of Ophthalmology and the European Society of Cataract and Refractive Surgeons' recommendations regarding povidone-iodine use also suggested 5% povidone-iodine before surgery and noted a 3-minute duration for its application[20]. Our study revealed that most of the centres used povidone-iodine routinely as part of the antiseptic strategy in post-cataract surgery endophthalmitis prophylaxis. With the available evidence and recommendations on the use of povidone-iodine, it is surprising that 5 centres in our study cohort do not use povidone iodine routinely. It was also noticed in our study, that centres that routinely perform conjunctival sac instillation of povidone-iodine had a significantly varied duration of application ranging from one to five minutes, or even no specific duration of application in some centres.

One strength of this study is the fact that data was obtained from anterior segment consultants or ophthalmic surgeons with high cataract surgery turnover in each training centre. A potential limitation of this study was the reliance on self-reported data from the training centres, as it may be subject to inaccuracies in reporting or recall bias. Direct observation or a review of medical records may provide a more objective assessment of prophylaxis practices. Not asking for specific consumable availability such as povidone-iodine and thus not analysing for its effect on the practice pattern of endophthalmitis prophylaxis, maybe another potential limitation.

In conclusion, this study has shown the diversity in the pharmacological practice pattern of endophthalmitis prophylaxis for cataract surgery across postgraduate ophthalmology training centres in Nigeria. Conjunctival sac application of 5% povidone-iodine is a routine practice, while the intracameral antibiotic injection is not routine in most centres. The variation in practices suggests a need for national guidelines that align with global best practices, particularly advocating for the use of intracameral antibiotics, which have been shown to significantly reduce the incidence of postoperative endophthalmitis. Training programs should emphasize the importance of evidence-based prophylaxis to ensure consistent and effective patient care.

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Retinoblastoma in Tanzania; Survival and prognostic factors: A retrospective cohort study

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ABSTRACT

Objective: To determine the 3-year survival rate and prognostic factors among patients with retinoblastoma diagnosed at Muhimbili National Hospital from January 2016 to December 2018.

Methods: A retrospective cohort study was conducted. Participants were consecutively recruited. Data were collected using a questionnaire. Variables included demographics, clinical presentation, treatment, and survival time. Statistical analysis was performed using Stata version11. Kaplan-Meier survival analysis was used to assess the survival rates, while the log rank test determined statistical significance. The hazard ratios were calculated using Cox regression. A P value < 0.005 was considered statistically significant.

Results: A total of 166 children were studied, with 69.3% having unilateral retinoblastoma and 30.7% bilateral. Fifty percent of the children were females. The overall mean age at diagnosis was 25.56 ± 15.56 months. The participant's mean age at diagnosis was 18.7± 11.6 months for bilateral and 31.3± 20.4 months for unilateral retinoblastoma. The most common complaints were leukocoria (90.4%) and eye protrusion (46.4%). The mean duration of symptoms was 7.9±5.3 months, and the mean total delay time was 9.4±5.6 months. At presentation, 51.8% of the study participants had disease stage 3 and 4 according to the International Retinoblastoma Staging System. The 3-year Kaplan-Meier survival rate was 52.3%. Multivariate Cox regression analysis identified age at diagnosis > 24 months (p=0.001), failure to complete treatment (p=<0.001), and extra-ocular disease invasion (p=0.008) as factors associated with lower survival rates.

Conclusion: The 3-year survival rate of patients with retinoblastoma in our setting was 52.3%. Age at diagnosis of >24 months, failure to complete treatment, and extraocular disease invasion were associated with a lower survival rate.

Key words: Survival rate, Retinoblastoma, Late presentation, Leukocoria

INTRODUCTION

Retinoblastoma (Rb) is the most common intraocular malignancy in young children, with an estimated incidence of 1 in 20,000 births worldwide (ranging from 1 in 14,000 to 1 in 34,000)[1, 2]. In high-income countries, Rb is curable, and deaths from this cancer are rare[3]. In Africa, however, Rb is the most prevalent life-threatening ocular cancer in children under five, associated with a higher mortality rate[4, 5]. Rb is a potentially curable disease with very high disease-free survival if early detected and managed appropriately[1,2]. However, late diagnosis and treatment result in significantly higher mortality and morbidity, leaving some survivors completely blind with severe emotional difficulties and limited participation in educational, economic, and social activities[6].

The survival rates for retinoblastoma vary significantly worldwide. The 3-year survival rate is 99.5% in high-income countries, 91.2% in upper-middle-income countries, 80.3% in lower-middle-income countries, and 57.3% in low-income countries[7]. Lower survival rates in developing countries, particularly in sub-Saharan Africa, are attributed to delays in seeking medical care, late diagnosis and treatment[9, 10]. Despite developing countries bearing greater (80–90%) of the disease burden, few studies have focused on retinoblastoma survival rates[6–8]. In spite of having a significant number of patients receiving treatment annually in our centre, the survival rate and prognostic factors remains unknown. Knowing the survival rates and prognostic factors may help in evidence based counselling to the parents and caretakers about Rb treatment. This can positively impact the decision of parents in accepting treatment without any delays and further increases the chances of survival. This study aimed at investigating the 3-year survival rate and associated prognostic factors among patients diagnosed with retinoblastoma at our centre from January 2016 to December 2018.

MATERIALS AND METHODS

Study design and study period: This was a retrospective cohort study conducted for a period of six months between June and December 2021.

Study setting: This study was conducted at Muhimbili National Hospital (MNH) which houses eye paediatric and paediatric oncology units providing both outpatient and inpatient services. The paediatric oncology and eye unit collaborates in a specialized programme dedicated for managing retinoblastoma patients. The two units are equipped for the diagnosis and management of early and late cases of retinoblastoma. An average of 60–80 cases of retinoblastoma are seen each year at MNH.

Study population: The study population included all patients with retinoblastoma diagnosed at MNH from January 1st, 2016 to December 31st, 2018.

Inclusion criteria: This study included all patients with a histologically confirmed diagnosis of retinoblastoma with complete 3 years follow-up time.

Exclusion criteria: All patients whose outcomes were unknown due to loss to follow-up and incomplete data.

Data collection procedure: Data was collected using a structured questionnaire. The principal investigator gathered information from the retinoblastoma data base and patients' files. This included demographic information, presenting complaints, duration of the symptoms, family history of retinoblastoma, disease laterality, disease stage according to the International Retinoblastoma Staging System (IRSS), types of treatment, time lag before treatment, and total delay time. It also collected information regarding the follow-up time and the survival status (alive or dead). Symptom duration was defined as the time from symptom onset, as noted by the parents or caretaker, to the first presentation at MNH. Total delay time was defined as the interval from the first time the parent noted the first symptom to the initiation of the first treatment at MNH.

Data analysis: Stata version 11.0 was used for data analysis. Kaplan-Meier survival analysis was performed to assess the survival rates, and statistical significance was tested by the log-rank test. Univariable and multivariable Cox regression were used to calculate unadjusted and adjusted hazards ratios. A p-value of <0.05 was considered statistically significant. The measure of outcome was survival. The survival time was measured from the date of diagnosis up to the 3-year follow-up time, or the time when death occurred.

Ethical consideration: Ethical clearance for the study was obtained from the Institutional Review Board of Muhimbili University of Health and Allied Science. Verbal consents were obtained from parents / caretakers through mobile phone calls. Participants had no risk in participating in this study and they were not paid anything. The study provided no direct benefit to the study participants but findings of the study if implemented can improve the survival rate in these patients.

RESULTS

Of the 184 patients diagnosed with retinoblastoma (Rb) from 2016 to 2018, 18 were excluded from the analysis due to loss to follow-up (15 patients) and incomplete data (3 patients). Of the 166 study participants included in the analysis, slightly more than half (51%) were females. The majority (99; 60%) of the participants were aged 2–24 months, 58 (34.9%) were aged 25–48 months, and nine (5.4%) were older than 48 months. The overall mean age at diagnosis was 25.56 months (± 15.56 months). The mean age at diagnosis was 18.7 (± 11.6) months for participants with bilateral retinoblastoma and 31.3 (± 20.4) months for those with unilateral retinoblastoma.

Table 1: Clinical characteristics and disease stage of the study participants at presentation

Characteristic	Frequency	
	No.	(%)
Laterality		
Unilateral	115	69.3
Bilateral	51	30.7
Presenting complaints		
Leukocoria	150	90.4
Eye protrusion	77	46.4
Eye redness/pain	46	27.7
Squint	16	9.6
Other symptoms	23	13.8
Recurrent tumour post enucleation	4	2.4

Family history of retinoblastoma	5	3.0
Duration of symptoms(months)		
< 3	30	18.1
3-6	54	32.5
>6	82	49.4
International Retinoblastoma Staging System (IRSS)		
Stage 1	40	24.1
Stage 11	40	24.1
Stage 111	48	28.9
Stage IV	38	22.9

Other symptoms included poor vision (12), nystagmus (4), headache (1), eye discharge (2), and vomiting (4).

Most (69.3%) participants had a unilateral disease. The most common (90.4%) presenting complaint was leukocoria. Nearly half (49.4%) of study participants had a duration of symptoms greater than 6 months. More than half (86; 51.8%) of the participants presented with advanced disease (stage 3 or 4) (Table 1).

The mean duration of symptoms was 7.9±5.3 months. The majority (122; 73.5%) of the study participants had a total delay time of ≥ 6 months, while only (44; 26.5%) had a total delay time of < 6 months from the onset of symptoms to treatment initiation. The mean total delay time from recognition of symptoms to treatment initiation was 9.4±5.6 months. In most (156; 94%) of study participants, the treatment was initiated within one month after diagnosis. About (7; 4.2%) of participants died in the course of treatment.

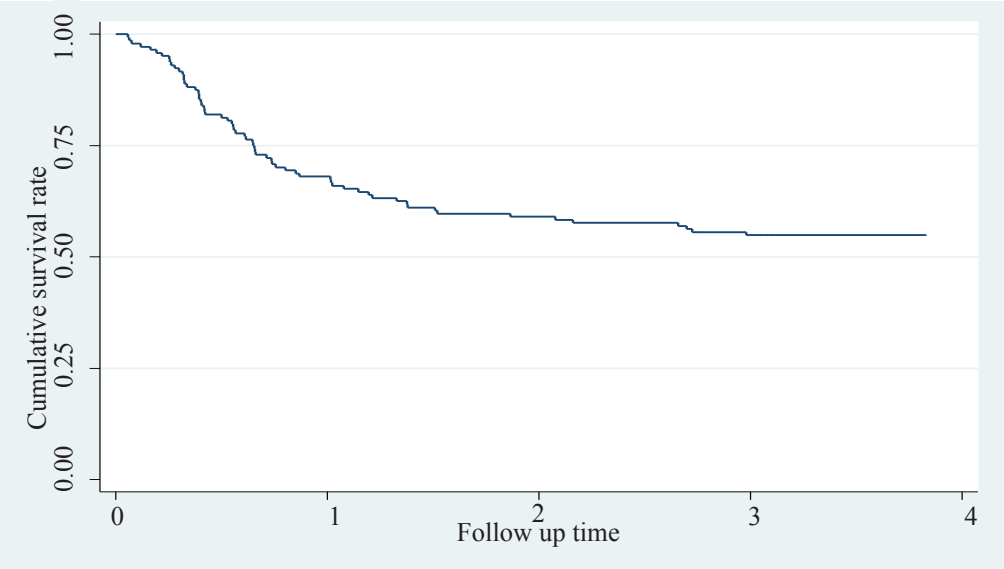
Table 2: Modality of treatments given to the study participants (n=166)

Variable	Frequency	
	No.	(%)
Modality of treatment given		
Primary enucleation alone	33	19.8
Primary enucleation with adjuvant chemotherapy	41	24.7
Primary enucleation with adjuvant chemotherapy and radiotherapy	06	3.6
Secondary enucleation with adjuvant chemotherapy	30	18.1
Secondary enucleation with adjuvant chemotherapy and radiotherapy	20	12.1
Palliative treatment	36	21.7

Many patients received more than one treatment modality. The patients who received chemotherapy without radiotherapy included those whose histology ruled out high-risk features. Three patients who were under the age of one year and eligible for radiotherapy did not receive it due to their young age. Twenty patients did not complete the required treatment.

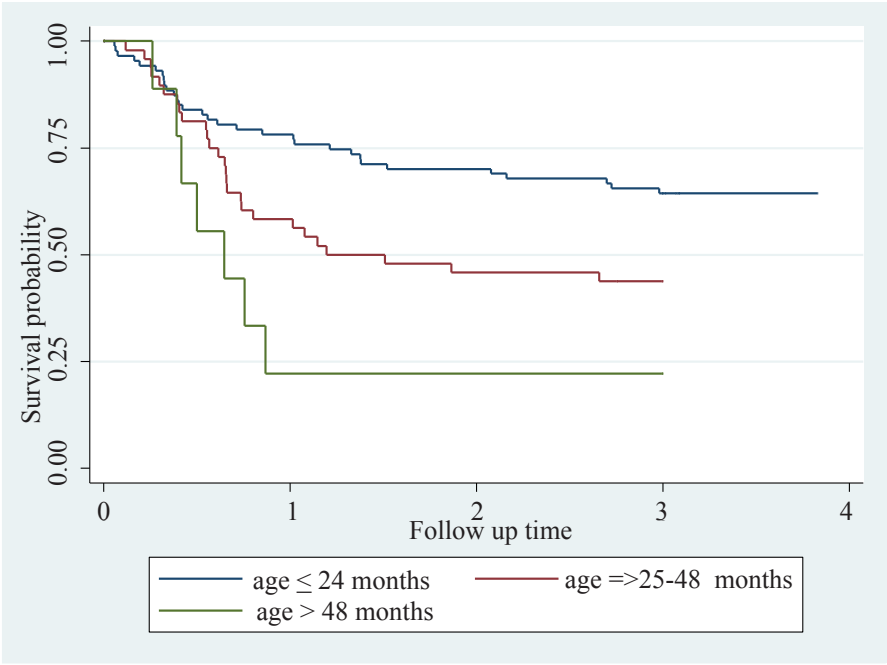
Survival rate analysis: The overall cumulative survival rate of the patients with retinoblastoma was 69%, 59.6% and 52.3% at 1, 2 and 3 years respectively (n=166) (Figure 1).

Figure 1: Kaplan -Meir survival rate for retinoblastoma patients



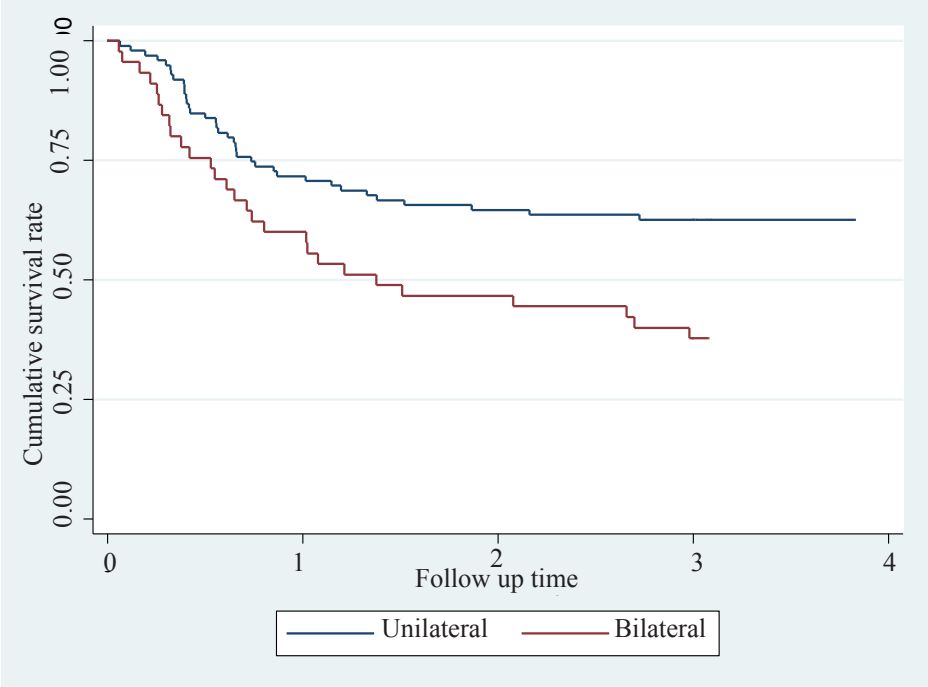
The 3- year survival rate was 99 (66%) for the participants diagnosed within the first 24 months of life. The survival rate for participants aged 25-48 months was 58 (44%) and 9 (22.2%) for participants aged 49 months and above. The survival rate difference between these age groups was statistically significant (log rank p= 0.0026). (Figure 2).

Figure 2: Kaplan-Meir survival rate of the study participants by age at diagnosis



The 3-year survival rate for participants with unilateral Rb was 115 (64.4%), while for bilateral Rb it was 51 (37.2%). The difference in survival rate between the two groups was statistically significant (log rank p = 0.0053) (Figure 3).

Figure 3: Kaplan-Meir survival rate of the study participants by disease laterality



The study participants with shorter duration of less than 3 months had a 3-year cumulative survival rate of 30 (86.6%), whereas those who presented after 3 months duration had cumulative survival rate of 54 (68.5%) and 82 (36.6%) for patients with symptoms lasting 3-6 months and >6 months respectively. There was a significant difference in survival rate between the groups (log rank p=0.0002).

Participants with time interval of less than six months from the first appearance of first symptom to the initiation of treatment had cumulative survival rate of 44 (86.4%) and those with time interval of greater than six months the survival rate was 122 (45.1%). There was a significant difference in survival rate between the two groups (log rank p=0.0004).

According to disease stage at diagnosis, participants with stage 1 disease had a survival rate of 40 (90%), stage 2 had a survival rate of 40 (77%), stage 3 had a survival rate of 48 (49.5%) and stage 4 had a survival rate of 38 (2.6%). The survival rate difference across the disease stages was statistically significant (log rank p= <0.0001).

Majority 130 (78.3%) of patients came with advanced disease which necessitated enucleation. Participants who underwent primary enucleation had higher survival rate (80; 80%) compared to those who underwent secondary enucleation (50; 58%). The difference in survival rate was statistically significant (p= <0.0001). Participants who had treatment initiated within one month of diagnosis had a higher survival rate (156; 59.6%) compared to those whose treatment was initiated after one month whereby all died. The observed difference was statistically significant (Log-rank p = 0.0019). Patients who abandoned treatment had 100% mortality, n=20. The difference in survival rate was statistically significant (Log rank p= <0.0001).

Table 3: Cox regression analysis for the factors associated with 3-year survival rate

Factor	Crude hazards ratio			Adjusted hazards ratio		
	HR	95% CI	P-value	HR	95% CI	P-value
Gender						
Male	1	-	-		-	-
Female	0.9	0.56 -1.43	0.549			
Age groups (months)						
≤ 24	1	-	-	1	-	-
25 -48	1.85	1.1 - 3.1	0.019	1.8	0.9- 3.8	0.034
> 48	3.46	1.5 - 7.9	0.003	3.7	1.4 - 9.9	0.001
Laterality						
Unilateral	1	-	-	1	-	-
Bilateral	1.98	1.2 - 3.2	0.006	1.4	0.8 - 2.6	0.216

Eye protrusion						
Yes	5.44	3.1 - 9.5	<0.001	1.5	0.6 - 3.8	0.364
No	1	-		-	-	
Duration of symptoms (months)						
< 3	1	-	-	1	-	-
3-6	2.26	0.7- 6.7	0.144	2.0	0.8 - 5.0	0.136
>6	5.13	1.8 - 14.3	0.002	4.5	1.7 - 9.4	0.112
Total delay time (months)						
< 6	1	-	-	1	-	-
≥ 6	4.09	1.7 - 9.4	0.001	0.3	0.07- 1.5	0.157
Disease stage						
1	1	-	-	1	-	-
2	2.48	0.7- 8.2	0.136	2.9	0.8 - 10.1	0.083
3	6.40	2.1 - 18.8	0.001	4.4	1.4 - 13.3	0.008
4	25.59	8.9 - 73.4	<0.001	5.2	1.5- 17.7	0.008
Treatment completion						
Yes	1	-				
No	17.8	9.1 -34.8	<0.001	13.7	5.0 - 37.4	<0.001

On both univariate and multivariate cox regression analysis, participants aged more than 24 months at diagnosis, extraocular disease (stage 3 and 4) and failure to complete treatment were found to be associated with lower survival.

DISCUSSION

Survival rates for patients with retinoblastoma vary significantly worldwide. In high-income countries, recent reports indicate 3-year survival rates as high as 99.5%. However, in developing countries, the survival rate remains low, with recent reports indicating a 3-year survival rate of 57.3%[7]. This study found a 3-year survival rate of 52.3%, which is higher than the rates reported in Uganda by Kalinaki *et al*[12] and in Kenya by Gichigo *et al*[11] which showed 3-year survival rates of 41.1% and 26.6%, respectively. However; this survival rate is slightly lower compared to that reported by the global retinoblastoma group (2022), which showed a 3-year survival rate of 57.3% of children from lower-income countries[7].

The 3-year survival rate observed in this study is significantly lower compared to the 3-year survival rates of over 80% reported in high- and middle-income countries[10,13,14]. The lower survival rate in this study is attributed to late presentation, which is due to underdeveloped primary eye care in Tanzania. Patients with retinoblastoma are first seen at primary and secondary health facilities where most health workers may have inadequate knowledge and skill to identify and appropriately refer them for tertiary care as previously reported by Mafwiri *et al*[15]. This leads to delay in presentation and late initiation of treatment. It is also reported that children in low-income countries present with a more biologically aggressive form of disease, which could have attributed to lower survival rate seen in this study[10]. Nevertheless, the current 3-year survival rate of this study is higher compared to that previously reported in Tanzania in 2008 by Bowman *et al*[16], which showed 30-months disease free survival probability of 23%. This shows that more children with Rb are surviving more compared to how it was 14 years ago. The improvement in survival rates for these patients can be attributed with the availability of well-established paediatric oncology free services, and improved follow-up of these patients.

Age at diagnosis was identified as an independent predictor of the survival with, a dramatic decline in survival rates for participants diagnosed after the age of 24 months. This has been widely reported in previous studies[4, 17]. It was observed that, many children who were diagnosed after 24 months of life had extraocular disease compared to those diagnosed earlier, which may have contributed to lower survival rate, supporting that retinoblastoma typically starts early in life.

Participants with unilateral retinoblastoma in this study had higher survival rate compared to those with bilateral retinoblastoma. The 3-year survival rate for both unilateral and bilateral retinoblastoma in this study

is lower compared to that reported in Turkey by Özkan *et al*[14] and in Singapore by Saw *et al*[13]. However; the global retinoblastoma group study (2022)[10] showed no difference in 3-year survival with regard to disease laterality. The lower survival rate in patients with bilateral retinoblastoma in this study may be explained by a large proportion of participants (approximately two-third) with bilateral disease who had advanced disease (stage 3 or 4) at presentation compared to patients with unilateral retinoblastoma (46.1%).

Advanced disease at presentation and poor patient outcomes are related to increased lag time before initiation of Rb treatment. This study showed that patients who presented with duration of symptoms of more than 6 months from the time when the parents / caretaker noted the first symptom to the diagnosis of Rb had lower survival rate compared to those who presented with duration of symptoms of less than 6 months. This observation has been reported widely in different studies[1, 17-20]. The lower survival rate in participants with longer duration of symptoms greater than 6 months before diagnosis is related to the greater risk of extraocular extension and central nervous system metastasis leading to poor survival rate in these patients[1, 21]. This indicates that lowering the lag time can be the effective first step towards improving survival in Rb patients. This can be achieved via targeted awareness of Rb campaigns and education programs, strengthening of red reflex test practices at the primary eye care level and shortening of referrals chains to the Rb treatment centres.

The advanced and metastatic disease stage (i.e., stage 3 and 4) at the time of first presentation to the hospital was present in half of the patients. These participants demonstrated a lower 3-year survival rate and all patients with CNS metastasis died. Similar findings have been reported in various studies.[1, 4, 11, 18, 19, 21-23]. The poor survival rate in these patients is because the disease already had the extraocular extension and CNS metastasis where by the disease became untreatable.

Participants who abandon treatment showed the dismal outcome. The main reason for treatment abandonment in this study was the refusal of enucleation. Similar findings have been reported by other authors[22-25]. The lower survival rate in this study was due to extraocular diseases advancement and CNS metastasis. Adequate information about the natural history of the disease and the importance of timely treatment should be given to all parents / care givers and their families so they can accept treatment. In addition, strict follow-up is also important to ensure that patients complete the required treatment regime in a required time period. Adequate and continuous counselling of parents is also necessary to ensure that patients complete treatment.

Nearly a quarter of the participants received palliative treatment due to presence of distance metastasis at the time of presentation. Two thirds of patients underwent enucleation and among them more than half received neoadjuvant and adjuvant chemotherapy. The patients with stage two disease and above also received the adjuvant radiotherapy post enucleation. In patients with bilateral retinoblastoma majority underwent bilateral enucleation and in a few patients, the fellow eye was salvaged. In those cases, the additional local therapy treatment was done which included cryotherapy, thermotherapy, intravitreal mephalan injection and subtenon carboplatin injection. The treatment modalities used in this study indicate the delayed presentation in diagnosis of these patients.

The patients whose treatment was initiated more than one month of diagnosis had lower survival rate compared to those whose treatment was initiated within one month of diagnosis. For patients whose treatment was initiated after one month from the diagnosis, the main reason was the initial refusal of enucleation. The lower survival rate in this is due to late treatment initiation resulting into disease progression and metastasis. Continuous comprehensive counselling is necessary to help the parents and the society to make timely decision regarding treatment for their children.

STUDY LIMITATIONS

Like any other retrospective study, our study also faced the challenges of incomplete data, and we had to exclude all such patients from the analysis thereby reducing the sample size and power of the study. In addition, the study could have faced the problem of recall bias on parents and caregivers reporting the onset of symptoms.

CONCLUSION

The 3-year survival rate of patients with retinoblastoma in our setting was 52.3%. Age at diagnosis of >24 months, failure to complete treatment, and extraocular disease invasion were associated with a lower survival rate.

RECOMMENDATIONS

Efforts to improve survival rate by early diagnosis, timely referral and timely initiation of appropriate treatment are necessary. This can be achieved by raising awareness of the disease to the primary and secondary health care workers and the community at large. Additionally thorough counselling for parents and caregivers to ensure treatment acceptance is necessary.

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