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

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ABSTRACT

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

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

INTRODUCTION

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

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

MATERIALS AND METHODS

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

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

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

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

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

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

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

RESULTS

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

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

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

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

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

Figure 1: Representative fundus photographs of the severity of DR

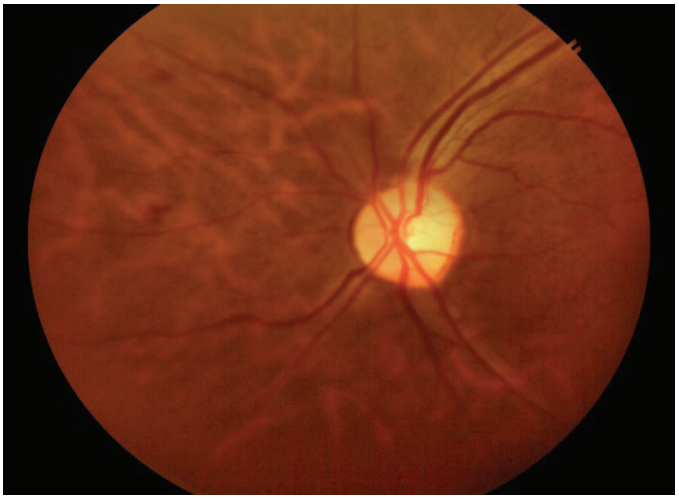

Figure 1.1: Mild NPDR: microaneurisms

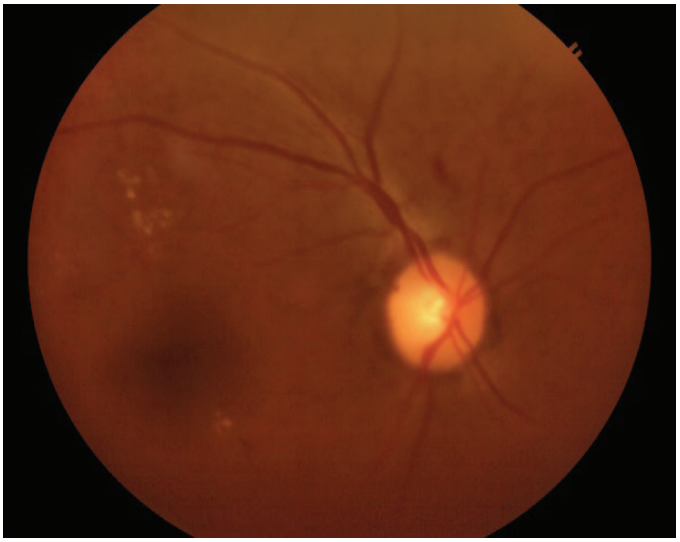

Figure 1.2: Moderate NPDR: exudates, MA, IR haemorrhage

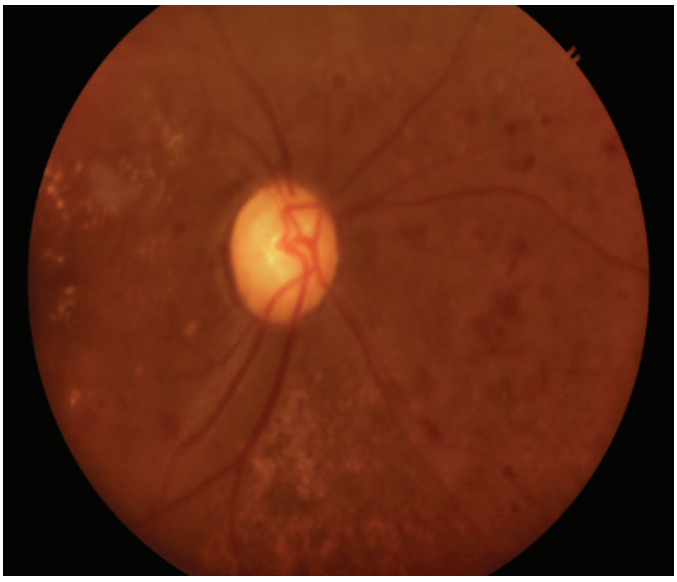

Figure 1.3: Severe NPDR: Venous beading

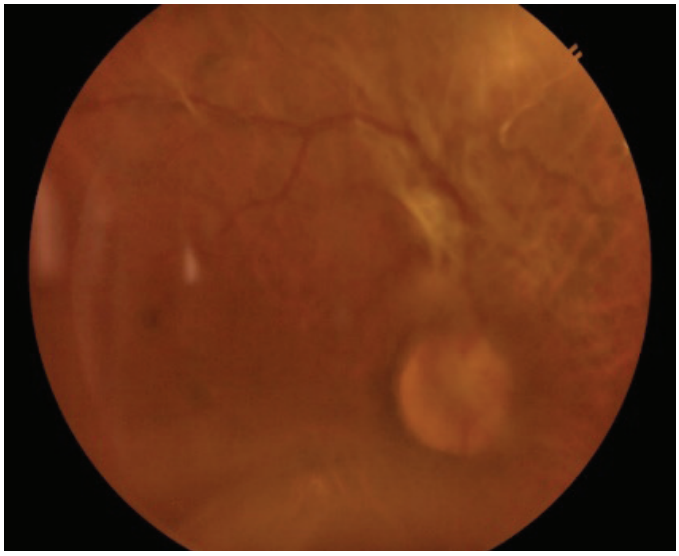

Figure 1.4: PDR: fibrovascular membranes

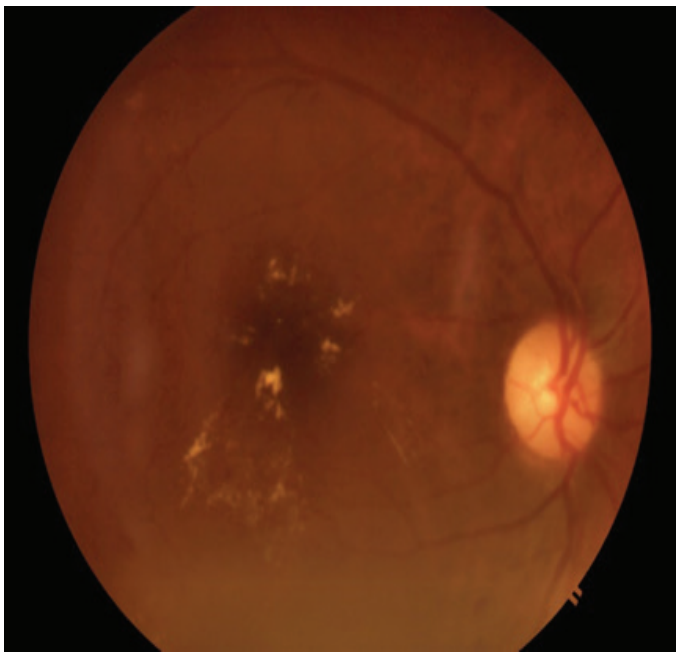

Figure 1.5: DME

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

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

CI: confidence interval, DR: diabetic retinopathy

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

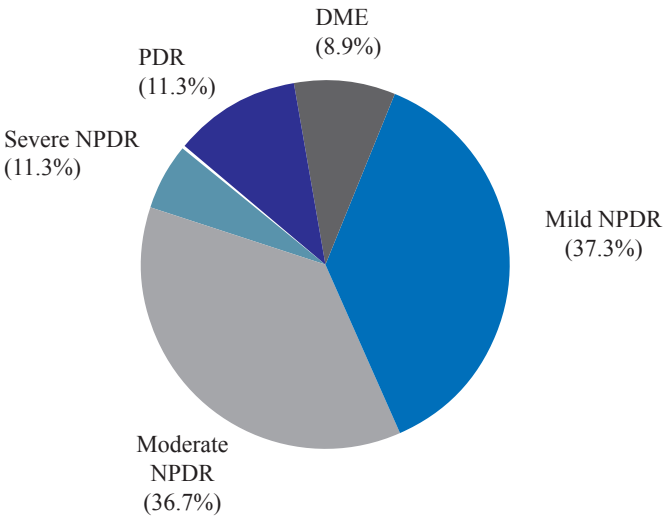

Table 3 shows factors associated with DR among DM patients. The multivariate model shows the main factors associated with any DR were: duration of DM with an Adjusted Odds Ratio (AOR) of 2.1 (95% CI 1.3 -3.5), poor glycemic control (AOR 1.9, 95% CI 1.2 - 3.0) and hypertension AOR 2.0 (95% CI 1.3 -3.4).

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

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

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

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

DISCUSSION

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

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

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

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

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

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