ORIGINAL RESEARCH

Prevalence of Diabetic Retinopathy and Its Associated Factors among Diabetic Patients at Debre Markos Referral Hospital, Northwest Ethiopia, 2019: Hospital-Based Cross-Sectional Study

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Background: Diabetic retinopathy is a well-known sight-threatening microvascular complication of diabetes mellitus. Currently, 93 million people live with diabetic retinopathy worldwide. There are insufficient studies addressing the prevalence of diabetic retinopathy and risk factors in Ethiopia.

Objective: To assess the prevalence of diabetic retinopathy and its associated factors among diabetic patients on follow-up at Debre Markos Referral Hospital, northwest Ethiopia, 2019.

Methods: This institution- based cross-sectional study was conducted among 302 patients. They were selected through systematic sampling. Explanatory data were extracted from medical records and interviews. Blood pressure, weight, height, and visual acuity tests were assessed. Retinal examination was performed with a Topcon TRC-NW7SF fundus camera. Data were entered in EpiData 3.1 and exported in to SPSS 20 for analyses. Binary logistic regression with 95% CIs was used for analyses. Simple binary logistic regression followed by multiple binary logistic regression analysis was conducted to identify associated factors.

Results: There were 302 patients in this study, of which 57 (18.9%) had diabetic retinopathy. Among the diabetic retinopathy patients, 75.4% had the preproliferative type. Four in ten (37.7%) of the patients had visual acuity problems. Poor glycemic control (AOR 4.58, 95% CI 1.86–11.31), > 10 years' diabetes duration (AOR 3.91, 95% CI 1.86–8.23), body-mass index >25 kg/m^2 (AOR 3.74, 95% CI 1.83–7.66), and hypertension (AOR 3.39, 95% CI 1.64–7.02) were factors significantly associated with diabetic retinopathy.

Conclusion: About a-fifth of diabetic patients had diabetic retinopathy. Diabetic retinopathy was significantly associated with glycemic control, hypertension, body-mass index, and duration of illness. Routine assessment and early control of those associated factors may be important in reducing both the prevalence and impact of diabetic retinopathy, as evidenced in the current study.

Keywords: diabetes mellitus, diabetic retinopathy, associated factor, Ethiopia

Background

Diabetic retinopathy (DR) is a well-known sight-threatening microvascular complication of diabetes mellitus (DM).[1–3] It is characterized by varying degrees of microaneurysm, hemorrhage, hard exudates, cotton-wool spots, venous changes,

and new vessel formation involved in the peripheral retina, macula, or both.[4–7] Globally, approximately 95 million (35.4%)diabetic patients have DR, of which a third have vision-threatening DR and 7.6% macular edema.[8,9] Global annual incidence of DR is 2.2%–12.7% and progression 3.4%–12.3-%. Progression to proliferative DR is higher in individuals with mild disease than those with no disease at baseline.[10]

The global prevalence of blindness is estimated to be 1.5 billion, of which 0.4 million is due to DR. Even though blindness and visual impairment has reduced globally, blindness due to DR increased from 0.2 million to 0.4 million and moderate–severe visual impairment from 1.4 million to 2.6 million from 1990 to 2015.[11] Though the combination of social, nutritional, and medical support has prevented or slowed the progression of DR, it is still a global issue, because of the epidemic rise of DM, for which the risk of visual loss is 25 times higher. Screening and treatment of DR is more challenging in developing countries, due to lack of finances and skills.[6,8,12] The cost of screening and treatment of DR is >US$3,190 per quality-adjusted life year. But financial loss due to social and blindness were not estimated.[13]

DR is the leading cause of new cases of blindness in middle-aged and elderly populations in the Asia–Pacific region. It has been estimated that it is the source of 51% of blindness and 56% of visual impairment cases globally, but awareness of DR among DM patients is 28%–84%.[14] In Africa, DR rangs 7%– 62.4%, of which 15% have severe DR. Ethiopia is among the top four countries with the highest (3.8%) adult diabetic populations in sub-Saharan Africa, but without sufficient studies, screening guidelines, standard referral criteria, or retinal photocoagulation.[15,16] Therefore, the aim of this study was to identify the prevalence and determinants of DR among DM patients in this area.

Methods
Study Area and Period
This was an institution-based, cross-sectional study. A total of 302 DM patients were recruited from the diabetes clinic at Debre Markos Referral Hospital through a systematic sampling method. Debre Markos Referral Hospital, in the town of Debre Markos, is 300 km from Addis Ababa, the capital of Ethiopia, and a major referral center for DM treatment in northwest Ethiopia, providing services Monday to Friday every week. Data collection

was conducted from April 1 to May 30, 2019 during routine working days.

Population and Eligibility Criteria
Source populations for this study were all patients with type 1 and type 2 DM according to World Health Organization criteria[17] and on stable anti-DM medication. Patients who were critically ill, did not complete the questionnaire, physical examination, or blood tests, pregnant, or had cataracts, glaucoma, or any other eye disease, and could not completed fundus examinations for any reason were excluded from the study.

Sample-Size Determination and Sampling Procedures
The required sample size was computed using a single-population proportion formula based on the assumption of 95% CI, 5% margin of error, and 41.4% proportion (P) of DR.[18] An added 10% estimated nonresponse rate made a final sample size of 302:

$$\frac{\left(Z_{\frac{\alpha}{2}}\right)^2 p(1-p)}{d^2} = \text{nf} = \frac{ni}{1+\frac{ni}{N}} = \frac{373}{1+\frac{373}{1026}} = 275 + 10\% = 302$$

Every third patient was selected through systematic random sampling to get a sample size of 302. The patient registry was used as a sampling frame. Data were collected from each study participant from the second visit and continued with intervals of three based on visiting-card order until the desired sample size had been obtained.

Operational Definition
The definition of DR was taken as the presence of microaneurysm, hemorrhage, exudates, cotton-wool spots, intraretinal microvascular abnormalities, vein beading, and/or new blood vessels in at least one eye on retinal camera examination.

Data-Collection Procedure and Study-Variable Measurement
Explanatory variables were sociodemographic (age, sex, level of education, marital status, occupation, residence, religion, and family history of DM), behavioral (history of smoking, history of alcohol consumption), clinical (duration of DM, chronic cardiac illness, and chronic kidney disease), DM care (treatment modality, follow-up frequency, and routine DR eye screening). Data were collected through a semistructured questionnaire. Blood pressure was measured using an Android digital sphygmomanometer,

keeping the respondent in a seating position. Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg for two consecutive measurements apart from four hours apart and ongoing treatment with antihypertensive drugs defined hypertension. Those with known chronic kidney disease had been diagnosed by a physician and recorded on their patient registry book. Glycemic level was coded as poor or good. Poor glycemic control was operationally defined as mean fasting blood glucose was >130 mg/dL for at least 6 months.[19] Height was measured with a movable headboard (stadiometer) and recorded to the nearest 0.1 cm. Weight was measured with a digital scale and recorded to the nearest 0.1 kg.[20] Visual acuity was tested at 6 m in a well-illuminated area using a Snellen chart. If the participant's vision were too poor to read any letters on the chart at 6 m, then counting finger, hand movement, and light perception were assessed.[21]

Fundus Examination and Diagnostic Criteria

Eye examinations were conducted by experienced ophthalmologists. Mydriasis of both eyes was assessed with 1% tropicamide and retinal examination, and a TRC-NW7SF fundus camera (Topcon, Tokyo, Japan) used to capture 45°C color digital images of the fundus of both eyes. Double-blind diagnoses were performed by two ophthalmologists from Debre Markose Referral Hospital. In cases of disagreement, a third ophthalmologist was consulted. According to the Early Treatment Diabetic Retinopathy Study, those with microaneurysms, hemorrhage, hard exudates, cotton-wool spots; retinal vein beading changes, microvascular abnormalities in the retina, and/or neovascularization lesions on fundus images were diagnosed with DR. On fundus examination, the presence of microaneurysms, cotton-wool spots, hemorrhage, vein beading, exudates, and/or intraretinal microvascular abnormalities were diagnosed as preproliferative DR, whereas the presence of new vessels on the dis or elsewhere and/or vitreous hemorrhage were diagnosed as as proliferative DR.[5]

Data-Quality Management

The questionnaire was translated into the local language (Amharic) from English, then back to English. One day's training was provided for the data collectors on how data were to be collected and recorded. Pretesting was done on 16 DM patients at Fenoteslam General Hospital to assess the validity of the instrument, estimate time needed for data collection, and modify the questionnaire accordingly. Data were checked daily for completeness and consistency.

Data Analysis

All data were entered in EpiData 3.1 and exported toSPSS 20. Data were checked, cleaned, coded, merged, categorized, and analyzed. Frequency distributions were computed for socio-demographic, behavioral, clinical and DM-care variables. Continuous variables are expressed as means ± SD and categorical variables as proportions. ORs and CIs were used to determine the strength of association between independent and dependent variables. All independent variables were cross-tabulated with dichotomized outcomes of DR (yes/no). Simple binary logistic regression followed by multiple binary logistic regression analysis was conducted to identifyfactors associated with DR in the study population. Variables were entered into the multiple logistic regression model if $P<0.25$ on simple binary logistic regression analysis.[22] $P<0.05$ wa considered a significant association between independent variables and DR. Finally, results were summarized and presented in text, tables, charts, and graphs.

Result
Sociodemographic Characteristics of Respondents

A total of 302 DM patients were included in the current study, with a 99.6% response rate. Respondents' mean age was 41.20±14.20 years. Two-thirds (67.5%) of the respondents were males, half (54%) > 40 years old, two-thirds (65.6%) married, and three-quarters (76.2%) urban dwellers. Though a third (37.4%) of respondents had a family history of DM, only 5.3% of them had developed DR. Half (45.0%) the respondents had a college education, and a third (35.1%) were governmental or nongovernmental employews (Table 1).

Behavioral, Clinical, and Diabetes-Care Characteristics of Respondents

Regarding prevalence of alcohol intake, 53 (17.5%) consumed alcohol once a month or less frequently, of whom 6.2% consumed alcohol once a week or more frequently. More than 94.3% of those who used alcohol once a month or less frequently had started before diagnoses of DM. Regarding prevalence of smoking, one (0.3.%) reported smoking regularly, but no respondents had stopped smoking. Four of ten (37.1%) had had DM >10 years. Mean body-mass index was 23.79±2.6 kg/m^2.

Table 1 Sociodemographic characteristics of patients (n=302) on follow-up

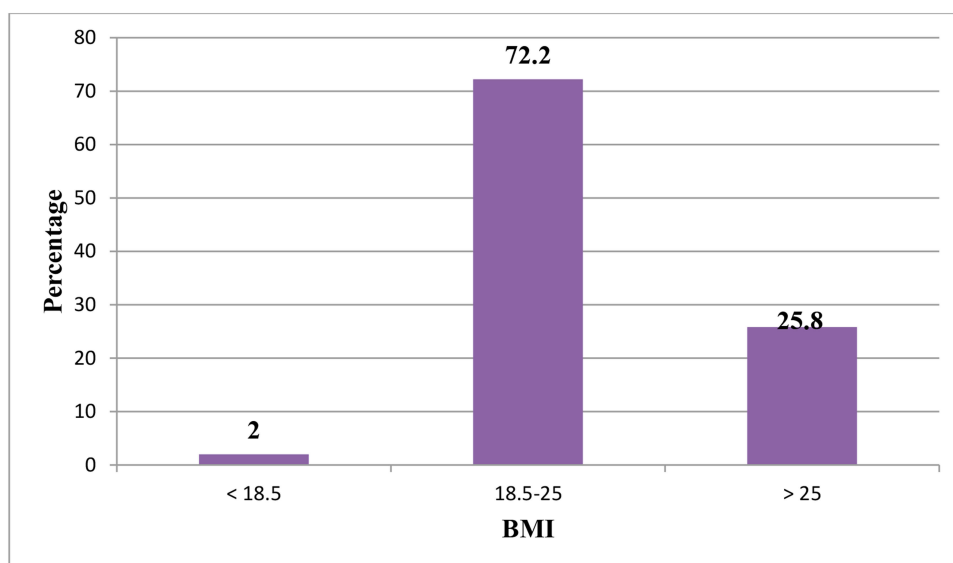|	Diabetic retinopathy		Total (%)
	Yes	**No**	
	n (%)	**n (%)**	
Sex			
Female	23 (7.62)	75 (24.83)	98 (32.45)
Male	34 (11.26)	170 (56.29)	204 (67.55)
Age			
≤40 years	9 (2.98)	130 (43.05)	139 (46.03)
>40 years	48 (15.89)	115 (38.08)	163 (53.97)
Religion			
Orthodox	53 (17.55)	226 (74.83)	279 (92.38)
Muslim	4 (1.32)	19 (6.29)	23 (7.62)
Residence			
Rural	8 (2.65)	64 (21.19)	72 (23.80)
Urban	49 (16.23)	181 (59.93)	230 (76.20)
Marital status			
Single	1 (0.33)	48 (15.890	49 (16.22)
Married	31 (10.26)	167 (55.30)	198 (65.56)
Divorced	5 (1.66)	11 (3.64)	16 (5.30)
Widowed	20 (6.62)	19 (6.30)	39 (12.91)
Education			
None	9 (2.98)	46 (15.23)	55 (18.21)
Primary	11 (3.64)	60 (19.86)	71 (23.51)
Secondary	2 (0.66)	38 (12.58)	40 (13.25)
College and above	35 (11.60)	101 (33.41)	136 (45.03)
Occupation			
Merchant	25 (8.28)	83 (27.48)	108 (35.76)
Employee	24 (7.95)	82 (27.15)	106 (35.10)
Farmer	8 (2.65)	49 (16.23)	57 (18.87)
Student	0	31 (10.26)	31 (10.26)
Family history of DM			
No	41 (13.58)	148 (49.01)	189 (62.59)
Yes	16 (5.30)	97 (32.12)	113 (37.42)

Table 2 Behavioral, clinical, and diabetes care–related characteristics of respondents (n=302)

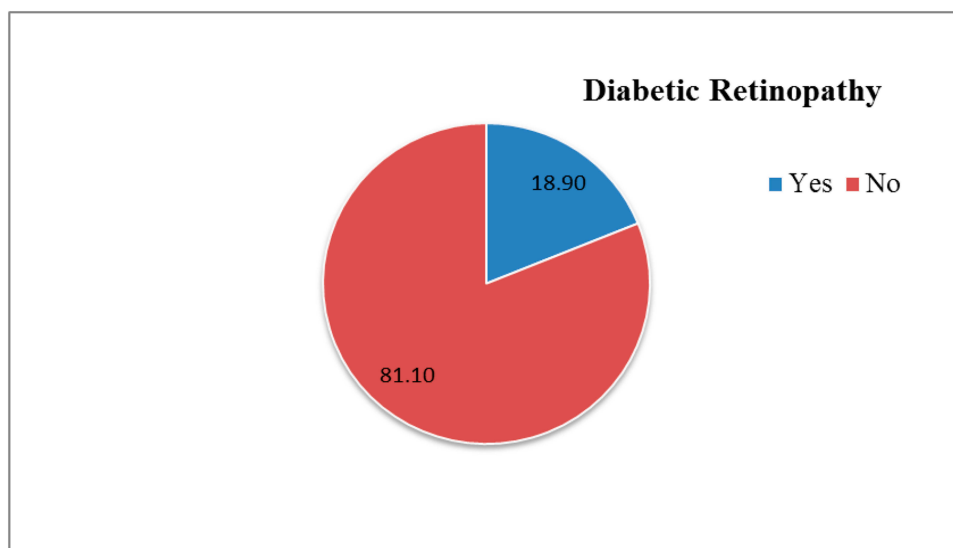|	Diabetic retinopathy		Total (%)
	Yes	**No**	
	n (%)	**n (%)**	
Alcohol consumption			
Never after diagnosis	43 (14.24)	206 (68.21)	249 (82.45)
Drinker	14 (4.64)	39 (12.91)	53 (17.55)
Duration of DM illness			
≤10 years	14 (4.64)	176 (58.28)	190 (62.92)
>10 years	43 (14.24)	69 (22.28)	112 (37.09)
Glycemic control			
Good	7 (2.32)	145 (48.01)	153 (50.33)
Poor	50 (16.56)	100 (33.11)	149 (49.34)
Hypertension			
No	25 (8.28)	207 (68.54)	232 (76.82)
Yes	32 (10.60)	38 (12.58)	68 (23.18)
Chronic cardiac illness			
No	49 (16.22)	243 (80.46)	292 (96.70)
Yes	8 (2.65)	2 (0.66)	10 (3.30)
Chronic kidney disease			
No	55 (18.21)	242 (80.13)	297 (98.35)
Yes	3 (0.99)	2 (0.66)	5 (1.65)
Type of diabetes			
2	41 (13.57)	127 (42.05)	168 (55.63)
1	14 (4.64)	117 (38.74)	131 (43.38)
Both	2 (0.66)	1 (0.33)	3 (0.99)
Follow-up frequency			
Every month	29 (9.60)	155 (51.32)	184 (60.92)
Every 2 months	28 (9.26)	90 (29.80)	118 (39.07)
Routine DR eye screening			
No	31 (10.26)	220 (72.85)	251 (83.11)
Yes	26 (8.61)	25 (8.28)	51 (16.88)
DR health education			
No	49 (16.22)	201 (66.56)	250 (82.87)
Yes	6 (2)	46 (15.23)	52 (17.23)

Three-quarters (72.2%) of respondents body-mass index was normal and a quarter (25.8%) were overweight/obese. A quarter (23.18%) had a history of hypertension. Mean fasting blood glucose was 131.06±26.79 mg/dL, and half (50.3%) had good glycemic control. More than half (55.6%) used oral antiglycemic agents, while 43.4% respondents took insulin for treatment. A total of 184 (60.92%) were visiting a health institution every month, and one in four (39.08%) were visiting a health institution every 2 months for DM follow-up (Table 2 and Figure 1).

Prevalence of Diabetic Retinopathy

Among the 302 participants, 57 (18.9%) had DR. Three-quarters (75.4%) of DR patients had nonproliferative DR, while a quarter (24.6%) had proliferative DR. There are no fundus picture is nongradable, and 6.4% of respondents had macular edema. Four in ten (37.7%) respondents had visual acuity problems and three-quarters (86%) of DR respondents had visual acuity problems (Figure 2).

Figure 1 Percentages of body mass–index values among DM patients on follow-up.

Figure 2 Prevalence of diabetic retinopathy among diabetic patients on follow-up.

Associated Factors for Diabetic Retinopathy among DM Patients

On bivariate analysis, DR had statistically significant associations with age, glycemic control, hypertension, body-mass index, type of DM, and duration of illness. On bivariate logistic regression, $P<0.25$ results were included in multivariate logistic regression. Glycemic control, hypertension, body-mass index, and duration of illness had statistically significant associations with DR. The odds of developing DR among those with poor glycemic control were about five times (AOR 4.58, 95% CI 1.86–11.31) those of patients with good glycemic control. The odds of developing DR in hypertensive patients were triple (AOR 3.39, 95% CI 1.64–7.02) those of nonhypertensive patients. The odds of developing DR among overweight/obese respondents were about four times more likely (AOR 3.74, 95% CI1.83–7.66) those of patients with normal body weight. The odds of developing DR among patients who had had DM >10 years were quadruple (AOR (95% CI 3.91 (1.86,8.23) those of their counterparts (Table 3).

Discussion

The findings of the current study showed that one in five (18.9%, 95% CI 14.5%–23.3%) DM patients had DR. This is consistent with studies conducted in Brazil (15%)[23] and

Table 3 Multivariate analysis of sociodemographic, clinical and diabetes care, and treatment modality–related characteristics of patients (n=302)

	Retinopathy		COR (95% CI)	AOR (95% CI)	P-value
	Yes	**No**			
Age					
≤40 years	9	130	1	1	
>40 years	48	115	6.03 (2.83–12.83)	1.39 (0.532–3.65)	0.500
Glycemic control					
Good	7	145	1	1	
Poor	50	100	10.35 (4.512–23.77)	4.58 (1.86–11.31)	0.001**
Hypertension					
No	25	207	1	1	
Yes	32	38	6.97 (3.72–13.1)	3.39 (1.64–7.02)	0.001**
Body-mass index					
18.5–25 kg/m^2	23	195	1	1	
>25 kg/m^2	34	44	6.55 (3.52–12.204)	3.74 (1.83–7.66)	0.001**
<18.5 kg/m^2	0	6	0	0	0.999
Type of diabetes					
2	41	127	1	1	
1	14	117	0.36 (0.19–0.69)	1.306 (0.51–3.35)	0.578
Both	2	1	1.5 (0.13–16.97)	1.52 (0.10–22.56)	0.762
Duration of DM					
≤10 years	14	176	1	1	
>10 years	43	69	7.83 (4.03–15.2)	3.91 (1.86–8.23)	0.001**

Note: **$P<0.05$.

India (21.2%)[24] and meta-analyses in China (18.45%).[25] It is higher than studies conducted in Beijing (8.1%)[26] and Arbamnech General Hospital (13%),[27] but lower than studies conducted in Armenia (36.2%),[28] Zimbabwe (28.4%),[29] Khartoum (82.6%),[30] and Jimma, Ethiopia (41.4%).[31] This discrepancy among studies might be due to variations in genetics, methodology, setting, DR-risk comorbidities, diagnostic method, quality of care, and health-seeking behavior among study participants. In our study, among DR patients, three-quarters (75.4%) had non-proliferative DR. This is lower than study results in India (85.3%)[30] and Armenia (90.2%),[28] but higher than studies in southern Iran (56.9%)[32] and Khartoum (51.7%).[30] This variation might be due to quality of care for DM patients and diagnostic methods. Four of ten (37.7%) respondents had visual acuity problems, and more than three-quarters (86%) of DR patients had visual acuity problems. This was higher than a study conducted at Nobel Medical College in Biratnagar (24.6%).[33] This variation might be due to quality of care for diabetic patients and lifestyle. In the multivariate logistic regression model, glycemic control, hypertension,

body-mass index, and duration of illness were significantly associated with DR. In this study, the odds of developing DR among those with poor glycemic control were about five times (AOR 4.58, 95% CI 1.86–11.31) those of patients with good glycemic control. This result is in line with systematic reviews in China,[25] southern Iran,[34] Tanzania,[35] and Jimma University Hospital.[31] The possible mechanism might be that poor glycemic control causes vascular cell apoptosis by abnormal glucose metabolism, activation of protein kinase C, formation of advanced glycosylation end product, and increased production of reactive oxygen species.[36–38] The odds of developing DR among hypertensive patients were three times (AOR 3.39 95% CI 1.64–7.02) those of nonhypertensive patients. This is consistent with studies conducted in Beijing,[26] Tanzania,[35] Kenya,[39] Khartoum,[30] Arbamnech General Hospital,[27] and Jimma University Hospital,[31] but inconsistent with a study conducted in Iran.[34] This discrepancy might be due to methodology, confounding effects, variations in self-care practices, and variations in hypertensive prevalence among studies. There also existed an association

between duration of DM and DR in our findings. The odds of developing DR among patients who had had DM >10 years (AOR 3.91, 95% CI 1.86_.23) were quadruple() those of their counterparts. This finding is in line with studies conducted in Armenia,[28] Beijing,[26] Iran,[32] Kenya,[39] Tanzania,[35] Zimbabwe,[29] Khartoum,[30] Arbamnech General Hospital,[27] and Jimma University Hospital.[31]

The odds of developing DR among overweight/obese respondents were (AOR (95% CI3.74 (1.83,7.66) were about quadruple those of patients with normal body weight. This result is in line with studies conducted in the US,[40] Iran,[32] and Beijing,[26] but inconsistent with studies in Croatia[41] and Minnesota.[42] Possible reasons for this discrepancy among studies might bemethodological differences, differences in study participants, lack of comprehensive anthropometric measurements, and confounding effects, but being overweight/obese causes increasing blood viscosity, oxidative stress, vascular growth factors, leptin, cytokines, and ICAM1, which leads to DR.[43,44]

Strengths and Limitations of the Study

There are many important strengths to the present study. This is the first study to investigate the prevalence of DR and associated factors in Debre Markose, Ethiopia. The use of a cross-sectional design also provided a sufficiently large sample and including many independent variables. Another strength is that fundus examinations were performed by experienced ophthalmologists. This study is not without limitations. The study design was cross-sectional, so we could not take account of the temporal relationship between potential risk factors and outcomes. Another limitation is its short duration. Despite these factors, we believe that this study is novel and its findings reflect the trend of rising DR frequency in developing countries. Moreover, fasting blood sugar was used to assess glycemic control, due to the lack of facilities to assess HbA_{1c} in the study area.

Conclusion and Recommendation

The prevalence of DR in this study was 18.9% (95% CI 14.3%–23.5%). Threequarters (75.4%) of DR patients had nonproliferative DR and a quarter (24.6%) proliferative DR. Poor glycemic control, hypertension, overweight, obesity, and longer DM duration were significantly associated with DR. The results emphasize that the Ministry of Health should establish strategies and polices to control DR. We recommend that health workers also provide sustainable health information to diabetic patients on possible risk factors of DR (hypertension, overweight/obese, and poor glycemic control), as these were evidenced in the current study.

Abbreviations

AOR, adjusted OR; BMI, body-mass index; COR, crude oOR; DM, diabetes mellitus; DR, diabetic retinopathy; FBS, fasting blood sugar; IRMAs, intraretinal microvascular abnormalities; NGO, nongovernmental organization; NPDR, nonproliferative dDRr; PDR, proliferative DR; SBP, systolic blood pressure; SLB, slit-lamp biomicroscopy; WHO, World Health Organization.

Data-Sharing Statement

The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the manuscript.

Ethics Approval and Consent to Participate

This study was performed in accordance with the revised Declaration of Helsinki guidelines for biomedical research involving human subjects,[45] and ethical clearance was obtained from the Institutional Review Board, College of Health Science, and Jimma University. Following endorsement from the university, Debre Markos Referral Hospital (study setting) was informed about the objectives of the study through a support letter from the Institutional Review Board. After obtaining informed consent (oral) from clients, data were collected. Study participants had the right to refuse to join, ask any question, or withdraw at any time. Privacy and confidentiality were assured. Respondents who were diagnosed with retinopathy were referred to the ophthalmic clinic for further management.

Consent for Publication

Not applicable.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, took part in drafting the article or revising it critically for important intellectual content, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Funding

There was no funding or sponsoring organization for this study.

Disclosure

All the authors declare that they have no competing interests.

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