ISSN 2475-5451

Research Article

International Journal of Diabetes & Metabolic Disorders

Diabetic Macular Edema Among Diabetic Patients at The University of Gondar Tertiary Eye Care and Training Center, North West Ethiopia

Endale Kabtu[1], Asamere Tsegaw[1*], Fisseha Admassu[1]

[1]*Department of Ophthalmology, University of Gondar, Ethiopia*

[*]**Corresponding author:**
Dr. Asamere Tsegaw, Department of OphthalmologyUniversity of Gondar, Ethiopia

Submitted: 28 Jun 2022; **Accepted**: 05 Jul 2022; **Published**: 13 Jul 2022

Citation: *EndaleKabtu, Asamere Tsegaw and FissehaAdmassu. (2022). Diabetic Macular Edema Among Diabetic Patients at The University of Gondar Tertiary Eye Care and Training Center, North West Ethiopia. Int J Diabetes MetabDisord, 7(2), 120-128.*

Abstract

Background: *Diabetic macular edema (DME) is the most common cause of visual impairment in patients with diabetes mellitus. The prevalence of DME globally is around 6.8 % and in Ethiopia range from 5.7% to 11%. Different factors are associated with DME including poor glycemic control, longer duration, hypertension, dyslipidemia.*

Objective: *To determine the prevalence and associated factors of diabetic macular edema among diabetic patients attending University of Gondar (UOG) hospital, tertiary eye care and training center, NW Ethiopia*
Methods:A hospital based cross-sectional study was conducted from March 2021 to October 2021. Socio-demographic, clinical and laboratory data of patients was gathered. The collected data was entered into epi-data 4.6 version, exported to SPSS version 20 and analyzed.

Results: *A total of 165 diabetic patients were enrolled with mean age of 54.71 ±13.66 years, 50.9% male, 85.5% urban dwellers, 79.9% type 2 DM,49.7% on oral hypoglycemic agents and the mean duration of diabetes was 7.93 years. Cataract was the commonest ocular morbidity and 42% of patients had at least mild vision impairment. The overall prevalence of DME was 17% and 5.5% of patients had clinically significant macular edema (CSME). The presence of proteinuria was 8.04 times more likely to have DME.*

Conclusion: *The prevalence of DME among our patients was high. The presence of proteinuria was significantly associated with DME. Screening of diabetic patients for sight threatening retinopathy early and appropriate treatment is recommended.*

Keywords: Prevalence, Diabetic Macular edema, Gondar, Ethiopia.

Introduction

Diabetic macular edema (DME) is the most common cause of visual reduction in patients with DM. It can occur in any stage of diabetic retinopathy [1]. Mechanism of DME ismulti factorial and due todisruption of the blood--retinal barrier following hyperglycemia induced damage, which leads to increased accumulation of fluid within the retinal layers of the macula [2].

The prevalence of DME globally is around 6.8 % [1].In western societies the reported prevalence ranges from 3.8% to 11.1% [1,3,4,5]. The prevalence in Africa is reported to be higher and ranges from 8.0% Cameroon, 12.5% South Africa, 20.8% South Africa, 33.3% Kenya [6,7,8,9]. In Ethiopia, the prevalenceranges from 5.7% to 11% [10,11].

Different factors have been found to be associated with DME including type-I diabetespoor glycemic control,longer duration of DM, systemic hypertension,dyslipidemia, insulin therapy, proteinuria and cataract surgery [12-21].

There has not been any study that specifically evaluated risk factors to develop DME among our patients and the aim of our study was therefore to determine the prevalence and investigate risk factors that are associated with DME among diabetic patients attending in the study center.

Methods and Materials

Study Design and Period

A hospital based cross-sectional study wasconducted at University of Gondar Tertiary eye care and training center from March 2021-October 2021.

Study Area

This study was conducted at University of Gondar tertiary eye care and training center which is a major ophthalmic center in Ethiopia. It is an ophthalmic referral center for the entire North-West Ethiopia of an estimated 14 million people. Over 50,000 patients are seen at the center annually as inpatient and outpatient basis. Currently there are 6 subspecialty clinics with 7 actively working ophthalmologists, 26 ophthalmology trainee residents, 38 optometrists, 35 general clinical nurses and ophthalmic nurses and other supporting staff working in the center.

Study Population

All diabetic patients who visited the tertiary eye care and training center during data collection period and fulfilled the inclusion criteria.

Inclusion Criteria

Medically diagnosed diabetic patients.
Adequate visualization of the fundus is possible.

Exclusion Criteria

Diabetic patients who had additional causes of macular edema
Patients age below 18 years old.

Data Collection Procedure

Semi-structured interviewer-administered questionnaire, document review, and ocular examination were used to collect data. The questionnaire consisted of three sections: sociodemographic variables (6 items), medical history (10 items), and checklist for clinical and laboratory data extraction (11 items). Data quality was ensured through pre-testing the questionnaire before the actual data collection period. Socio-demographic data and relevant medical history were filled into the pretested semi-structured questionnaire. Laboratory test results of a single record of the most recent fasting blood glucose (FBG) level, HgA1c, urine analysis, lipid profile was obtained. Blood pressure was measured in sitting position after 5–10 min of rest. Hypertension is defined as systolic BP of ≥140 mmHg and/or diastolic BP of ≥90 mmHg [22].BMI was calculated from weight in kilograms and height in meters squared and categorized according to WHO classification [23].

Best-corrected visual acuity was taken using Tumbling E Snellen visual acuity chart and patient sitting at 6 m position, and classified according to WHO grading of visual acuityas follows: visual acuity better or equal to 6/18 – normal; visual acuity ≤6/24 and better than or equal to 6/60 – moderate visual impairment; visual acuity <6/60 and better than or equal to counting fingers at 3 m – severe visual impairment; visual acuity less than counting fingers at 3 m – blindness; the results for the eye with better visual acuity was recorded [24].

Anterior and posterior segment examinations were done using slit-lamp biomicroscope and 90D condensinglens was used for detailed evaluation of the retina after dilating the pupil with 1% tropicamide. Grading of the retinal changes was made using the Diabetic Retinopathy (DR) Study guidelinesand recorded in six categories: mild, moderate, and severe nonproliferative retinopathy and early, high risk, and advanced proliferative retinopathy [25]. DME was diagnosed when there were hard exudates on the macula and/or macular thickening obvious on slit-lamp examination and clinically significant macular edema (CSME) was diagnosed based on ETDRS study criteria [26]. In cases of asymmetric involvement of eyes, the eye with the most severe DR grade was taken. In patients with concomitant central or branch retinal vein occlusion, the DR grade in the eye not involved in the vein occlusion was used. All data were collected and recorded by an ophthalmologist, and all diagnoses were confirmed by a retina specialist at the retina clinic of the study center.

Data Processing and Analysis

The collected data was checked for accuracy and consistency and manual data clean up and correction of any errors was done. Data was coded and entered into epi-data4.6 and exported to statistical package for social sciences (SPSS) version 20 for analysis. Simple binary logistic regression analysis was done and the explanatory variables with pre-set p-value of <0.2 were taken for further analysis with multiple binary logistic regression to identify the factors independently associated with diabetic macula edema. Associations were shown in terms of calculated odds ratio and p-values. Results are described in terms of numbers, percentages, means and medians, and are displayed on tables,pie chart and bar graphs.

Ethical Considerations

The study was conducted after ethical clearance was obtained from University of Gondar ethical review board (ID=UOG/ER/130/2021).Informed written consent was obtained from the study participants after clear explanation concerning the purpose and importance of the study. The identity of the patient was not exposed in any way and confidentiality of patient record was respected.

Results

A total of 165 diabetic patients were included in the study.The mean age was 54.71±13.66 years andrange 19-87 years. A majority 84 (50.95%) were males and 141 (85.5%) were urban dwellers. (Table 1)

Table 1: Socio-demographic characteristics of Diabetic patients presented to UOG tertiary eye care and training center, North West Ethiopia, 2021 (n=165)

variable	categories	frequency	Percent (%)
Age in year			
	Less than 30 years	12	7.3
	30-45 years	23	13.9
	>45 years	130	78.8
Sex			
	Male	84	50.9
	Female	81	49.1
Residency			
	Rural	24	14.5
	Urban	141	85.5
Marital status			
	Married	117	70.9
	Single	17	10.3
	Divorced	11	6.7
	Widowed	20	12.1
Educational status			
	Can't read and write	34	20.6
	Can read and write only	23	13.9
	Primary school	30	18.2
	Secondary school	28	17
	College/University	50	30.3
Occupation			
	Farmer	11	6.7
	Business owner	19	11.5
	Government employee	44	26.7
	private employee	31	18.8
	House wife	29	17.6
	Pension	9	5.5
	Unemployed	22	13.3

Most of the patients had type-II DM 131 (79.4%),the mean duration of diabetes was 7.93 years (range 1-30 years) and a majority of them were on oral hypoglycemic agents 85 (49.7%). (Figure-I) (Table 2)

Table 2: Clinical characteristics of diabetic patients presented to UoGtertiary eye care and training center, North West Ethiopia, 2021 (n=165)

Variable	categories	Frequency (number)	Percent (%)
Type of DM			
	Type 1	34	20.6
	Type 2	131	79.4
	Less than 5 years	74	44.8
Duration of DM			
	5-10 years	48	29.1
	11-20 years	31	18.8
	Greater than 20 years	12	7.3

	Dietary	10	6.1
Form of DM therapy			
	OHA	82	49.7
	Insulin	50	30.3
	Combination	23	13.9

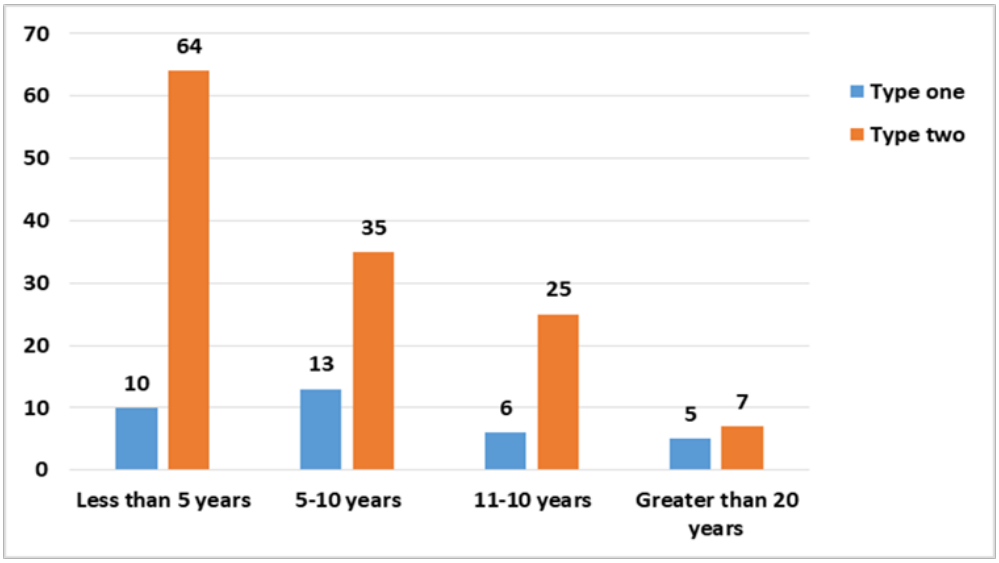

Figure I: Disease durationamong type I and type II diabetic patients at UOG tertiary eye care and training center, North West Ethiopia, 2021 (n=165)

Systemic hypertension was the most common known systemic co-morbidity 69 (41.8%) followed by dyslipidemia 22 (13.3%) and 21(12.7%) of patient had high systolic blood pressure measurements. (Table-III)

Table 3: Concomitant systemic co-morbidities among patients among withdiabetes at UOG tertiary eye care and training center, North West Ethiopia, 2021 (n=165)

variable		frequency (%)
Known Hypertension	Yes	69(41.8%)
	No	96(58.2%)
Kidney disease	Yes	1(0.6%)
	No	164(99.4%)
Dyslipidemia	Yes	22(13.3%)
	No	143(86.7%)
History of smoking	Yes	3(1.8%)
	No	162(98.2%)
Alcohol history	Yes	19(11.5%)
	No	146(88.5%)
Systolic BP	<140 mmHg	134(81.2%)
	>=140 mmHg	21(12.7%)
Diastolic BP	<90 mmHg	149(90.3%)
	>=90 mmHg	6(3.6%)
BMI	<18.5	9(6%)
	18.5-24.9	74(49.33%)
	25-29.9	50(33.33%)
	>30	17(11.33%)

Cataract was the most common concomitant ocular pathology 28 (17%), followed by Glaucoma 2(1.2%) and corneal opacity 2 (1.2%).

The means of FBS, HbA1c, cholesterol and triglycerides were 158.92 mg/dL, 8.86 mmol/mol, 178.96mg/dL and 175.01 mg/dl respectively. (Table-IV and Table-V)

Table 4: Laboratory Investigation results (all in mg/dl except specified)of diabetic patients presented to UOG tertiary eye care and training center, North West Ethiopia, 2021 (n=65)

Variable name	Minimum	maximum	Mean	SD
FBS	51	459	158.92	±68.36
HbA1c (mmol/mol)	6.7	12.6	8.86	±1.38
Total cholesterol	56	345	178.96	±53.72
Triglyceride	46	490	175.01	±78.62
LDL	25	220	99.82	±35.06

Table 5: Category ofLaboratory Investigation results versus the presence or absence of DME among diabetic patients at UOG tertiary eye care and training center, North West Ethiopia, 2021.

variable	Lab ranges	No DME	DME
FBS mg/dl (n=165)	< 126	51(83.6%)	10(16.4%)
	126-200	48(78.7%)	13(21.3%)
	>200	34(89.5%)	4(10.5%)
HbA1CMMol/mol (n=26)	<7	1(100%)	0
	7 to 9	13(81.2%)	3(18.8%
	>9	7(77.8%)	2(22.2%
Triglyceride level mg/dl(n=38)	<150	45(84.9%)	8(15.10%)
	150-199	41(91.1%)	4(8.9%)
	150-199	41(91.1%)	4(8.9%)
	>=200	25(71.4%)	10(28.6%)
LDL level mg/dl(n=97)	<130	72(91.1%)	7(8.9%)
	130-159	5(50%)	5(50%)
	>=160	4(80%)	1(20%)
	<200	81(87.1%)	12(12.9%)
Cholesterol level mg/dl(n=140)	201-239	20(83.3%)	4(16.7%)
	>=240	12(66.7%)	6(33.3%)

The prevalence of DR in the worst affected eye was 110 (33.3%), ranging from mild NPDR 30(18.2%) to PDR 3(1.8%). The overall prevalence of DME was 17% of which 11.5% hadNon-CSME and 5.5% had CSME in the worst affected eye. (Table-VI)

Table 6: DR and DME grading amongdiabetic patients at UOG tertiary eye care and training center, North West Ethiopia, 2021 (n=165)

Variable	Grade of Diabetic retinopathy	Number (%)
Grade of DR	No DR	110 (66.70%)
	Mild DR	30 (18.20%)
	Moderate NPDR	13 (7.90%)
	Sever NPDR	9 (5.50%)
	PDR	3 (1.80%)
Grade of DME	No DME	137 (83.00%)
	DME	19 (11.50%)
	CSME	9 (5.50%)

Seventy one(43%) of patients had visual impairment, out of this 35(21.2%) had mild visual impairment, 17 (10.3%) had moderate visual impairments and 19(11.5%) were blind.. (Table VII)

Table 7: Visual acuity versus the presence or absence of DME among diabetic patients at UOG tertiary eye care and training center, North West Ethiopia, 2021 (n=165)

Visual acuity	No DME	Yes DMETotal
6/6-6/18	85(51.5%)	9(5.4%)94(56.9%)
<6/18-6/60	27(16.3%)	8(4.8%)35(21.2%)
<6/60-3/60	10(6%)	7(4.2%)17(10.3%)
<3/60	13(7.9%)	6(3.6%)19 (11.5%)

A binary logistic regression analysis was done for every independent variable to include into the final multivariable logistic regression model. Then the variables with p-value of less than 0.2 were included into the final model and association of the independent variables with DME.

The bi-variable logistic regression analysis showed that,Residency,Type of DM,Duration of DM,Hypertension,History of cataract surgery,proteinuriaand higher Diastolic BPwere found to have association (P< 0.2) with outcome (the presence or absence) DME.

In the final multivariable logistic regression analysis patients having proteinuria on urine examination (P<0.01) and those with severe NPDR and PDR (P<0.01) were significantly associated with development of DME.

Accordingly, patients with proteinuria in Urine analysis resultwere 8.04 times highly likely to develop DME ascompared with DM patients with normal Urine analysis result (AOR = 8.04, 95% CI (2.48-26.09).

Similarly, DM patients with severe NPDR and PDR were 22.04 times highly likely to have DME as compared with those without DR (AOR = 22.04, 95% CI 2.1-231). (Table VIII)

Table 8: Multivariate logistic regression offactors associated with DME amongdiabetic patients at UoGtertiary eye care and training center, North West Ethiopia, 2021 (n=165)

		Freq. (%)	Freq. (%)	P value	AOR	Lower	Upper
Residency							
	Rural	16(66.7)	8(33.3)				
	Urban	120(85.1)	21(14.9)	0.269	0.393	0.075	2.06
Type of DM							
	Type 1	25(73.5)	9(26.5)		1.321	0.242	7.216
	Type 2	111(84.7)	20(15.3)	0.748			
Duration of DM							
	< 5 years	62(83.8)	12(16.2)	0.084			
	5-10 years	41(85.4)	7(14.6)	0.651	1.49	0.265	0.651
	>=10 years	32(74.4)	11(25.6)	0.589	1.555	0.313	7.714
Hypertension							
	Yes	51(73.9)	18(26.1)	0.66	1.392	0.319	6.073
	No	85(88.5)	11(11.5)				
History of cataract surgery							
	Yes	8(57.1)	6(42.9)	0.633	1.77	0.169	18.513
	No	128(84.4)	23(15.2)				
Urine analysis							
	trace and negative	112(90.3)	12(9.7)				

	+1 &above	11(44.0)	14(56.0)	0.01	8.04	2.481	26.095
Diastolic BP							
	<90mm/Hg	120(96.8)	24(92.3)				
	>=90 mm/Hg	4(3.2)	2(7.7)	0.63	0.532	0.041	6.955
severe NPDR and/or PDR							
	No	134(87.6)	19(12.4%)				
	Yes	1(8.3%)	11(91.7%)	0.01	22.04	2.101	231.33

Discussion

The overall prevalence of Diabetic Macular Edema and clinically significant macular edema in this study was 17% and 5.5 % respectively.The prevalence of CSME in this study issimilar with results of studies from Jima south west Ethiopia and Iran which were 6 %, 5.8%, respectively [27, 28]. The overall prevalence of DME in this study is also in line with results of studies from South Africa, 20.8%, and Turkey, 15.8% [8,21].

However,the reported prevalence of DME in previous studies in this regionof NW Ethiopia,11%, 6.4% and 5.7%, is lower than our report and this may be because of the differences in the study setting, method of data collection and sample size [10,11,29].Similar diabetic clinic-based studies in Cameroon 8% and in South Africa 12.5%,also reporteda lowerprevalence of DME than ours [6,7].

The prevalence of DME in USA and England ranges from 3.8-7.12% which isalso lower than this study and this could be due to the differencesin sample size, study setting and better medical care and follow up for diabetic patients [3,5].

A study done in Kenya reported that the prevalence of DME was 33.3% which was much higher than this study and thiscould be due to the different sampling method used and also included only patients age above 50 years old [9].

The prevalence of diabetic retinopathy in this study 33.3% is higher than diabetic clinic based previous reports from this region 16 %and18.9 % however a study done in Jimma South West Ethiopia and another study done in NW Ethiopia reported higher figures than this study, 42.2% and 41.4% respectively [10,11,28,29].This may be due to the differences in data collection technique, sample size and study setting.

The prevalence of DR in our study is higher than reports from other parts of Africa, in Cameroon, 24.3%, in South Africa24.8% but slightly lower than a Kenyanreport 35.9 %[6,7,9].
The presence of severe NPDR and/or PDR was 22.04 times more likely to haveDME than Early or No DR in this study with P value <0.001. A similar finding was reported with a slightly lower figure than ours from Boston USA which was 6.2 times and 7.7 times for severe NPDR and PDR respectively [13].

A retrospective study of electronic medical records in the UK showed that the presence of any degree of DR was 6.25 times more likely to have DME than absence of DR [30].

Our study showed that patients with proteinuria in Urine analysis result were 8.04 times more likely to develop DME as compared with DM patients with normal Urine analysis result. Many studies have also shown that the presence of proteinuria hadsignificant association with the development of diabetic macular edema.

In the Wisconsin Epidemiologic Study of Diabetic Retinopathy patients with proteinuria were three times more likely to have DME [3].

Two retrospective studies done in China and Japan also showed that the presence of microalbuminuria and proteinuria was significantly associated with development of DME [15,20].

A majority ofparticipants in this study,79.4%, were type-II DM patientsand this is similar with previous studies done in Ethiopia,88.4% in Gondar, 72.8% in Jimmaand 60.92% Debre marcos Longer duration of DM was strongly associated with diabetic macular edema in many studies [2,3,10,11,28,29].However, our study did not find association between duration ofdiabetes with development ofDME and this may be because nearly half of our study patients, 44.8%, had duration of diabetes less than five years.

A majority of DM patients in this study were on oral hypoglycemic agents, 49.9%, and 33.9 % of patients were on Insulin alone or combination therapy.Insulin therapy was reported to have significant association with DME in some studies [3,14,31]. However, this study didn't show any significant association.

Poor glycemic control, uncontrolled blood pressure and high lipid level (cholesterol level and LDL) have been associated with the development of DME in some studies but our study did not show any association [12, 15,16,17,18,19]. The small sample size and our inability to determine HgA1c and lipid level for all patients might have contributed to this discrepancy. These are also the limitations of this study.

The absence of imaging studies like OCT might have also underestimated the prevalence of DME in our patients as the diagnosis of DME was made based on clinical examination only.

Conclusion

The prevalence of Diabetic macular Edema among our patients was very high and this implies the need to establish early screening and proper treatment services to prevent vision loss from DME. The presence of proteinuria was independently associated with the

development of diabetic macular edema.Diabetic patients must be taught about the need for regular eye examination to detect and treat DME early [32].

References

1. Varma, R., Bressler, N. M., Doan, Q. V., Gleeson, M., Danese, M., Bower, J. K., ... &Turpcu, A. (2014). Prevalence of and risk factors for diabetic macular edema in the United States. JAMA ophthalmology, 132(11), 1334-1340.
2. Bhagat, N., Grigorian, R. A., Tutela, A., &Zarbin, M. A. (2009). Diabetic macular edema: pathogenesis and treatment. Survey of ophthalmology, 54(1), 1-32.
3. Klein, R., Klein, B. E., Moss, S. E., Davis, M. D., &DeMets, D. L. (1984). The Wisconsin epidemiologic study of diabetic retinopathy: IV. Diabetic macular edema. Ophthalmology, 91(12), 1464-1474.
4. Xie, J., Ikram, M. K., Cotch, M. F., Klein, B., Varma, R., Shaw, J. E., ... & Wong, T. Y. (2017). Association of diabetic macular edema and proliferative diabetic retinopathy with cardiovascular disease: a systematic review and meta-analysis. JAMA ophthalmology, 135(6), 586-593.
5. Minassian, D. C., Owens, D. R., & Reidy, A. (2012). Prevalence of diabetic macular oedema and related health and social care resource use in England. British journal of ophthalmology, 96(3), 345-349.
6. Jivraj, I., Ng, M., Rudnisky, C. J., Dimla, B., Tambe, E., Nathoo, N., & Tennant, M. T. (2011). Prevalence and severity of diabetic retinopathy in Northwest Cameroon as identified by teleophthalmology. TELEMEDICINE and e-HEALTH, 17(4), 294-298..
7. Sukha, A. Y., & Rubin, A. (2009). Demographic, medical and visual aspects of Dia-betic Retinopathy (DR) and Diabetic Macular Edema (DME) in South African diabetic patients. African Vision and Eye Health, 68(2), 70-81.
8. Webb, E. M., Rheeder, P., & Roux, P. (2016). Screening in primary care for diabetic retinopathy, maculopathy and visual loss in South Africa. Ophthalmologica, 235(3), 141-149.
9. Mathenge, W., Bastawrous, A., Peto, T., Leung, I., Yorston, D., Foster, A., &Kuper, H. (2014). Prevalence and correlates of diabetic retinopathy in a population-based survey of older people in Nakuru, Kenya. Ophthalmic epidemiology, 21(3), 169-177.
10. Tsegaw, A., Alemu, S., Dessie, A., Patterson, C. C., Parry, E. H., Phillips, D. I., & Trimble, E. R. (2021). Diabetic Retinopathy in Type 2 Diabetes Mellitus Patients Attending the Diabetic Clinic of the University of Gondar Hospital, Northwest Ethiopia. Journal of Ophthalmology, 2021.
11. Ejigu, T., & Tsegaw, A. (2021). Prevalence of diabetic retinopathy and risk factors among diabetic patients at University of Gondar Tertiary Eye Care and Training Center, North-West Ethiopia. Middle East African Journal of Ophthalmology, 28(2), 71.
12. Yau JW, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. (2012). Global prevalence and major risk factors of diabetic retinopathy. Diabetes care.35(3):556-64.
13. Lopes de Faria, J. M., Jalkh, A. E., Trempe, C. L., &Mcmeel, J. W. (1999). Diabetic macular edema: risk factors and concomitants. Acta OphthalmologicaScandinavica, 77(2), 170-175.
14. Wang Y, Lin Z, Zhai G, Ding XX, Wen L, Li D, et al. (2020). Prevalence of and risk factors for diabetic retinopathy and diabetic macular edema in patients with early and late onset diabetes mellitus. Ophthalmic research.
15. Tan, G. S., Cheung, N., Simo, R., Cheung, G. C., & Wong, T. Y. (2017). Diabetic macular oedema. The lancet Diabetes & endocrinology, 5(2), 143-155.
16. Bek, T. (2020). Systemic risk factors contribute differently to the development of proliferative diabetic retinopathy and clinically significant macular oedema. Diabetologia, 63(11), 2462-2470.
17. Martín-Merino, E., Fortuny, J., Rivero-Ferrer, E., Lind, M., & Garcia-Rodriguez, L. A. (2017). Risk factors for diabetic macular oedema in type 2 diabetes: A case-control study in a United Kingdom primary care setting. Primary care diabetes, 11(3), 288-296.
18. Liu, E., Craig, J. E., & Burdon, K. (2017). Diabetic macular oedema: clinical risk factors and emerging genetic influences. Clinical and Experimental Optometry, 100(6), 569-576.
19. Eldem, B., Ozdek, S., Saatci, A. O., Ozmert, E., Ulay, E., &Nomak, G. (2017). Clinical Characteristics of Patients with Newly Diagnosed Diabetic Macular Edema in Turkey: A Real-Life Registry Study—TURK-DEM. Journal of ophthalmology, 2017.
20. Zhuang X, Cao D, Yang D, Zeng Y, Yu H, Wang J, et al. (2019). Association of diabetic retinopathy and diabetic macular oedema with renal function in southern Chinese patients with type 2 diabetes mellitus: a single-centre observational study. BMJ open. (9): e031194.
21. Acan, D., Calan, M., Er, D., Arkan, T., Kocak, N., Bayraktar, F., &Kaynak, S. (2018). The prevalence and systemic risk factors of diabetic macular edema: a cross-sectional study from Turkey. BMC ophthalmology, 18(1), 1-8.
22. Gabb GM, Mangoni AA, Anderson CS, Cowley D, Dowden JS, Golledge J, et al. (2016). Guideline for the diagnosis and management of hypertension in adults - 2016. The Medical journal of Australia.205(2):85-9.
23. Review executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight andadult body mass index obesity in adults. Arch Intern Med 1998; 158:1855-67.
24. World Health Organization. Consultation on Development of Standards for Characterization of Vision Loss and Visual Functioning. Geneva: World Health Organization; 2003.
25. Liu, E., Craig, J. E., & Burdon, K. (2017). Diabetic macular oedema: clinical risk factors and emerging genetic influences. Clinical and Experimental Optometry, 100(6), 569-576.
26. Relhan, N., & Flynn, H. W. (2017). The Early Treatment Diabetic Retinopathy Study historical review and relevance to today's management of diabetic macular edema. Current opinion in ophthalmology, 28(3), 205-212.

27. Javadi, M. A., Katibeh, M., Rafati, N., Dehghan, M. H., Zayeri, F., Yaseri, M., ... &Ahmadieh, H. (2009). Prevalence of diabetic retinopathy in Tehran province: a population-based study. BMC ophthalmology, 9(1), 1-8.
28. Sharew, G., Ilako, D. R., Kimani, K., &Gelaw, Y. (2013). Prevalence of diabetic retinopathy in Jimma University Hospital, Southwest Ethiopia. Ethiopian medical journal, 51(2), 105-113.
29. Tilahun, M., Gobena, T., Dereje, D., Welde, M., &Yideg, G. (2020). Prevalence of Diabetic retinopathy and its associated factors among diabetic patients at Debre Markos referral hospital, Northwest Ethiopia, 2019: hospital-based cross-sectional study. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy, 13, 2179.
30. Chu, C. J., Johnston, R. L., Buscombe, C., Sallam, A. B., Mohamed, Q., Yang, Y. C., & United Kingdom Pseudophakic Macular Edema Study Group. (2016). Risk factors and incidence of macular edema after cataract surgery: a database study of 81984 eyes. Ophthalmology, 123(2), 316-323.
31. Jingi, A. M., Noubiap, J. J. N., Essouma, M., Bigna, J. J. R., Nansseu, J. R. N., Ellong, A., &Mvogo, C. E. (2016). Association of insulin treatment versus oral hypoglycaemic agents with diabetic retinopathy and its severity in type 2 diabetes patients in Cameroon, sub-Saharan Africa. Annals of translational medicine, 4(20).
32. Kabtu, E., & Tsegaw, A. (2022). Prevalence of diabetic macular edema and risk factors among diabetic patients at the University of Gondar Tertiary Eye Care and Training Center, North West Ethiopia. medRxiv.