Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/13559
DOI URL: http://dx.doi.org/10.21474/IJAR01/13559

RESEARCH ARTICLE

THE PREVALENCE AND RISK FACTORS ASSOCIATED WITH TYPE 2 DIABETIC RETINOPATHY IN RWANDA

A. Niyodusenga[1,2], T.N. Kiama[2], C. Muhizi [3] and F. Bukachi[2]

1. University of Rwanda, School of Medicine and Pharmacy, Department of Clinical Biology, Huye, Rwanda.
2. University of Nairobi, School of Medicine, Department of Medical Physiology, Nairobi, Kenya.
3. University of Rwanda, School of Medicine and Pharmacy, Department of Surgery, Huye, Rwanda.

Manuscript Info

Manuscript History
Received: 19 August 2021
Final Accepted: 22 September 2021
Published: October 2021

Key words:-
Type 2 Diabetes Mellitus, Retinopathy, Risk Factors, Rwanda

Abstract

Objective: To determine the prevalence and risk factors associated with type 2 diabetic retinopathy in Rwanda.

Methods: A case-control study was conducted from January to September 2019 in four hospitals within the Republic of Rwanda. Type 2 diabetic patients were screened for retinopathy. Patients with retinopathy were considered as cases and those without retinopathy as controls. A study sample of 592 participants were enrolled, 66 cases and 526 controls. Diabetic retinopathy was assessed by indirect ophthalmoscopy performed for each eye with a slit-lamp +90D lens. Plasma glucose and Glycated hemoglobin (HbA_{1c}) were measured by colorimetric enzymatic tests. Albuminuria was measured by quantitative spectrophotometric method. Triglycerides, Total, HDL and LDL cholesterol, Urea and Creatinine were assayed by colorimetric methods. A questionnaire was used to assess medical history and demographic status. Data were analyzed by use of SPSS version 20. Statistical analyses were performed by Chi square to show association between nominal and ordinal data. Multivariate logistic regression analysis to select independent variables was performed. Odds ratio was used as a measure of association.

Results: The prevalence of diabetic retinopathy in this study population was 11.2%. Independent risk factors associated with diabetic retinopathy were long duration of diabetes, hyperglycemia, LDL cholesterol, triglycerides, and albuminuria.

Conclusion: The prevalence of diabetic retinopathy is high and is associated with traditional modifiable risk factors. Early detection and management of diabetes mellitus and these risk factors, combined with good adherence to scheduled eye examination would greatly improve the quality of life of affected patients.

Copy Right, IJAR, 2021,. All rights reserved.

Introduction:-

Diabetic retinopathy (DR) is an eye disease, in which damage occurs to the retina mainly due to ischemia resulting from blood vessels fragility, rupture and blood cell aggregation as a result of uncontrolled hyperglycemia and glycation of structural proteins (MacCance and Huether, 2006). It is usually the main cause of blindness in diabetic

Corresponding Author:- A. Niyodusenga
Address:- University of Rwanda, School of Medicine and Pharmacy, Department of Clinical Biology, Huye, Rwanda.

patients and is the fifth leading cause of blindness globally (Glover et al. 2012). Whereas in developed countries the prevalence and incidence of DR is well documented, there is scanty published data on prevalence of diabetic retinopathy from sub-Saharan Africa (Glover et al. 2012). In the US, DR is documented as the main cause of vision loss in people aged 25-74 years (Abdhish et al. 2012), and in India its prevalence in 2014 was found to be about 22% (Gadkari et al. 2016).

In African populations, studies showed the prevalence of DR to be between 30.2 - 31.6%, proliferative DR 0.9 - 1.3%, and maculopathy 1.2 - 4.5%. In clinical surveys, the reported prevalence range for DR was 7.0 - 62.4%, proliferative DR 0 - 6.9%, and maculopathy 1.2 - 31.1% (Burgess et al. 2013). Recent studies conducted in Zimbabwe and Ethiopia reported a prevalence of 28.4% and 16% respectively (Pasipanodya et al. 2017, Tsegaw et al. 2021). In Rwanda the national prevalence of T2DM is about 3.16%, and mortality rate 2% per annum (WHO, 2016). In the Rwanda countryside there are no recent studies on ocular complications. Based on studies done in Kigali University Teaching Hospital, 20.4% of the patients with renal failure requiring hemodialysis suffered from T2DM (Igiraneza et al., 2018). The prevalence of diabetic retinopathy (diabetes mellitus type 1& 2) was 23% (Rudasingwa et al., 2012). The aim of this study was to determine the prevalence and risk factors associated with retinopathy in type 2 diabetic patients in Rwanda.

Methods:-

Study Design

A case-control study was conducted from January to September 2019 in four hospitals of Rwanda namely: University Teaching Hospital of Butare, Ruhengeri hospital, Kabutare and Kabgayi district hospitals. The patients were recruited from the routine diabetes clinics in these hospitals. They were consecutively consented to participate and the study information availed to them. Participants were screened for retinopathy and those with a positive result categorized as cases while those negative became controls. Of the 592 participants enrolled, 66 were cases and 526 controls.

Study Population

All type 2 diabetic patients receiving healthcare at the four mentioned hospitals were recruited. The inclusion criteria were age 25 years and above, with fasting plasma glucose above 7.0 mmol/l, be on regular oral antidiabetic drugs for at least 6 months, and willing to give informed consent and able to communicate orally.

Study tool: Type 2 diabetic patients were identified through hospital registries. The participants were interviewed guided by a questionnaire that collected information on medical history, demographic status, and anthropometric measurements performed.

Study Procedure

Morning urine and blood specimens were collected. Plasma glucose was measured by enzymatic colorimetric test (Abbott kits, Germany). Glycated hemoglobin (HbA_{1c}) was measured by colorimetric enzymatic test (Glycohemoglobin $HbA1_C$ liquicolor test kit, Human company, Germany), using Humastar 80 (Human, SN 20888, 2011, Germany).

Serum urea, creatinine, total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides were determined using colorimetric test kits (Human Company, German). Values were obtained by measuring the increase in absorbance at a wave length of 546nm, 510nm, 545nm, 600nm, 546nm, and 545nm (Humastar 80 2000; Human,SN 20888, 2011Germany) respectively.

Albuminuria was assayed by quantitative spectrophotometry. For positive albuminuria cases, full blood count, erythrocyte sedimentation rate and urinalysis were performed to rule out other causes of albuminuria. Specimens with urinary infection were not confirmed for albuminuria. Their albuminuria assays were run one month later after the infection cleared. The C - reactive protein was assayed by qualitative method using CRP reagent kit.

Diabetic retinopathy was assessed by indirect ophtalmoscopy performed for each eye with a slitlamp +90 D lens (Shin- Nippon, 2010, Japan).

Blood pressure was measured using a digital sphygmomanometer (AMRON, MI plus, Hem- 4011C-E, China). Body Mass index (BMI) was calculated as follows: BMI= Body weight (Kg)/ Height (m^2). Waist and hip circumferences were determined using a tape measure (cm).

Ethical Consideration

The study was approved by the relevant Institutional Review Boards before commencement as follows: College of Medicine and Health Sciences, University of Rwanda (Permit no. 288/CMHS IRB/2018) and Kenyatta National Hospital/University of Nairobi (Ref.KNH/ERCA3).

Data analysis:

Data obtained were analyzed on SPSS version 20. Statistical analysis to determine interactions of risk factors was performed by Chi square (x^2). Multivariate logistic regression analysis was performed for independent variables. Odds ratio (OR) was used as a measure of association. Statistical significance was set at $p < 0.05$.

Results:-

Of the 592 type 2 diabetic patients, 526 were controls and 66 cases. The mean age for controls and cases was 56 years (SD ± 0.50464, CI 95%) and 58 years (SD ± 1.46768, CI 95%) respectively. The age range for the controls was 26-86 while in the cases it was 34-89 years. Twenty eight (42.42%) of cases and 169 (32.13%) of controls were males. Majority of the participants resided in the rural area: 37 (56.06%) cases and 322 (61.21%) controls. Forty eight (72.72%) out of the 66 cases and 264 (50.19%) of controls were hypertensive. Forty six (69.69%) out of 66 cases and 356 (67.68%) out of 526 controls had a history of alcohol consumption.

The prevalence of retinopathy was 11.2%, (mild non proliferative 8.61%, moderate non proliferative 1.7%, severe non proliferative 0.34% and proliferative retinopathy 0.5%). Of the 592 participants, 78 (13.2%) had cataract and 22 (3.7%) had maculopathy.

Table 1:- Age, Gender, anthropometric measures and diabetic retinopathy.

Risk factor/Outcome		**Diabetic retinopathy**				**Total**	**x^2**	**CI**	**p**
		66 Cases	**%**	**526 Controls**	**%**				
Age	25 - 34	2	10.0	18	90.0	20	4.460	95%	0.813
	35 - 44	9	11.8	67	88,2	76			
	45 - 54	12	7.8	141	92.2	153			
	55 - 64	27	13.0	180	87.0	207			
	65 and above	16	11.8	120	88.2	136			
BMI	< 18.5	4	12.9	27	87.1	31	4.383	95%	0.625
	18.5 - 24.9	36	12.7	247	84.3	283			
	25 -29.9	16	8.3	176	91.7	192			
	30 - 34.9 and above	10	11.6	76	88.4	86			
Waist circum.	Lower risk (< 94 cm for men, < 80 cm for women)	37	13.6	236	86.4	273	3.384	95%	0.194
	Increased risk (94 – 102 cm for men, 80 -88 cm for women)	9	7.8	107	92.2	116			
	Substantially increased risk (> 102 cm for men , > 88 cm for women)	20	9.9	183	90.1	203			
		66 Cases		526 Controls		Total	OR	CI	P
Gender	Male	28		169		197	1.557	95%	0.094
	female	38		357		395			
Waist : Hip Ratio	Lower risk	23		135		158	0.646	95%	0.112
	Increased risk	43		391		434			

Table 1 shows age, gender and anthropometric variables. In univariate analysis, age, gender, BMI, waist circumference, and waist:hip ratio were not statistically associated with diabetic retinopathy. ($p > 0.05$).

Table 2:- Medical risk factors and retinopathy.

		Diabetic retinopathy			OR	CI	P
Risk Factor/Outcome							
		66 cases	526 controls	Total			
Hypertension	yes	48	264	312	**2.646**	95%	**0.001**
	no	18	262	280			
Stress	yes	21	246	267	0.531	95%	0.021
	no	45	280	325			
Alcohol consumption	yes	46	356	402	1.098	95%	0.741
	no	20	170	190			
Smoking	yes	11	125	136	0.642	95%	0.196
	no	55	401	456			
HIV infection	yes	6	22	28	2.291	9%	0.077
	no	60	504	564			
T2DM in the fam.	yes	15	149	164	0.744	95%	0.338
	no	51	377	428			
Abandonment of treatment	yes	10	67	77	1.223	95%	0.583
	no	56	459	515			
soft drink consumption	yes	26	173	199	1.326	95%	0.292
	no	40	353	393			
		Cases	Controls	Total	$\mathbf{x^2}$	CI	P
Duration of T2DM (years)	½ - 5	19	333	352	**49.418**	**95%**	**0.000**
		5.4 %	94.6 %	100.0%			
	6 - 10	19	132	151			
		12.6 %	87.4%	100.0%			
	11 - 15	19	39	58			
		32.8%	67.2%	100.0%			
	16 years and above	9	22	31			
		29.0%	71.0%	100.0%			

Table 2 above shows variables of medical history studied here. In univariate analysis hypertensive diabetic participants had 2.6 times the risk of developing diabetic retinopathy (OR 2.646, p 0.001) compared to non-hypertensive participants. Having T2DM in a period of 11 - 15 years was associated with diabetic retinopathy (32.8 % of DR, $\mathbf{x^2} = 49.418$, $p = 0.000$).

Table 3:- Socio – demographic risk factors and retinopathy.

Risk factor/Outcome		Diabetic retinopathy				Total	x^2	CI	p
		cases	%	controls	%				
Marital status	single	0	0.0	17	100.0	17	4.769	95%	0.312
	married	45	10.3	376	89.3	421			
	divorced	0	0.0	8	100.0	8			
	separated	2	14.3	12	85.7	14			
	widowed	19	14.4	113	85.6	132			
Education	none	17	15.7	91	85.3	108	3.151	95%	0.369
	primary	30	9.5	285	90.5	315			
	secondary	17	11.3	133	88.7	150			
	university	2	10.5	17	89.5	19			
Residence	town	26	12.7	179	87.3	205	3.454	95%	0.327
	agglomeration	3	10.7	25	89.3	28			
	village	31	12.0	227	88.0	258			
	Stand alone	6	5.9	95	94.1	101			
Profession	farmer	36	11.4	280	88.6	316	1.925	95%	0.859
	employed	4	8.5	43	81.5	47			
	private	12	11.4	93	88.6	105			
	retired	6	16.7	30	83.3	36			
	student	0	0.0	1	100	1			
	unemployed	8	9.2	79	90.8	87			
Transport	public	5	10.0	45	90.0	50	0.244	95%	0.970
	private	1	14.3	6	85.7	7			
	motor/bicycle	9	12.3	64	87.7	73			
	walking	51	11.0	411	89.0	462			

		Cases		Controls		Total	OR	CI	P
History of exercise	yes	29		240		269	0.934	95%	0.795
	no	37		286		323			

Table 3 above shows the association between socio- demographic variables, physical activity and DR. In univariate analysis, marital status, education, residence, profession, transport and physical activity were not associated with DR (p value > 0.05).

Hyperglycemia was associated with diabetic retinopathy (19.8% of DR, x2 = 31.229, p = 0.000). Elevated glycosylated Hemoglobin > 7.5 % and positive C - reactive protein were associated with diabetic retinopathy. (glycosylated HbA_{1C} > 7.5%, 24.3 % of DR, $\mathbf{x^2}$ = 32.506, p = 0.000, and positive CRP, 18.8 % of DR, $\mathbf{x^2}$ =10.130, p = 0.001). High levels of plasma creatinine was associated with DR, (high creatinine 23.6% of DR, x^2 =12.858, p = 0.000). High levels of LDL cholesterol, triglycerides and microalbuminuria were associated with diabetic retinopathy (x^2 = 15.077, 19.014, 67.413, and p = 0.002, 0.000, 0.000) respectively.

Table 4:- Biomarkers and T2DM retinopathy.

		Diabetic retinopathy					$\mathbf{x^2}$	P
Biomarkers/ Outcomes								
		cases	%	controls	%	Total		
Blood glucose	70 - 126 normal	18	5.4	316	94.6	334	**31.229**	**0.000**
(mg/dl)	< 70 hypoglycemia	0	0.0	15	100.00	15		
	> 126 hyperglycemia	48	19.8	195	80.2	243		
HbA1c	< 6.5 % optimal	23	6.5	331	94.9	354	**32.506**	**0.000**
	6.5 - 7,5% fair	9	9.2	89	90.8	98		
	> 7.5% poor	34	24.3	106	75.7	140		
Plasma creatinine: mg/dl	0.5 -1.2 normal	49	9.4	471	90.6	520	**12.856**	**0.000**
	> 1.2 high	17	23.6	55	76.4	72		
Serum urea: mg/dl	10 -50 normal	59	10.6	500	89.4	559	3..573	0.059
	> 50 high	7	21.2	26	78.8	33		
Total cholesterol	< 200 Normal	41	9.6	387	90.4	428	3.841	0.147
(mg/dl)	200 -239 Borderline high	14	15.2	78	84.8	92		
	> 240 High	11	15.3	61	84.7	72		
HDL Cholesterol	< 40 low	21	11.9	156	88.1	177	0.327	0.849
(mg/dl)	40 - 60 normal	40	11.1	320	88.9	360		
	> 60 high	5	9.1	50	90.9	55		
LDL cholesterol	< 130 normal	52	11.3	407	88.7	459	**15.077**	**0.002**
(mg/dl)	130 – 159 borderline high	2	2.4	80	97.3	82		
	160 – 189 high	9	**26.5**	25	73.5	34		
	>190 very high	3	17.6	14	82.4	17		
Triglycerides	40 – 160 normal	32	7,8	379	92.2	411	**19.014**	**0.000**
(mg/dl)	>160 – 200	11	13.8	69	86.3	80		
	Borderline high > 200 high	**23**	**22.8**	78	77.2	101		
C reactive protein	negative	41	8.9	418	91.1	459	**10.130**	**0.001**
	positive	25	18.8	108	81.2	133		
Albuminuria	30 – 300 microalbuminuria	27	36.5	47	63.5	74	**67.413**	**0.000**
(mg)	> 300 macroalbuminuria	4	**44.3**	5	55.7	9		
	< 30 normal	35	6.9	474	93.1	509		

In multivariate analysis, long duration of T2DM (p = 0.0013), elevated triglycerides (p = 0.0022), elevated LDL cholesterol (p = 0.0374), hyperglycemia (p = 0.0011), and microalbuminuria (p = 0.0009) were statistically significantly associated with diabetic retinopathy.

Table 5:- Multivariate analysis (risk factors and diabetic retinopathy).

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
							Lower	Upper
Hypertension	0.4659	0.3289	2.0056	1	0.1567	1.593479	0.8361	3.0365
DurationB			13.1476	2	**0.0013**			
Duration(1)	-1.4615	0.4046	13.0472	1	0.0003	0.231873	0.1049	0.5124
Duration(2)	-0.8816	0.3963	4.9473	1	0.0261	0.414096	0.1904	0.9005
Triglycerides	1.01549	0.3318	9.3614	1	**0.0022**	2.760724	1.4404	5.2909
LDLchole			5.2376	2	0.0728			
LDLchole(1)	-0.0096	0.4512	0.0004	1	0.9828	0.990369	0.4089	2.3982
LDLchole(2)	-1.7581	0.8449	4.3298	1	**0.0374**	0.172364	0.0329	0.9029
Glucose			13.5478	2	**0.0011**			
Glucose(1)	-1.2301	0.3342	13.5478	1	0.0002	0.292249	0.1518	0.5626
Glucose(2)	-19.4508	9703.8	4.02E-06	1	0.9984	3.57E-09	0	.
GhycoHB			0.8912	2	0.6404			
GhycoHB(1)	0.01429	0.3945	0.0013	1	0.9710	1.014402	0.4681	2.1982
GhycoHB(2)	-0.4045	0.4785	0.7143	1	0.3980	0.667314	0.2611	1.7049
CRP(1)	-0.3797	0.3353	1.2826	1	0.2574	0.68404	0.3545	1.3197
Albuminuria	-0.6313	0.1911	10.9126	1	**0.0009**	0.531893	0.3657	0.7735
Creatinin	0.24084	0.4084	0.34775	1	0.5553	1.272318	0.5714	2.8329
Constant	-0.4724	0.9976	0.2242	1	0.6358	0.623487		

Discussion:-

In the present study the prevalence of Type 2 diabetic retinopathy was 11.2% (non proliferative 10.65% and proliferative retinopathy 0.5%). Studies conducted in other Sub-Saharan African countries namely Zimbabwe, Ethiopia, Kenya and Uganda reported higher prevalences respectively 26.7%, 16%, 35. 9%, 19.5% (Pasipanodya et al., 2017, Tsegaw et al. 2021, Wanjiku et al., 2014, Tejal et al., 2019). The studies in Zimbabwe, Ethiopia and Uganda were conducted in a single hospital, while the current one was conducted in four hospitals and may therefore be said to be more representative of the Rwanda's population. The study conducted in Kenya reported higher prevalence compared to ours, this difference may be attributed to various factors such as the age of participants which was $\geq$ 50 years (Wanjiku et al., 2014) compared to the present study where the range was 26-89 years.

In the present study, the univariate analysis for hypertension was associated with diabetic retinopathy compared to multivariate logistic regression analyses which was not. The lack of statistical association between hypertension and diabetic retinopathy here is similar to the results of earlier studies (Pasipanodya et al., 2017, Tsegaw et al., 2021). This demonstrates the effect of better control of blood pressure on reduction of incidence and progression of diabetic retinopathy as reported in the previous studies (Glover et al., 2012, Stratton et al., 2001).

The duration of type 2 diabetes mellitus was an independent risk factor associated with diabetic retinopathy in the current study similar to previous studies (Tsegaw et al., 2021, Seyoum et al., 2001, Macky et al., 2011). In the current study there was increased chance of developing diabetic retinopathy after 11years of being diagnosed with type 2 diabetes. Also hyperglycemia was an independent risk factors associated with DR which is similar to previous studies (Pasipanodya et al., 2017, Gill et al., 2008).

Elevated LDL cholesterol and high triglycerides in univariate and multivariate analyses were independently associated with DR. This is similar to findings of other studies that high LDL cholesterol and high triglycerides were independent predictive factors for retinal complications in diabetic patients (Hadjadj et al., 2004, Wong et al., 2008). This study also found that significant albuminuria indicated by microalbuminuria and macroalbuminuria was strongly associated with DR. The study found that diabetic patients with microalbuminuria and macroalbuminuria had 7.78 and 10.83 times respectively, the risk of developing DR compared to those without albuminuria. A similar association between albuminuria and DR was reported in a previous study (Padmaja et al., 2011). The association between advanced degrees of DR and macroalbuminuria was reported by other authors (Wirta et al., 1999, Looker et al., 2003).

The present study showed that positive C – reactive protein and high levels of plasma creatinine were associated with DR in univariate logistic analyses, but not in multivariate analyses. C-reactive protein is an acute-phase protein and is mainly synthesized by the liver or adipose tissue when microbial infection or tissue damage occurs (Genes, 2010). The measurement of CRP is useful in clinical settings for the diagnosis and treatment of some acute or chronic inflammatory diseases (Lim et al. 2010). Some studies reported higher levels of CRP in patients with proliferative diabetic retinopathy than in non proliferative diabetic retinopathy (Chen, 2010, Cai et al., 2006). In this study, C-reactive protein was affected by duration of T2DM and the severity of diabetic retinopathy where the majority of DR, 8.6% had mild retinopathy. The severity of DR was associated with progressive renal function decline and albuminuria progression (Hayne et al., 2019). The strong association between DR and chronic kidney disease (CKD) was reported in an earlier study and the presence of CKD almost always accompanies DR (Parving et al., 1988). Elevated creatinine and microalbuminuria as markers of renal function increase with increasing levels of retinopathy (Kamran, 2018). In the current study plasma creatinine was also affected by duration of T2DM and severity of DR.

This study also found that obesity as indicated by BMI $\geq$ 30 kg/m^2 and waist:hip ratio >1, was not associated with DR. On meta-analysis Wei Zhu and colleagues found an association between obesity and DR (Zhu et al., 2018). A population-based cohort study found that BMI was associated with DR in risk, age and sex adjusted multivariate models (Grauslund et al. 2009), and increased waist:hip ratio was associated with DR in women (Raman et al., 2010). The lack of association between obesity and DR in the current study was attributed to general population fitness, where the majority of the patients came to hospital on foot and are in general of ectomorph body constitution as confirmed by the low prevalence of obesity in Rwandan population which was 5.8% in 2016 (Index Mundi, 2016).

Conclusion:-

The prevalence of diabetic retinopathy in this study was 11.2% (mild non proliferative 8.61%, moderate non proliferative 1.7%, severe non proliferative 0.34% and proliferative retinopathy 0.5%) in type 2 diabetic patients. The prevalence of cataract and maculopathy were 13.2% and 3.7% respectively. The major independent risk factors associated with diabetic retinopathy were long duration of T2DM, hyperglycemia, LDL cholesterol, triglycerides, and albuminuria (microalbuminuria and macroalbuminuria) It is expected that the management of these modifiable risk factors of diabetic retinopathy shall help significantly decrease its incidence or delay its onset. The Adherence to annual eye examination in diabetic patients for early diagnosis and management of DR and other causes of visual impairment such as cataracts and maculopathy is highly recommended to improve the quality of life of patients.

Acknowledgements:-

The Researchers thank the participants for their contribution to the study. The PI would like to acknowledge the Rwanda Education Board for financial support towards his Doctoral research.

Conflicts of Interest

There are no conflicts of interest.

References:-

1. **Abdhish** R. B., Atebara N. H., Drouilhet J. H. (2012). Diabetic retinopathy. On line http://emedicine.medscape.com/article/1225122-overview. Reviewed September 4th, 2021.
2. Burgess P. I., MacCormick I. J. C., Harding S. P., Bastawrous A., Beare N. A. V., and Garner P. (2013). Epidemiologyof diabetic retinopathy and maculopathy in Africa: a systematicreview, *Diabetic Medicine*, Volume 30 (4):399–412.
3. Cai X. L., Wang F., Ji L. N. (2006). Risk factors of diabetic retinopathy in type 2 diabetic patients. *Chin Med J (Engl)*. Volume 119:822–826.
4. Chen Y. S. (2010). Contents changes and correlations between Hcy and Cystatin C in patients with diabetic retinopathy in type 2 diabetes mellitus. *International Journal of Ophthalmology*. Volume 10: 2107–2110.
5. Gadkari S. S., Maskati Q. B., Nayak B. K. (2016)Prevalence of diabetic retinopathy in India.The All India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2014. *Indian Journal of Ophthalmology*: Volume 64 (1): 38-44.
6. Genes J. (2010). C-reactive protein: risk factor, biomarker and/or therapeutic target? *Can J Cardiol*., volume 26, Suppl A:41– 44.
7. Gill G., Gebrekidan A., English P., Wile D., Tesfaye S. (2008). Diabetic complications and glycemic control in remote North Africa. *QJM*, vol. 101(10):793 – 798.

8. Glover S.J., Burgess P.I, Cohen D. B., Harding S. P., Hofland H. W. C., Zijlstra E. E., et al. (2012). Prevalence of diabetic retinopathy, cataract and visual impairment in patients with diabetes in sub-Saharan Africa. *Br J Ophthalmol*. Volume 96 (2):156–161.
9. Grauslund J., Green A., Sjolie A. K. (2009). Prevalence and 25 year incidence of proliferative retinopathy among Danish type 1 diabetic patients. *Diabetologia*. Volume 52:1829– 1835.
10. Hadjadj S., Duly-Bouhanick B., Bekherraz A., BrIdoux F., Gallois Y., Mauco G., Ebran J., Marre M. (2004). Serum triglycerides are a predictive factor for the development and the progression of renal and retinal complications in patients with type 1 diabetes. *Diabetes Metab*., volume 30 (1): 43–51.
11. Hayne C. P., Young-Ki L., AJin C., Chae hoon Han, Jung-Woo N., Young J. S., Bae S. H., Hakyoung K. (2019). Diabetic retinopathy is a prognostic factor for progression of chronic kidney disease in the patients with type 2 diabetes mellitus, *Plos One*, volume 14 (7): 1 -12.
12. Igiraneza G.**,** Ndayishimiye B., Nkeshimana M., Dusabijambo V., Onyembo O. (2018) Clinical profile and outcome of patients with acute kidney injury requiring hemodialysis: Two years experience at a tertiary hospital in Rwanda. *BioMed. Research International*, volume 2018: 1 – 6.
13. Index Mundi. (2016). Obesity – adult prevalence rate Rwanda. https://www.indexmundi.com/g/g.aspx?c=rw&v=2228. Reviewed August 30, 2020
14. Kamran M. A. A. (2018). Association of Diabetic Retinopathy and Maculopathy with Elevated HbA1c, Blood Pressure, Serum Creatinine, Microalbuminuria, Spot Urine Protein, Nephropathy and Diabetic Kidney Disease. An Experience from Data Analysis of 10,580 Diabetic Patients. *Journal of Endocrinology and Diabetes*. Volume 5 (1): 1 - 11.
15. Lim L. S., Tai E. S., Mitchell P., Wang J. J., Tay W.T., Lamoureux E. et al. (2010). C - reactive protein, Body Mass Index, and Diabetic Retinopathy. *Investigative Ophthalmology & Visual Science*, volume 51:4458 – 4463.
16. Looker H. C., Krakoff J., Knowler W. C., Bennett P.H., Klein R., Hanson R. L. (2003). Longitudinal studies of incidence and progression of diabetic retinopathy assessed by retinal photography in Pima Indians. *Diabetes Care*. Volume 26 (2): 320–326.
17. MacCance K. L. and Huether S. E. (2006). Pathophysiology, the biologic basis for disease in adults and children. Fifth edition, Elsevier Mosby. Endocrine system, pp. 700 -707.
18. Macky T. A., Khater N., Al-Zamil M. A., El Fishawy H., and Soliman M. M. (2011). Epidemiology of diabetic retinopathy in Egypt: a hospital-based study, *Ophthalmic Research*, volume 45(2):73–78.
19. Padmaja K. R., Rajiv R., Gupta A., Swakshyar S. P., Kulothungan V., and Tarun S. (2011). Albuminuria and Diabetic Retinopathy in Type 2 Diabetes Mellitus**.** Sankara Nethralaya Diabetic Retinopathy Epidemiology And Molecular Genetic Study (SN-DREAMS, report 12). *Diabetol. Metab. Syndr, volume* 2011: 3- 9.
20. Parving H. H., Hommel E., Mathiesen E., Skott P., Edsberg B., Bahnsen M., *et al*. (1988). Prevalence of microalbuminuria, arterial hypertension, retinopathy and neuropathy in patients with insulin dependent diabetes. *Br Med J (Clin Res Ed).* Vol. 296 (6616):156–160.
21. Pasipanodya I. M., Macheka B., Mukona M., Kudzanai M., Parmenas N.O., Exnevia G. (2017). Prevalence and risk factors associated with retinopathy in diabetic patients at Parirenyatwa Hospital outpatients' clinic in Harare, Zimbabwe. *Arch Med Biomed Res*., Volume 3:104-111.
22. Raman R., Rani P. K., Gnanamoorthy P., *et al.* (2010). Association of obesity with diabetic retinopathy: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS Report no. 8). *Acta Diabetol*. Volume 47: 209 - 215.
23. Rudasingwa G.J, Amendezo E., and Twagirumukiza M. (2012). Clinical patterns and complications of African diabetic patients: preliminary data from Kigali University Teaching Hospital, Rwanda. *African Journal of Diabetes Medicine*. Volume 20 (2):39 -41.
24. Seyoum B., Mengistu Z., Berhanu P., et al. (2001). Retinopathy in patients of tikur anbessa hospital diabetic clinic, *Ethiopian Medical Journal*, vol. 39 (2):123–131.
25. Stratton I. M., Kohner E. M., Aldington S. J. et al. (2001). UKPDS 50: risk factors for incidence and progression of retinopathy in type II diabetes over 6 years from diagnosis, *Diabetologia*, volume 44 (2):156–163.
26. Tejal M., Pouncey A., Kunal G., Katta M., Posner M., Davey C. (2019). Prevalence and severity of diabetic retinopathy in patients attending the endocrinology diabetes clinic at Mulago Hospital in Uganda, *Diabetes Research and Clinical Practice*, Volume 152:65-70.
27. Tsegaw A., Alemu S., Abere D., Patterson C. C., Parry E. H. O., Phillips D. I. W., and 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, Volume 2021: 1-7.

28. Wanjiku M., Bastawrous A., Tunde P., Leung I., Yorston D., Foster A. *et al*. (2014). Prevalence and Correlates of Diabetic Retinopathy in a Population-based Survey of Older People in Nakuru, Kenya. *Ophthalmic epidemiology*, volume 21 (3):169 – 177.
29. WHO (World Health Organization)**.** Global report on diabetes. Part1. Global burden of diabetes, Geneva**.** 2016, pp. 21 – 23.
30. Wirta O., Pasternack A., Mustonen J., Laippala P., Lähde Y. (1999). Retinopathy is independently related to microalbuminuria in type 2 diabetes mellitus. *Clin Nephrol*. Volume 51:329–334.
31. Wong T. Y., Cheung N.,Tay W.T., Wang J. J., Aung T., Saw S. M., Lim S. C., Tai E. S., Mitchell P. (2008). Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. Ophthalmology, volume 115 (11):1869–1875.
32. Zhu W., Wu Y., Yi-Fang M., Xing Q., Jian-Jun T., Jiong L. (2018). Association of obesity and risk of diabetic retinopathy in diabetes patients. A meta-analysis of prospective cohort studies. *Medicine*, Volume 97 (32):1 - 7.