Open Access

Original Article

Identifying Risk Factors Associated with the Development of Diabetic Retinopathy in the Local Population

Erum Tariq, Palvasha Waheed, Amir Rashid, Asifa Majeed

Army Medical College/National University of Medical Sciences (NUMS), Rawalpindi Pakistan

ABSTRACT

Objective: To identify the risk factors for developing diabetic retinopathy.
Study Design: Cross-sectional study.
Place and Duration of Study: Department of Biochemistry and Molecular Biology, Army Medical College, Rawalpindi, Pak Emirates Military Hospital (PEMH), Rawalpindi and Armed Forces Institute of Ophthalmology (AFIO), Rawalpindi Pakistan, from Jun 2021 to May 2022.
Methodology: A total of one hundred and fifty participants aged 25-70 years were included in the study. All participants were divided into three equal groups. Group-I was of age and gender-matched healthy individuals (n=50), Group-II was of people with diabetes without retinopathy (n=50), and Group-III was of diabetic patients having retinopathy (n=50). All the data of the participants were recorded on an especially designed proforma, and 5ml of venous blood was also drawn from the subjects to measure serum lipid levels.
Results: Male gender was more common with 33(66%), 30(60%) and 33(66%) in Group-I, Group-II, and Group-III respectively. Most of the retinopathy cases had sedentary lifestyle 33(66%), poor dietary habits 34(68%), cardiovascular disease 38(76%), diabetic foot ulcers 44(88%) and increased levels of TAGS (*p*-value 0.001). Nephropathy and smoking showed no significant link with dr.
Conclusion: It can be concluded that a sedentary lifestyle, poor dietary habits, cardiovascular disease, diabetic foot and increased TAGS may be risk factors for the development of diabetic retinopathy. These findings can help in the early identification and better prognosis of the disease in high-risk individuals.

Keywords: Diabetic Retinopathy, Risk factors, Type 2 diabetes.

How to Cite This Article: *Tariq E, Waheed P, Rashid A, Majeed A. Identifying Risk Factors Associated with the Development of Diabetic Retinopathy in the Local Population. Pak Armed Forces Med J 2022; 72(6): 2170-2173. DOI: https://doi.org/10.51253/pafmj.v72i6.9044*

INTRODUCTION

According to the International Diabetes Federation (IDF) diabetes atlas 2017, Pakistan is ranked 10 out of 221 countries worldwide with 7.5 million cases of DM aged 20–79 years.[1,2] Half the diabetics are more prone to develop diabetic complications because of a lack of awareness. The chronic complications of DM are divided into micro-vascular and macro-vascular.[3] Microvascular compli-cations (nephropathy, retinopathy and neuropathy) have a much higher prevalence as compared to macro-vascular complications (stroke, peripheral artery disease (PAD) and cardiovascular disease). There are also some other complications of DM that cannot be categorized into the two categories.[4,5]

One of the most serious and dangerous complications of DM is diabetic retinopathy (DR).[6] Based on the presence or absence of neo-angiogenesis and vascular lesions, DR can be classified as proliferative (PDR) or non-proliferative diabetic retinopathy (NPDR). Only micro-aneurysms may be present in mild NPDR. When found together, retinal haemorrhages, hard exudates and micro-aneurysms may cause moderate NPDR.[7] Among the US working-age population, DR is one of the most threatening causes of blindness or vision loss.[8]

In a study done in 2017 in China, different risk factors for different forms of DR were characterized. Long diabetes duration, higher blood glucose level, hypertension, young age and high HbA1c all were found to be important risk factors for causing DR.[9] Many complications other than eye complications can also be related to the development of DM. These include peripheral neuropathy, cardiovascular diseases, nephropathy or low density of bones. All complications can decrease the quality of life and can cause an increased rate of mortality.[10] Therefore. This study was conducted to identify the risk factors leading to DR in the local population so that this highly debilitating condition may be prevented through early diagnosis and appropriate management.

Correspondence: Dr Erum Tariq, Department of Biochemistry, Army Medical College, Rawalpindi, Pakistan
Received: 19 Jul 2022; revision received: 31 Oct 2022; accepted: 02 Nov 2022

METHODOLOGY

This study was conducted at the Department of Biochemistry and Molecular Biology, Army Medical College (AMC), in collaboration with the Armed Forces Institute of Ophthalmology (AFIO) and Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan, after approval from the Army Medical College Ethical Review Board (ERC/ID/110). Non-probability consecutive sampling technique was employed. The study was completed in one year, from June 2021 to May 2022. The sample size was calculated using the WHO sample size calculator with the reference prevalence of DM as 11.77%.[11]

Inclusion Criteria: All the patients of T2DM and healthy controls of both genders aged between 25-70 years, with or without DR, with any duration of diabetes, including the newly diagnosed patients, were included in the study.

Exclusion Criteria: All T1DM subjects, all the patients with retinopathy due to causes other than diabetes such as atherosclerosis, hypertension, systemic vasculitis, systemic infections, blood dyscrasias, radiations etc., patients with ocular diseases other than DR like cataracts, glaucoma, papillopathy, and ocular surface diseases such as retinal vein occlusion and retinal macro-aneurysms etc., patients with a history of retinal laser therapy or ocular surgeries, patients with gestational diabetes were excluded from the study.

Total subjects enrolled in the study were 150. All the subjects were equally divided into three groups. Group-I was of age and gender-matched healthy individuals (n=50), Group-II was of people with diabetes without retinopathy (n=50), and Group-III was of diabetic patients having retinopathy (n=50). Consent of the study subjects was taken before the conduct of the study.

The medical and surgical histories of all patients, along with their demographic data, were recorded on the pre-designed proforma. The demographic data consisted of age, gender, weight, height etc. Other parameters that may affect the progression of diabetic retinopathy were also noted, like duration of diabetes, diet, lifestyle, hypertension, diabetic nephropathy, diabetic neuropathy, cardiovascular disease, diabetic foot or any other significant medical or surgical history. Under aseptic conditions, 5ml of venous blood was also drawn from the subjects and stored in plain tubes to be taken to the laboratory for measuring serum lipid levels. In addition, a fasting lipid profile was performed on the samples. The lipid profile of all the participants included total serum cholesterol, serum HDL cholesterol, serum triglycerides (TAGS) and serum LDL cholesterol.

Statistical Package for Social Sciences (SPSS) version 24.0 was used for data analysis. Frequency and percentage were calculated for qualitative variables like gender, diet, lifestyle, history of smoking, hypertension, nephropathy, neuropathy, duration of diabetes, CVD, and the presence or absence of diabetic foot. Mean±SD was presented for quantitative varia-bles like total serum cholesterol, serum triglycerides, serum LDL cholesterol and serum HDL cholesterol. Finally, all the variables between the three groups were compared to determine the value of significance between the groups using One-way ANOVA and Post-hoc Tukey test. The *p*-value of ≤0.05 was considered significant statistically.

RESULTS

Table-I: Demographic data of the study Groups (n=150)

Variables	Group-I (n=50)n(%)	Group-II (n=50)n(%)	Group-III (n=50) n(%)	*p*-value
Age(years)				
25-45	33(66)	17(34)	5(10)	0.001
46-70	17(34)	33(66)	45(90)	
Gender				
Male	33(66)	30(60)	33(66)	-
Female	17(34)	20(40)	17(34)	
Diet				
Healthy	34(68)	24(48)	16(32)	0.001
Poor	16(32)	26(52)	34(68)	
Lifestyle				
Sedentary	6(12)	25(50)	33(66)	0.001
Less active	20(40)	13(26)	8(16)	
Active	24(48)	12(24)	9(18)	
Smoking				
Smokers	3(6)	4(8)	4(8)	0.908
Non smokers	47(94)	46(92)	46(92)	
Hypertension				
Present	0(0)	14(28)	25(50)	0.001
Absent	50(100)	36(72)	25(50)	
Neuropathy				
Present	0(0)	14(28)	30(60)	0.001
Absent	50(100)	36(72)	20(40)	
Nephropathy				
Present	0(0)	2(4)	1(2)	0.365
Absent	50(100)	48(96)	49(98)	
CVD				
Present	0(0)	5(10)	12(24)	0.001
Absent	50(100)	45(90)	38(76)	
Duration of DM				
<15 years	0(0)	31(62)	18(36)	0.001
>15 years	0(0)	19(38)	32(64)	
Diabetic Foot Ulcer				
Present	0(0)	0(0)	6(12)	0.002
Absent	50(100)	50(100)	44(88)	

In above Table-I, male gender was more common with 33(66%), 30(60%) and 33(66%) in Group-I, Group-II, and Group-III respectively. The age of the patients increased as they progressed towards retinopathy, with a *p*-value of 0.001. Around 45(90%) of the subjects with retinopathy had ages above 45 years. 33(66%) of the retinopathy cases adopted a sedentary lifestyle and 34(68%) adopted poor dietary habits, with the *p*-value of both variables being around 0.001. Our findings showed that hypertension and neuropathy were found in 25(50%) and 30(60%) cases of DR with a *p*-value of 0.001.

When the lipid profile was measured for all the subjects, the results showed that lipid derangement also occurs along the development of DR. Mostly, increased levels of TAGS were observed in both groups of cases (DM & DR) (*p*-value 0.001). Whereas LDL cholesterol was also slightly increased in the borderline range in these two groups (*p*-value 0.001)(Table-II).

Table-II: Comparison of Lipid Profile of the study Groups (n=150)

Parameters (mean)	Group-I (n=50) Mean±SD	Group-II (n=50) Mean±SD	Group-III (n=50) Mean±SD	*p*-value
Total cholesterol (mmol/l)	3.79±0.60	4.53±1.28	4.76±1.85	0.001
Serum TAGS (mmol/l)	1.38±0.34	2.011±0.95	3.14±2.19	0.001
Serum LDL cholesterol (mmol/l)	2.23±0.40	3.17±1.05	3.09±1.33	0.001
Serum HDL cholesterol (mmol/l)	1.19±0.17	1.02±0.19	1.13±0.47	0.026

Intra-group association of blood lipid profile showed that total serum cholesterol and serum LDL cholesterol showed significance when Group-I was compared with Group-II and Group-III (Table-III).

Table-III: Intra-group comparison of the study Groups (n=150)

Parameters			Group II vs. Group III
	Group-I vs. Group II	Group-I vs. Group III	
Total cholesterol	0.018	0.001	0.676
Serum TAGS	0.065	0.001	0.001
Serum LDL cholesterol	0.001	0.001	0.907
Serum HDL cholesterol	0.022	0.619	0.190

DISCUSSION

Our results showed that age, diet, lifestyle, hypertension, neuropathy, duration of DM >15 years, CVD, DFU and serum TAGS positively affect the progression of DR from DM. According to the results of other studies, quality of life was seen to be affected more in the DR subjects compared to people with diabetes without nephropathy. Furthermore, a decrease in quality of life was recorded with increased duration or severity of DR.[12,13] The patients of DR suffer more from different complications, as observed in our study.

According to a meta-analysis done in 2017, a connection between DR patients with T2DM and smoking was studied. However, surprisingly, according to the results of this study, T2DM subjects, when compared with non-smokers, the risk of having PDR and DR was significantly low in the group of smokers (*p*=0.02) for DR.[14] Our study showed no significant association between smoking with the development of DM or DR. According to a study done in 2018, low physical activity was found to be strongly linked to high mortality rates, followed by smoking and dietary risks.[15] This factor is observed in our study as well that most patients of DR had a sedentary lifestyle.

At Arbaminch General Hospital, a cross-sectional study including 400 DM patients was performed. The results of the study clearly showed that age, family history of the DM, duration of DM in years and hypertension were all the risk factors identified that may play a role in the pathogenesis of DR.[16] Hypertension, age, increased duration of DM (>15years) shown a positive association in our study as well.

A meta-analysis was done in China in 2020 to determine the diagnostic significance of DR for patients with CVD. The results clearly showed that in all T2DM subjects, the DR patients had a higher CVD mortality rate than the non-DM cases.[17] Our study also showed that the risk of getting CVD increases along with the development of DR from DM or a healthy state.

According to the results of the study performed from 1987 to 2014, the prevalence of retinopathy depending on the duration of diabetes was 63% after more than 30 years of DM and 58.7% after 25 to 30 years of the disease.[18] According to a review conducted on Diabetic Foot Ulcer (DFU) patients, out of 100 DFU patients, 55 (55%) had PDR, and 90 patients (90%) had DR. No significant link was found with the

DFU severities and DR.[19] Our study showed that more cases of DFU were observed in DR subjects as compared to other two groups.

TAGS were found to play a role in the development and occurrences of micro-aneurysms in CVD patients (p=0.003). Nevertheless, in the subjects, who underwent lifestyle modifications like eating a healthy diet and exercising regularly, especially in overweight and obese subjects, the development of retinal micro-aneurysms was less. In addition, early microangiopathy was seen to develop in the diabetic subjects with elevated serum TAGS levels.[20] Our study also showed an increase in TAGS levels along with progressing age and DR development.

ACKNOWLEDGEMENT

The authors are thankful to the Department of Biochemistry, AMC, Rawalpindi and the National University of Medical Sciences (NUMS), Rawalpindi.

LIMITATIONS OF THE STUDY

The limitations of the study were the small sample size and restricted funding. In addition, it was a single institute study. Therefore, multicenter trials and the provision of proper funding and resources should be performed.

CONCLUSION

Measures to prevent the progression of diabetes can be initiated early by identifying the risk factors. Vision-threatening DR can be avoided by early detection of the disease at the non-proliferative stages.

This study concludes that risk factors significantly affect the development and progression of diabetic retinopathy in T2DM subjects and healthy controls.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

ET & PW: Conception, study design, drafting the manuscript, approval of the final version to be published.

AR & AM: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Petersmann A, Müller-Wieland D, Müller UA, Landgraf R.. Definition, Classification and Diagnosis of Diabetes Mellitus. Exp Clin Endocrinol Diabetes 2019; 127(S 01): S1-S7.
2. Federation ID. IDF Diabetes Atlas 8th edition. International Diabetes Federation, 2017, [Internet] avalable at: https://5lkasjdfasdjfasjd diabetesatlas.org/upload/resources/previous/files/8/IDF_DA_8e-EN-final.pdf
3. Cho NH, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, et al. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res Clin Pract 2018; 138: 271-281. doi: 10.1016/j.diabres. 2018.02.023.
4. Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of Diabetes 2017. J Diabetes Res 2018; 2018: 3086167. doi: 10.1155/2018/3086167.
5. Dendup T, Feng X, Clingan S, Astell-Burt T. Environmental Risk Factors for Developing Type 2 Diabetes Mellitus: A Systematic Review. Int J Environ Res Public Health 2018; 15(1): 78. doi: 10.3390/ijerph15010078.
6. Giuliari GP, Sadaka A, Chang PY, Cortez RT. Diabetic papillopathy: current and new treatment options. Curr Diabetes Rev 2011; 7(3): 171-175. doi: 10.2174/157339911795843122.
7. Lechner J, O'Leary OE, Stitt AW. The pathology associated with diabetic retinopathy. Vision Res 2017; 139: 7-14. doi: 10.1016/j. visres.2017.04.003.
8. Kempen JH, O'Colmain BJ, Leske MC, Haffner SM, Klein R, Moss SE, et al; Eye Diseases Prevalence Research Group. The prevalence of diabetic retinopathy among adults in the United States. Arch Ophthalmol 2004; 122(4): 552-63. doi: 10.1001/arch opht.122.4.552.
9. Liu Y, Yang J, Tao L, Lv H, Jiang X, Zhang M, et al. Risk factors of diabetic retinopathy and sight-threatening diabetic retinopathy: a cross-sectional study of 13 473 patients with type 2 diabetes mellitus in mainland China. BMJ Open 2017; 7(9): e016280.
10. Moriya T, Tanaka S, Sone H, Ishibashi S, Matsunaga S, Ohashi Y, et al. Patients with type 2 diabetes having higher glomerular filtration rate showed rapid renal function decline followed by impaired glomerular filtration rate: Japan Diabetes Complica-tions Study. J Diabetes Complications 2017; 31(2): 473-478. doi: 10.1016/j.jdiacomp.2016.06.020.
11. Mumtaz SN, Fahim MF, Arslan M, Shaikh SA, Kazi U, Memon MS. Prevalence of diabetic retinopathy in Pakistan; A systematic review. Pak J Med Sci 2018; 34(2): 493-500. doi: 10.12669/p jms.342.13819.
12. Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. J Pak Med Assoc 2016; 66(12): 1637-1642.
13. Pereira DM, Shah A, D'Souza M, Simon P, George T, D'Souza N, et al. Quality of Life in People with Diabetic Retinopathy: Indian Study. J Clin Diagn Res 2017; 11(4): NC01-NC06. doi: 10.7860/JC DR/2017/24496.9686.
14. Campagna D, Alamo A, Di Pino A, Russo C, Calogero AE, Purrello F, et al. Smoking and diabetes: dangerous liaisons and confusing relationships. Diabetol Metab Syndr. 2019; 11: 85. doi: 10.1186/s13098-019-0482-2.
15. Elling D, Surkan PJ, Enayati S, El-Khatib Z. Sex differences and risk factors for diabetes mellitus - an international study from 193 countries. Global Health 2018; 14(1): 118. doi: 10.1186/s129 92-018-0437-7.
16. Chisha Y, Terefe W, Assefa H, Lakew S. Prevalence and factors associated with diabetic retinopathy among diabetic patients at Arbaminch General Hospital, Ethiopia: Cross sectional study. PLoS One 2017; 12(3): e0171987. doi: 10.1371/journal.po ne.0171987.
17. Xu XH, Sun B, Zhong S, Wei DD, Hong Z, Dong AQ. Diabetic retinopathy predicts cardiovascular mortality in diabetes: a meta-analysis. BMC Cardiovasc Disord 2020; 20(1): 1-8. doi:10.1186/s12872-020-01763-z.
18. Voigt M, Schmidt S, Lehmann T, Köhler B, Kloos C, Voigt UA, et al. Prevalence and progression rate of diabetic retinopathy in type 2 diabetes patients in correlation with the duration of diabetes. Exp Clin Endocrinol Diabetes 2018; 126(9): 570-576.
19. Hwang DJ, Lee KM, Park MS, Choi SH, Park JI, Cho JH, et al. Association between diabetic foot ulcer and diabetic retinopathy. PLoS One 2017; 12(4): e0175270. doi: 10.1371/jou rnal.pone.0175270.
20. Aro A, Kauppinen A, Kivinen N, Selander T, Kinnunen K, Tuomilehto J, et al. Life Style Intervention Improves Retinopathy Status-The Finnish Diabetes Prevention Study. Nutrients 2019; 11(7): 1691. doi: 10.3390/nu11071691.