Original Article

Co-Relation between Metabolic Status and Stage of Diabetic Retinopathy in Patients Visiting Mayo Hospital, Lahore

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ABSTRACT

Purpose: To find out correlation of metabolic status (HbA1c, liver function tests, renal function tests, and hemoglobin (Hb)) with stage of diabetic retinopathy.

Study Design: Observational correlational study.

Place and Duration of Study: Mayo hospital Lahore, from April 2016 to October 2016.

Methods: After approval from the Institutional Review Board of King Edward Medical University,188 patients with diabetic retinopathy (DR) in any one of their eyes, were enrolled. The mean age of subjects was 54.43 ± 9.17 years. Staging of diabetic retinopathy was done by an ophthalmologist and relevant blood workup was carried out. If a patient had DR in both eyes, the eye in the advanced stage was recorded. Spearman rho (ρ) correlation coefficients were analyzed. The determination coefficient (r^2) was also evaluated.

Results: The male-to-female ratio was 1:1. There were 161 (85%) patients with Non proliferative diabetic retinopathy (NPDR), 16 (8.5%) had Proliferative diabetic retinopathy (PDR), and 11 (5.8%) had Adevanced diabetic eye disease. Spearman rho correlation of stage of retinopathy with HbA1c, BUN, Serum creatinine, Bilirubin, SGPT, SGOT, ALP, and Hb were -0.20, 0.160, 0.052, 0.008, -0.13, 0.119, 0.294 and -0.61 respectively; showing positive correlation to BUN, Serum creatinine, Bilirubin, SGOT, and Alkaline phosphate, and negative to HbA1c, SGPT, and Hb. The correlation was significant with BUN and ALP; $p = 0.03$ and $p < 0.001$ respectively.

Conclusion: Stages of DR showed a positive correlation with BUN, Serum creatinine, Bilirubin, SGOT, and ALP, and negative to HbA1c, SGPT, and Hb. Metabolic state of the diabetic patients should be determined and kept under control while managing diabetic retinopathy.

Key Words: Diabetic retinopathy, Serum creatinine, Bilirubin, Hemoglobin, Alkaline phosphate.

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INTRODUCTION

Diabetes mellitus is a major global health problem.[1] According to WHO, there were 437.9 million cases of type 2 diabetes in 2019, which represents a 49% increase since 1990.[2] Diabetes Association (DA) has defined diabetes mellitus as high blood glucose, of > 126 after fasting or random > 200 mg/dl including the presence of symptoms of hyperglycemia.[3] In Type I diabetes, the immune system destroys the pancreas and ultimately decreases the production of insulin. Type II diabetes occurs as a result of insulin deficiency.[4,5]

Hemorrhages and microvascular abnormalities are hallmark of this disease. Microvascular abnormalities caused by Non-proliferative diabetic retinopathy

(NPDR) include microaneurysms, and dilation of vessels in the posterior retina and macula. In NPDR, visual loss is noted with diabetic macular edema (DME). PDR occurs when there is proliferation of new vessels on the retina.[6,7] High blood pressure is also a risk factor for development of diabetic retinopathy.[8] For the diagnosis of diabetes, the HbA1c is the most preferable criterion. However, DM is diagnosed by blood glucose level in fasting and after 2 hours of the meal.[9]

To check the renal fuctions, (BUN) blood urea nitrogen is very important which measures the total amount of nitrogen in blood.[10] The breakdown product of protein is urea nitrogen. The range of normal value of BUN is between7 – 20. Liver fuction tests are also diaturbed in uncontrolled diabetes.[11]

Decrease insulin production is not the only cause of diabetes. Sometimes there is metabolic disturbance and genetic factors resulting in insulin resistance.[12]

This study assessed the renal, function, liver function, diabetes control and hemoglobin levels in patients with diabetic retinopathy.With the help of this study, patients can control or stabilize their metabolic status through early diagnosis of diabetic retinopathy.

METHODS

Ethical clearance to conduct the study was obtained from the College of Ophthalmology and Allied Vision Sciences, King Edward Medical University Lahore. A total of 188 patients who were diagnosed with diabetic retinopathy by the Diabetic Clinic, Mayo Hospital Lahore were included. The participants who were not willing, had any other systemic disease like asthma, nephropathy, or ischemic heart disease, cataract, glaucoma, uveitis and other fundus anomalies, history of any co-morbid condition (except that related to vision loss), psychological disorders or taking psychiatric medications were excluded. A consent form in containing information related tothe purpose, significance, and intended procedures of the research study was completed and signed by each participant. Data were collected by clinical examination and self-designed proforma. Venous blood samples were collected in Dipotassium EDTA and tested within 1 hour of collection to minimize variations due to old sample. Metabolic functions like Liver function test, Renal function tests, HbA1c, and Hemoglobin levels were done using an automatic blood counter system kx-21 in the hematology laboratory of the pathology department at KEMU Lahore. Samples were maintained at room temperature. The collection of quality blood specimens from patients requires specific tools for obtaining the sample and for post-collection processing, handling, shipping, and storage. The following were needed: Dipotassium EDTA vacuolated collection tubes, tourniquet (to cause blood to pool in the area and to enlarge the veins, making them easier to palpate), alcohol wipes (to disinfect the skin before blood collection), adhesive bandages/tape (to protect the vein puncture site after collection), syringes disposal unit, gloves (worn to protect the patient and the phlebotomist). A non-mydriatic fundus camera Canon no 300191 CR- 1 retinal imaging camera was used for the grading of diabetic retinopathy.

Improperly collected samples and hemolyzed and clotted samples were discarded. Samples were maintained at room temperate. Fundoscopy of selected patients was done by an ophthalmologist according to the defined protocol in the ophthalmology department of KEMU Lahore.

Data was entered and analyzed in SPSS-20. Quantitative Variables like age were presented as mean ± standard deviation. Qualitative Variables like gender were presented as frequency and percentages. Comparison of grading and values were checked with spearman rho and r. To maintain confidentiality the use of a code rather than the participant's name was employed.

RESULTS

The male-to-female ratio was 1:1. There were 161 (85%) patients with NPDR, 16 (8.5%) had PDR, and 11 (5.8%) had Adevanced diabetic eye disease. Spearman rho correlation of stage of retinopathy with HbA1c, BUN, Serum creatinine, Bilirubin, SGPT, SGOT, ALP, and Hb were -0.20, 0.160, 0.052, 0.008, -0.13, 0.119, 0.294 and -0.61 respectively; showing positive correlation to BUN, Serum creatinine, Bilirubin, SGOT, and Alkaline phosphate, and negative to HbA1c, SGPT, and Hb. The correlation was significant with BUN and ALP; $p = 0.03$ and $p < 0.001$ respectively. See Table 1 for details.

Table 1: *Correlation of diabetic retinopathy with metabolic status.*

			Stage of DR	HbA1c	BUN	Serum Creatinine	Bilirubin	SGPT	SGOT	ALP	Hb
Spearman Rho Test	**Stage of DR**	Correlation coefficient	1	-0.02	.160*	0.052	0.008	-0.013	0.119	.294**	0.061
		Sig. (2-tailed)		0.783	0.03	0.49	0.914	0.866	0.112	0	0.408
		N	188	188	186	178	184	182	180	188	187
	HbA1c	Correlation coefficient	-0.02	1	-.232**	-0.145	-0.088	-.165*	-0.11	-.172*	-0.014
		Sig.(2-tailed)	0.783	.	0.001	0.054	0.235	0.026	0.143	0.018	0.848
		N	188	188	186	178	184	182	180	188	187
	BUN	Correlation coefficient	.160*	-.232**	1	.427**	-0.041	-0.051	-0.041	0.014	0.066
		Sig. (2-tailed)	0.03	0.001	.	0	0.584	0.5	0.59	0.852	0.372
		N	186	186	186	178	182	180	178	186	185
	Serum Creatinine	Correlation coefficient	0.052	-0.145	.427**	1	-0.015	-0.111	-0.051	-0.018	.190*
		Sig. (2-tailed)	0.49	0.054	0	.	0.842	0.146	0.507	0.812	0.011
		N	178	178	178	178	174	173	171	178	177
	Bilirubin	Correlation coefficient	0.008	-0.088	-0.041	-0.15	1	0.094	0.062	0.025	-.146*
		Sig. (2-tailed)	0.914	0.235	0.584	0.842	.	0.213	0.417	0.74	0.049
		N	184	184	182	174	184	178	176	184	183
	SGPT	Correlation coefficient	-0.013	-.165*	-0.051	-0.111	0.094	1	0750**	288*	-0.097
		Sig. (2-tailed)	0.866	0.026	0.5	0.146	0.213	.	0	0	0.193
		N	182	182	180	173	178	182	180	182	181
	SGOT	Correlation coefficient	0.119	-0.11	-0.041	-0.051	0.062	.750**	1	.218**	-0.061
		Sig. (2-tailed)	0.112	0.143	0.59	0.507	0.417	0	.	0.003	0.419
		N	180	180	178	171	176	180	180	180	179
	ALP	Correlation coefficient	.294**	-.172*	0.014	-0.018	0.025	.288**	.218**	1	0.044
		Sig. (2-tailed)	0	0.018	0.852	0.812	0.74	0	0.003	.	0.55
		N	188	188	186	178	184	182	180	188	187
	Hb	Correlation Coefficient	0.061	-0.014	0.066	.190*	-.146*	-0.097	-0.061	0.044	1
		Sig. (2-tailed)	0.408	0.848	0.372	0.011	0.049	0.193	0.419	0.55	.
		N	187	187	185	177	183	181	179	187	187

DISCUSSION

Diabetic retinopathy (DR) is a metabolic syndrome. Early diagnosis and management is mandatory to prevent complications. Use of intravitreal Anti-vascular endothelial growth factors has revolutionized the treatment of DR.[13,14] For any treatment to be effective, the metabolic control is of primary importance. In the present study, metabolic prameters including, renal fuction tests (RFT), liver function tests (LFT), HBA1C and Hb levels were assessed and correlated with the severity of DR.

The mean value of HbA1C was 9.46 which was quite higher. It increased with the increase in the severity of DR. Other studies have shown that higher values of HbA1c were associated with fundus changes.[15]

In this particular study, LFTs and Bilirubin were also affected but in the borderline. The bilirubin levels were not affected in Mild NPDR cases. BUN and serum creatinine also had deranged values but the BUN values were more prone to affect DR than creatinine. The value of Hb was also not affected in

Mild stages of DR. In another study, HbA1c was found to be higher in diabetics even without retinopathy as compared to the controls and the highest values were seen in the mild NPDR.[16]

The total number of patients with moderate NPDR were 74 in our study. The values of HbA1c, BUN and serum creatinine were higher in moderate NPDR than mild NPDR. The liver functions were also deranged, similar to a previous study in which the LFT were more deranged in severe DR than mild disease.[17]

According to one study, a positive relationship between incidence and progression of retinopathy and glycosylated hemoglobin was found even after controlling for duration of diabetes, age, sex, and baseline retinopathy. These data suggest a strong and consistent relationship between hyperglycemia and incidence and progression of retinopathy.[18] In an African research, a J-shaped relationship was reported between poor control of glycemia ≥ 126 mg/dL and the severity of non proliferative diabetic retinopathy.[19] Thus, as the values of blood glucose are increased the stage of diabetic retinopathy was also higher.

The status of Hb remained the same until late stages of the disease. At late stages, Hb showed a significant inverse association with the severity of DR.[20,21]

The limitation of our study is that it was a single center study with a one time correlational design. Further research can be done by following up the patients by controlling the variables and then finding their correlation with DR.

CONCLUSION

Control of metabolic status and diabetic retinopathy goes side by side. One factor affects other factors as well. Therefore, LFTs, RFTs, HbA1C and Hb must be checked in all patients with DR on regular basis.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board **(10330/REG/KEMU/2016).**

Conflict of Interest: Authors declared no conflict of interest.

REFERENCES

1. **King H, Aubert RE, Herman WH.** Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care, 1998; **21 (9):** 1414-1431. doi: 10.2337/diacare.21.9.1414.
2. **Safiri S, Karamzad N, Kaufman JS, Bell AW, Nejadghaderi SA, Sullman MJM, et al.** Prevalence, Deaths And Disability-Adjusted-Life-Years (Dalys) Due To Type 2 Diabetes And Its Attributable Risk Factors In 204 Countries And Territories, 1990-2019: Results From The Global Burden Of Disease Study 2019. Front Endocrinol. 2022; **13:** doi:10.3389/fendo.2022.838027.
3. **Nathan DM, Davidson MB, DeFronzo RA, Heine RJ, Henry RR, Pratley R, et al.** American Diabetes Association. Impaired fasting glucose and impaired glucose tolerance: implications for care. Diabetes Care, 2007; **30 (3):** 753-759. doi: 10.2337/dc07-9920.
4. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care, 2014; **37 Suppl 1:** S81-90. doi: 10.2337/dc14-S081.
5. **Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al.** Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care, 2003; **26 (11):** 3160-3167. doi: 10.2337/diacare.26.11.3160.
6. American Diabetes Association. Standards of medical care in diabetes--2010. Diabetes Care, 2010; **33 Suppl. 1 (Suppl. 1):** S11-61. doi: 10.2337/dc10-S011. Erratum in: Diabetes Care, 2010 Mar; **33 (3):** 692.
7. **Mettler M, Kemper DW.** Information therapy: The strategic role of prescribed information in disease self-management. Stud Health Technol Inform. 2006; **121:** 373-383.
8. **Liu L, Quang ND, Banu R, Kumar H, Tham YC, Cheng CY, et al.** Hypertension, blood pressure control and diabetic retinopathy in a large population-based study. PLoS One, 2020; **15 (3):** e0229665. doi: 10.1371/journal.pone.0229665.
9. **Pippitt K, Li M, Gurgle HE.** Diabetes Mellitus: Screening and Diagnosis. Am Fam Physician, 2016; **93 (2):** 103-109. Erratum in: Am Fam Physician, 2016; **94 (7):** 533.
10. **Qiu J, Yard BA, Krämer BK, van Goor H, van Dijk P, Kannt A.** Association Between Serum Carnosinase Concentration and Activity and Renal Function Impairment in a Type-2 Diabetes Cohort. Front Pharmacol. 2022; **13:** 899057. doi: 10.3389/fphar.2022.899057.
11. **Cuthbertson DJ, Brennan G, Walsh S, Henry E.** Hepatic glycogenosis: abnormal liver function tests in Type 1 diabetes. Diabet Med. 2007; **24 (3):** 322-323. doi: 10.1111/j.1464-5491.2007.02085.x.

12. **Alqahtani N, Khan WA, Alhumaidi MH, Ahmed YA.** Use of Glycated Hemoglobin in the Diagnosis of Diabetes Mellitus and Pre-diabetes and Role of Fasting Plasma Glucose, Oral Glucose Tolerance Test. Int J Prev Med. 2013; **4 (9):** 1025-1029.
13. **Brown AE, Walker M.** Genetics of Insulin Resistance and the Metabolic Syndrome. Curr Cardiol Rep. 2016; **18 (8):** 75. doi: 10.1007/s11886-016-0755-4.
14. **Chatziralli I, Loewenstein A.** Intravitreal Anti-Vascular Endothelial Growth Factor Agents for the Treatment of Diabetic Retinopathy: A Review of the Literature. Pharmaceutics, 2021; **13 (8):** 1137. doi: 10.3390/pharmaceutics13081137
15. **Behl T, Kotwani A.** Exploring the various aspects of the pathological role of vascular endothelial growth factor (VEGF) in diabetic retinopathy. Pharmacol Res. 2015; **99:** 137-148. doi: 10.1016/j.phrs.2015.05.013.
16. **Jamshaid S, Hanif A, Malik IQ, Zahid N, Imtiaz HS.** Relationship between HbA1c Levels and Severity of Diabetic Retinopathy. Pak J Ophthalmol. 2021; **37 (4):** 352-355. Doi: 10.36351/pjo.v37i4.1210
17. **Mukherjee B, Shankar S, Ahmed R, Singh K, Bhatia K.** Association of Glycated Haemoglobin and Serum Apolipoproteins with Diabetic Retinopathy: An Indian Overview. J Clin Diagn Res. 2017; **11 (9):** BC19-BC23. doi: 10.7860/JCDR/2017/25933.10667.
18. **Arkkila PE, Koskinen PJ, Kantola IM, Rönnemaa T, Seppänen E, Viikari JS.** Diabetic complications are associated with liver enzyme activities in people with type 1 diabetes. Diabetes Res Clin Pract. 2001; **52 (2):** 113-118. doi: 10.1016/s0168-8227(00)00241-2.
19. **Klein R, Klein BE, Moss SE, Davis MD, DeMets DL.** Glycosylated hemoglobin predicts the incidence and progression of diabetic retinopathy. JAMA. 1988; **260 (19):** 2864-2871.
20. **Longo-Mbenza B, Muaka M, Mbenza G, Mbungu-Fuele S, Mabwa-Mbalanda L, Nzuzi-Babeki V, et al.** Risk factors of poor control of HBA1c and diabetic retinopathy: Paradox with insulin therapy and high values of HDL in African diabetic patients. Int J Diabetes & Metabolism, 2008; **16:** 69-78.
21. **Traveset A, Rubinat E, Ortega E, Alcubierre N, Vazquez B, Hernández M, et al.** Lower Hemoglobin Concentration Is Associated with Retinal Ischemia and the Severity of Diabetic Retinopathy in Type 2 Diabetes. J Diabetes Res. 2016; **2016:** 3674946. doi: 10.1155/2016/3674946.

Authors Designation and Contribution

Umara Gul; Optometrist: *Concepts, Design, Literature seach, Data acquisition, Statistical analysis.*

Fatima Zahid; Lecturer: *Data analysis, Statistical analysis, Manuscript preparation, Manuscript editing.*

Zehwa Mazhar; Demonstrator: *Literature search, Manuscript review.*

Ubaidullah Jan; Optometrist: *Literature search, Manuscript review.*