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 Advanced 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.


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.\textsuperscript{6,7} High blood pressure is also a risk factor for development of diabetic retinopathy.\textsuperscript{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.\textsuperscript{9}

To check the renal functions, (BUN) blood urea nitrogen is very important which measures the total amount of nitrogen in blood.\textsuperscript{10} The breakdown product of protein is urea nitrogen. The range of normal value of BUN is between 7 – 20. Liver function tests are also disturbed in uncontrolled diabetes.\textsuperscript{11}

Decrease insulin production is not the only cause of diabetes. Sometimes there is metabolic disturbance and genetic factors resulting in insulin resistance.\textsuperscript{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 containing information related to the 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 temperature. 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 Advanced 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.
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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{18} In an African research, a J-shaped relationship was reported between poor control of glycemia $\geq 126$ mg/dL and the severity of non proliferative diabetic retinopathy.\textsuperscript{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.\textsuperscript{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.


Authors Designation and Contribution
Umara Gul; Optometrist: Concepts, Design, Literature search, Data acquisition, Statistical analysis.

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Ubaidullah Jan; Optometrist: Literature search, Manuscript review.