Association of Biochemical Markers with Presence of Retinopathy Among Patients Managed with Type-II Diabetes

Syed Ali Ghawas, Muhammad Faheem*, Anam Manzoor**, Ahsan Mehmood***, Muhammad Adil****, Mustajab Alam*****

Department of Medicine, Combined Military Hospital Skardu/National University of Medical Sciences (NUMS) Pakistan, *Department of Medicine, 2 mountain medical battalion, ** Department of Gynae, Combined Military Hospital Skardu/National University of Medical Sciences (NUMS) Pakistan,***Department of Medicine, Pak Emirates Military Hospital/National University of Medical Sciences (NUMS), Rawalpindi Pakistan,****Department of Anesthesia, Fauji Foundation Hospital, Rawalpindi Pakistan,***** Department of Pathology, Combined Military Hospital Skardu/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To look for association of uric acid levels, erythrocyte sedimentation rate, LDL-cholesterol and microalbuminuria with presence of retinopathy among patients managed with Type-II Diabetes

Study Design: Comparative cross-sectional study

Place and Duration of Study: Department of Medicine, Combined Military Hospital Skardu from November 2021 to June 2022 Subjects and Methods: The sample population comprised of 120 type II diabetes patients managed either with oral hypoglycemic agents or insulin. Diabetic retinopathy was diagnosed by consultant ophthalmologist of our own hospital. Patients underwent all baseline investigations including biochemical markers included in the study. Association of uric acid levels, erythrocyte sedimentation rate, LDL-cholesterol and microalbuminuria was established with presence of diabetic retinopathy among the study participants.

Results: Out of 120 patients of type-II diabetes mellitus included in the study, 76(63.3%) were male while 44(36.7%) were female. Mean age of the patients was 44.59±6.175 years. Mean duration of type-II Diabetes Mellitus in the study participants was 4.23±4.56 years. Out of 120 patients, 75(62.5%) patients had no diabetic retinopathy while 45(37.5%) patients had retinopathy. Statistical analysis revealed that hyperuricemia and microalbuminuria had statistically significant association with presence of diabetic retinopathy in study participants (p-value<0.05).

Conclusion: Considerable number of patients with type-II diabetes mellitus had diabetic retinopathy in our data set. Patients with raised serum uric acid levels and presence of microalbuminuria were found more at risk of having diabetic retinopathy as compared to those patients who did not have these biochemical abnormalities.

Keywords: Diabetic retinopathy; Microalbuminuria; Type II DM; uric acid

INTRODUCTION

Metabolic disorders including diabetes make a big chunk of all the multisystem disorders which are managed in outpatients and wards of health care facilities.[1,2] Number of complications ranging from minor to life threatening may occur in patients suffering from diabetes mellitus during the course of illness.[3] Number of methods and assessment procedures have been in practice to look for glycemic control and complications in these patients.[4]

Diabetic retinopathy is one of the most common and debilitating complication which occur during the course of diabetes. Even patients with good glycemic control have been found to be high risk for this complication.[5] Usually clinical exams are part of routine protocol in western countries to pick the complications early. In our part of the world with limited health resources we need to identify high risk cases with basic examination and baselines investigations to prevent complications.[6]

Studies have been done in recent past regarding association of various biochemical abnormalities with presence of diabetic retinopathy. Guo et al. in 2022 published a systemic review and meta-analysis regrading relationship of uric acid abnormalities with diabetic retinopathy. It was concluded that in patients with advanced DM, uric acid levels were found deranged in most of the patients with diabetic retinopathy.[7]A Swedish study studied children of Type-I DM regarding LDL-cholesterol derangements in patients with diabetic retinopathy. It was revealed that high levels of LDL cholesterol was a risk factor for retinopathy and neuropathy among children suffering from Type-I DM.[8] Dash *et al.* studied correlation of

Correspondence: Dr Syed Ali Ghawas, Department of Medicine, Combined Military Hospital Skardu Pakistan
Received: 05 Jul 2022; revision received: 25 Jul 2022; accepted: 26 Jul 2022

microalbuminuria with presence of diabetic retinopathy. They came up with the findings that severe diabetic retinopathy was significantly associated with microalbuminuria in their study participants.[9]

Burden of diabetes mellitus is enormous in our part of the world. If disease is controlled in early phase and complications could be prevented, it is a huge success of treating team. A recent local article summarized that statistical data about diabetic retinopathy in Pakistan. They revealed a high prevalence of this complication in Pakistani population.[10] Limited local data has been available regarding role of biochemical markers in predicting various complications of DM including diabetic retinopathy. We therefore planned this study with the rationale to look for association of various biochemical markers with presence of retinopathy among patients managed with Type-II Diabetes at our hospital in Gilgit/Baltistan.

METHODOLOGY

This comparative cross-sectional study was conducted at Medicine department of Combined Military Hospital Skardu between November 2021 to June 2022. Non-probability consecutive sampling technique was used to gather the sample for the study. Sample size was calculated by using the WHO sample size calculator by using population prevalence of diabetic retinopathy in type II diabetes patients as 24.8%[11]and keeping margin of error as 10%.

Inclusion Criteria: Sample was drawn from the type II diabetic patients between age 25 and 60 years with duration of DM more than one year, managed either by oral hypoglycemic or insulin at our hospital.

Exclusion Criteria: Patients with type I diabetes or those having diabetic ketoacidosis or coma with in last three months. Patients with uncontrolled comorbid HTN, IHD, RA, autoimmune illnesses, bleeding disorders, or malignant conditions were also not recruited. Patients having history of retinopathy or any retinal disease prior to onset of diabetes were excluded from study. Those taking any medications which could interfere with retinal vascular bed in any capacity were also not included in the study.

After IREB approval via letter number A/07 dated 29Jun 22, study commenced in CMH Skardu and patients of type II DM were enrolled after informed consent. Detailed history was taken by one of the members of research team to exclude all the confounding variables. All patients underwent detailed examination by consultant ophthalmologist and diabetic retinopathy was diagnosed on the basis of retinal findings picked by ophthalmologist.[12] Patients also underwent baseline blood investigations including those which were made part of the study. Ranges for normal serum uric acid,[13] serum LDL-cholesterol,[14] microalbuminuria,[15] and erythrocyte sedimentation rate,[16] were used as per international standards. Chemical pathology department of laboratory of our own hospital was taken on board for this study. All the socio-demographic, clinical and laboratory parameters were noted on a personalized proforma for each patient designed by researchers before the start of study.

All statistical analysis was performed using Statistics Package for Social Sciences version 24.0. Frequency and percentage was calculated for the gender of the patients participating in the study and patients with and without retinopathy and biochemical derangements. Mean and standard deviation was calculated for age of the patients and duration of diabetes mellitus Chi-square test was used to look for biochemical derangements associated with diabetic retinopathy. The *p*-values were considered significant if less than or equal to 0.05.

RESULTS

Out of 120 patients of type-II diabetes mellitus included in the study, 76(63.3%) were male while 44(36.7%) were female. Mean age of the patients was 44.59±6.175 years. Table-I showed characteristic of type-II DM patients included in the study. Mean duration of type-II Diabetes Mellitus in the study participants was 4.23±4.56 years. Out of 120 patients, 75(62.5%) patients had no diabetic retinopathy while 45(37.5%) patients had retinopathy as shown in Figure-I.
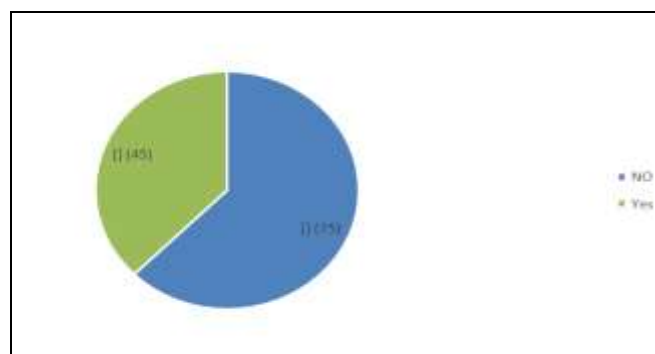

Figure-I: Percentage of patients having diabetic retinopathy (n=120)

56(46.6%) patients had BMI within normal range while 64(53.4%) were overweight or obese. Out of total 120 patients, 54(45%) patients were managed with oral hypoglycaemic agents while 66(55%) were managed with different regimes of insulin.

Table-II summarized the results of Statistical analysis. It was revealed that hyperuricemia (*p*-value-0.006) and microalbuminuria (*p*-value-0.003) had statistically significant association with presence of diabetic retinopathy in study participants while ldl-cholesterol (*p*-value-0.056) and erythrocyte sedimentation rate (*p*-value-0.258) had no significant association with diabetic retinopathy in our data set.

Table-I: Characteristics of Study Participants (n=120)

Study parameters	n(%)
Age (years)	
Mean + SD	44.59±6.175 years
Range (min-max)	25 years - 59 years
Gender	
Male	76(63.3%)
Female	44(36.7%)
Duration of Diabetes mellitus	4.23±4.56 years
Body mass index	
Normal	
Obese and over	56(46.6%)
weight	64 (53.4%)
Type of treatment	
Oral hypoglycemic	54(45%)
Insulin	66(55%)

Table-II: Association of Various Biochemical Factors with Presence of Diabetic Retinopathy (n=120)

Factors	No diabetic retinopathy	Diabetic retinopathy	*p*-value
Uric acid levels			
Normal	68(90.7%)	32(71.1%)	0.006
Deranged	07(9.3%)	13 (28.9%)	
Microalbuminuria			
No	67(89.3%)	30(66.6%)	0.003
Yes	08(10.7%)	15(33.4%)	
LDL-Cholesterol			
Normal	53(70.7%)	24(53.3%)	0.056
Deranged	22(29.3%)	21(46.7%)	
Erythrocyte sedimentation rate			
Normal	55(73.3%)	37(82.2%)	0.258
Raised	20(26.7%)	08(17.8%)	

DISCUSSION

Biochemical abnormalities like albuminuria and hyperuricemia were associated with diabetic retinopathy in our study participants. Multisystem abnormalities have been reported commonly by patients suffering from diabetes. Association of these abnormalities with each other and underlying glycemic control had always been an area of interest from clinical researchers. As it is a multisystem disorder therefore treating team has to cater for all aspects of management especially in those patients who have long duration of illness, poorly controlled illness or disease related complications. Usually compilations are directly related to main underlying abnormality in these patients i-e. glycemic control but a lot of other factors may also contribute. This study was conducted to look for association of various biochemical markers with presence of retinopathy among patients managed with Type-II Diabetes at our hospital in Gilgit/Baltistan.

Chawla *et al*. in 2021 published a study with an objective to look for relationship of microalbuminuria and other risk factors with diabetic retinopathy among patients managed for Type-II DM.[17] They revealed that HbA1c, BMI, duration of diabetes, microalbuminuria and peripheral neuropathy were significantly associated with diabetic retinopathy. Our results were also similar and microalbuminuria had statistically significant association with presence of diabetic retinopathy in our study participants.

A recent study published in China evaluated role of uric acid levels in predicting complications of DM. they concluded that high levels of uric acid were associated with chronic complication of DM including retinopathy.[18] Our results showed that considerable number of patients with type-II diabetes mellitus had diabetic retinopathy in our data set. Patients with raised serum uric acid levels and presence of microalbuminuria were found more at risk of having diabetic retinopathy as compared to those patients who did not have these biochemical abnormalities.

A case control study was published by Liu et al. in 2022 regarding association between increased parameters of lipid profile and presence of diabetic retinopathy among patients suffering from diabetes mellitus.[19] They revealed that deranged lipid profile parameters were predictors of diabetic retinopathy in their study participants. Our results were slightly different as uric acid derangement and microalbuminuria were associated with diabetic retinopathy in our study participants but LDL

cholesterol levels did not have such association in our study participants. Small sample size and other limitations may be responsible for this finding.

Another study published by Hu *et al.* in 2021 concluded that hyperuricemia was an independent risk factor for fatty liver disease in patients suffering from DM.[20] Diabteic retinopathy was found around 1/3rd of our study participants and raised uric acid levels significantly predicted presence of diabetic neuropathy.

LIMITATION OF STUDY

One hospital of Gilgit/Baltiistan was targeted so burden of diabetes or diabetic retinopathy could not be assessed for whole population of this area. Moreover, no information of status of these biochemical markers was available prior to diagnosis of diabetes or diabetic retinopathy so it cannot be concluded that diabetic retinopathy was secondary to these biochemical abnormalities. The study was cross-sectional which provides a weak evidence with many confounding variables that can lead to bias. Multicentre studies are needed on a large cohort of diabetics to further elucidate the role of biochemical markers in the prediction of DR.

CONCLUSION

Considerable number of patients with type-II diabetes mellitus had diabetic retinopathy in our data set. Patients with raised serum uric acid levels and presence of microalbuminuria were found more at risk of having diabetic retinopathy as compared to those patients who did not have these biochemical abnormalities.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

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

SAG & MF: Data acquisition, data analysis, critical review, approval of the final version to be published.

AM & AM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MA & MA: Conception, data acquisition, drafting the manuscript, 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. Uloko AE, Musa BM, Ramalan MA, et al. Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. Diabetes Ther. 2018; 9(3): 1307-1316.

2. Bullard KM, Cowie CC, Lessem SE, et al. Prevalence of Diagnosed Diabetes in Adults by Diabetes Type - United States, 2016.MMWR Morb Mortal Wkly Rep. 2018; 67(12): 359-361. https://doi:10.15585/mmwr.mm6712a2

3. Al Mansari A, Obeid Y, Islam N, et al. GOAL study: clinical and non-clinical predictive factors for achieving glycemic control in people with type 2 diabetes in real clinical practice. BMJ Open Diabetes Res Care. 2018; 6(1): e000519. https://doi:10.1136/bmjdrc-2018-000519

4. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomark Insights. 2016; 11: 95-104. https://doi:10.4137/BMI.S38440

5. Widyaputri F, Rogers SL, Kandasamy R, Shub A, Symons RCA, Lim LL. Global Estimates of Diabetic Retinopathy Prevalence and Progression in Pregnant Women With Preexisting Diabetes: A Systematic Review and Meta-analysis. JAMA Ophthalmol. 2022; 140(5): 486-494. https://doi:10.1001/jamaophthalmol.2022.0050

6. Chung, Yu-Chien et al. "Early Screening for Diabetic Retinopathy in Newly Diagnosed Type 2 Diabetes and Its Effectiveness in Terms of Morbidity and Clinical Treatment: A Nationwide Population-Based Cohort." Frontiers in public health vol. 10 771862. 26 Apr. 2022, https://doi:10.3389/fpubh.2022.771862

7. Guo Y, Liu S, Xu H. Uric Acid and Diabetic Retinopathy: A Systematic Review and Meta-Analysis. Front Public Health. 2022; 10(3): 906760. https://doi:10.3389/fpubh.2022.906760

8. Rathsman B, Haas J, Persson M, et al. LDL cholesterol level as a risk factor for retinopathy and nephropathy in children and adults with type 1 diabetes mellitus: A nationwide cohort study. J Intern Med. 2021; 289(6): 873-886. https://doi:10.1111/joim.13212

9. Dash S, Chougule A, Mohanty S. Correlation of Albuminuria and Diabetic Retinopathy in Type-II Diabetes Mellitus Patients. Cureus. 2022; 14(2): e21927.https://doi:10.7759/cureus.21927

10. 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. https://doi:10.12669/pjms.342.13819

11. Hashemi H, Rezvan F, Pakzad R, Ansaripour A, Heydarian S, Yektaet al A. Global and Regional Prevalence of Diabetic Retinopathy; A Comprehensive Systematic Review and Meta-analysis. Semin Ophthalmol. 2022; 37(3): 291-306. https://doi:10.1080/08820538.2021.1962920

12. Pearce E, Sivaprasad S. A Review of Advancements and Evidence Gaps in Diabetic Retinopathy Screening Models. Clin Ophthalmol. 2020; 14(3): 3285-3296. https://doi:10.2147/OPTH.S267521

13. Desideri G, Castaldo G, Lombardi A, Mussap M, Testa A, Pontremoliet R al. Is it time to revise the normal range of serum uric acid levels?. Eur Rev Med Pharmacol Sci. 2014; 18(9): 1295-1306.

14. Moidu S, Oomen AT, Pillai G, Vs S. Microalbuminuria as an Independent Risk Factor for Developing Concentric Left Ventricular Hypertrophy in Primary Hypertension: A Single-Center Observational Study From South India. Cureus. 2022; 14(1): e21119. https://doi:10.7759/cureus.21119

15. Ahn JH, Ahn Y, Jeong MH, et al. Optimal low-density lipoprotein cholesterol target level in Korean acute myocardial infarction patients (<70 mg/dL vs. <55 mg/dL): Based on Korea acute myocardial infarction registry-National Institute of Health. Int J Cardiol. 2022; 351(3): 15-22. https://doi:10.1016/j.ijcard.2021.12.020

16. Asawapattanakul T, Pintapagung T, Piratae S, Juntautsa S, Chancharoen P. Erythrocyte sedimentation rate, C-reactive protein, and interleukin-6 as inflammatory biomarkers in dogs naturally infected with Ehrlichia canis. Vet World. 2021; 14(9): 2325-2331. https://doi:10.14202/vetworld.2021.2325-2331

17. Chawla S, Trehan S, Chawla A, et al. Relationship between diabetic retinopathy microalbuminuria and other modifiable risk factors. Prim Care Diabetes. 2021;15(3):567-570. https://doi:10.1016/j.pcd.2021.01.012

18. Xiong Q, Liu J, Xu Y. Effects of Uric Acid on Diabetes Mellitus and Its Chronic Complications. Int J Endocrinol. 2019; 2019(1): 9691345. https://doi:10.1155/2019/9691345

19. Liu Z, Shao M, Ren J, Qiu Y, Li S, Cao W. Association Between Increased Lipid Profiles and Risk of Diabetic Retinopathy in a Population-Based Case-Control Study. J Inflamm Res. 2022; 15(2): 3433-3446.https://doi:10.2147/JIR.S361613

20. Hu Y, Li Q, Min R, Deng Y, Xu Y, Gao L. The association between serum uric acid and diabetic complications in patients with type 2 diabetes mellitus by gender: a cross-sectional study. PeerJ. 2021; 9(1): e10691. https://doi:10.7717/peerj.10691

....