# Albuminuria and its Association with Diabetic Retinopathy among Type-2 Diabetic Patients at a Specialized Diabetic Clinic

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## Abstract

**Background:** Diabetes mellitus is one of the leading non-communicable diseases with an increasing prevalence around the globe. Diabetic Nephropathy and Retinopathy are common complications of diabetes that can be prevented by early interventions.

**Objective:** To assess the association between micro and macro-albuminuria with diabetic retinopathy in patients having Diabetes Mellitus type-2.

**Methodology**: This hospital-based cross-sectional study was conducted on patients having Diabetes Mellitus type-2, visiting eye clinic at AIMS Diabetes Hospital and Research Center Hayatabad, Peshawar from October 2016 to March 2017. All patients having Diabetes Mellitus type-2 were included in the study using purposive sampling. After taking informed consent from patients, data were collected on a pre-designed questionnaire and analyzed using STATA-14. Linear regression was done for the assessment of an association of albuminuria with diabetic retinopathy and other independent variables.

**Results:** A total of 141 type-2 diabetic patients were examined. The mean age of participants was 53.4±9.42 years and 73 (51.77%) were female. Of these patients, microalbuminuria was 88 (62.41%) and macroalbuminuria was 26 (18.4%). Overall, the frequency of Diabetic Retinopathy was 93 (65%), in which 62 (43%) were non-proliferative, and 31 (21.9%) were proliferative DR. On multivariate regression analysis, albuminuria was significantly associated with male gender, old age group (60 years and above), overweight, obesity, and occurrence of both NPDR and PDR (p-value <0.05).

**Conclusion:** Increased level of albuminuria in patients with Diabetes Mellitus type-2 enhances the risk of developing diabetic retinopathy. The risk for developing Diabetic Retinopathy increases with an increase in BMI and age of the patients.

**Keywords**: Diabetes Mellitus, Diabetic retinopathy, Microalbuminuria, Type 2 diabetes

**Article Citation:** Arooj A, Fazid S, Khan AJ, Adeeb H, Jawaid H, Ihsanullah, Albuminuria and its Association with Diabetic Retinopathy among Type-2 Diabetic Patients at a Specialized Diabetic Clinic. JSZMC 2021;12(3):17-21. **DOI:** https://doi.org/10.47883/jszmc.v12i3.177

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## Introduction

Diabetes mellitus (DM), a metabolic disease in which there is hyperglycemia due to deficiency in insulin secretion, the problem with insulin activity, or both. DM can affect different organs, especially the eyes, kidneys, heart, and blood vessels, and nerves.[1] The worldwide number of individuals with diabetes will increase twofold in the next 25 years.[2] As per the American Diabetes Association, around 1.5 million new cases of diabetes are diagnosed every year in the United States, and diabetes is the leading cause of end-stage renal disease, adult-onset blindness, and non-traumatic lower-limb amputations.[3]

As opposed to western countries, the largest proportion of patients affected with DM in Asia are between 45 to 64 years of age. Due to the chronicity of the disease, they are prone to long-term disease complications, including diabetic retinopathy which is the most common preventable cause of blindness.[4] Patients having diabetic retinopathy (DR) are having around 25 higher chances of becoming blind as compared to normal individuals. Worldwide statistics show that there are 93M people with DR, 21M macular edema, and 17M with proliferative DR.[5] Poor glycemic control and the longevity of DM with hypertension are strong risk factors for DR.[6]

The duration of disease in this chronic condition is a significant association for DR. In DM Type 2, 40% of patients using insulin and 24% of those not on insulin have retinopathy in patients more than 30 years with disease duration of fewer than 5 years. These percentages then go up to 84% and 53%, if the

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duration of the disease is increased to 19 years. Proliferative diabetic retinopathy is found in 2% of DM Type-2 patients who have had the disease for less than 5 years, and in 25% of patients who have the disease for a longer duration. Similarly, glycaemic control is an important modifiable risk factor and poses a significant risk for retinopathy than the disease duration. The target HbA1c should be less than 7% to prevent diabetic retinopathy.[7] Diabetic nephropathy occurs in 25% of type-2 diabetics and is one of the main reasons for end-stage renal failure. There is an early period of diabetic renal disease called incipient diabetic nephropathy which can be identified by urinary excretion of albumin (Microalbuminuria). Microalbuminuria precedes the development of overt diabetic nephropathy by 10-14 years.

It is regularly associated with other microvascular complications like retinopathy and neuropathy, so it can be a marker for microvascular damage in patients with DM and is acknowledged as the main clinical finding for the diagnosis of diabetic nephropathy.[8] As diabetic nephropathy progresses, the development of microalbuminuria eventually leads to macroalbuminuria and then to dynamic loss of glomerular filtration rate (GFR). Type-2 diabetes patients may also get parenchymal renal disease due to having hypertension, atherosclerosis, and lipid toxicity.[9] Some researchers have explored the potential relationship between microalbuminuria and diabetic retinopathy in patients, having DM type-2. The association of microalbuminuria and diabetic retinopathy (DR) has been well reported in patients with type-1 diabetes; however, for type-2 diabetes, there is limited data, especially from population-based studies.[10-12]

The patients with microalbuminuria are twice more prone to have DR than those without microalbuminuria, and this risk becomes 6 folds in the presence of macroalbuminuria.[13] A comparative study of Hispanics vs non-Hispanics in the US also showed a strong association of over albuminuria and Diabetic Retinopathy.[7] The objective of this study was to assess the association of micro and macro-albuminuria with diabetic retinopathy in patients having Diabetes Mellitus type-2.

## Methodology

The present cross-sectional study was done at the Eye Clinic of AIMS Diabetes Hospital & Research Centre Hayatabad, Peshawar from October 2016 to March 2017. All type-2 diabetic patients of both genders and all ages were enrolled in the study using purposive sampling. Those who were not willing to participate were excluded from the study. Data was collected after taking informed written consent and confidentiality was ensured. Ethical approval was sought from the Ethical Committee of the Hospital.

Data regarding age, gender, weight, height, history of diabetes, and fundoscopy results were recorded on a structured Performa.

Visual acuity was assessed by using the Snellen acuity chart at a 6m distance; Tropicamide 1% was used for pupil dilation. Fundoscopy was performed by using a Direct Ophthalmoscope and slit lamp bimicroscopy with 78D lens. After screening for diabetic retinopathy, patients had their HbA1C and urine microalbumin tests done, in the laboratory of under study hospital. Data were analyzed by using STATA-14. Mean and SD was calculated for age and BMI while the Chi-square test was used for cross-tabulation between albuminuria status with independent variables, i.e. age, gender, HbA1c level, BMI, duration of diabetes, and diabetic retinopathy. Multivariate regression analysis was used to assess the association of albuminuria levels with the independent variables while controlling for potential confounders. A p-value of $<0.05$ was considered statistically significant.

## Results

A total of 141 type-2 diabetes patients were examined for this study. Out of the total patients, 68 (48.23%) were males, and 73 (51.7%) were female.Almost half of the patients 61 (43.26%) were below 50 years of age, and 32 (22.7%) were in the 60 years and above age group. On the BMI cut-offs, 41 (29%) were normal weight, 66 (46.8%) were overweight and 34 (24.11%) were obese. Of the total, 27 (19.15%) patients were having normal albumin levels, 88 (62%) were having microalbuminuria followed by macroalbuminuria 26 (18%). Among these patients, 62 (43.9%) were having non-proliferative diabetic retinopathy while 29 (20.5%) were having vision-threatening proliferative diabetic retinopathy.

**Table I: Characteristic of the participants by albuminuria level (n=141)**

| Variables | Normal N (%) | Microalbuminuria N (%) | Macroalbuminuria N (%) | P-value |
|---|---|---|---|---|
| **Gender** | | | | |
| Male | 16 (59.26) | 37 (42.05) | 15 (57.69) | 0.166 |
| Female | 11 (40.74) | 51 (57.95) | 11 (42.31) | |
| **Age Groups** | | | | |
| ≤50 | 13 (48.15) | 42 (47.73) | 6 (23.08) | 0.154 |
| 51-60 | 9 (33.33) | 29 (32.95) | 10 (38.46) | |
| ≥61 | 5 (18.52) | 17 (19.32) | 10 (38.46) | |
| **Duration (years)** | | | | |
| 1 - 5 | 6 (22.22) | 11 (12.5) | 2(7.69) | 0.04 |
| 6 – 10 | 16 (59.26) | 31 (35.23) | 8 (30.77) | |
| 11 – 15 | 1 (3.7) | 19 (21.59) | 5 (19.23) | |
| 16 – 20 | 4 (14.81) | 27(30.68) | 11 (42.31) | |
| **HbA1c** | | | | |
| ≤8 | 2 (7.41) | 16 (18.18) | 2 (7.69) | 0.215 |
| >8 | 25 (92.59) | 72 (81.82) | 24 (92.31) | |
| **BMI** | | | | |
| Normal Weight | 14 (51.85) | 24 (27.27) | 3 (11.54) | 0.01 |
| Overweight | 11 (40.74) | 41 (46.59) | 14 (53.85) | |
| Obese | 2 (7.41) | 23 (26.14) | 9 (34.62) | |
| **Diabetic Retinopathy (DR) Status** | | | | |
| No DR | 15 (55.56) | 30 (34.09) | 3 (11.54) | <0.001 |
| Non-proliferative DR | 10 (37.04) | 41 (46.59) | 11 (42.31) | |
| Proliferative DR | 2 (7.41) | 17 (19.32) | 12 (46.15) | |

**Table-II: Linear regression analysis of the participant characteristics associated with albuminuria (n=141)**

| Variables | Un-adjusted | | | Adjusted | | |
|---|---|---|---|---|---|---|
| | Coef. | 95% CI | P-value | Coef. | 95% CI | P-value |
| **Gender** | | | | | | |
| Female | Ref | Ref | Ref | Ref | Ref | Ref |
| Male | 30.49 | -5.35, 66.34 | 0.09 | 45.72 | 11.93, 79.50 | 0.008 |
| **Age** | | | | | | |
| ≤50 | Ref | Ref | Ref | Ref | Ref | Ref |
| 51-60 | 35.52 | -4.98, 76.02 | 0.08 | 28.31 | -8.75, 65.36 | 0.13 |
| ≥61 | 61.47 | 15.65, 107.29 | 0.01 | 51.49 | 9.62, 93.37 | 0.01 |
| **Duration of Diabetes (In years)** | | | | | | |
| ≤5 | Ref | Ref | Ref | Ref | Ref | Ref |
| 6- 10 | 16.86 | -39.16, 72.89 | 0.55 | 0.56 | -49.40, 50.53 | 0.98 |
| 11- 15 | 47.06 | -17.01, 111.13 | 0.15 | 26.08 | -35.92, 88.09 | 0.41 |
| 16 & above | 67.14 | 8.93, 125.34 | 0.02 | 40.78 | -15.99, 97.55 | 0.16 |
| **HbA1c** | | | | | | |
| ≤ 8 mmol | Ref | Ref | Ref | Ref | Ref | Ref |
| >8 mmol | 18.75 | -33.02, 70.51 | 0.47 | 19.91 | -26.87, 66.69 | 0.40 |
| **BMI** | | | | | | |
| Normal Weight | Ref | Ref | Ref | Ref | Ref | Ref |
| Overweight | 61.77 | 20.72, 102.83 | 0.003 | 69.64 | 30.68, 108.60 | 0.001 |
| Obese | 77.46 | 29.57, 125.35 | 0.002 | 93.11 | 45.27, 140.95 | <0.001 |
| **Diabetic Retinopathy** | | | | | | |
| No DR | Ref | Ref | Ref | Ref | Ref | Ref |
| Non-proliferative DR | 58.90 | 21.79, 96.02 | 0.002 | 53.24 | 15.14, 91.34 | 0.007 |
| Proliferative DR | 125.68 | 80.11, 171.26 | <0.001 | 85.16 | 34.46, 135.86 | 0.001 |

On cross-tabulation between albuminuria and other independent variables, we found that albuminuria (micro and macro) was associated with the duration of diabetes, BMI, and diabetic retinopathy status (p-value <0.05). (Table-I) On univariate linear regression, we found that an increase in albuminuria is associated with increased age, i.e. 60 years and above, history of diabetes more than 15 years, overweight & obese, and occurrence of DR (p-value <0.05).

However, it also showed there is no association of albuminuria with gender, age below 60 years, and level of HbA1c. On multivariate linear regression, the adjusted results showed that the increase in albuminuria is associated with male gender, age group 60 years and above, overweight & obese, and occurrence of DR (p-value <0.05). On adjusted rates, it showed that there is no association of albuminuria with DR in patients of less than 60 years of age and also it has no association with the duration of diabetes and HbA1c level in type-2 diabetic patients. (Table-II)

## Discussion

Diabetic retinopathy is a serious and common microvascular complication of DM. It is the leading cause of acquired blindness worldwide. The burden of DR is rising with an increase in the prevalence of DM type-2.[9] The risk factors associated with DR include a raised HbA1c, dyslipidemia, hypertension, chronicity of the disease, age at the onset, smoking, and microalbuminuria.[10]

Microalbuminuria is usually due to a pathophysiological vascular insufficiency, which makes the patient prone to organ damage. The persistence of microalbuminuria with DM is not only a risk for kidney and heart diseases but also for vision-related morbidity. Microalbuminuria is thought to be an indicator of diabetic nephropathy in obese patients with DM type 2. Several studies have indicated that microalbuminuria might be an independent risk factor for DR in DM type-2. In this study, we noted that albuminuria (micro and macro) was associated with a history of diabetes (duration), BMI, and diabetic retinopathy status (p-value <0.05).

We found a significant association of diabetic retinopathy with microalbuminuria. Several other studies found a similar association. A study in Iran reported that diabetic retinopathy and renal involvement were highly positively related.[10] In another study,[11] a significant association of diabetic retinopathy with microalbuminuria was noted. Similarly, another study,[12] also reported a strong association between diabetic retinopathy and microalbuminuria. A cross-sectional study was conducted,[13] on 284 patients showed a significant association between DR and microalbuminuria. A study conducted by M.C. Boelter,[14] on 1214 DM type-2 patients noted that patients having proliferative DR more often presented with renal involvement and increased urine albumin excretion. Another retrospective study was conducted,[15] among 917, type-2 diabetic patients to correlate the link between retinopathy and nephropathy caused by complications of diabetes mellitus type-2. Their investigation likewise shows that the relationship amongst DR and DN was factually noteworthy and had a unidirectional connection, DN goes before DR, and the level of renal impedance is corresponding to the level of harm to the eye. Also, it has been reported that[16] assessment of diabetic retinopathy may provide useful information on the renal function and risk of kidney disease.

Giuseppe Giuffre,[17] noted that DR has a strong association with the duration of diabetes. Similarly, in another study conducted by Snjezana Kastelan,[18] reported in their study that DR progression was correlated with diabetes duration, BMI, and HbA1c. Pavel Kotlars,[15] suggested in his study that DR is affected positively by diabetes duration and HbA1c. A study conducted by Manaviat MR,[10] also reported that risk factors HbA1c and BMI were significantly associated but had no association with gender.

We found similar results and found that albuminuria (micro and macro) was associated with the history of diabetes (duration), BMI of the patients and diabetic retinopathy status (p-value <0.05), increased age, i.e. 60 years and above, duration more than 15 years, overweight and obese with the risk of occurrence of DR (p-value <0.05). However, in patients less than 60 years old, it showed no association of albuminuria and DR and also not associated with gender, duration of diabetes, and level of HbA1c.

## Conclusion

It was revealed that Diabetes Retinopathy in type-2 diabetes patients, who are above 60 years are significantly associated with gender, Albuminuria,

HbA1c, BMI, and with duration of diabetes. Microalbuminuria in patients with retinopathy most probably would reflect diabetic nephropathy. This study suggests that every diagnosed patient of type 2 diabetes mellitus should have a detailed fundus examination and should be screened for microalbuminuria. This will help us in early detection and prompt treatment of these complications saving a large number of patients from morbidity and mortality

**Authors Contribution: AA:** Conception of work, Acquisition and Analysis of data and Drafting. **SF:** Acquisition and Analysis of data and Drafting. **AJK:** Design of work and Drafting. **HA:** Acquisition and Analysis of data and revising. **HJ:** Interpretation of data and drafting. **IU:** Interpretation of data and Drafting.
All authors critically revised and approve its final version.

**Conflict of Interest**: Authors has declared no conflict of interest.

**Sources of Funding:** The source of funding was self.

**Disclaimer:** None

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