

Diabetic Retinopathy Among Type II Diabetics; with and without Microalbuminuria

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ABSTRACT

Objective: To determine the frequency of diabetic retinopathy among type ii diabetics, with and without microalbuminuria at tertiary care Hospital. **Study Design:** Cross-sectional study. **Settings:** Diabetes Management Centre, Services Hospital Lahore-Pakistan. **Duration:** Six months duration from May 2015 to November 2015. **Methodology:** Patients with type II diabetes mellitus diagnosed for >10 years and whose random blood sugar level was ≥ 200 mg/dl or fasting blood sugar level is ≥ 126 mg/dl at the time of diagnosis, both gender and age between 25 to 70 years were included. Patient were said to have diabetic retinopathy if any one of the following changes were seen on his/her funduscopy by retinal camera: Microaneurysm, blot and dot hemorrhages, hard exudates, beading, and venous looping, soft exudates, maculopathy and formation of fresh vessel. All the data was recorded in the proforma. **Results:** Total 300 patients were studied; their age range was 35-70 years. 43% were male and 57% were female. Out of 300 diabetics, 90 were diagnosed as patients of retinopathy and 86 were found to have microalbuminuria i.e., 28.7%. Frequency of retinopathy was greater among microalbuminuria cases (45.4%) while among cases without microalbuminuria it was 24.3%. **Conclusion:** It was concluded that the frequency of retinopathy was higher among patients with microalbuminuria as compare to those without microalbuminuria. After these findings' microalbuminuria can be used as a predictor of diabetic retinopathy.

Keywords: Diabetes mellitus, Diabetic retinopathy, Microalbuminuria.

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Submitted for Publication: 12-07-2019

Accepted for Publication: 29-08-2019

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Citation: Butt A, Mateen F, Hafeez S, Ali H, Waheed K, Ahmad A. Diabetic Retinopathy Among Type II Diabetics, with and without Microalbuminuria. APMC 2019;13(3):236-40.

INTRODUCTION

Diabetes mellitus (DM) is a syndrome with metabolic disorder and unacceptable hyperglycemia because of either an insulin secretion deficiency or combination of insufficient secretion to compensate and insulin resistance.¹ Diabetes is a major factor of mortality and morbidity globally, and is 6th major factor of death within United States representing >71,000 deaths yearly.² The great majority of diabetic subjects are categorized into 1 of 2 broad groups: type-1 diabetes having an absolute insulin deficiency, and type 2 distinguished by insulin resistance with an insufficient compensatory rise in secretion of insulin. Besides the major two forms, it can as well develop in the course of pregnancy and secondary to endocrinopathies, pancreatic infection, and drugs etc.³ Chronic hyperglycemia encourages the glucose reaction with arterial wall components to result in advanced glycation end products. These products cross-link with collagen, thus raising arterial rigidity which along with raised levels of cholesterol and low-density lipoprotein (LDL) encourages atherogenesis. Thus high levels of blood glucose result in endothelial impairment - manifesting as macrovascular or microvascular impairment.⁴ The diabetic subject is prone to a sequence of complications that result in premature mortality and morbidity.⁵ Diabetic complications impose a heavy burden on health services because poor glycaemic control in diabetic patients also has been associated directly with raised general costs of health care.^{6,7} Micro vascular disease also has a noticeable effect on the life of T2DM subjects.⁸ Diabetic

retinopathy is a most severe ocular complication of diabetes. The incidence of diabetic retinopathy ranges between 21.0% and 60.0% in diabetic subjects for < 5 years and ≥ 15 years, correspondingly. Proliferative retinopathy ranges between 1.20% and 67.0% in diabetic subjects for >10 years and ≥ 35 years, respectively. The incidence of blindness in diabetic cases was 16.0%.⁹ In type 2 diabetes, microalbuminuria is rarely reversible¹⁰ however, instead, advances to overt proteinuria among 20.0% to 40.% of cases.¹¹ Among 10.0% to 50.% of cases with proteinuria, chronic renal disorder develops that eventually needs transplantation or dialysis.^{12,13} 40.0% to 50.0% of T2DM patients with microalbuminuria ultimately die of CVD;^{14,15} this is thrice as high a rate of death associated with cardiac factors as among diabetes patients without renal disorder.¹⁶ Many studies have shown microalbuminuria is correlated with the incidence of retinopathy among diabetic cases and with the existence of proliferative disorder among younger-onset people. People with microalbuminuria were further likely to have retinopathy contrasted to those without microalbuminuria. The data propose that microalbuminuria can possibly be a predictor for the risk of proliferative retinopathy.^{17,18}

METHODOLOGY

Study Design: This was a cross-sectional study.

Settings: Diabetes Management Centre, Services Hospital Lahore Pakistan.

Duration: Six months from May 2015 to November 2015.

Sample Size: Total 300 patients were studied

Inclusion Criteria: Patients with type II diabetes mellitus diagnosed for >10 years and whose random blood sugar level is ≥ 200 mg/dl or fasting blood sugar level is ≥ 126 mg/dl at the time of diagnosis, Both gender and age between 35 to 70 years.

Exclusion Criteria: All the patients who have had laser therapy of retina, taking ACE inhibitors, hypertension, positive protein on dipstick (macroalbuminuria), patients with BUN > 20 mg/dl and creatinine > 1.20 mg/dl on labs and Patients with RBC cast, WBC cast and tubular cast on urine microscopy were excluded.

Methods: Patient were said to have diabetic retinopathy if any one of the following changes were seen on his/her funduscopy by retinal camera: Microaneurysm, blot and dot hemorrhages, hard exudates, beading, and venous looping, soft exudates, maculopathy and formation of fresh vessel. Effect modifiers like age, poor glycemic control subjected to HbA1c and treatment taken were controlled through stratification. Data collection was done by computer and analysis was carried out by SPSS version 16.

RESULTS

Overall 300 cases with T2MD diagnosed for >10 years were selected from the Diabetes Management Centre of Services Hospital Lahore. Out of 300 cases, 43.0% were males and 57.0% were females. Females were found more than males. Figure 1 shows bar graphs showing the percentages of males and females. Most of diabetic subjects were aged 45-64 (68.70%). There were some patients at the extremes of age groups, with the minimum and maximum age of 35 and 70 respectively. Mean age was $52.18 \pm$ SD of 8.993. Out of 300 patients 86 (28.7 %) patients were found to have microalbuminuria and 214 (71.3%) patients did not have microalbuminuria. Out of 300 patients 91 (30.3 %) patients were found to have retinopathy and 209 (69.7%) patients did not have retinopathy. There were 86 patients who had microalbuminuria 39 (45.4%) patients also had retinopathy, however, remaining 47 (54.6%) patients did not have retinopathy. Among the 214 patients who had no microalbuminuria, the frequency of retinopathy was 52 (24.3%). 162 (75.7%) patients had no retinopathy and microalbuminuria. It clearly shows that patients with microalbuminuria have more frequency of retinopathy (45.3%) as compared to the patients without microalbuminuria (24.3%). Out of 300 patients 267 patients were taking treatment for diabetes mellitus. Out of these 267 patients 72 (27%) developed retinopathy, however, remaining 195 (73%) did not have retinopathy. Those 33 patients who were not taking any treatment had higher frequency of retinopathy i.e., 19 (56.7%). It clearly shows that retinopathy develops more frequently in patients who do not take treatment for diabetes. Out of 267 patients who were taking treatment for diabetes microalbuminuria developed in 71 (26.6%) patients. On the other hand, frequency of microalbuminuria in patients not taking any treatment was 15 out of 33 i.e., 45.5%. It shows that frequency of microalbuminuria can be reduced by taking treatment for diabetes. Out of 300 patients 192 patients had fair

control of diabetes as shown by HbA1c less than 7.5, 108 patients had poor control as their HbA1c was more than 7.5. In patients with HbA1c less than 7.5, 23 (12%) patients out of 192 developed microalbuminuria. In patients with HbA1c more than 7.5, 63(58%) patients out of 108 developed microalbuminuria. It shows that patients who had bad control of diabetes developed microalbuminuria more frequently. Out of 192 patients who had HbA1c less than 7.5, retinopathy developed in 30 (15.6%) patients. On the other hand frequency of retinopathy in patients with higher HbA1c was 61 out of 108 i.e., 56.5%. It shows that patients who had bad control of diabetes developed retinopathy more frequently.

Table 1: Frequency distribution of demographic and clinical characteristics

Variables	Frequency	Percent	
Gender	Male	129	43.0
	Female	171	57.0
Age groups	35-44 yrs	61	20.3
	45-55 yrs	119	39.7
	55-64 yrs	87	29.0
	65-70yrs	33	11.0
Microalbuminuria	Yes	86	28.7
	No	214	71.3
Retinopathy	Yes	91	30.3
	No	209	69.7

Table 2: comparison of retinopathy with respect to different variables

		Presence of retinopathy		p-value
		Yes	No	
Microalbuminuria	Yes	39(45.4%)	47(54.6%)	0.001
	No	52(24.3%)	162(75.7%)	
Treatment taken for diabetes	Yes	72(27%)	195(73%)	0.001
	No	19(57.6%)	14(42.4%)	
HbA1c to see glycemic control	7.5 or less	30(15.6%)	162(84.4%)	0.001
	>7.5	61(56.5%)	47(43.5%)	

DISCUSSION

The prevalence of diabetes mellitus is fast raising in our part of the world.¹⁹ Being a chronic disorder, much of its morbidity and mortality is related to the incidence of associated long-standing complications.²⁰ As per World Health Organization, diabetes affects >170 million individuals globally, and this rate will increase upto 370 million by 2030.²¹ Around 33% of those affected will ultimately have progressive worsening of kidney functions.¹¹ The first clinical sign of kidney failure in diabetic patients is usually microalbuminuria,²² which develops among 2.0% to 5.0% of cases annually.¹⁶ In T2DM, unlike type 1 diabetes,⁷ microalbuminuria is rarely reversible⁷ however, rather, progresses to overt proteinuria among 20.0% to 40.0% of cases.¹⁰ Blindness is the most dreaded complication of diabetes. In 2002, 124 million individuals suffered from low vision and 37,000,000 were blind.²³ In western nations, diabetes

mellitus is the first cause in loss of vision among younger patients.²⁴ The pathogenesis of diabetic retinopathy and nephropathy is same, that's why it has been postulated that microalbuminuria can be used as a predictor of retinopathy, and can be used as a marker to refer the patients for screening of retinopathy.¹⁸ In this study an attempt has been made to determine the microalbuminuria frequency in T2DM and frequency of retinopathy in patients with and without microalbuminuria. Several studies were conducted to assess the incidence of microalbuminuria and retinopathy in Type 2 diabetes. These studies produced different rates from 16.00% to 53.40% for retinopathy.²⁵⁻²⁷ In a study the incidence of diabetic retinopathy was 39.30%.¹⁸ Our study exhibited the rate of 30.30% which is in median range. The disparity in rate can possibly be due to different techniques applied in those studies, the races and or the population involved, or difference in controlling the level blood sugar.

The microalbuminuria incidence in current study was 28.70%. Parving et al documented 22.0% incidence of microalbuminuria among T2DM cases²⁸ while Lunetta documented an incidence of 15.0%.²⁹ In a study the frequency of microalbuminuria was 153 (25.9%) out of 590 patients.¹⁸ The above-stated studies exhibited a non-significant correlation between microalbuminuria and the extent of retinopathy.

However, few studies do not favor such correlations. Erasmus et al exhibited that among 113 cases suffering from NIDDM, the prevalence of microalbuminuria was upto 54.0% in men and 59% in women. Incidence of retinopathy was 16.0%. As per their conclusion microalbuminuria can possibly not forecast retinopathy and takes place independently from either raised levels of blood pressure or glycaemic control.³⁰ The population selected for the study effects the different prevalence achieved in different studies.

This study shows that patients having microalbuminuria had high frequency of retinopathy i.e., 45.4% and patients without microalbuminuria had 24.3% retinopathy.

The method used to measure microalbuminuria has also significant influence on difference in frequency of microalbuminuria. In this study immunoturbiditic method was used and only one sample was sent for microalbuminuria but in a study Clinitek 100 (made by Bayer Corporation-Elkhart, USA) was utilized for measuring microalbuminuria. Three urine specimens were collected during 3 to 6 months and if two specimens were positive, microalbuminuria was affirmed.¹⁸

In this study the method to measure microalbuminuria is simple and economical but it has higher chances of getting false positive reports.

This study only shows the frequency of microalbuminuria and retinopathy in cases with type II diabetes for above 10 years. The frequency of macroalbuminuria and overt nephropathy was not determined in this study.

Moreover, in this study the diabetic retinopathy is not graded and the correlation of severity of retinopathy with microalbuminuria is not studied. In previous studies it has been studied and established a significant correlation between severity of retinopathy and microalbuminuria.^{18,31}

This study only shows the frequency of retinopathy in cases without and with microalbuminuria, which clearly showed that frequency of retinopathy increased with presence of microalbuminuria.

More studies are needed to better comprehend the association between retinopathy and microalbuminuria. Understanding this correlation will lead to better insight into the pathophysiology of microvascular complications of diabetes. This will enable us to introduce novel diagnostic modalities and treatment which can diminish mortality and morbidity associated to diabetic microvascular complications. In this study other factor that can affect the frequency of diabetic retinopathy and nephropathy like age, HbA1c and treatment taken for diabetes are also studied. This study shows that frequency of diabetic retinopathy and microalbuminuria increases with increasing age. This is also shown in another study that duration of diabetes and age has a positive relation with retinopathy.⁹

This study also shows that control of diabetes contributes significantly in progression of diabetic retinopathy and presence of microalbuminuria. In this study we divided the patients into two groups on the basis of diabetic control shown by their HbA1c. The patients with HbA1c of less than 7.5% had low frequency of retinopathy and microalbuminuria. These results were consistent with many previous studies, which showed that with HbA1c of more than 6.1% is associated increased incidence of retinopathy³² and hyperglycemia promotes damage to glomerulus causing proteinuria (P=0.05).³³ This shows the importance of adequate diabetic control to prevent retinopathy as well as nephropathy.

CONCLUSION

It was concluded that the retinopathy frequent complication among patients having diabetes. Patients with microalbuminuria are on high risk as compare to those without microalbuminuria. However, it is not clear that microalbuminuria can be used as a predictor of presence of diabetic retinopathy in type II diabetics. This predictor function required additional studies for validating its efficacy.

CONFLICT OF INTREST






There is no conflict of interest in this study.

REFERENCES

1. Masharani U. Diabetes mellitus and hypoglycemia. *Curr Med Diagnos Treatment* 2005;1157-201.
2. Arias E, Anderson RN, Kung H-C, Murphy SL, Kochanek KD. Deaths: final data for 2001. *National Vital Stat Reports* 2003;52(3):1-116.
3. Kumar P, Clark M. Diabetes mellitus and other disorders of metabolism. *Clinical medicine* 2002;2:1069-71.
4. Cooper ME, Bonnet F, Oldfield M, Jandeleit-Dahm K. Mechanisms of diabetic vasculopathy: an overview. Oxford University Press; 2001. p. 475-84.
5. Wilson JD. Approach to the patient with endocrine and metabolic disorders. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL et al. *Harrison's principles of internal medicine*. 14th ed. New York: Mc Graw-Hill, 1998: 2074-5.

6. Gilmer TP, O'connor PJ, Manning WG, Rush WA. The cost to health plans of poor glycemic control. *Diabet Care* 1997;20(12):1847-53.
7. Menzin J, Langley-Hawthorne C, Friedman M, Boulanger L, Cavanaugh R. Potential short-term economic benefits of improved glycemic control. *Diabet Care* 2001;24(1):51-5.
8. Papadopoulos AA, Kontodimopoulos N, Frydas A, Ikonomakis E, Niakas D. Predictors of health-related quality of life in type II diabetic patients in Greece. *BMC Public Health* 2007;7(1):1-9.
9. Bamashmus MA, Gunaid AA, Khandekar RB. Diabetic retinopathy, visual impairment and ocular status among patients with diabetes mellitus in Yemen: a hospital-based study. *Indian J Ophthalmol* 2009;57(4):293-8.
10. Parving H-H, Lehnert H, Bröchner-Mortensen J, Gomis R, Andersen S, Arner P. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *New Engl J Med* 2001;345(12):870-8.
11. Remuzzi G, Schieppati A, Ruggenti P. Nephropathy in patients with type 2 diabetes. *N Engl J Med* 2002;2002(346):1145-51.
12. Brenner BM, Cooper ME, de Zeeuw D, Keane WF, Mitch WE, Parving H-H, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *New Engl J Med* 2001;345(12):861-9.
13. Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *New Engl J Med* 2001;345(12):851-60.
14. Eurich DT, Majumdar SR, Tsuyuki RT, Johnson JA. Reduced mortality associated with the use of ACE inhibitors in patients with type 2 diabetes. *Diabet Care* 2004;27(6):1330-4.
15. Parving HH, Mauer M, Ritz E. Diabetic nephropathy. In: Brenner BM, ed. *Brenner & Rector's The kidney*. 7th ed. Vol. 2. Philadelphia: Saunders, 2004:1777-818.
16. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Int* 2003;63(1):225-32.
17. Boelter MC, Gross JL, Canani L, Costa L, Lisboa H, Trés GS, et al. Proliferative diabetic retinopathy is associated with microalbuminuria in patients with type 2 diabetes. *Brazilian J Med Biolog Res* 2006;39(8):1033-9.
18. Manaviat MR, Afkhami M, Shoja MR. Retinopathy and microalbuminuria in type II diabetic patients. *BMC Ophthalmol* 2004;4(1):1-4.
19. Shafique M, Rehman K, Haider Z, Sidiqui A, Shehzad A. . Microvascular complications in Pakistani NIDDM (non-insulin dependant diabetes mellitus). *Pak Postgraduate MJ* 1998;9:1-4.
20. Powers AC. Diabetes mellitus. In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL, Jameson JL. *Harrison's principles of internal Medicine*. 15th ed. New York: McGraw-Hill 2001: 2109-37.
21. Jermendy G, Ruggenti P. Preventing microalbuminuria in patients with type 2 diabetes. *Diabet /Metabol Res Rev* 2007;23(2):100-10.
22. Ritz E. Albuminuria and vascular damage--the vicious twins: *N Engl J Med*. 2003 Jun 5;348(23):2349-52.
23. Aiello LP. Angiogenic pathways in diabetic retinopathy. *Mass Medical Soc*; 2005. p. 839-41.
24. Frank R. Diabetic Retinopathy. *N Engl J Med* 2004;350(48-58).
25. Sobngwi E, Mbanya J-C, Moukouri EN, Ngu KB. Microalbuminuria and retinopathy in a diabetic population of Cameroon. *Diabet Res Clin Pract* 1999;44(3):191-6.
26. Wirta O, Pasternack A, Mustonen J, Laippala P, Lähde Y. Retinopathy is independently related to microalbuminuria in type 2 diabetes mellitus. *Clin Nephrol* 1999;51(6):329-34.
27. Liu D, Molyneaux L, Chua E, Wang Y, Wu C, Jing H, et al. Retinopathy in a Chinese population with type 2 diabetes: factors affecting the presence of this complication at diagnosis of diabetes. *Diabet Res Clin Pract* 2002;56(2):125-31.
28. Parving H-H, Hommel E, Mathiesen E, Skøtt P, Edsberg B, Bahnsen M, et al. Prevalence of microalbuminuria, arterial hypertension, retinopathy, and neuropathy in patients with insulin dependent diabetes. *Br Med J* 1988;296(6616):156-60.
29. Lunetta M, Infantone L, Calogero AE, Infantone E. Increased urinary albumin excretion is a marker of risk for retinopathy and coronary heart disease in patients with type 2 diabetes mellitus. *Diabet Res Clin Pract* 1998;40(1):45-51.
30. Erasmus R, Oyeyinka G, Arije A. Microalbuminuria in non-insulin-dependent (type 2) Nigerian diabetics: relation to glycaemic control, blood pressure and retinopathy. *Postgraduate Med J* 1992;68(802):638-42.
31. Asensio-Sánchez V, Rodríguez-Delgado B, García-Herrero E, Cabo-Vaquera V, García-Loygorri C. Microalbuminuria and diabetic retinopathy. *Arch Soc Esp Oftalmol* 2008;83(2):85-8.
32. Tapp R, Zimmet P, Harper C, De Courten M, McCarty D, Balkau B, et al. Diagnostic thresholds for diabetes: the association of retinopathy and albuminuria with glycaemia. *Diabet Res Clin Pract* 2006;73(3):315-21.
33. Al-Ghamdi AA. Role of HbA1c in management of diabetes mellitus. *Saudi Med J* 2004;25(3):342-5.

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