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Research Article

**AN ASSESSMENT OF RETINOPATHY IN CASES OF TYPE-II
DIABETES MELLITUS WITH MICROALBUMINURIA**¹Dr. Hadia Jabeen, ²Dr. Anum Asjad Cheema, ³Dr. Faheem Murtaza¹Woman Medical Officer, Lahore General Hospital Lahore² Medical Officer, Al-Shifa General Hospital, Bahawalpur³ST1, Princess Royal Hospital Telford, UK**Article Received:** October 2019 **Accepted:** November 2019 **Published:** December 2019**Abstract:****Objective:** To assess the retinopathy in cases of type-II diabetes mellitus with microalbuminuria.**Materials and methods:**

This cross-sectional study was conducted at Department of Medicine Lahore General Hospital, Lahore from October 2018 to April 2019 over the period of 6 months. Total 295 cases of type-II diabetes mellitus with microalbuminuria having age 45-80 years either male or female were selected for this study. Retinopathy was assessed in selected patients.

Results: Total 295 patients were selected for this study. Mean age of the patients was 58.13 ± 9.412 years. Out of 295 patients, retinopathy was noted in 67 (23%) patients. Out of 147 (49.83%) male patients, retinopathy was noted in 39 (26.5%) patients. Out of 148 (50.17%) female patients, retinopathy was noted in 28 (18.9%) patients. Statistically insignificant association of retinopathy with gender was noted with p value 0.119.

Conclusion: The prevalence of retinopathy in diagnosed type 2 diabetes mellitus patients is relatively high in this study. The high prevalence of diabetes mellitus underlines the importance of detailed ophthalmic examination for early detection of diabetes retinopathy

Keywords: Retinopathy, Diabetes mellitus type II, Microalbuminuria**Corresponding author:****Dr. Hadia Jabeen,**

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INTRODUCTION:

Type 2 diabetes (T2D), once considered an illness restricted to adults, is progressively affecting more and more adolescents as population rates of obesity increase. Estimates suggest that T2D represents 20–25% of new-onset cases in adolescents and those certain ethnic or racial groups are disproportionately affected.¹ International Diabetic Federation (IDF) database on Diabetics shows that Pakistan currently stands at number seven in the list of countries with the highest number of Diabetic cases. The estimation of diabetic population in Pakistan was 6.9 million in 2007 and its projection is 11.5 million by the year 2025 with ranking Pakistan at 5th in the IDF list.²

In numerous studies carried out by the Diabetic Association of Pakistan, 10% of the general population aged 30 years or above is said to be suffering from Diabetes type-II. Undiagnosed Diabetes and related retinopathy due to virtually non-existent primary eye care centers are common in the general population and is associated with impaired visual status of the community, especially in the third world countries like Pakistan, where resources are limited and budgetary allocation to health is inadequate. Very few studies have been carried out to evaluate the role of Diabetes related blindness (DRB) in the context of the local population.³

Subjects with diabetes mellitus (DM) are associated with microvascular complications, e.g. diabetic retinopathy (DR). It is one of the main causes of visual loss in individuals with increasing age and is present in more than 77% of patients with DM type 2 who survive for over 20 years with the disease.⁴ However there is no available data on the prevalence of complications like retinopathy in newly diagnosed patients with type 2 diabetes mellitus.⁵

Despite the morbidity and mortality associated with retinopathy, nephropathy, and neuropathy, cardiovascular disease remains the leading cause of death in type 2 diabetes mellitus. Consequently, the treatment of confounding risk factors of obesity, hypertension, and hyperlipidemia assumes major importance and must be coordinated with good glycemic control for reduction in total mortality in type 2 diabetes mellitus.⁶

The progression of retinopathy is gradual, advancing from mild abnormalities to moderate and then to severe non-proliferative diabetic retinopathy and finally proliferative retinopathy. This may end up in retinal hemorrhages, retinal detachments, glaucoma and finally blindness. Several factors include types and diabetes has been identified as determinants for the development of DR and its progression. These factors includes types and

duration of DM, age, gender, glycosylated hemoglobin (HbA1C), hypertension, body mass Index (BMI), smoking, serum lipids and presence of micro-albuminuria (MA).⁷

Oral hypoglycemic agents and lifestyle modifications such as diet and physical activity are the mainstay of therapy in patients with type 2 diabetes. Further health issues need to be addressed such as foot care, peripheral diabetic neuropathy, as well as nephropathy and retinopathy monitoring. Many oral hypoglycemic agents exist that have proven to be successful in lowering significant parameters in disease monitoring such as HbA1C lowering, fasting blood glucose reduction and peak postprandial plasma glucose. Currently, many oral hypoglycemic agents are FDA approved and have shown to be very effective in type 2 diabetes. Several factors are of importance in choosing the best agent, such as tolerability, effectiveness, contraindicating disease, and side effects profile. Also patient cofactors play an additional important role.⁸

Operational definitions:**Type II diabetes mellitus along with microalbuminuria****Type II diabetes mellitus:**

- The type II diabetes patients of less than five years duration was confirmed according to WHO criteria: raised venous glucose on 2 separate occasion--- fasting ≥ 126 mg/dl (confirmed on laboratory investigation).
- Samples was taken one week apart

Microalbuminuria:

Random urine albumin-to-creatinine ratio (ACR) of 30-300 mg/g (confirmed on laboratory investigations)

Diabetic retinopathy: presence of any one of the following on fundus examination was deemed as positive:

- Grade I (Background Diabetic Retinopathy): presence of microaneurysms and retinal hemorrhage \pm any exudates.
- Grade II (Diabetic Maculopathy): presence of focal/diffuse maculopathy and macular oedema.
- Grade III (Pre-proliferative Diabetic Retinopathy): presence of venous beading, venous reduplication, intraretinal microvascular abnormality and blot hemorrhage.
- Grade IV (Proliferative Diabetic Retinopathy): presence of new vessels on disc (NVD), pre-retinal/vitreous

hemorrhage and pre-retinal fibrosis ± tractional retinal detachment.

MATERIALS AND METHODS:

This cross-sectional study was conducted at Department of Medicine Lahore General Hospital, Lahore from October 2018 to April 2019 over the period of 6 months. Total 295 cases of type-II diabetes mellitus with microalbuminuria having age 45-80 years either male or female were selected for this study.

Already diagnosed and under treatment patients for diabetic retinopathy (on history and medical record), already under treatment for microalbuminuria (on history and medical record), not willing to participate in the study and hypertensive patients with retinopathy were excluded from the study.

Study was approved by the ethical committee and written informed consent was taken from every patient.

Detailed history for diabetes mellitus and microalbuminuria considering their medical record with lab investigations was asked and cases was followed for funduscopy by single consultant ophthalmologist of the hospital to avoid any bias for diagnosis of retinopathy.

Findings were recorded in pre-designed proforma along with demographic profile of the patients.

Data was entered and analyzed in SPSS version for 14.0. Mean and standard deviation was calculated for quantitative variable like age of the patients and duration of disease. Frequencies and percentages were calculated for qualitative variables like gender and diabetic retinopathy in diagnosed type II diabetes mellitus patients along with microalbuminuria. Stratification for duration of diabetes mellitus type II, age and gender was

recorded to address the effect modifiers. Post stratification chi square test was applied. P value ≤ 0.05 was taken as significant.

RESULTS:

Total 295 patients were selected for this study. Mean age of patients was 58.13 years with standard deviation of 9.412 years. The median age of patients was 57 years, minimum age of patients was 45 years, maximum age of patients was 80 years and range age of patients was 35 years.

Out of 295 patients, retinopathy was noted in 67 (23%) patients. (Fig. 1)

Out of 147 (49.83%) male patients, retinopathy was noted in 39 (26.5%) patients. Out of 148 (50.17%) female patients, retinopathy was noted in 28 (18.9%) patients. Statistically insignificant association of retinopathy with gender was noted with p value 0.119. (Table 1)

Patients were divided into 3 age groups, age group 45-57 years, age group 58-68 years and age group 69-80 years. Total 148 (50.17%) patients belonged to age group 45-57 years and retinopathy was noted in 36 (24.3%) patients. Out of 100 (33.90%) patients of age group 58-68 years, retinopathy was seen in 19 (16%) patients. Out of 47 (15.93%) patients of age group 69-80% patients, retinopathy was noted in 12 (25.5%) patients. Statistically insignificant association of retinopathy with age groups was noted with p value 0.544. (Table 2)

Out of 129 (43.73%) patients of 1-3 years duration of DM group, retinopathy was noted in 31 (24.00%) patients. Among the 166 (56.27%) patients of 4-5 years of duration of DM, retinopathy was noted in 36 (21.7%) patients. Statistically insignificant association of retinopathy with duration of DM was noted with p value 0.634. (Table 3)

Figure 1: Frequency of retinopathy

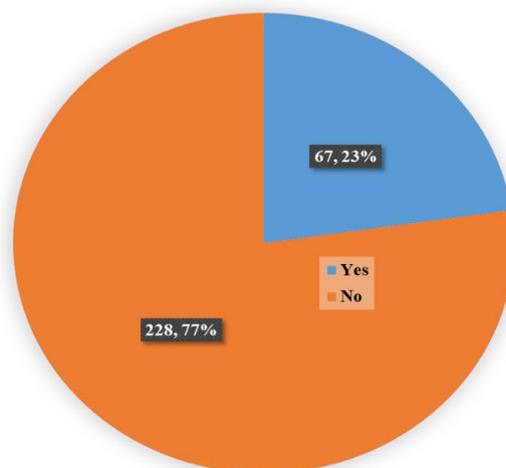


Table 1: Association of retinopathy with gender

Gender	Retinopathy		Total	p-value
	Yes	No		
Male	39 26.5%	108 73.5%	147 (49.83%)	0.119
Female	28 18.9%	120 81.1%	148 (50.17%)	
Total	67 22.7%	228 77.3%	295	

Table 2: Association of retinopathy with age group

Age groups	Retinopathy		Total	p-value
	Yes	No		
45-57	36 24.3%	112 75.7%	148 50.17%	0.544
58-68	19 19.0%	81 81.0%	100 33.90%	
69-80	12 25.5%	35 74.5%	47 15.93%	
Total	67 22.7%	228 77.3%	295	

Table 3: Association of retinopathy with duration of DM

Duration of DM (Years)	Retinopathy		Total	p-value
	Yes	No		
1-3	31 24.0%	98 76.0%	129 43.73%	0.634
4-5	36 21.7%	130 78.3%	166 56.27%	
Total	67 22.7%	228 77.3%	295	

DISCUSSION:

Diabetic retinopathy (DR) is a well-known complication of diabetes mellitus (DM) and it is a major public health problem that is approaching epidemic proportions globally. The number of diabetes worldwide in the year 2000 was estimated to be about 171 million; this figure being 11% higher than the previous estimate of 154 million. Diabetic retinopathy is one of the most frequent and most serious complications of diabetes mellitus. It is one of the leading causes of blindness not only in Pakistan but also worldwide. Since type 2 diabetes mellitus may be present well before its clinical diagnosis is made, it is not uncommon to see its micro vascular complications at the time of diagnosis. Reported prevalence of diabetic retinopathy at the time of diagnosis of type 2 diabetes varies from 5-35%. Blindness from diabetic retinopathy can be delayed with timely detection and appropriate therapy. Therefore, newly diagnosed diabetic patients should be screened for retinopathy as early diagnosis and treatment can prevent its morbidity.⁹⁻¹⁰

Our study, which is a clinic-based rather than population-based survey, reflects the prevalence of diabetic retinopathy of 22.71%. These results of our study were comparable to the results of other study done locally and internationally. Chowdhury *et al*¹¹ evaluated 292 patients (165 South Asians) for cardiovascular risk factors of early onset diabetes at diagnosis and found significantly higher prevalence of diabetic retinopathy in South Asians (17.5% versus 7.9 %). The prevalence of retinopathy was also reported as high as 29% in newly diagnosed patients in Sri Lanka.¹²

In a study conducted by Ramavat PR *et al*¹³ showed that prevalence of DR in type 2 patients of western India was 33.9%. Prevalences of non-proliferative DR and proliferative DR were 25.5% and 8.33% respectively. Statistically significant differences (p value<0.05) were observed between prevalences of DR in each group of patients which was classified, and duration of diabetes. Prevalence of CSME (clinically significant macular oedema) was 6.5%. Associated hypertension showed a statistically

significant (p value $< 0.05\%$), higher prevalence of DR.

In another study conducted by Li N *et al*¹⁴ showed that One thousand one hundred patients with type 2 diabetes mellitus were recruited. The prevalence of DR was 32.1% (353/1100) in the study population. Sixty-three percent (652/1035) of patients had glycated hemoglobin (HbA1c) level less than 7.0%. The majority of patients (85.4%, 916/1072) conducted a diet control, 77.3% (827/1070) exercised, 56.0% (609/1088) monitored blood glucose regularly, 56.8% (416/733) detected HbA1c more than once every six months, 71.7% (762/1062) had ophthalmologic examination after the diagnosis of diabetes mellitus, and 47.9% (525/1097) had mydriatic check-up.

Jammal H *et al*¹⁵ showed in their study that 7.9% had DR. Of those with DR, 40% already had clinically significant macular edema necessitating laser photocoagulation or intravitreal injections. Multivariate analysis revealed that age and HbA1c were significantly associated with DR. The odds of DR increased by 11% for each 1 year increase in age (odds ratio [OR] 1.11; 95% confidence interval [CI] 1.02-1.20). For each 1% increase in HbA1c, the odds of DR increased by 43% (OR 1.43; 95% CI 1.09-1.88).

In another study conducted by Kostev K *et al*¹⁶ showed that there were 12,524 patients with newly diagnosed type 2 diabetes mellitus in the general practices. The mean age was 65 years with slightly more male patients (56%). The prevalence of diagnosed retinopathy was 19.0% (95% CI 18.3%, 19.7%). The median time to first retinopathy diagnosis was 309 (interquartile range 50-693) days. Factors independently associated with retinopathy in multivariate logistic regression were age, male sex, HbA(1c), systolic blood pressure and antihypertensive drugs. No significant relationships were observed for obesity and diastolic blood pressure.

Looker HC *et al*¹⁷ in their study showed that the prevalence at first screening of any retinopathy was 19.3%, and for referable retinopathy it was 1.9%. For individuals screened after a year the prevalence of any retinopathy was 20.5% and referable retinopathy was 2.3%. Any retinopathy at screening was associated with male sex (OR 1.19, 95% CI 1.14, 1.25), HbA(1c) (OR 1.07, 95% CI 1.06, 1.08 per 1% [11 mmol/mol] increase), systolic BP (OR 1.06, 95% CI 1.05, 1.08 per 10 mmHg increase), time to screening (OR for screening > 1 year post diagnosis = 1.12, 95% CI 1.07, 1.17) and obesity (OR 0.87, 95% CI 0.82, 0.93) in multivariate analysis.

In another study conducted by Buková L *et al*¹⁸ showed that Prevalence of diabetic retinopathy in men was 0.85% and in women 1.2%. The prevalence of diabetic distal symmetric polyneuropathy in men was 53% and in women 62%. The median of glomerular filtration based on a simplified MDRD4 equation.

A study conducted by Al-Zuabi H *et al*¹⁹ showed that out of the 92 newly diagnosed type 2 diabetes mellitus patients, diabetic retinopathy was present in 7 (7.6%) patients. Two of the 7 patients had maculopathy that needed treatment by photocoagulation. High glycated hemoglobin in 51 patients (55.4%), microalbuminuria in 25 (27.2%), hypertension in 29 (31.5%), hyperlipidemia in 69 (75%), obesity in 45 (48.9%) and overweight in 37(40.2%) were noted in the study population. Microalbuminuria was weakly associated with the presence of retinopathy ($p = 0.08$) at the time of diagnosis of diabetes mellitus, but other risk factors were not statistically significant.

In a local study conducted in Karachi by Mahar PS *et al*²⁰ showed that out of the cohort of 19211 subjects, 1677 patients were found Diabetic, giving the prevalence of DM in Gaddap town at 8.73%, with 1258 (6.55%) known and 419 (2.18%) newly diagnosed cases. DR was seen in 460 (27.43%) of the Diabetic cases with 126 (7.51%) patients requiring urgent intervention for vision threatening complications.

In another local study conducted by Hayat AS *et al*²¹ showed that total 100 patients were included, with mean age 45.1 \pm 3.2 years, 60% of them were females. Overall, 17% of type 2 diabetic patients had retinopathy within one month of diagnosis. Background retinopathy was predominant (12%) followed by pre-proliferative (4%) and proliferative (1%) lesions.

Manaviat MR *et al*²² in their study showed the overall prevalence of retinopathy was 39.3% (232 patients), 5.4% of which showed to be proliferative diabetic retinopathy (PDR). The diabetic retinopathy had significant inverse correlation with body mass index (BMI) ($P = 0.02$). HbA1C was higher in patients with PDR (mean = 10.5%) than in patients with no signs of retinopathy (mean = 9.5%) and this difference was statistically significant ($P = 0.001$). The prevalence of microalbuminuria was 25.9% while 14.5% of the patients revealed to have macroalbuminuria. As expected, diabetic retinopathy and renal involvement were highly positively correlated. ($P = 0.001$).

The variation in rates could be as a result of the different methods used in those studies, the population and or the races involved, or variations in

controlling blood sugar levels. Smaller sample sizes, referral biases and cross-sectional studies are major limitations due to which results are difficult to extrapolate in larger populations. Its strength lies in the fact that this is a first study of its kind which assessed the prevalence of DR in South Punjab population by using retinal photographs and standard grading technique.

CONCLUSION:

The prevalence of retinopathy in diagnosed type 2 diabetes mellitus patients is relatively high in this study. The high prevalence of diabetes mellitus underlines the importance of detailed ophthalmic examination for early detection of diabetes retinopathy in all diagnosed patients of diabetes mellitus type-II. We suggest population-based studies with larger sample sizes to determine a better estimation of prevalence of diabetic retinopathy in Pakistan and its associated risk factors.

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