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Original Research Article

Correlation of microalbuminuria and diabetic retinopathy: a retrospective study

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ABSTRACT

Background: By 2030, the number of people with diabetes is estimated to increase to 366 million. As the number of people with diabetes increases, the development of microvascular complications also rises. DR is responsible for 4.8% of the 37 million cases of blindness worldwide. The present population-based study was carried out to estimate the prevalence of microalbuminuria in type 2 diabetes mellitus. This study aimed to investigate the relationship between microalbuminuria and the presence and severity of diabetic retinopathy in individuals with diabetes.
Methods: Patients with diabetic retinopathy who underwent urine albumin excretion testing in the retina clinic in 2022 were taken. The sample collected was a total of 200 patients with diabetic retinopathy. Each patient's clinical findings, OCT, and spot urine albumin were noted. Reports of other risk factors were collected. All parameters were compared between two groups (with and without nephropathy).
Results: The prevalence of microalbuminuria in patients with diabetic retinopathy and maculopathy is higher. Patients with microalbuminuria mostly had severe NPDR and PDR.
Conclusions: Patients with microalbuminuria would have more severe retinopathy compared to those without nephropathy. This study helps ophthalmologists in the early detection of the risk of developing diabetic retinopathy and prevents its progression by careful monitoring.

Keywords: Diabetes, Diabetic retinopathy, Microalbuminuria, Risk factors

INTRODUCTION

Diabetes is slowly becoming a vital chronic disease burden worldwide, especially in developing countries like India. India has turned into the country with the second-largest diabetes inhabitants, with 1 in 6 adults having diabetes in the world being from India. International Diabetes Federation (IDF) estimates that 500 million people worldwide are currently living with diabetes, a number that is expected to increase to 30% in 2045.[1-3] The southern region of India has higher prevalence rates than other parts of India.[4] The prevalence of diabetes ranged from 2.02% in rural Madhya Pradesh to 40.3% in Tamil Nadu.[3]

The etiology of diabetes in India is multifactorial and includes genetic factors along with environmental influences. An upsurge in early-onset diabetes is also responsible for the development of diabetic complications due to the longer duration of the disease.[5]

Risk factors for diabetes

Indians are highly susceptible to diabetes. Racial predisposition toward diabetes is evident from the studies in Asian Indians and migrant Indian populations in many parts of the world.[5]

Genetic susceptibility

Asian Indians have a strong genetic predisposition to diabetes. Approximately 75% of type 2 diabetic patients in India have a first-degree family history.[6]

Age

Asian Indians are developing diabetes at least 10-15 years earlier than the Caucasian population. The national urban diabetes survey in India reveals that more than 50% of diabetic patients had onset at less than 50 years of age.[7]

Cardiometabolic risk factors

Indians tend to have higher rates of risk factors, like abdominal obesity, hyperlipidemia, and insulin resistance. The presence of diabetes itself is said to increase the CVD risk by two to fourfold.[8]

Dyslipidaemia

Raised LDL and lowered HDL levels lead to beta-cell dysfunction, thus inhibiting insulin secretion and consequently type 2 diabetes.[9]

Hypertension

Hypertension aggravates the sympathetic nervous system activity leading to a decrease in glucose uptake. This leads to insulin resistance and finally type 2 diabetes.

Smoking

Smokers are 30-40% more likely at risk to develop type 2 diabetes when compared to non-smokers.[10] Due to smoking, the level of nicotine increases in the body. This leads to a reduction in muscle glucose intake and insulin resistance, eventually leading to type 2 diabetes.

Complications in diabetes

A study from Chennai shows that the prevalence of complications in type 2 diabetes are as follows: retinopathy 23.7%; nephropathy 5.5%; peripheral neuropathy 27.5%; CVD 11.4%; peripheral vascular disease 4.0%; and stroke 0.9%.[11]

Microvascular complications

Diabetic retinopathy: In the Chennai Urban Rural Epidemiology (CURES) cohort study, the prevalence of retinopathy was 17.6%.[12] The risk factors for developing diabetic retinopathy were duration of diabetes mellitus and poor glycaemic control.

Diabetic nephropathy: Diabetic nephropathy is the major cause of end-stage renal disease worldwide, and it is suggested that 20% of type 2 diabetic patients reach end-stage renal disease during their lifetime.[13] The prevalence varies from 0.9% to 62.3% in India. Poor glycaemic control, long duration of diabetes, and higher blood pressure were the risk factors for developing overt nephropathy.

Diabetic neuropathy: The prevalence of diabetic neuropathy in India ranges from 10.5% to 44.9%.[14] Similar to the above-mentioned complications, poor glycaemic control and increased duration of diabetes were significantly associated with diabetic neuropathy.

Macrovascular complications

More than 65% of patients with T2DM die due to cardiovascular disease; of which, nearly 80% are due to coronary artery disease (CAD).[15] Mortality after an acute coronary event is 40% higher in Asian Indian patients. The presence of T2DM itself has a 3-4 times higher risk of cardiovascular disease for Asian Indian individuals than for their white counterparts.

In the CURES cohort study, the prevalence of PVD was 8.6%. Increased age, female sex and duration of disease were all related to increased incidence of PVD.[16]

Microalbuminuria and diabetic retinopathy

Diabetic retinopathy is a common microvascular complication of diabetes mellitus and is responsible for the leading causes of acquired blindness. Microalbuminuria reflects a pathophysiological state of vascular dysfunction and organ damage. It is identified that a rise in urinary albumin excretion is seen in the early phase of diabetic retinopathy. Thus, microalbuminuria is more of a marker of endothelial dysfunction than renal impairment [17,18]. In contrast, macroalbuminuria is a specific marker of renal impairment.

This study aimed to investigate the relationship between microalbuminuria and severity of diabetic retinopathy in individuals with diabetes. Primary objectives of this study were to detect the prevalence of microalbuminuria among patients with diabetic retinopathy. Also to compare the severity of diabetic retinopathy with microalbuminuria. Secondary objectives were to determine the association of diabetic retinopathy with factors like hypertension, anemia, fasting lipid profile, serum urea, creatinine, HBA1C, and central foveal thickness.

METHODS

This is a Retrospective comparative study done from January 1, 2022 to December 2022 at Aravind Eye Hospital, Salem. Patients who had diabetes retinopathy undergone urine albumin testing were selected. A total Sample size of 200 patients was collected.

Inclusion criteria

This study included patients with diabetic retinopathy with and without diabetic nephropathy, above 18 years of age.

Exclusion criteria

Patients who had undergone intervention for diabetic retinopathy, cataract or media opacity interfering with fundus view, macular thickening due to other causes like ARMD, retinal vein occlusion, ERM, or vitreomacular traction were excluded.

History, visual acuity, anterior segment findings, and fundus findings of each patient were noted. Reports of macular thickness measured by OCT and albuminuria measured by spot urine albumin creatinine ratio are collected. The presence of DR was assessed by an expert ophthalmologist using dilated fundoscopy. Patients were classified into the following categories: absent DR; mild, moderate, or severe nonproliferative DR (non-PDR); proliferative DR (PDR); or maculopathy according to early treatment diabetic retinopathy study (ETDRS). DR grade depends on the worst eye. The presence of diabetic nephropathy was assessed by measuring albuminuria. Patients were assigned based on the following categories of albuminuria (mg/24 h): normoalbuminuria (AER 30), microalbuminuria (AER 30-299), or macroalbuminuria (AER 300). Reports of other risk factors like blood sugars, lipid profile, HBA1C, and renal status (urea, creatinine) were collected. Diabetic retinopathy status, duration of DM and HTN, visual acuity, central foveal thickness, and HBA1C were compared between two groups (with and without nephropathy).

Statistical analysis

This study used a retrospective comparative study design to investigate patients with diabetes retinopathy undergone urine albumin testing. The sample size collected is 200 patients. Data were collected using various evaluation methods. The collected data were analyzed using statistical methods to draw meaningful conclusions. Inferential statistics, such as the chi-square test, were used to test for significant differences between groups. Student t-test will be used for comparing data and SPSS 16 software for data analysis. The statistical analysis helped to identify important associations and relationships between variables, which can guide clinical decision-making and improve patient care.

RESULTS

The results suggested that diabetic retinopathy was more common in the age group of 51-60 years (Table 1) and male gender (Table 2). Prevalence of PDR was higher (Table 3). The duration of diabetes was compared with the severity of DR and there is no significant association ($p>0.05$) found between the two variables (Table 4). A higher prevalence of microalbuminuria in patients with diabetic retinopathy is noted (Table 5). Patients with macroalbuminuria had a higher prevalence of PDR, while patients with microalbuminuria had a higher prevalence of severe NPDR and PDR (Table 6,7). The severity of DR and urine albuminuria excretion was compared and there was a significant association found between the two variables with a $p<0.05$. The presence of macular edema with albuminuria was compared in the above table, and there was a significant association found between the two variables with a p value <0.05. Diabetic retinopathy associated with maculopathy was more common in patients with microalbuminuria (Table 8). Overall, there is an increased prevalence of microalbuminuria in patients with severe NPDR and PDR with more preponderance towards the PDR category. There was no statistically significant association between the severity of maculopathy with various systemic risk factors like total cholesterol, triglyceride, HDL, LDL, HBA1C, urea, or creatinine (Table 9,10).

Table 1: Distribution of cases according to age group.

Age (years)	N (%)
≤50	27 (13.5)
51-60	84 (42.0)
61-70	74 (37.0)
>70	15 (7.5)
Total	200 (100.0)

Table 2: Distribution of cases according to gender.

Gender	N (%)
Male	115 (57.5)
Female	85 (42.5)
Total	200 (100.0)

Table 3: Distribution of cases according to severity of diabetic retinopathy.

Severity of diabetic retinopathy	N (%)
Mild NPDR	6 (3.0)
Moderate NPDR	20 (10.0)
Severe NPDR	36 (18.0)
PDR	138 (69.0)
Total	200 (100.0)

Table 4: Duration of diabetes and severity of diabetic retinopathy.

Diabetic duration	Severity of DR					
	Mild NPDR N (%)	Moderate NPDR N (%)	Severe NPDR N (%)	PDR N (%)	Total N (%)	P value[F]
Below 5 years	3 (1.5)	11 (5.5)	17 (8.5)	55 (27.5)	86 (43.0)	0.199 (NS)
6-10 years	1 (0.5)	4 (2)	15 (7.5)	40 (20)	60 (30.0)	
11-15 years	2 (1.0)	1 (0.5)	2 (1.0)	20 (10)	25 (12.5)	
Above 15 years	0 (0)	4 (2)	2 (1.0)	23 (11.5)	29 (14.5)	
Total	6 (3.0)	20 (10)	36 (18.0)	138 (69.0)	200 (100.0)	

F-Fisher's Exact test; NS-Not Significant (p>0.05)

Table 5: Distribution of cases according to urine albumin excretion.

Albuminuria	N (%)
Macro albuminuria	22 (11.0)
Micro albuminuria	156 (78.0)
Normal albuminuria	22 (11.0)
Total	200 (100.0)

Table 6: Distribution of cases according to severity of diabetic retinopathy and urine albumin excretion.

Severity of diabetic retinopathy	Albuminuria				
	Normal albuminuria N (%)	Micro albuminuria N (%)	Macro albuminuria N (%)	Total N (%)	P-value[F]
Mild NPDR	2 (1.0)	4 (2.0)	0 (0.0)	6 (3.0)	0.041(S)
Moderate NPDR	4 (2.0)	15 (7.5)	0 (0.0)	20 (10.0)	
Severe NPDR	1 (0.5)	33 (16.5)	2 (1.0)	36 (18.0)	
PDR	15 (7.5)	104 (52.0)	20(10.0)	138 (69.0)	
Total	22 (11)	156 (78)	22 (11)	200 (100.0)	

F-Fisher's Exact test; S- Significant (p<0.05)

Table 7: Distribution of cases according to severity of diabetic retinopathy and microalbuminuria.

Severity	N (%)
Mild NPDR	4 (2.0)
Mod NPDR	15 (7.5)
Severe NPDR	33 (16.5)
PDR	104 (52.0)
Total (N=)	156 (78)

Table 8: Distribution of cases according to severity of macular edema and urine albumin.

Macular edema	Albuminuria				
	Micro albuminuria N (%)	Macro albuminuria N (%)	Normal albuminuria N (%)	Total N (%)	P-value[F]
Yes	10 (5.0)	107 (53.5)	10 (5.0)	127 (63.5)	0.020 (S)
No	12 (6.0)	49 (24.5)	12 (6.0)	73 (36.5)	
Total	22 (11.0)	156 (78.0)	22 (11.0)	200 (100.0)	

F-Fisher's Exact test; S- Significant (p<0.05)

Table 9: Severity of diabetic retinopathy and systemic risk factors.

Variables in mg/dl except HB1AC		Total n=200	Diabetic retinopathy				P value[F]
			Mild NPDR n=5 N (%)	Moderate NPDR n=18 N (%)	Severe NPDR n=28 N (%)	PDR n=109 N (%)	
T. cholestrol	<200	122	4 (3.3)	15 (12.3)	22 (18.0)	81 (66.4)	0.612
	200-220	28	1 (3.6)	3 (10.7)	6 (21.4)	18 (64.3)	
	>220	10	-	-	-	10 (100.0)	
Triglyceride	<150	67	2 (2.9)	8 (11.9)	9 (13.4)	48 (71.6)	0.909
	150-200	62	2 (3.2)	7 (11.3)	14 (22.6)	39 (62.9)	
	>200	31	1 (3.2)	3 (9.7)	5 (16.1)	22 (70.9)	
HDL	<40	33	-	3 (9.1)	5 (15.1)	25 (75.8)	0.736
	40-50	81	3 (3.7)	11 (13.6)	12 (14.8)	55 (67.9)	
	>50	46	2 (4.4)	4 (8.7)	11 (23.9)	29 (63.0)	
LDL	<100	66	4 (6.1)	8 (12.1)	13 (19.7)	41 (62.1)	0.543
	100-150	90	1 (1.1)	10 (11.1)	15 (16.7)	64 (71.1)	
	>150	4	-	-	-	4 (100.0)	
Urea	<30	61	3 (4.9)	7 (11.5)	11 (18.0)	40 (65.6)	0.846
	30-60	98	2 (2.0)	11 (11.1)	17 (17.4)	68 (69.4)	
	>60	1	-	-	-	1 (100.0)	
Creatinine	<1.2	109	5 (4.6)	12 (11.0)	20 (18.4)	72 (66.1)	0.526
	1.2-5	51	-	6 (11.8)	8 (15.7)	37 (72.6)	
HBA1C (in %)	<5.7	2	-	-	-	2 (100.0)	0.829
	5.8-6.4	10	1 (10.0)	1 (10.0)	1 (10.0)	7 (70.0)	
	6.5-9	54	2 (3.7)	8 (14.8)	10 (18.5)	34 (62.9)	
	9.1-13	74	1 (1.4)	6 (8.1)	14 (18.9)	53 (71.6)	
	Above 13	17	1 (5.9)	2 (11.8)	3 (17.8)	11 (64.7)	

F-Fisher's Exact Test; %-Row percentage; P>0.05

Table 10: Maculopathy based on OCT and systemic risk factors.

Variables in mg/dl except HB1AC		Total n=200	OCT					P value[F]
			151-250 n=9 N (%)	251-350 n=57 N (%)	351-450 n=25 N (%)	451-550 n=15 N (%)	Above 550 n=39 N (%)	
T.cholestrol	<200	109	5 (4.6)	42 (38.5)	18 (16.5)	13 (11.9)	31 (28.4)	0.161
	200-220	26	1 (3.9)	11 (42.3)	7 (26.9)	1 (3.9)	6 (23.0)	
	>220	10	3 (30.0)	4 (40.0)	-	1 (10.0)	2 (20.0)	
Triglyceride	<150	54	4 (7.4)	18 (33.3)	13 (24.1)	8 (14.8)	11 (20.4)	0.268
	150-200	61	2 (3.3)	29 (47.5)	9 (14.8)	4 (6.6)	17 (27.9)	
	>200	30	3 (10.0)	10 (33.3)	3 (10.0)	3 (10.0)	11 (36.7)	
HDL	<40	28	2 (7.1)	10 (35.7)	7 (25.0)	3 (10.7)	6 (21.43)	0.909
	40-50	73	3 (4.1)	31 (42.5)	11 (15.1)	8 (10.9)	20 (27.4)	
	>50	44	4 (9.1)	16 (36.4)	7 (15.9)	4 (9.1)	13 (29.5)	
LDL	<100	58	3 (5.2)	22 (37.9)	9 (15.5)	8 (13.8)	16 (27.6)	0.621
	100-150	83	5 (6.0)	32 (38.6)	16 (19.3)	7 (8.4)	23 (27.7)	
	>150	4	1 (25.0)	3 (75.0)	-	-	-	
Urea	<30	56	5 (8.9)	24 (42.9)	10 (17.9)	4 (7.1)	13 (23.2)	0.673
	30-60	88	4 (4.5)	33 (37.5)	15 (17.1)	11 (12.5)	25 (28.4)	
	>60	1	-	-	-	-	1 (100.0)	
Creatinine	<1.2	99	8 (8.1)	40 (40.4)	17 (17.2)	9 (9.1)	25 (25.3)	0.644
	1.2-5	46	1 (2.2)	17 (36.9)	8 (17.4)	6 (13.0)	14 (30.4)	
HBA1C (in %)	<5.7	1	-	-	1 (100.0)	-	-	0.767
	5.8-6.4	8	1 (12.5)	3 (37.5)	-	2 (25.0)	2(25.0)	
	6.5-9	48	2 (4.2)	17 (35.4)	11 (22.9)	4 (8.3)	14 (29.2)	
	9.1-13	69	5 (7.3)	27 (39.1)	12 (17.4)	7 (10.1)	18 (26.1)	
	Above 13	16	1 (6.3)	8 (50.0)	1 (6.3)	2 (12.5)	4 (25.0)	

F-Fisher's Exact Test; %-Row percentage; P>0.05

DISCUSSION

This present study is a retrospective comparative study done for one year conducted in a tertiary care hospital. The study was done to estimate the prevalence of microalbuminuria among type 2 diabetes mellitus patients with retinopathy and to find a correlation between different stages of diabetic retinopathy and urine microalbumin.

Song et al reported the prevalence of any DR in people with DM kept rising from 12.55% in adults aged 30-39 to 20.44% in those 60-69 years old.[19] Then the prevalence of any DR in people with DM started to decrease, to 11.22% in the elderly aged 80 years and above. Our study shows a higher prevalence of DR in people aged 51-60 years constituting 84 patients (42%), similar to the above-mentioned study prevalence decreased to 7.5% in patients aged above 70 years.

Ozawa et al, advanced retinopathy in type 1 diabetes appears to be more common in males, and the presence and severity of diabetic retinopathy at the time of diagnosis in type 2 diabetes appears to be more associated with male sex.[20] This study population also shows a higher predominance of male patients (57.5%) than female patients (42.5%).

Yau et al analyzed about 35 studies and showed that the overall prevalence of any DR was 34.6%, PDR was 6.96%, DME was 6.81%, and VTDR was 10.2%.[21] In our study, out of 200 cases of diabetic retinopathy, 3% had mild NPDR, 10% had moderate NPDR, 18% had severe NPDR and 69% had PDR.

Song et al noted the DM duration-specific prevalence of any DR ranged from 9.00% in people with newly detected DM to 55.52% in those who had been diagnosed with DM for 10 years or longer.[19] By the estimated DM duration-specific prevalence of any DR in subgroup meta-analysis, longer DM duration was additionally recognized as a significant risk factor for any DR.

Yau et al also noted the prevalence of retinopathy increased with duration of diabetes,0-4 years,-9.2%; 5-9 years-23.1%;10-19 years-33.3%;20 years-57.1%.[21] In this study population, DR is more prevalent in patients diagnosed with diabetes for less than 5 years. Patients with a longer duration of diabetes for more than 15 years had higher grades of DR (PDR). On analysis, 78% of the study population (156 patients) had microalbuminuria 11% (22 patients) had macroalbuminuria and 11% (22 patients) had urine albumin levels within the normal range. Several studies conducted in the past have reported variable incidences. Parving et al noted a 22% incidence rate of microalbuminuria in type 2 diabetics, while Lunetta et al noted an incidence of 15% of microalbuminuria in diabetics.[22,23]

Wisconsin epidemiologic study on diabetic retinopathy noted that microalbuminuria is associated significantly with diabetic retinopathy, and also noted the presence of proliferative disease in younger-onset individuals.[24] Singh et al noted that patients with diabetic retinopathy had microalbuminuria test positive and the level was significantly higher in patients with proliferative retinopathy than in patients with background retinopathy.[25] Rani et al noted the prevalence of microalbuminuria as 15.9%.[26] Manaviat et al in their study noted that the overall prevalence of retinopathy was 39.3% of which 5.4% were proliferative diabetic retinopathy (PDR) and concluded that microalbuminuria is associated with diabetic retinopathy in type II diabetic patients and is a reliable marker of retinopathy.[27]

In our study there, is an increased prevalence of microalbuminuria in patients with severe NPDR and PDR with more preponderance towards the PDR category. Lee et al in their study noted that diabetic nephropathy is closely associated with diabetic retinopathy and macular edema.[28] Dutta et al noted that 88.24% with microalbuminuria had severe NPDR and 93.06% of patients with microalbuminuria had clinically significant macular edema.[29] Our study showed macular edema in 63.5% of patients, of which 53.5% had microalbuminuria.

In our study, there was no statistically significant association between the severity of maculopathy with various systemic risk factors like total cholesterol, triglyceride, HDL, LDL, HBA1C, urea, or creatinine. Patients having dyslipidemia may be on treatment with lipid-lowering agents, also diabetic patients may be on oral hypoglycemic agents and hence glycemic status under control. This may be the reason why the severity of maculopathy is not related to lipid profile or HBA1C. However, those with higher values of risk factors had a positive correlation with PDR.

It is a retrospective study with a limited sample size. Long-term follow-up and visual prognosis of cases were not done.

CONCLUSION

Among the group of patients with mild, moderate, and severe NPDR, a statistically significant correlation was found between the degree of retinopathy and microalbuminuria. This study was a hospital-based retrospective study with a limited sample size. However, an analytical community-based study with a larger sample size is required for external validation of the results. In this study, there is a chance of bias in the duration of diabetes mellitus. This study suggests that early intervention is recommended to improve visual outcomes and reduce the risk of complications. Medical professionals must raise awareness among patients regarding diabetic retinopathy screening, and patients

also should understand the importance of regular follow-up.

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