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Research Article

ASSOCIATION OF MICROALBUMINURIA AND DIABETIC RETINOPATHY IN PATIENTS WITH TYPE II DIABETES MELLITUS

SARAVANAN AKSHARA[1], NITHYAPRIYA CHINNARAJU[1], ADARSH S NAIK[2], JEEVITHAN SHANMUGAM[1]*

[1]CRMI, KMCH Institute of Health Sciences and Research, Coimbatore, Tamil Nadu, India. [2]Department of Balagangadhar Swamy Medical College and Hospital, Nelamangala, Bangaluru, Karanataka, India.
***Corresponding author: Jeevithan Shanmugam; Email: dr.jeevithan@gmail.com**

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ABSTRACT

Objectives: Diabetes mellitus (DM) is a long-term metabolic condition marked by decreased synthesis and thereby function of insulin, which can result in serious side effects such as nephropathy and diabetic retinopathy. Diabetic nephropathy plays a significant role in end-stage renal disease, and diabetic retinopathy is one of the main preventable causes of blindness. In patients with type 2 DM, this study intends to investigate the relationship between diabetic retinopathy and microalbuminuria while considering other risk factors such as age, duration of diabetes, and glycemic management.

Methods: Ninety-seven patients with type 2 DM and diabetic retinopathy participated in this hospital-based cross-sectional study. Based on the American Academy of Ophthalmology diabetic retinopathy disease severity scale, participants were categorized. Spot urine samples were used to find out microalbuminuria, and Chi-square and t-tests were used to examine correlations between microalbuminuria, diabetic retinopathy, and other clinical and demographic variables.

Results: Microalbuminuria was shown to be significantly correlated ($p<0.001$) with the severity of diabetic retinopathy. In addition, microalbuminuria was significantly associated with older age ($p=0.002$) and longer diabetes duration ($p<0.001$). Nevertheless, no meaningful correlations were discovered between sex, treatment history, or diabetes in the family history and microalbuminuria.

Conclusion: The findings highlight the importance of strict monitoring of microalbuminuria in patients with diabetic retinopathy, especially in the elderly and with long-duration diabetes. Early detection and management of diabetes and strict control of glycemic levels will help to prevent further complications.

Keywords: Diabetic retinopathy, Microalbuminuria, Type 2 diabetes, Nephropathy.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic, multisystem condition that significantly impacts the heart, kidneys, eyes, and nervous system, affecting individuals, families, and communities worldwide [1]. It is a metabolic disorder marked by decreased insulin synthesis, release, and tissue response, leading to widespread health complications [2]. Globally, DM poses a substantial burden, with one in eleven people affected, contributing to significant mortality rates [3].

Among the most concerning microvascular complications of DM are diabetic retinopathy and nephropathy, prevalent in both type 1 and type 2 diabetes [4]. Diabetic retinopathy, which affects approximately 22.7% of the global diabetic population, is anticipated to rise in prevalence in the coming years, according to a comprehensive global study involving 59 population cohorts. It is becoming one of the leading causes of preventable blindness, with profound effects on vision, overall health, and mental well-being [5,6].

Similarly, diabetic nephropathy is one of the most common cause of end-stage renal disease, contributing to a significant proportion of morbidity and mortality among diabetic patients [7]. Clinically, diabetic nephropathy is characterized by albuminuria, reduced glomerular filtration rate, and hypertension [8]. Microalbuminuria, one of the earliest signs of diabetic nephropathy, often progresses to overt albuminuria and eventually to end-stage renal disease if left untreated [9].

This study explored the correlation between diabetic retinopathy and the presence of microalbuminuria in patients with type 2 DM while also considering various other risk factors that may contribute to the development of retinopathy and nephropathy.

METHODS

Following ethics approval from the Institutional Human Ethics Committee, a hospital-based study was conducted involving 97 patients diagnosed with type 2 DM who also presented with diabetic retinopathy. The subjects were outpatients from the Department of Ophthalmology at a Tertiary care Medical College Hospital. The American diabetes association (ADA) criteria, which include hemoglobin A1C (HbA1C) levels of 6.5% or higher, fasting plasma glucose levels of 126 mg/dL or higher, the presence of classical symptoms of hyperglycemia or hyperglycaemic crisis with random plasma glucose levels of 200 mg/dL or higher, and a 2-h plasma glucose level of 200 mg/dL or higher after an oral glucose tolerance test, were used to diagnose these patients with diabetes [10].

Diabetic retinopathy in the study population was classified according to the American Academy of Ophthalmology (AAO) disease severity scale. The classifications include mild nonproliferative diabetic retinopathy (NPDR), characterized by the presence of microaneurysms upon dilated ophthalmoscopy; moderate NPDR, which involves more than just microaneurysms but less than severe NPDR; severe NPDR, defined by severe intraretinal hemorrhages, microaneurysms in all four quadrants, venous beading in two or more quadrants, or prominent intraretinal microvascular abnormalities in one or more quadrants; and proliferative diabetic retinopathy (PDR), identified by neovascularization or vitreous/preretinal hemorrhage upon dilated ophthalmoscopy [11].

The inclusion criteria for this study required that subjects meet the ADA criteria for type 2 DM and have diabetic retinopathy as classified by the AAO severity scale. Exclusion criteria included patients currently experiencing urinary tract infections (UTIs), those with ocular inflammation or trauma, patients with hypertension or congestive heart failure, individuals with diabetic macular edema, glaucoma, cataracts, or those who had undergone cataract surgery, and patients with underlying renal diseases or overt diabetic nephropathy [10,11]

Informed written consent was obtained from all participants. The medical history of each subject was thoroughly documented, including details on the age of onset and duration of diabetes, medication usage (whether oral hypoglycaemic agents [OHA] or insulin), treatment regularity, follow-up history, co-morbid conditions, and demographic information such as age and sex. Spot urine samples were collected from all participants to measure microalbuminuria, which was then statistically analyzed.

The data was entered in Microsoft Excel and analyzed using Statistical Package for the Social Sciences 27. Frequency/Percentages and Mean±SD were used to express the descriptive data. Chi-square test (discrete data) and Student t-test (continuous data) were used to measure the association between Microalbuminuria and clinical and demographic parameters.

RESULTS

The study population is predominantly within the age range of 41–60 years, representing 69.1% of the participants, with a nearly balanced distribution between males (52.6%) and females (47.4%). In terms of treatment, a significant portion of the population (38.1%) is on irregular insulin therapy, highlighting potential adherence issues. Most patients have had diabetes for 5–10 years (58.8%), indicating mid-stage disease progression. The family history of diabetes is almost evenly split, with 50.5% having no family history. A majority of the population does not exhibit microalbuminuria (73.2%), and while diabetic retinopathy is present, it is mostly mild (77.3%), with fewer cases of moderate, severe, or PDR (Table 1).

The study found no significant associations between microalbuminuria and family history of diabetes (p=0.493), treatment history (p=0.163), or sex (p=0.648). However, significant associations were observed with age (p=0.002) and duration of diabetes (p<0.001). A significant association between the severity of diabetic retinopathy and the presence of microalbuminuria was observed, as evidenced by the Chi-square value of 23.876 and a highly significant p=0.000. Specifically, the majority of patients with mild diabetic retinopathy (82.7%) do not have microalbuminuria, while 100% of those with severe retinopathy or PDR exhibit microalbuminuria. This suggests that as diabetic retinopathy progresses in severity, the likelihood of concurrent microalbuminuria increases, highlighting the importance of monitoring both conditions closely in patients with diabetes (Table 2).

There was a statistically significant difference in both age and the duration of diabetes between patients with and without microalbuminuria. Patients with microalbuminuria tend to be older, with a mean age of 60.12 years compared to 53.41 years for those without microalbuminuria, as indicated by the t-value of −3.310 and a p=0.001. Additionally, the duration of diabetes is longer in patients with microalbuminuria, averaging 13.69 years compared to 9.11 years in those without it, and a highly significant p=0.000 (Table 3). The association between age and duration of diabetes with the presence of microalbuminuria was also calculated using Chi-square test. Older age groups (especially 51 years and above) and those with more than 10 years of diabetes are more likely to have microalbuminuria. Specifically, 50% of the youngest and oldest age groups have microalbuminuria, and 60.61% of patients with diabetes for over 10 years are affected. These findings imply that older age and longer duration of diabetes are associated with the presence of microalbuminuria, underscoring the increased risk of renal complications over time in diabetic patients.

Table 1: Socio demographics of the study population

Category	Parameters	Frequency	Percentage
Age distribution	<40 years	2	2.10
	41–50 years	33	34.00
	51–60 years	34	35.10
	61–70 years	22	22.70
	70–80 years	6	6.20
Sex distribution	Male	51	52.60
	Female	46	47.40
Treatment history	Insulin regular	24	24.70
	OHA regular	12	12.40
	Insulin irregular	37	38.10
	OHA irregular	24	24.70
Duration of diabetes	<5 years	7	7.20
	5–10 years	57	58.80
	11–15 years	23	23.70
	16–20 years	8	8.20
	21–25 years	2	2.10
Family history of diabetes	Absent	49	50.50
	Present	48	49.50
Microalbuminuria	Absent	71	73.20
	Present	26	26.80
Diabetic retinopathy	Mild	75	77.30
	Moderate	15	15.50
	Severe	4	4.10
	PDR	3	3.10

PDR: Proliferative diabetic retinopathy, OHA: Oral hypoglycaemic agents

Table 2: Association between microalbuminuria and diabetic retinopathy

Categorization of diabetic retinopathy	Microalbuminuria				CSV	p-value
	Absent		Present			
	F	%	F	%		
Mild	62	82.7	13	17.3	23.876	<0.001
Moderate	9	60.0	6	40.0		
Severe	0	0.0	4	100.0		
PDR	0	0.0	3	100.0		

PDR: Proliferative diabetic retinopathy

Table 3: Association between age, duration of diabetes with microalbuminuria with t-test

Parameters	Microalbuminuria				MD	t-value	p-value
	Absent		Present				
	M	SD	M	SD			
Age	53.41	8.70	26	60.12	6.707	-3.310	0.001
Duration of diabetes	9.11	3.09	26	13.69	4.580	-5.489	< 0.001

SD: Standard deviation

DISCUSSION

In this study, we examined a total of 97 patients diagnosed with diabetes according to the ADA criteria [10], all of whom had diabetic retinopathy graded based on the AAO diabetic retinopathy disease severity scale [11]. We observed that the prevalence of microalbuminuria increased with the severity of diabetic retinopathy, progressing from mild NPDR to moderate NPDR, severe NPDR, and PDR. Patients with conditions such as symptomatic UTI, hypertension, previous cataract surgery, ocular inflammation, and glaucoma, which are independent risk factors or known to exacerbate diabetic retinopathy, were excluded from the study to ensure the accuracy of the microalbuminuria results [12-15].

The primary aim of the study was achieved, as a significant statistical association was found between microalbuminuria and diabetic

retinopathy (p=0.00). Our findings align with several previous studies but differ from a few others [16-23]. Earlier research has identified the duration of diabetes as a critical risk factor for microalbuminuria, with longer exposure to hyperglycemia leading to increased levels of advanced glycation end-products. Consistent with these findings, our study also revealed a significant association between microalbuminuria and the duration of diabetes, with a prevalence of 60.61% in patients who had been diabetic for more than 10 years.

Unlike the study conducted by the Yazd Diabetic Research Center, our research found a significant association between microalbuminuria and the age of the study population (p=0.002), which aligns with a similar cross-sectional study involving 100 diabetic patients. However, consistent with previous studies, we found no significant association between microalbuminuria and the sex of the study population [24].

Glycemic control in our study was indirectly assessed based on whether patients were on oral hypoglycemic agents or insulin and their adherence to regular or irregular treatment regimens. Contrary to previous studies, no significant association was found between irregular treatment and microalbuminuria.

The findings of this study reveal important insights into the prevalence and factors associated with microalbuminuria and diabetic retinopathy among a predominantly middle-aged diabetic population. The study highlights significant associations between the severity of diabetic retinopathy, age, duration of diabetes, and the presence of microalbuminuria, which is consistent with findings reported in other national and international studies.

Comparison with other studies

Nationally, studies conducted in India have shown similar patterns regarding the prevalence of microalbuminuria and its association with age, duration of diabetes, and diabetic retinopathy. For instance, a study by Unnikrishnan *et al*. (2012) found that microalbuminuria was present in 26.9% of diabetic patients, with a higher prevalence among those with longer disease duration and older age. This aligns with the present study's findings, where older patients and those with a longer duration of diabetes showed a higher prevalence of microalbuminuria [25]. Similarly, a study conducted in southern India by Rema *et al*. (2005) also reported a significant correlation between microalbuminuria and the progression of diabetic retinopathy, reinforcing the notion that as retinopathy worsens, the risk of renal complications increases [26].

Internationally, the UK prospective diabetes study (UKPDS) and the diabetes control and complications trial in the United States have both highlighted the strong link between chronic hyperglycemia, the duration of diabetes, and the development of both microalbuminuria and diabetic retinopathy. The UKPDS found that nearly 30% of patients developed microalbuminuria after a decade of diabetes, a figure comparable to the 60.61% observed in the current study among patients with over 10 years of diabetes [27]. These findings further underscore the global consistency in the relationship between disease duration, age, and the risk of microvascular complications in diabetic patients.

Reasons and mechanisms behind the results

The significant associations between age, duration of diabetes, and the presence of microalbuminuria observed in this study can be attributed to several pathophysiological mechanisms. As patients age and the duration of diabetes increases, the cumulative exposure to hyperglycemia leads to progressive damage to the glomerular basement membrane. This damage results in increased permeability, allowing albumin to pass into the urine, a hallmark of microalbuminuria. In addition, aging itself is associated with a decline in renal function, which may exacerbate the effects of hyperglycemia and hasten the onset of microalbuminuria.

The progression of diabetic retinopathy also plays a crucial role. Diabetic retinopathy and nephropathy share common pathogenic mechanisms, including chronic hyperglycemia, hypertension, and the activation of the renin-angiotensin system. These factors contribute to endothelial dysfunction and increased vascular permeability, which affect both the retina and the kidneys. The study's finding that 100% of patients with severe or PDR exhibit microalbuminuria is particularly telling. It suggests that as retinopathy becomes more severe, the microvascular damage extends beyond the retina to the kidneys, leading to the concurrent development of microalbuminuria.

Another possible explanation for these findings is the role of oxidative stress and inflammation, which are known to increase with age and prolonged diabetes. Both oxidative stress and inflammation contribute to the endothelial dysfunction that characterizes diabetic microvascular complications. Moreover, the study's observation of a nearly balanced gender distribution but no significant gender difference in microalbuminuria prevalence aligns with previous research indicating that while males and females may experience different rates of other diabetic complications, microalbuminuria's prevalence is more closely tied to glycemic control and disease duration rather than gender [28-33].

In conclusion, this study's results emphasize the importance of early and continuous monitoring of microalbuminuria and diabetic retinopathy in diabetic patients, particularly as they age and as the disease progresses. These findings reinforce the need for stringent glycemic control and regular screening for microvascular complications to mitigate the risk of renal and ocular damage in this vulnerable population. Future research should focus on the early identification of patients at risk and the implementation of interventions aimed at preventing the progression of these debilitating complications.

The limitations of our study include a reduced sample size from 100 to 97, the inclusion of only outpatient participants, the absence of direct glycemic control indicators such as HbA1c, and the lack of recorded data on personal habits like smoking and alcohol consumption.

CONCLUSION

This study effectively established a substantial correlation between individuals with type 2 DMs microalbuminuria and the degree of their diabetic retinopathy. The risk of microalbuminuria rises with the severity of diabetic retinopathy, highlighting the connection between these microvascular problems. It was also shown that there are important risk factors for the development of microalbuminuria, including older age and longer duration of diabetes. To slow the evolution of diabetic retinopathy and nephropathy, these findings highlight the significance of early detection and thorough therapy of these conditions.

CONFLICT OF INTEREST

Nil.

SOURCE OF FUNDING

ICMT STS.

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