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Original Research Article

Assessment of Microalbuminuria and Hs-CRP for Early Detection of Diabetic Nephropathy in Type 2 Diabetes

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Abstract: ***Background*:** Diabetic nephropathy is one of the most prevalent complications of type 2 diabetes and is associated with an increased risk of end-stage renal disease in patients whose disease is not diagnosed in time. Formerly, microalbuminuria was used as the first marker, but recently, high-sensitivity c-reactive protein (hs-CRP) may be useful for early diagnosis. ***Aims and Objectives*:** This study aimed to compare microalbuminuria and hs-CRP in type 2 diabetic patients and test their efficiency in diagnosing early diabetic nephropathy. ***Methods*:** This is a cross-sectional observational study with 75 patients with type 2 DM. Demographic variables, microalbuminuria, and hs-CRP were measured and recorded. Microalbuminuria and positive or negative CRP were used to stratify patients into groups of MG, LG, and control. The t-test was used to test for differences in hs-CRP levels between the groups. ***Results*:** As for renal markers, microalbuminuria was elevated at 60% among these patients. The hs-CRP levels were higher in patients with microalbuminuria compared to patients without it (3. 1 ± 1. 2 mg/L versus 1. 5 ± 0. 8 mg/L, respectively; p = 0.001). Patients with microalbuminuria were older, their diabetes duration was longer, HDL was lower, and triglyceride levels were higher in comparison to patients without microalbuminuria. These observations were consistent with the CRP-positive group compared with the CRP-negative group. ***Conclusions*:** The research suggested a relationship between increased hs-CRP concentrations and microalbuminuria among patients with type 2 diabetes. This indicates that hs-CRP could be a potential biomarker for detecting diabetic renal disease early enough. Therefore, screening for hs-CRP in combination with screening for microalbuminuria could increase the early detection of kidney complications in type 2 diabetes. More large-cohort longitudinal follow-up studies are warranted to determine the diagnostic value of hs-CRP for predicting the development of diabetic nephropathy and to define optimal cut-off levels.

Keywords: Microalbuminuria, Nephropathy, Hs-CRP, Diabetic.

INTRODUCTION

Diabetes mellitus is one of the most prevalent noncommunicable diseases in the world, diagnosed in millions of people, and the most prevalent type is type 2 diabetes [1]. Among its serious complications, diabetic nephropathy is an important consideration and can progress to end-stage renal disease if not recognized and managed early. Diabetic nephropathy can be identified at early stages through timely testing, which helps to implement successful intervention measures for the

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patient [2]. Conventionally, microalbuminuria, ranging between 30 and 300 mg of albumin per day, has been regarded as one of the earliest signs of diabetic nephropathy. Over the years, studies have focused on searching for a link between inflammatory markers in the leucocyte and the occurrence of this complication; however, more recent research has opened up the possibility of the involvement of high-sensitivity C-reactive protein in this complication [3]. There is renewed cognizance to investigate more possibilities of early identification of inflammation and risk stratification of DN due to their close association yet complex interaction. The subclinical inflammation that is characteristic of patients with T2DM may further intensify endothelial dysfunction and vascular permeability, which in turn may worsen microalbuminuria and renal involvement in the disease [4]. The purpose of this study is to compare microalbuminuria and hs-CRP in type 2 diabetic patients to assess whether both tests have the ability to predict DN in the early stages. A combined analysis of these markers may provide an improved understanding of the pathophysiology of inflammation in diabetic kidney disease and help to identify more specific biomarkers that can clearly signal the early stages of the disease [5]. The research shows how knowledge of microalbuminuria and hs-CRP could potentially enhance the concepts of microalbuminuria and hs-CRP absolute risk assessment and individualized intervention [6]. This research might be useful to refine screening methods in order to allow doctors to have a clearer picture of the population at risk and act to prevent these outcomes [7].

Our aim in this, please, is to clarify the interplay of the above biomarkers and augment the knowledge on the pathophysiology of diabetic nephropathy to benefit the patients. This research signifies an effort in the right direction of preventing or early diagnosis of kidney complications amongst patients with type 2 diabetes, thereby reducing end-stage renal disease and overall patient quality of life [8].

MATERIAL AND METHODS

This cross-sectional observational study was done in the outpatient department of nephrology and medicine at Community Based Medical College, Bangladesh from January 2023 to December 2023. The total sample size taken from the research was 75 patients with type 2 diabetes mellitus. The study inclusion criteria consisted of patients over the age of 30 who had been diagnosed with T2DM for at least one year. Contraindications for the study were evidence of urinary protein excretion >500 mg/day, poorly controlled hypertension, any acute or chronic infection, malignancy, immunosuppressive therapy, or treatment with ACE inhibitors and ARBs. Basic demographic information such as age, gender, duration since diagnosis of diabetes, and body mass index (BMI) were gathered from all the patients. The serum hs-CRP was also determined with the high-sensitivity immunoturbidimetric assay kits. Microalbuminuria was defined using spot urine sample-specific gravity measured by urinary albumin to creatinine ratio (ACR), where ACR > 30 and ≤300 mg/g as per the harmonized definition. Statistical analysis was carried out with the aid of the Statistical Package for the Social Sciences (SPSS version 25). Continuous variables were described as mean ± standard deviation, while categorical variables were presented as absolute numbers and distributions. This was done by performing a Student's t-test to compare the hs-CRP levels between the groups as classified by the presence or absence of microalbuminuria. The overall comparison of the HGF levels between both groups was found to be statistically significant with a p-value <0.05.

RESULTS

This study involved 75 participants with type 2 diabetes, as hitherto described in Table 1. With regard to the gender distribution of participants, 40 out of the participants were male (53.3%) while 35 were female (46.7%), as depicted in Figure 1 below. It also emerged that the mean age of the study population was 50 years. Seven years, with most of the patients being. 46.7% within the age bracket of 50–60 years, as shown below in Figure 2. Figure 2: Age distribution of patients Timeline Distribution Age Group Number of patients % % <45 8 10. 5 45-50 16 20. 5 50-60 36 46. 7 >60 20 25. 5 Total.

Table 1: Distribution of the patients according demographic (N=75*)*

Variable	Frequency	Percentage
Gender		
Male	40	53.3
Female	35	46.7
Age Group		
30-40	08	10.7
41-50	25	33.3
50-60	35	46.7
>60	07	09.3
Mean ± SD	**50.9 ± 8.7**	

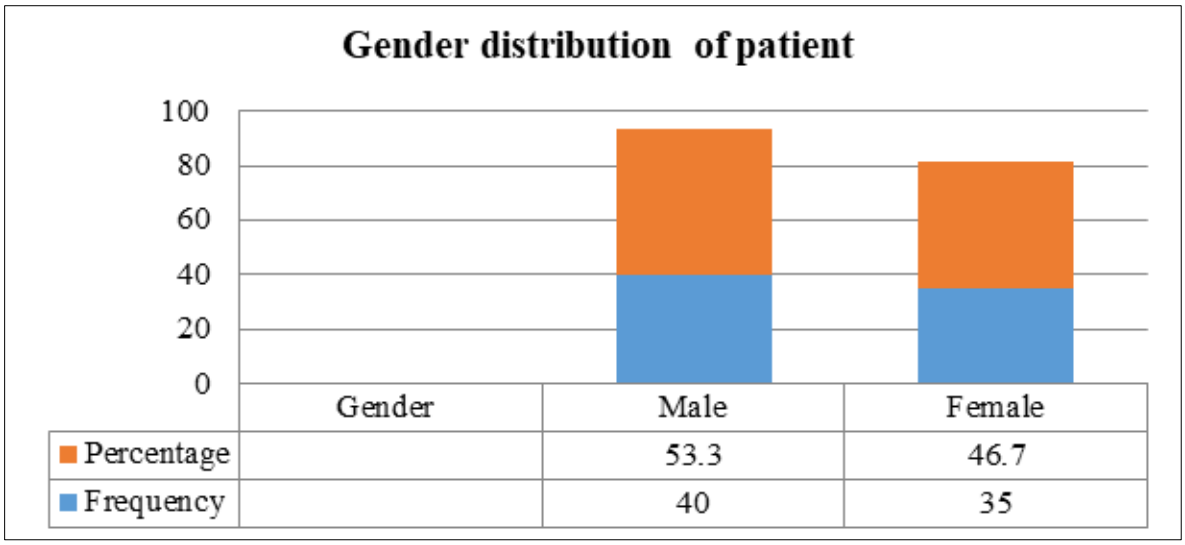

Figure 1: Column chart showed gender wise distribution (N=75)

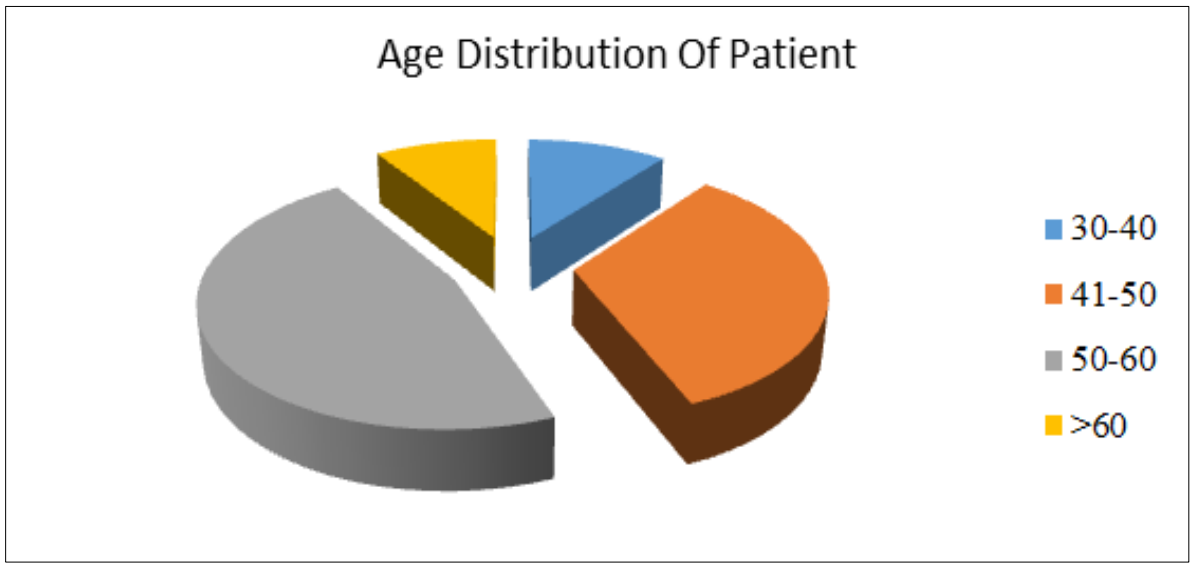

Figure 2: Pie chart showed Ager wise distribution (N=75)

Table 2 shows the time the participants had been diabetic. The mean was 24 days, which implies that the duration of social media content delivery varies depending on the content type, the content producer, and the platform being used. For two years, the largest share of respondents (46.7%) have been living with diabetes for 6–10 years, as shown in Figure 3 below.

Table 2: Distribution of the patients according Duration of diabetes (N=75)

Duration of diabetes	Frequency	Percentage
1 year	05	6.7
2-5 years	20	26.7
6-10 years	35	46.7
>10 years	15	20
Mean ± SD	**24.3 ± 3.2**	

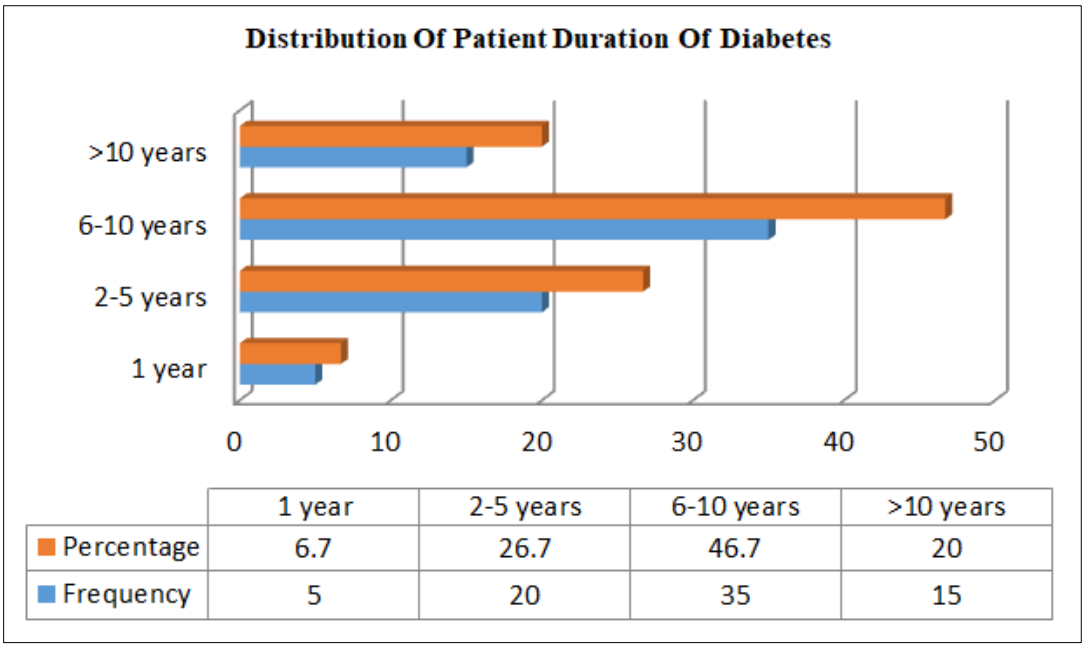

Figure 3: Bar chart showed Duration of diabetes wise distribution (N=75)

The distribution of body mass index is given in Tab. 3 and depicted in Fig. 4. Of these, 40 percent of patients were a little overweight with a body mass index of 23–24.9 kilograms per square meter, while 30.7% had a high weight status (>25 BMI), and 26% had a high obesity rate. About seven percent had their BMI fall within the standard range of 18.5-22.9 kg/m. Finally, to determine the mean BMI, it was calculated as twenty-four.

Table 3: Distribution of the patients according BMI (N=75)

BMI	Frequency	Percentage
Underweight (<18.5kg kg/m2)	02	02.7
Normal range (18.5-22.9 kg/m2)	20	26.7
Overweight (23-24.9 kg/m2)	30	40.0
Obese (eH25)	23	30.7
Mean±SD	**24.5 ± 3.2**	

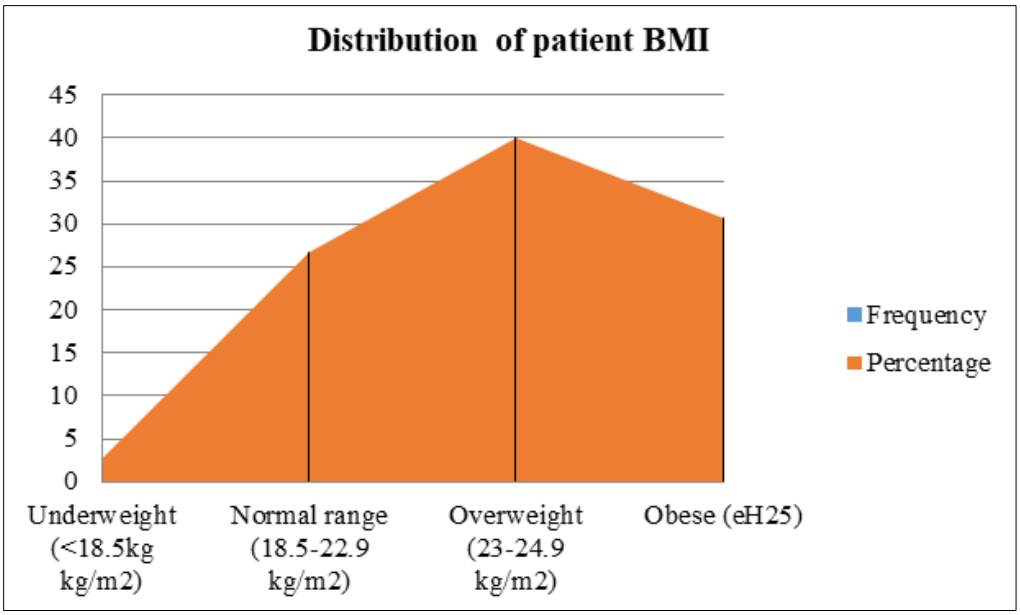

Figure 4: Area chart showed BMI wise distribution (N=75)

As highlighted in Table 4, one of the notable findings of the present work includes microalbuminuria. Urinary albumin excretion rates above 15 mg/day were observed in 45 patients (60%), while the remaining 30 patients (40%) remained in the normal range. Importantly, we found that there was evidence of a statistically significant difference in the means of hs-CRP in these two groups. We compared hs-CRP levels between patients with and without microalbuminuria: 3. 1 ± 1. 2 mg/L and 1. 5 ± 0. 8 mg/L, respectively, p = 0.001.

Table 4: Association between hs-CRP levels and microalbuminuria in type 2 DM patients (n=75).

Variable	With micro- albuminuria (N=45)	Without micro albuminuria (N=30)	p value
hs-CRP (mg/L)	3.1±1.2	1.5±0.8	0.001

These findings, especially the one that emphasizes an independent correlation between hs-CRP levels and microalbuminuria, point to the presence of a relationship between inflammation and incipient DN markers. This discovery reveals that there is a possibility of using hs-CRP to differentiate and establish other signs of early renal involvement in type 2 diabetic patients.

We also compared the clinical and biochemical profiles of patients with diabetes with and without microalbuminuria and positive and negative CRP tests, as presented in Tables 5 and 6.

Table 5: Characteristics of diabetics with and without micro albuminuria

Parameters	Micro albuminuria Positive (N = 30)	Microalbuminuria Negative (N = 45)	P-value
Age (years)	55.17 ± 10.58	48.71 ± 8.21	0.002
Diabetes duration (years)	7.60 ± 6.62	3.95 ± 2.97	0.01
BMI (kg/m^2)	25.44 ± 2.20	26.02 ± 2.70	0.27
Systolic BP (mmHg)	121.11 ± 16.19	119.76 ± 15.73	0.69
Diastolic BP (mmHg)	75.11 ± 13.46	75.95 ± 11.54	0.76
Cholesterol (mg/dL)	216.60 ± 44.77	211.95 ± 30.83	0.58
HDL (mg/dL)	42.93 ± 8.23	48.80 ± 11.22	0.006
LDL (mg/dL)	124.77 ± 36.44	130.80 ± 27.63	0.40
Triglyceride (mg/dL)	266.71 ± 76.98	167.57 ± 54.30	< 0.001
Glucose (mg/dL)	135.04 ± 19.47	140.95 ± 18.51	0.15
Creatinine (mg/dL)	1.04 ± 0.25	1.02 ± 0.24	0.69
HS-CRP (mg/L)	4.98 ± 1.45	2.82 ± 2.10	< 0.001

Table 6: Characteristics of diabetic patients with positive and negative C-reactive protein tests

Parameters	CRP Positive (N = 35)	CRP Negative (N = 40)	P-value
Age (years)	55.17 ± 10.58	48.71 ± 8.21	0.002
Diabetes duration (years)	7.60 ± 6.62	3.95 ± 2.97	0.01
BMI (kg/m^2)	25.44 ± 2.20	26.02 ± 2.70	0.27
Systolic BP (mmHg)	121.11 ± 16.19	119.76 ± 15.73	0.69
Diastolic BP (mmHg)	75.11 ± 13.46	75.95 ± 11.54	0.76
Cholesterol (mg/dL)	216.60 ± 44.77	211.95 ± 30.83	0.58
HDL (mg/dL)	42.93 ± 8.23	48.80 ± 11.22	0.006
LDL (mg/dL)	124.77 ± 36.44	130.80 ± 27.63	0.40
Triglyceride (mg/dL)	266.71 ± 76.98	167.57 ± 54.30	< 0.001
Glucose (mg/dL)	135.04 ± 19.47	140.95 ± 18.51	0.15
Creatinine (mg/dL)	1.04 ± 0.25	1.02 ± 0.24	0.69

In the study, the patients with microalbuminuria were older in age than the patients without the microalbuminuria (55.1 ± 10.58. vs. 48.71 ± 8.21 years; p = 0.002), and their duration of diabetes was also longer than the control group. They also had a lower total cholesterol to HDL ratio (4. 00 ± 1. 13 vs. 3. 62 ± 0. 80, p = 0.03) and a lower high-density lipoprotein level (42.93 ± 8.23 vs. 48.80 ± 11.22 mg/dL, p = 0.006). However, hs-CRP concentrations were higher among the microalbuminuria group (4.98 ± 1.45 vs. 2.82 ± 2.10

mg/L; F = 14.03; p <0.001), which corroborates the main findings of the study.

In the comparison of pairs of variables—CRP-positive and CRP-negative patients—both showed similar trends. A comparison of patients with positive CRP to those with negative CRP showed that positive CRP patients had a higher age, longer disease duration, lower HDL specific gravity, and higher triglyceride levels. Since microalbuminuria reflects an increased cardiovascular risk in diabetic patients, these findings indicate that positive CRP positivity also exhibits an equivalent risk profile to that observed with microalbuminuria.

DISCUSSION

By conducting this research, we have found out that high levels of hs-CRP are very much related to the development of microalbuminuria among patients with type 2 diabetes. This study therefore provides support for existing literature on inflammation in the development of DN. They aid in developing an understanding of the possibility of hs-CRP as another predictor of kidney complications in diabetes [9]. The patients who had microalbuminuria had significantly higher hs-CRP levels, and the following mechanisms may be considered to explain this finding: Low-grade inflammation and oxidative stress, which are observed in individuals with type 2 diabetes, may promote endothelial dysfunction and increased permeability of the blood vessels, resulting in microalbuminuria [10]. This is supported by the finding of Stehouwer and his colleagues [11], who established that endothelial dysfunction and chronic inflammation are two factors that are independently linked with increased urine albumin spilling in type 2 diabetes. In light of the mentioned theories, our study provides evidence for this idea, as inflammatory processes may occur before or concurrently with the onset of microalbuminuria. Further, the inflammation triggers a direct assault on the glomerular filtration barrier, which worsens albumin leakage. The above hypothesis is consistent with the study by Navarro *et al*., [12], which observed elevated urinary concentrations of inflammatory biomarkers, including tumor necrosis factor alpha, in type 2 diabetes patients in a manner that was positively associated with clinical indices of glomerular and tubulointerstitial damage. The present work builds on these observations by showing that there is a positive correlation between a marker of inflammation, the high-sensitivity CRP (hs-CRP), and the level of microalbuminuria, indicating that there may exist a link between local renal inflammation and systemic inflammation in diabetes [13]. Hs-CRP levels were also found to be higher in patients with microalbuminuria compared to those without (3. 1 ± 1. 2 mg/L vs. 1. 5 ± 0. 8 mg/L, respectively; p = 0.001) and could therefore be useful as a marker for the identification of diabetic nephropathy at a preclinical stage [14]. This observation is in agreement with the study done by Bashir *et al*., [15], who noted that diabetic patients with microalbuminuria exhibited a higher hs-CRP concentration than the other group of patients [16]. However, our study quantifies the magnitude of this difference and therefore may be useful in the definition of diagnostic thresholds in future diagnostic criteria for autism [17]. The presented data on age distribution and duration of diabetes can be considered close to the typical characteristics of patients with diabetic nephropathy [18]. The mean age is 50.7 years, and the majority of patients are in their fifties, supporting the findings of Unnikrishnan *et al*., [19], in their population-based epidemiological study of diabetic nephropathy in urban south India. The fact that different investigations from various parts of the world have found similar age distributions of patients with diabetes and its complications further highlights the worldwide problem of this disease [20]. The mean duration of diabetes in our study was 24. 3 ± 3. 2 years, which was comparatively higher than in some of the prior studies. For example, in the study by Pojskiæ *et al*., [21], the mean duration of diabetes in patients was estimated to be 11 years on average. 8 years in their study on microalbuminuria and hs-CRP. These differences could be due to differences in the population studied or advanced medical management resulting in more survival from diabetes. But it also emphasizes the necessity of prolonged examination of the evolution of diabetic nephropathy [22]. Overweight and obesity were seen in the majority of our patients (70.7%), thus underscoring the role of lifestyle interventions, including weight loss, in managing type 2 diabetes and its complications. This rate is higher than the one documented by Bashir *et al*., [15], who observed that 45% of their diabetic subjects were either overweight or obese. It is also noteworthy that the results underscore the necessity of more stringent lifestyle modification efforts in diabetes treatment and kidney disease prevention. It is worthy of note that the prevalence of microalbuminuria in this study was significantly higher than that reported in some previous studies (60%) [23]. For example, the Chennai Urban Rural Epidemiology Study (CURES) done by Unnikrishnan *et al*., [19], found a prevalence of 26 percent. of 9% for microalbuminuria among their urban Indian population. This could have been due to variations in the study sample, the duration of diabetes, or approaches to diabetes management [24]. It may also point to the rising severity of complications for diabetic patients, an aspect that deserves further study [25]. The relationship of hs-CRP with microalbuminuria that we have identified is important in view of the existing literature on the

predictive role of these indexes [26]. Analyzing the data of a prospective cohort study, Hayashino *et al*., [27], established a positive correlation between high hs-CRP levels and the risk of developing diabetic nephropathy, but not for its progression. In line with this concept, our cross-sectional data imply that hs-CRP might be best used as a sign of early kidney complications of diabetes [28].

To summarize, the findings of the present investigation support the notion that an increased concentration of hs-CRP is independently linked with microalbuminuria in patients with type 2 diabetes. The findings are helpful in advancing knowledge of inflammation involvement in diabetic nephropathy and indicate that incorporating the hs-CRP test into general microalbuminuria tests may improve the identification of early kidney deterioration [29]. In order to show that hs-CRP indeed predicts the progression of diabetic kidney disease, longitudinal studies are required in the future; furthermore, the best cut-off value for hs-CRP needs to be identified. With a progressive understanding of the molecular and cellular mechanisms of DN, using inflammation-based markers to enhance the risk profiling approach in diabetes management may open up novel directions in the future.

CONCLUSION

The results of this research support the hypothesis that type 2 diabetic patients with increased basal hs-CRP have higher rates of microalbuminuria. Based on the results of the study, a possibility of increasing the efficiency of early diagnosis of diabetic nephropathy through the simultaneous measurement of hs-CRP along with the traditional microalbuminuria screening has been indicated. This could mean that individuals with type 2 diabetes could be diagnosed and treated earlier, which could lead to more favorable results in the long term. These changes, which involve the assessment of inflammatory markers and microalbuminuria at the same time, can provide a better understanding of the pathophysiological changes in diabetic nephropathy. More prospective studies are also required to assess the prognostic significance of hs-CRP in the development of diabetic nephropathy as well as to identify the appropriate cut points for hs-CRP that are helpful in clinical practice.

Limitations

Interpreting this study's results has several limitations: The presence of a cross-sectional design that restricts the assessment of causality, the small number of patients included in the study, the lack of control for other confounding variables, and the presence of a single-center design may also constitute potential biases in the study.

Conflict of Interest: There are no conflicts of interest that the authors have to report about the conduct of the study or the preparation of this manuscript.

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