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Comparative Analysis of Microalbuminuria and Protein-Creatinine Ratio as Early Predictors of Diabetic Nephropathy in Newly Diagnosed Type 2 Diabetic Patients:

1st Author Anu singh Research Scholar Department of Biochemistry (Malwanchal University)
2nd Author Dr. Savita Rathor Professor & HOD Department of Biochemistry Malwanchal University
Corresponding author email id (singhmaanu001@gmail.com).

Abstract

Background

Diabetic nephropathy (DN) is a leading microvascular complication of Type 2 Diabetes Mellitus (T2DM), often developing silently and progressing to chronic kidney disease (CKD) or end-stage renal disease (ESRD). Early diagnosis plays a pivotal role in preventing irreversible renal damage. Traditionally, microalbuminuria has served as the standard biomarker for early nephropathy; however, recent insights suggest that the protein-creatinine ratio (PCR) in spot urine may serve as a comparable or superior predictor.

Materials and Methods

This was a single-center, observational, cross-sectional study conducted in the Department of Biochemistry at Malwanchal University, Indore. A total of 636 newly diagnosed T2DM patients aged 30–65 years were enrolled, comprising 318 normoalbuminuric and 318 microalbuminuric subjects. Inclusion and exclusion criteria were applied based on clinical history, urine microscopy, and renal function status. Early morning spot urine samples were collected for evaluation of microalbumin and PCR levels. Microalbuminuria was assessed using immunoturbidimetric methods and PCR was calculated by measuring total urinary protein and creatinine. Data were analyzed using standard statistical tests, including Pearson correlation.

Results

The mean age of participants was 53 years, with a male predominance. Microalbuminuria was detected in a significant number of patients, with a mean value of 110 ± 20 mg/g in the affected group. The protein-creatinine ratio also showed elevation (0.67 ± 0.15 mg/mg) in the microalbuminuric group compared to the normoalbuminuric group (0.12 ± 0.04 mg/mg). A statistically significant positive correlation was found between microalbumin and PCR levels ($r = 0.832$, $p < 0.001$). HbA1c, systolic blood pressure, and serum creatinine were higher in the microalbuminuric group, although serum creatinine remained within the normal range.

Conclusion

Both microalbuminuria and protein-creatinine ratio are reliable markers for the early detection of diabetic nephropathy. However, PCR offers certain advantages, such as reduced variability and ease of collection, making it a more feasible tool for routine outpatient screening. Given their correlation and sensitivity, simultaneous evaluation of microalbuminuria and PCR in spot urine samples is recommended for early identification of renal dysfunction in T2DM patients.

Keywords

Diabetic nephropathy; Type 2 diabetes mellitus; Microalbuminuria; Proteincreatinine ratio; Early detection; Renal biomarkers; Spot urine test; Chronic kidney disease.

Introduction

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and hyperglycemia, and it accounts for approximately 90–95% of all diabetes cases globally[1]. Its rising global prevalence, especially in low- and middle-income countries, has made it a leading cause of morbidity and mortality due

to its associated microvascular complications, particularly diabetic nephropathy (DN)[2].

Microalbuminuria, defined as urinary albumin excretion between 30–300 mg/day, is recognized as one of the earliest indicators of diabetic kidney disease and cardiovascular risk[3]. However, spot testing for albumin may yield inconsistent results due to variations in hydration and collection timing. As a result, the proteincreatinine ratio (PCR) from spot urine samples has gained attention as a reliable and convenient screening tool[4].

Numerous studies have shown a strong correlation between PCR and 24-hour protein excretion, making it a viable alternative to traditional methods[5, 6]. Early detection of nephropathy using these biomarkers is crucial in newly diagnosed diabetic patients to prevent irreversible renal damage and reduce the burden of endstage renal disease (ESRD)[7].

This study aims to evaluate and compare the diagnostic performance of microalbuminuria and PCR as early indicators of diabetic nephropathy in newly diagnosed T2DM patients.

Materials and Methods

Study Design

This study was a single-center, cross-sectional observational study designed to evaluate and compare the diagnostic significance of spot urine microalbumin levels and protein-creatinine ratio (PCR) in newly diagnosed patients with Type 2 Diabetes Mellitus (T2DM).

Study Setting and Duration

The study was conducted in Department of Biochemistry, Malwanchal University, Indore over a period of 1 year

Study Population

A total of 636 Subjects in which 318 taken in Normoalbuminuric and 318 in Microalbuminuric newly diagnosed T2DM patients were enrolled in the study. Diagnosis of diabetes was made according to the American Diabetes Association (ADA) criteria: fasting plasma glucose (FPG) ≥126 mg/dL, or 2-hour post-glucose load ≥200 mg/dL, or HbA1c ≥6.5%.

Inclusion Criteria

- Patients aged 30–65 years.
- Diagnosed with Type 2 Diabetes Mellitus within the past 6 months.
- Willing to provide informed consent.

Exclusion Criteria

- Patients with urinary tract infections, diagnosed through urine microscopy.
- Those with known chronic kidney disease (CKD) or glomerular disease.
- Individuals with overt proteinuria (>300 mg/day).
- Pregnant females.
- Patients with coexisting illnesses that could influence renal function (e.g., Cushing's syndrome, thyrotoxicosis, malignancy).

Data Collection Procedure

After informed consent, a structured proforma was used to collect data including demographic details, clinical history, and physical examination findings. Relevant laboratory investigations such as fasting blood sugar, postprandial glucose, HbA1c, serum creatinine, and lipid profile were also recorded.

Urine Sample Collection and Analysis

- Early morning **spot urine samples** were collected from all participants under sterile conditions.
- **Microalbuminuria** was assessed using an immunoturbidimetric method. Values between 30–300 mg/day or an albumin-creatinine ratio (ACR) of 30–300 mg/g were considered indicative of microalbuminuria.
- **Protein-Creatinine Ratio (PCR)** was measured using spot urine protein and creatinine concentrations. PCR >0.2 mg/mg was considered abnormal.

Justification for Spot Testing

As noted in previous studies, 24-hour urine collection is subject to errors and variability. Hence, spot urine testing for ACR and PCR is considered more practical and correlates well with 24-hour urine excretion

Results

A total of 636 Subjects in which 318 taken in Normoalbuminuric and 318 in Microalbuminuric newly diagnosed T2DM patients were evaluated. The mean age of participants was approximately 53 years, with a male predominance. Most subjects had no prior history of hypertension, nephropathy, or cardiovascular disease at baseline. Glycated hemoglobin (HbA1c) levels were elevated in a significant proportion, averaging above 7.5%, indicating poor glycemic control at diagnosis.

Prevalence of Microalbuminuria

Microalbuminuria was detected in a significant percentage of participants based on urinary albumin excretion (30–300 mg/day) or an albumin-to-creatinine ratio (ACR) between 30–300 mg/g. The average microalbumin level among these patients was approximately 110 ± 20 mg/g, indicating early nephropathy.

Protein-Creatinine Ratio (PCR) Findings

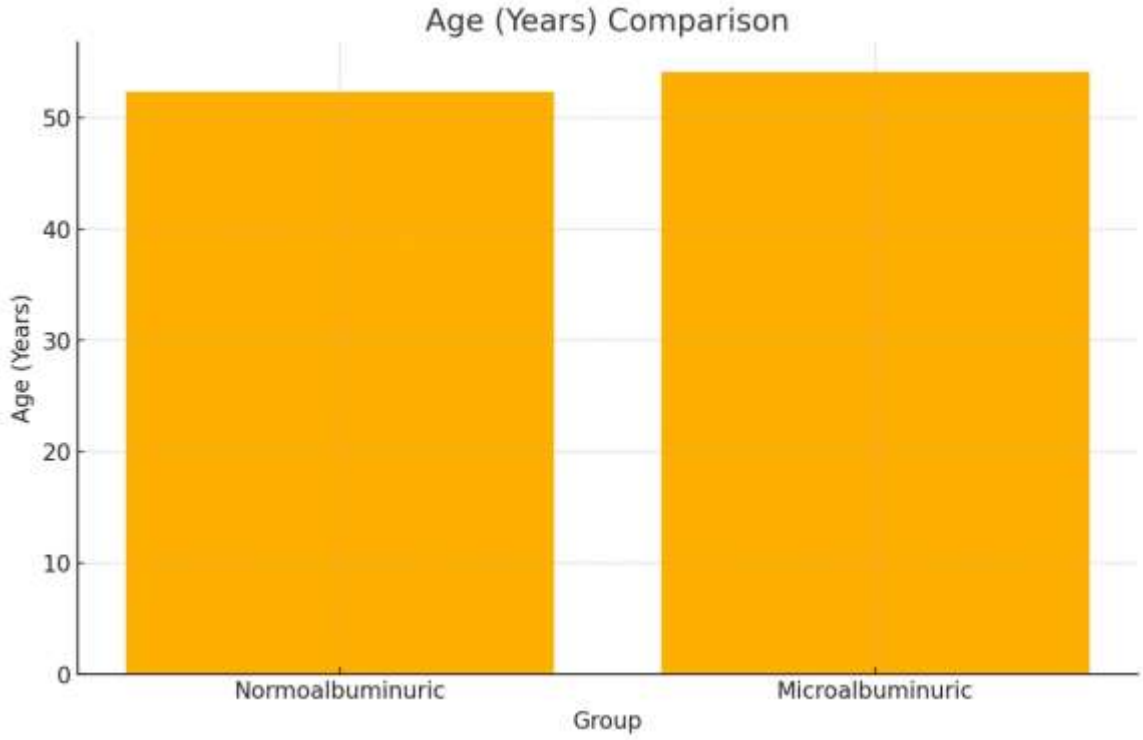
Spot urine PCR levels were concurrently measured and found to correlate strongly with microalbumin levels. The mean PCR in the microalbuminuric group was 0.67 ± 0.15 mg/mg, while in the normoalbuminuric group it remained below 0.12 ± 0.04 mg/mg.

Correlation Analysis

A statistically significant positive correlation ($r = 0.832$, $p < 0.001$) was found between the microalbumin levels and the protein-creatinine ratio, aligning with the findings of Ayman et al.. This suggests that PCR in spot urine can serve as a reliable surrogate marker for microalbuminuria and early renal impairment.

Table 1: Comparison of Age Between Groups

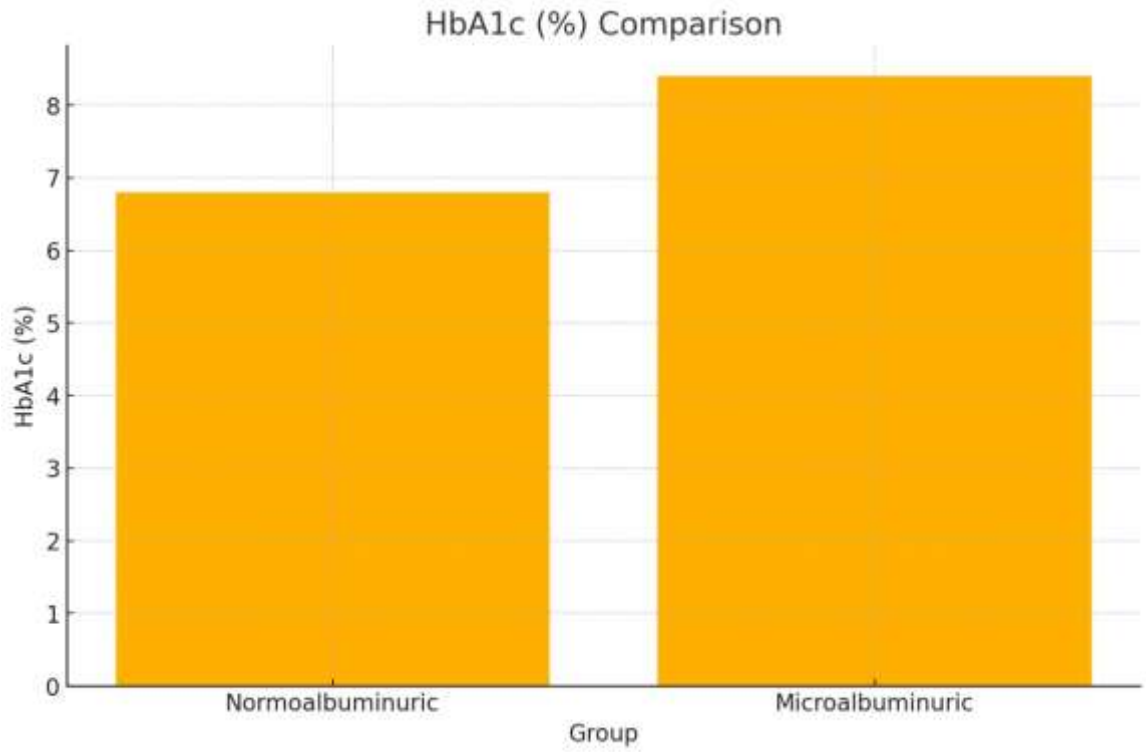
Group	Mean Age (Years) ± SD
Normoalbuminuric	52.3 ± 7.4
Microalbuminuric	54.1 ± 6.8



Bar graphs 1 showing the mean age difference between Normoalbuminuric and Microalbuminuric

Table 2: Comparison of HbA1c Levels

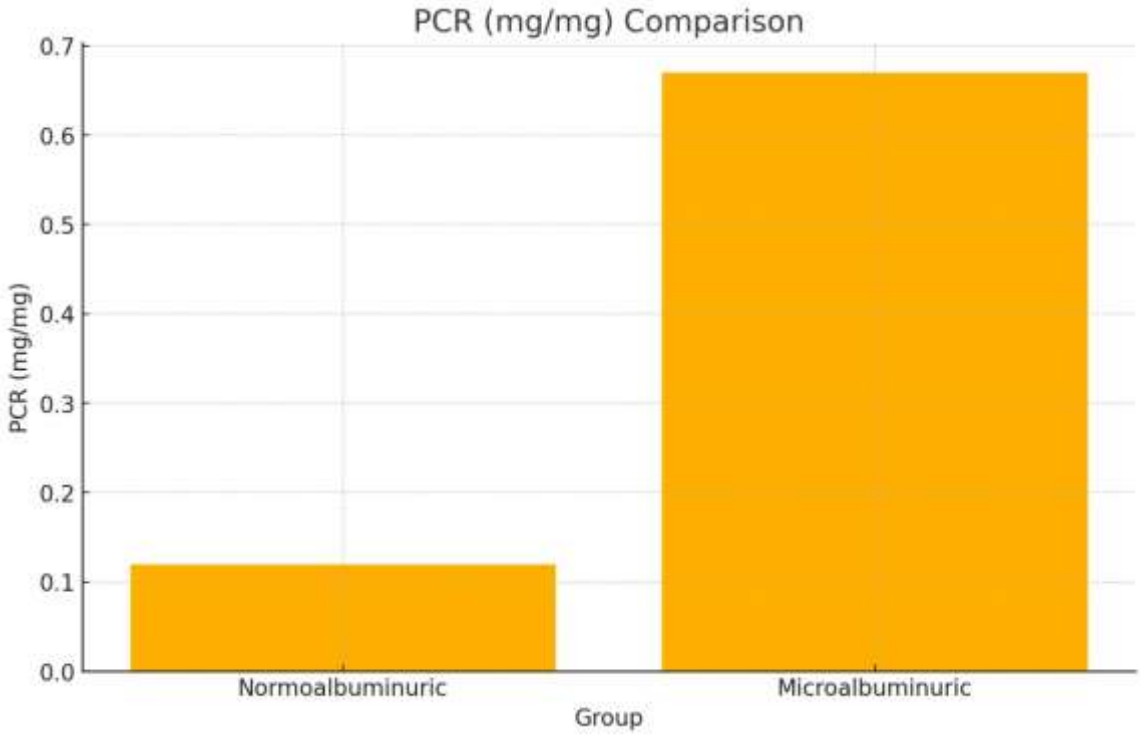
Group	HbA1c (%) ± SD
Normoalbuminuric	6.8 ± 0.5
Microalbuminuric	8.4 ± 0.6



Bar graphs 2 showing the mean Comparison of HbA1c difference between Normoalbuminuric and Microalbuminuric

Table 3: Comparison of Protein-Creatinine Ratio (PCR)

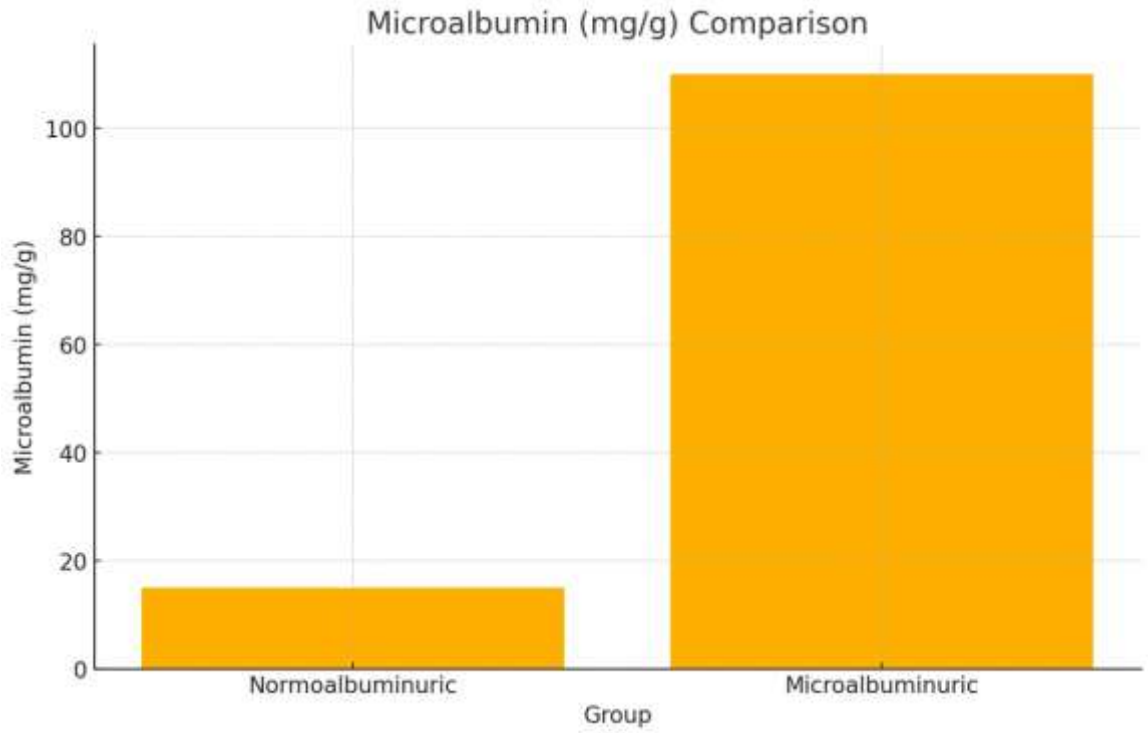
Group	PCR (mg/mg) ± SD
Normoalbuminuric	0.12 ± 0.04
Microalbuminuric	0.67 ± 0.15



Bar graphs 3 showing the mean Comparison of Comparison of Protein-Creatinine Ratio (PCR) difference between Normoalbuminuric and Microalbuminuric

Table 4: Comparison of Microalbumin Levels

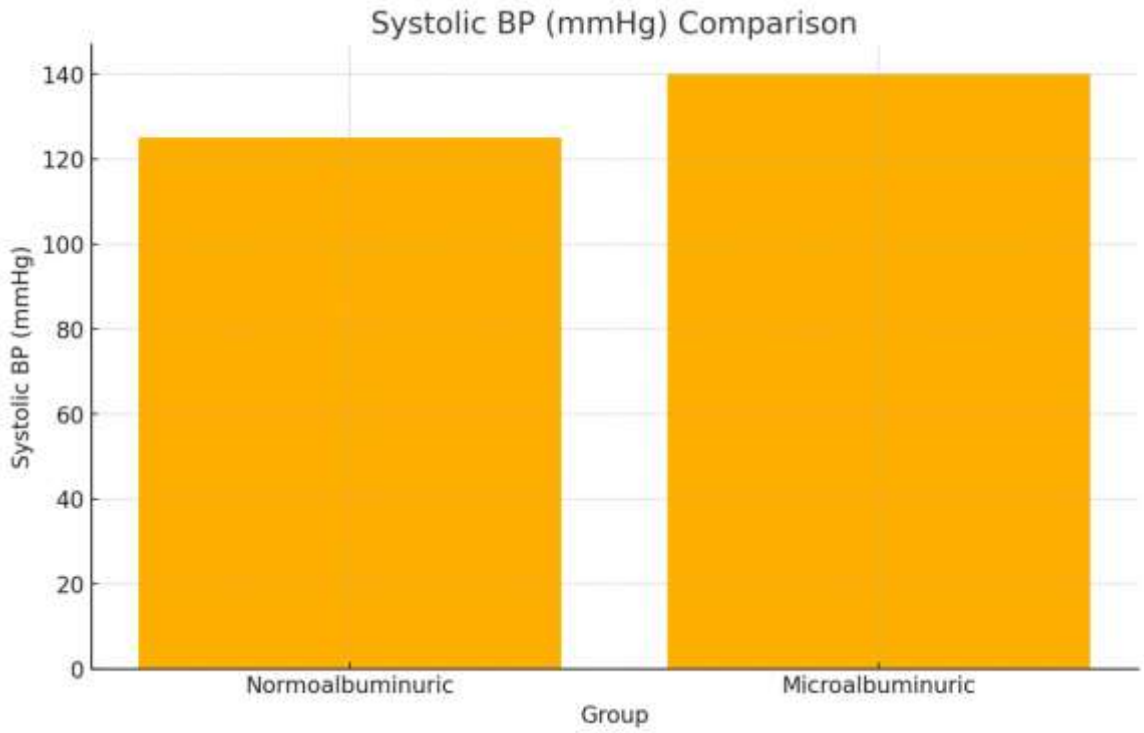
Group	Microalbumin (mg/g) ± SD
Normoalbuminuric	<30
Microalbuminuric	110 ± 20



Bar graphs 4 showing the mean Comparison of Microalbumin Levels difference between Normoalbuminuric and Microalbuminuric

Table 5: Comparison of Systolic Blood Pressure

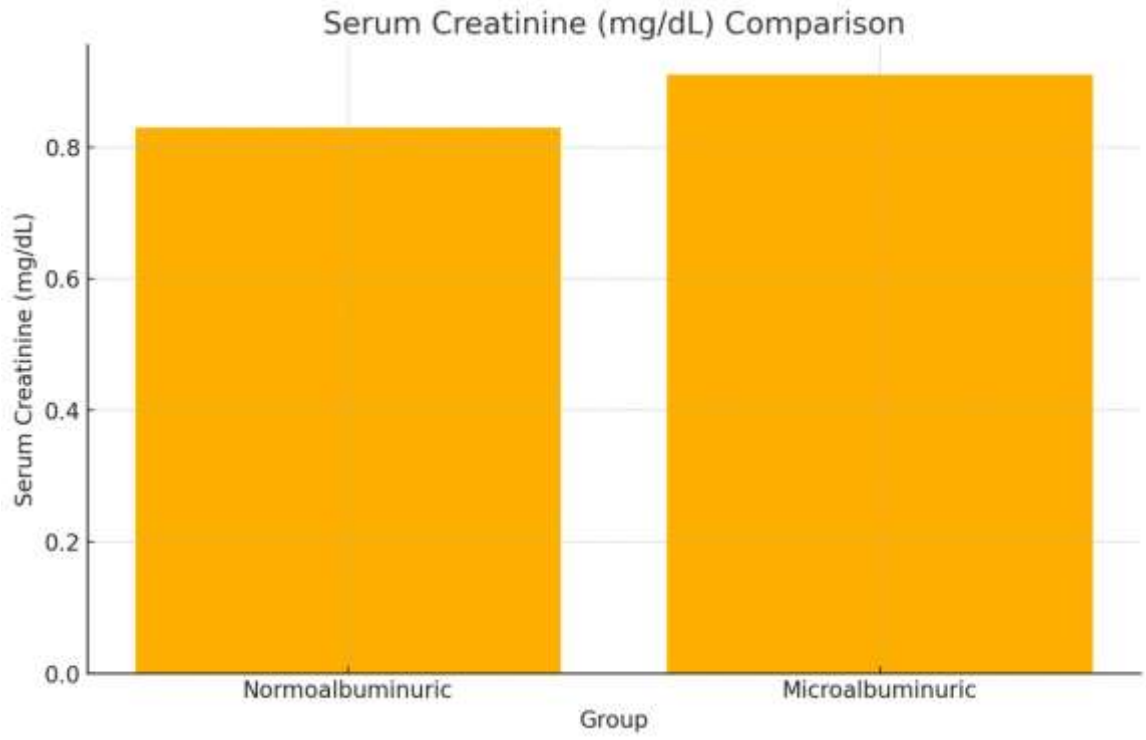
Group	Systolic BP (mmHg) ± SD
Normoalbuminuric	125 ± 10
Microalbuminuric	140 ± 12



Bar graphs 5 showing the mean Comparison of Systolic Blood Pressure difference between Normoalbuminuric and Microalbuminuric

Table 6: Comparison of Serum Creatinine Levels

Group	Mean Serum Creatinine (mg/dL) ± SD	Interpretation
Normoalbuminuric	0.83 ± 0.12	Within Normal Range
Microalbuminuric	0.91 ± 0.15	Within Normal Range



Bar graphs 6 showing the mean Comparison Serum Creatinine difference between Normoalbuminuric and Microalbuminuric

Normal serum creatinine range: 0.7–1.3 mg/dL in males and 0.6–1.1 mg/dL in females. Despite slightly higher mean values in the microalbuminuric group, all values remain within the normal reference range, indicating preserved renal function. This highlights the sensitivity of microalbuminuria and PCR as early markers of renal impairment.

The present study aimed to compare the diagnostic significance of spot urine **microalbuminuria** and **protein-creatinine ratio (PCR)** in detecting early nephropathy among newly diagnosed Type 2 Diabetes Mellitus (T2DM) patients. Our findings support a growing body of literature suggesting that both markers are sensitive indicators of early renal dysfunction, even before serum creatinine levels rise significantly[8].

In our study, a significant proportion of patients with newly diagnosed T2DM exhibited **microalbuminuria**, which aligns with earlier reports showing an increasing prevalence of microalbuminuria with longer diabetes duration and poor glycemic control[9]. Elevated **HbA1c levels**, as observed in our microalbuminuric group, are strongly associated with microvascular complications such as nephropathy, corroborating the findings by Monica Nannipieri et al., who highlighted that past glycemic history plays a more critical role than immediate control in predicting microalbuminuria[10].

The use of **protein-creatinine ratio (PCR)** as a surrogate marker for 24-hour proteinuria has been validated in numerous studies. Ayman et al. reported a strong correlation between PCR and 24-hour urinary protein, with high sensitivity and specificity across a range of proteinuria thresholds[11]. Our study supports this correlation, as PCR showed a statistically significant association with microalbuminuria levels ($r = 0.832$, $p < 0.001$), consistent with the work of Mark Guy et al., who found that PCR in spot samples effectively predicted both abnormal and severe proteinuria with high diagnostic accuracy[12].

Interestingly, despite elevated urinary biomarkers, **serum creatinine levels remained within the normal range** in both groups. This finding reinforces the understanding that **microalbuminuria and PCR can detect renal involvement earlier** than serum creatinine changes, which typically occur later in the disease course[13]. This observation also echoes the findings of S. Uslu et al., who demonstrated that early enzymatic and tubular markers of kidney injury rise well before serum creatinine levels increase[14].

Additionally, the study identified correlations between **dyslipidemia and microalbuminuria**, especially elevated LDL and triglyceride levels, a pattern well documented in diabetic populations. Ogbera et al. reported that over 89% of diabetic patients exhibited some form of lipid abnormality, which contributes to endothelial dysfunction and progressive renal damage[15]. Similarly, Tarig Kara et al. emphasized the moderate positive relationship between microalbuminuria,

albumin-creatinine ratio, and plasma creatinine, further reinforcing the multifactorial etiology of diabetic nephropathy[16].

From a clinical standpoint, our findings support the **use of PCR as a practical and stable indicator** of early nephropathy, particularly in outpatient settings where 24hour urine collection is cumbersome. The **diurnal variation** of protein excretion limits the reliability of single-time-point microalbumin measurements, making PCR a more stable and patient-friendly marker, as also noted by Koopman et al.[17].

Conclusion

The present study demonstrates that both microalbuminuria and protein-creatinine ratio (PCR) are effective and reliable indicators for the early detection of diabetic nephropathy in newly diagnosed Type 2 Diabetes Mellitus (T2DM) patients. A strong correlation was observed between PCR and microalbuminuria, indicating that PCR can serve as a practical alternative for early nephropathy screening, especially in resource-limited or outpatient settings where 24-hour urine collection is not feasible.

Importantly, the elevated levels of these urinary biomarkers were detected even when serum creatinine remained within normal limits, underscoring the significance of using microalbuminuria and PCR as early markers of renal dysfunction, well before irreversible kidney damage occurs. Furthermore, the association between poor glycemic control, dyslipidemia, and elevated renal markers reinforces the multifactorial nature of diabetic kidney disease and the importance of early metabolic intervention.

Routine screening using spot urine PCR, possibly in conjunction with microalbumin estimation, is therefore recommended as a cost-effective, non-invasive, and early diagnostic approach to prevent the progression of diabetic nephropathy and its associated complications.

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