Section: Miscellaneous

Original Research Article

ASSOCIATION OF SERUM CYSTATIN C WITH EGFR AND VITAMIN D IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AS A MARKER OF PRECLINICAL KIDNEY DISEASE. A CROSS-SECTIONAL STUDY IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: Diabetic kidney disease (DKD) is a major microvascular complication of type 2 diabetes mellitus (T2DM) and a leading cause of chronic kidney disease worldwide. Early detection of renal dysfunction remains a clinical challenge. Serum cystatin C has emerged as a sensitive biomarker for identifying subtle declines in renal function, while vitamin D deficiency has been implicated in the progression of diabetic nephropathy. This study aimed to evaluate the correlation of serum cystatin C with estimated glomerular filtration rate (eGFR) and vitamin D levels as markers of preclinical kidney disease in patients with T2DM. **Materials and Methods:** This hospital-based cross-sectional study was conducted at a tertiary care centre and included 100 patients with T2DM. Demographic, clinical, and biochemical parameters were recorded. Serum cystatin C and 25-hydroxy vitamin D were measured using immunoassay techniques, and eGFR was calculated using the CKD-EPI equation. Preclinical kidney disease was defined by reduced eGFR and/or elevated cystatin C in the absence of overt nephropathy. Statistical analysis was performed using SPSS, with Pearson's correlation and appropriate significance tests applied. A p-value <0.05 was considered statistically significant. **Results:** The prevalence of preclinical kidney disease was 8%. Serum cystatin C demonstrated a strong negative correlation with eGFR ($r = -0.72$, $p < 0.001$) and a strong positive correlation with serum creatinine ($r = 0.68$, $p < 0.001$). Patients with preclinical kidney disease had significantly higher cystatin C levels (1.42 ± 0.21 mg/L vs. 0.97 ± 0.18 mg/L; $p < 0.001$) and lower eGFR (68.5 ± 9.6 vs. 98.7 ± 14.5 mL/min/1.73 m²; $p < 0.001$). Vitamin D levels were significantly reduced in affected individuals (15.6 ± 4.8 ng/mL vs. 24.3 ± 8.4 ng/mL; $p = 0.003$), with vitamin D deficiency significantly associated with preclinical kidney disease ($p = 0.021$). **Conclusion:** Serum cystatin C is a sensitive and reliable biomarker for detecting early renal dysfunction in patients with T2DM. Its significant correlation with eGFR, serum creatinine, and vitamin D highlights its utility in the early identification and risk stratification of preclinical diabetic kidney disease.

Keywords: Type 2 diabetes mellitus, Cystatin C, eGFR, Vitamin D, Preclinical kidney disease, Diabetic nephropathy, Biomarkers.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become a major public health challenge worldwide, with a disproportionately high burden in low- and middle-income countries such as India. According to the International Diabetes Federation (IDF) Diabetes Atlas (2024), approximately 89.8 million adults in India are living with diabetes, accounting for nearly 10.5% of the adult population and placing India second globally in terms of disease burden. Recent estimates further suggest that this number may exceed 90 million and is projected to rise to over 150 million by 2050, reflecting the rapidly escalating epidemic.[1,2] Furthermore, the Indian Council of Medical Research–India Diabetes (ICMR–INDIAB) study reported that over 101 million people in India are living with diabetes, highlighting the alarming magnitude of the disease.[3]

Diabetic kidney disease (DKD) is one of the most common and serious microvascular complications of T2DM and represents a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide.[4-6] In India, the increasing prevalence of diabetes has contributed significantly to the rising incidence of CKD, thereby escalating morbidity, mortality, and healthcare expenditure. Early detection of renal dysfunction is crucial, as structural and functional alterations often occur long before clinical symptoms become apparent.[7,8]

Traditionally, renal function is assessed using serum creatinine and estimated glomerular filtration rate (eGFR). However, serum creatinine is influenced by factors such as age, gender, muscle mass, and dietary intake, which limit its sensitivity in detecting early renal impairment.[9-11] Consequently, there is a growing need for more reliable biomarkers that can identify kidney dysfunction at a preclinical stage. Serum cystatin C, a low-molecular-weight protein produced by all nucleated cells, has emerged as a sensitive and specific endogenous marker of glomerular filtration. It is freely filtered by the glomerulus and is relatively unaffected by extrarenal factors, making it superior to creatinine for the early detection of renal dysfunction.[12]

In addition to cystatin C, vitamin D deficiency has been increasingly recognized as an important contributor to the pathogenesis and progression of diabetic complications, including nephropathy. Beyond its classical role in calcium and bone metabolism, vitamin D exerts pleiotropic effects such as modulation of the renin–angiotensin–aldosterone system, anti-inflammatory actions, and inhibition of renal fibrosis.[13-14] Studies have demonstrated an association between low vitamin D levels, reduced eGFR, and increased albuminuria, suggesting its potential role as both a biomarker and a therapeutic target in diabetic kidney disease.[15]

Despite advancements in diagnostic strategies, early detection of preclinical kidney disease in patients with T2DM remains a challenge, particularly in resource-limited settings. The combined assessment of serum cystatin C, eGFR, and vitamin D may provide valuable insights into early renal dysfunction and facilitate timely intervention. However, data evaluating these associations in the Indian population, especially in tertiary care settings, remain limited.

Therefore, the present study aims to evaluate the correlation of serum cystatin C with eGFR and vitamin D levels in patients with type 2 diabetes mellitus as markers of preclinical kidney disease. This cross-sectional study conducted in a tertiary care centre seeks to contribute to improved early detection and management of diabetic nephropathy.

Objectives

1. To evaluate the correlation between serum cystatin C and estimated glomerular filtration rate (eGFR) in patients with type 2 diabetes mellitus as markers of preclinical kidney disease.
2. To assess the association of serum cystatin C with serum vitamin D levels in patients with type 2 diabetes mellitus and determine their utility in the early detection of diabetic kidney disease.

MATERIALS AND METHODS

This hospital-based cross-sectional analytical study was conducted in the Department of physiology in collaboration with the Departments of General Medicine and Nephrology at a tertiary care centre. The study was carried out over a period of 2 years, after obtaining approval from the Institutional Ethics Committee. The study included patients diagnosed with type 2 diabetes mellitus (T2DM) attending outpatient and inpatient services of the tertiary care hospital during the study period.

Inclusion Criteria

- Patients aged ≥18 years.
- Diagnosed cases of type 2 diabetes mellitus as per the American Diabetes Association (ADA) criteria.
- Patients willing to provide written informed consent.
- Patients without clinically evident kidney disease, to evaluate preclinical renal dysfunction.

Exclusion Criteria

- Patients with known chronic kidney disease or end-stage renal disease.
- Individuals with acute kidney injury.
- Patients with a history of thyroid disorders, liver disease, malignancy, or chronic inflammatory conditions.
- Pregnant and lactating women.
- Patients on vitamin D supplementation within the past three months.
- Patients receiving corticosteroids or nephrotoxic drugs.

Sample size calculation: As per study by Pradeepa R et al, proportion of patients with impaired eGFR in type 2 Dm patients was 3.7%,[8] Assuming that 4% of the subjects in the population have the factor of interest, a population size of 10000 and an expected response rate of 60%, the study would require a sample size of: 98 for estimating the expected proportion with 5% absolute precision and 95% confidence.[16] Thus a sample size of 100 is taken.

Sampling method: A total of 100 patients with T2DM were enrolled in the study using a convenient sampling technique.

Data Collection

After obtaining informed consent, detailed demographic and clinical information was recorded using a structured proforma. The following data were collected:

- Age and gender
- Duration of diabetes
- Body mass index (BMI)
- Blood pressure
- Glycemic parameters

Sample Collection

Approximately 5 mL of fasting venous blood was collected under aseptic conditions. The samples were processed and analyzed in the central laboratory of the institution.

Biochemical Analysis

The following parameters were measured:

Parameter	Method
Fasting Plasma Glucose	Glucose Oxidase–Peroxidase (GOD-POD) method
Serum Creatinine	Modified Jaffe's/Kinetic method
Serum Cystatin C	Particle-Enhanced Immunoturbidimetric Assay (PETIA) or ELISA
Serum 25-Hydroxy Vitamin D [25(OH)D]	Chemiluminescent Immunoassay (CLIA)
HbA1c	High-Performance Liquid Chromatography (HPLC)

All analyses were performed using standardized, calibrated automated analyzers with appropriate quality control measures.

Estimation of eGFR

Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation based on serum creatinine values. Renal function was classified according to kidney disease: Improving Global Outcomes (KDIGO) guidelines.

Definition of Variables

- **Preclinical Kidney Disease:** Reduced eGFR (<90 mL/min/1.73 m²) in the absence of clinically evident kidney disease.
- **Vitamin D Status (based on serum 25(OH)D):**
  - Deficiency: <20 ng/mL
  - Insufficiency: 20–29 ng/mL
  - Sufficiency: ≥30 ng/mL
- **Normal Reference Range of Serum Cystatin C:** 0.6–1.2 mg/L.

Quality Control

Internal and external quality control procedures were followed throughout the study to ensure accuracy and reliability of laboratory results. Standard operating protocols were strictly adhered to.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 28.

- Continuous variables were expressed as mean ± standard deviation (SD).
- Categorical variables were presented as frequencies and percentages.
- Normality of data was assessed using the Shapiro–Wilk test.
- Pearson's correlation coefficient was used to assess correlations between serum cystatin C and eGFR and vitamin D levels.
- Independent t-test was used where data was normally distributed and Mann whitney U test was used where data distribution was not normal, for comparison between groups.

A p-value <0.05 was considered statistically significant.

RESULTS

The study included 100 patients with type 2 diabetes mellitus. The mean age of the participants was 52.4 ± 9.6 years. The majority of patients belonged to the 41–50 years age group (32%), followed by those aged 51–60 years (30%), >60 years (20%), and 30–40 years (18%). There was a male predominance, with 58% males and 42% females enrolled in the study. Regarding the duration of diabetes, 40% of patients had diabetes for 5–10 years, 36% had a duration of less than 5 years, and 24% had diabetes for more than 10 years. The mean duration of diabetes was 7.8 ± 4.2 years. [Table 1]

Table 1: Demographic and Clinical Characteristics of the Study Population (n = 100)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	30–40	18	18.0
	41–50	32	32.0
	51–60	30	30.0
	>60	20	20.0
Mean Age (years)	—	**52.4 ± 9.6**	—

Gender	Male	58	58.0
	Female	42	42.0
Duration of Diabetes (years)	<5	36	36.0
	5–10	40	40.0
	>10	24	24.0
Mean Duration of DM (years)	—	**7.8 ± 4.2**	—

The mean systolic and diastolic blood pressures of the study population were 132.6 ± 14.8 mmHg and 82.4 ± 9.6 mmHg, respectively. The glycaemic profile indicated suboptimal control, with a mean fasting blood glucose of 156.8 ± 42.5 mg/dL and a mean HbA1c of 7.9 ± 1.4%. Assessment of renal function showed a mean serum creatinine level of 0.94 ± 0.21 mg/dL and a mean estimated glomerular filtration rate (eGFR) of 96.4 ± 18.2 mL/min/1.73 m^2, suggesting largely preserved kidney function in the study cohort. The mean serum cystatin C level was 1.01 ± 0.26 mg/L, supporting its potential role as an early biomarker for detecting subtle renal impairment. The mean serum 25-hydroxy vitamin D level was 23.6 ± 8.7 ng/mL, indicating an overall trend toward vitamin D insufficiency among patients with type 2 diabetes mellitus. [Table 2]

Table 2: Physical and Biochemical Parameters of the Study Population (n = 100)

Parameter	Mean ± SD
Systolic Blood Pressure (mmHg)	132.6 ± 14.8
Diastolic Blood Pressure (mmHg)	82.4 ± 9.6
Fasting Blood Glucose (mg/dL)	156.8 ± 42.5
HbA1c (%)	7.9 ± 1.4
Serum Creatinine (mg/dL)	0.94 ± 0.21
Serum Cystatin C (mg/L)	1.01 ± 0.26
Serum 25-Hydroxy Vitamin D (ng/mL)	23.6 ± 8.7
Estimated GFR (mL/min/1.73 m^2)	96.4 ± 18.2

Preclinical kidney disease was identified in 8 (8.0%) of the 100 patients with type 2 diabetes mellitus. Figure 1]

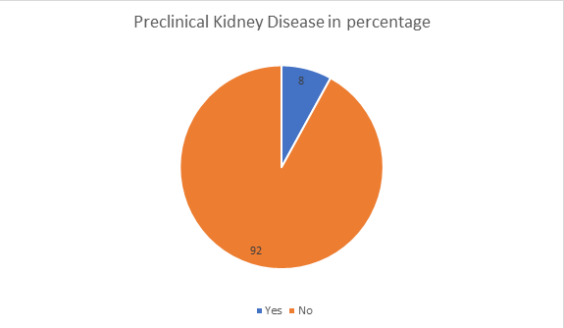

Figure1: Prevalence of Preclinical Kidney Disease in the Study Population

Preclinical Kidney Disease	Frequency (n)	Percentage (%)
Yes	8	8.0
No	92	92.0

Vitamin D deficiency was significantly associated with preclinical kidney disease, observed in 6 of 8 (75.0%) affected patients compared to 26 of 92 (28.3%) without the disease, while no cases were noted among vitamin D–sufficient individuals (p = 0.021). [Table 3]

Table 3: Association Between Vitamin D Status and Preclinical Kidney Disease

Vitamin D Status	Preclinical Kidney Disease Present n (%)	Preclinical Kidney Disease Absent n (%)	Total	p-value
Deficient (<20 ng/mL)	6 (75.0)	26 (28.3)	32	
Insufficient (20–29 ng/mL)	2 (25.0)	38 (41.3)	40	
Sufficient (≥30 ng/mL)	0 (0.0)	28 (30.4)	28	
Total	**8 (100)**	**92 (100)**	**100**	**0.021***

Chi-square test; statistically significant at $p < 0.05$.

Patients with preclinical kidney disease exhibited significantly higher systolic blood pressure (142.5 ± 12.4 vs. 131.7 ± 14.6 mmHg; p = 0.038), diastolic blood pressure (88.3 ± 7.2 vs. 81.9 ± 9.5 mmHg; p = 0.049), fasting blood glucose (182.4 ± 35.6 vs. 154.5 ± 41.8 mg/dL; p = 0.041), HbA1c (8.9 ± 1.2% vs. 7.8 ± 1.3%; p = 0.028), serum creatinine (1.18 ± 0.19 vs. 0.92 ± 0.18 mg/dL; p = 0.001), and serum cystatin C (1.42 ± 0.21 vs. 0.97 ± 0.18 mg/L; p < 0.001), along with significantly lower serum 25-hydroxy vitamin D levels (15.6 ± 4.8 vs. 24.3 ± 8.4 ng/mL; p = 0.003) and eGFR (68.5 ± 9.6 vs. 98.7 ±

14.5 mL/min/1.73 m²; p < 0.001) compared to those without preclinical kidney disease. [Table 4]

Table 4: Comparison of Clinical and Biochemical Parameters Across Preclinical Kidney Disease

Parameter	Preclinical Kidney Disease Present (n = 8) Mean ± SD	Preclinical Kidney Disease Absent (n = 92) Mean ± SD	p-value
Systolic Blood Pressure (mmHg)	142.5 ± 12.4	131.7 ± 14.6	0.038*
Diastolic Blood Pressure (mmHg)	88.3 ± 7.2	81.9 ± 9.5	0.049*
Fasting Blood Glucose (mg/dL)	182.4 ± 35.6	154.5 ± 41.8	0.041*
HbA1c (%)	8.9 ± 1.2	7.8 ± 1.3	0.028*
Serum Creatinine (mg/dL)	1.18 ± 0.19	0.92 ± 0.18	0.001*
Serum Cystatin C (mg/L)	1.42 ± 0.21	0.97 ± 0.18	<0.001*
Serum 25(OH) Vitamin D (ng/mL)	15.6 ± 4.8	24.3 ± 8.4	0.003*
eGFR (mL/min/1.73 m²)	68.5 ± 9.6	98.7 ± 14.5	<0.001*

Statistically significant at p < 0.05 (Independent Student's t-test).

Pearson's correlation analysis revealed a strong negative correlation between serum cystatin C and eGFR (r = −0.72, p < 0.001) and a strong positive correlation with serum creatinine (r = 0.68, p < 0.001), indicating its reliability as a sensitive marker of early renal dysfunction. [Table 5]

Table 5: Correlation of Serum Cystatin C with eGFR and Serum Creatinine (n = 100)

Parameter	Correlation Coefficient (r)	p-value	Interpretation
eGFR (mL/min/1.73 m²)	**−0.72**	**<0.001***	Strong negative correlation
Serum Creatinine (mg/dL)	**+0.68**	**<0.001***	Strong positive correlation

Statistically significant at p < 0.05.

DISCUSSION

The present cross-sectional study evaluated the correlation of serum cystatin C with estimated glomerular filtration rate (eGFR) and vitamin D levels as markers of preclinical kidney disease in patients with type 2 diabetes mellitus (T2DM). The findings underscore the importance of early detection of renal dysfunction using sensitive biomarkers.[17]

This study included 100 patients with type 2 diabetes mellitus, with a mean age of 52.4 ± 9.6 years. The majority belonged to the 41–50 years age group (32%), followed by 51–60 years (30%), >60 years (20%), and 30–40 years (18%). These findings are consistent with the ICMR–INDIAB study, which reported a higher prevalence of T2DM among middle-aged adults in India.[3] These findings are comparable with those of Alsenany et al., who reported a mean patient age of 58 years.[17] Similarly, Pradeepa and Mohan observed that diabetes commonly affects individuals in the fifth and sixth decades of life.[6] Sharma P et al. further noted that diabetes prevalence increases with age, peaking at 55–59 years in males and 65–69 years in females.[18]

The present study demonstrated a male predominance, with 58% males and 42% females. Regarding disease duration, 40% of patients had diabetes for 5–10 years, 36% for <5 years, and 24% for >10 years, with a mean duration of 7.8 ± 4.2 years. These findings are comparable with those of Alsenany et al., who reported a diabetes prevalence of 42% in males and 58% in females, and mean ages of diabetes onset of 34 years in males and 39 years in females.[17] Similarly, Sharma P et al. observed a higher likelihood of diabetes among males (44%) compared to females (40%).[18]

In the present study, the mean systolic and diastolic blood pressures were 132.6 ± 14.8 mmHg and 82.4 ± 9.6 mmHg, respectively. The glycaemic profile reflected suboptimal control, with a mean fasting blood glucose of 156.8 ± 42.5 mg/dL and a mean HbA1c of 7.9 ± 1.4%. These findings are comparable to those reported by Kumar S. P. et al., who documented a mean fasting blood glucose of 156.73 ± 54.0 mg/dL and a postprandial glucose level of 232.94 ± 6.42 mg/dL.[19]

Assessment of renal function in the present study revealed a mean serum creatinine level of 0.94 ± 0.21 mg/dL and a mean estimated glomerular filtration rate (eGFR) of 96.4 ± 18.2 mL/min/1.73 m², indicating largely preserved kidney function among the participants. These findings are consistent with those reported by Asmamaw T et al., where most patients with type 2 diabetes mellitus exhibited normal or elevated GFR (≥90 mL/min/1.73 m²). Additionally, 15% were classified as stage 2 CKD (GFR 60–89 mL/min/1.73 m²), 5% as stage 3 CKD (GFR 30–59 mL/min/1.73 m²), and one patient as stage 4 CKD (GFR 15–29 mL/min/1.73 m²).[20]

The mean serum cystatin C level in the present study was 1.01 ± 0.26 mg/L, underscoring its potential as an early biomarker for detecting subtle renal impairment. This observation is consistent with the findings of Asmamaw T et al., who reported significantly elevated serum creatinine and cystatin C levels in patients with type 2 diabetes mellitus compared to healthy controls.[20]

The mean serum 25-hydroxy vitamin D level was 23.6 ± 8.7 ng/mL, indicating a trend toward vitamin

D insufficiency among the study population. Furthermore, preclinical kidney disease was identified in 8 (8.0%) of the 100 patients with type 2 diabetes mellitus, highlighting the importance of early screening for renal dysfunction.

Vitamin D deficiency was significantly associated with preclinical kidney disease in the present study, observed in 6 of 8 patients (75.0%) compared to 26 of 92 patients (28.3%) without renal involvement, while no cases occurred among vitamin D–sufficient individuals ($p = 0.021$). These findings are supported by Nam H et al., who reported type 2 diabetes prevalence rates of 22.6%, 22.5%, 18.4%, and 12.7% among individuals with severely deficient, deficient, insufficient, and sufficient vitamin D levels, respectively, demonstrating that higher serum 25(OH)D levels were associated with a reduced risk of T2DM.[21] Similarly, Bashir et al. observed significant differences in vitamin D status between groups ($p < 0.001$), with deficiency and insufficiency reported in 37.4% (n = 112) and 29.1% (n = 87) of patients with diabetic nephropathy, compared to 8.0% (n = 8) and 9.0% (n = 9), respectively, among T2DM patients without nephropathy. Conversely, vitamin D sufficiency was higher in patients without nephropathy (83.0%, n = 83) than in those with diabetic nephropathy (33.4%, n = 100). The relative risk of vitamin D deficiency and insufficiency was significantly lower among T2DM patients without nephropathy (RRR = 0.09, 95% CI: 0.04–0.19, $p < 0.001$ and RRR = 0.13, 95% CI: 0.06–0.26, $p < 0.001$, respectively), indicating a 91% and 87% reduced risk. These findings collectively highlight the strong association between hypovitaminosis D and diabetic renal complications.[15]

In the present study, patients with preclinical kidney disease exhibited significantly elevated systolic blood pressure (142.5 ± 12.4 vs. 131.7 ± 14.6 mmHg; $p = 0.038$), diastolic blood pressure (88.3 ± 7.2 vs. 81.9 ± 9.5 mmHg; $p = 0.049$), fasting blood glucose (182.4 ± 35.6 vs. 154.5 ± 41.8 mg/dL; $p = 0.041$), and HbA1c (8.9 ± 1.2% vs. 7.8 ± 1.3%; $p = 0.028$). Renal function parameters were also significantly deranged, with higher serum creatinine (1.18 ± 0.19 vs. 0.92 ± 0.18 mg/dL; $p = 0.001$) and serum cystatin C (1.42 ± 0.21 vs. 0.97 ± 0.18 mg/L; $p < 0.001$), accompanied by lower serum 25-hydroxy vitamin D levels (15.6 ± 4.8 vs. 24.3 ± 8.4 ng/mL; $p = 0.003$) and reduced eGFR (68.5 ± 9.6 vs. 98.7 ± 14.5 mL/min/1.73 m²; $p < 0.001$) compared to patients without preclinical kidney disease. These findings align with Bashir et al., who reported poorer glycaemic control and renal function in patients with diabetic nephropathy, including higher HbA1c (8.2 [7.5–9.0]% vs. 7.3 [6.8–7.7]%; $p < 0.001$), fasting blood sugar (149 [135–162] mg/dL vs. 142 [130–155] mg/dL; $p = 0.0005$), urea (31 [24–38] mg/dL vs. 22 [18–27] mg/dL; $p < 0.001$), and creatinine (1.35 [1.0–1.7] mg/dL vs. 0.82 [0.7–0.9] mg/dL; $p < 0.001$).[15]

Pearson's correlation analysis in the present study demonstrated a strong negative correlation between serum cystatin C and eGFR ($r = -0.72$, $p < 0.001$) and a strong positive correlation with serum creatinine ($r = 0.68$, $p < 0.001$), highlighting its reliability as a sensitive marker of early renal dysfunction. These findings are consistent with those of Sagar et al., who reported significantly elevated cystatin C and creatinine levels in patients with chronic kidney disease compared to controls ($p < 0.0001$), with cystatin C exhibiting a stronger negative correlation with eGFR ($r = -0.91$) than creatinine ($r = -0.896$).[22] Similarly, J. D. Sa et al. observed significant increases in serum creatinine and cystatin C across CKD stages ($p < 0.001$), with a positive correlation between cystatin C and creatinine ($r = 0.875$, $p < 0.001$) and negative correlations with eGFR ($r = -0.736$ for cystatin C and $r = -0.719$ for creatinine). Notably, in patients with eGFR ≥60 mL/min/1.73 m², median serum creatinine remained within normal limits (1.01 mg/dL), whereas cystatin C was elevated (1.34 mg/L).[23] Furthermore, Dhupper V et al. demonstrated a stronger Pearson correlation of cystatin C with eGFR ($r = -0.877$; CI: 1.44–1.96; $p = 0.000$) compared to serum creatinine ($r = -0.777$; CI: 1.88–3.06; $p = 0.000$).[24] Collectively, these findings reinforce the superiority of serum cystatin C as an early and sensitive biomarker of renal dysfunction.

CONCLUSION

In this cross-sectional study prevalence of preclinical kidney disease was found to be 8%, highlighting the importance of early screening in diabetic individuals. Serum cystatin C showed a strong negative correlation with eGFR ($r = -0.72$, $p < 0.001$) and a strong positive correlation with serum creatinine ($r = 0.68$, $p < 0.001$), underscoring its reliability in detecting early renal dysfunction. Patients with preclinical kidney disease had significantly higher serum cystatin C levels (1.42 ± 0.21 mg/L vs. 0.97 ± 0.18 mg/L; $p < 0.001$) and lower eGFR (68.5 ± 9.6 vs. 98.7 ± 14.5 mL/min/1.73 m²; $p < 0.001$) compared to those without renal impairment.

Vitamin D deficiency was notably associated with early kidney dysfunction. Individuals with preclinical kidney disease exhibited significantly lower serum 25-hydroxy vitamin D levels (15.6 ± 4.8 ng/mL vs. 24.3 ± 8.4 ng/mL; $p = 0.003$), with 75% of affected patients being vitamin D deficient ($p = 0.021$). Additionally, poorer glycaemic control and higher blood pressure were observed among patients with renal impairment, including elevated fasting blood glucose (182.4 ± 35.6 mg/dL vs. 154.5 ± 41.8 mg/dL; $p = 0.041$) and HbA1c (8.9 ± 1.2% vs. 7.8 ± 1.3%; $p = 0.028$).

In conclusion, serum cystatin C demonstrates superior sensitivity for detecting early renal

dysfunction and correlates significantly with eGFR, serum creatinine, and vitamin D levels. Its integration with conventional renal markers and vitamin D assessment may enhance the early diagnosis and risk stratification of preclinical diabetic kidney disease in patients with type 2 diabetes mellitus, particularly in tertiary care settings.

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