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Serum Cystatin C versus Creatinine: A Cross Sectional Study of GFR Estimation in Type II Diabetic Patients

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KEYWORDS

Type II diabetes mellitus, Glomerular filtration rate, Cystatin C

ABSTRACT:

Introduction: Diabetic nephropathy is a leading cause of chronic kidney disease. Accurate estimation of glomerular filtration rate (GFR) is essential for early detection of renal impairment. Serum creatinine is widely used but influenced by non renal factors, whereas serum Cystatin C offers greater sensitivity.

Aim: To evaluate and compare GFR estimation using serum Cystatin C (Hoek's formula) and serum Creatinine (Cockcroft–Gault formula) in patients with type II diabetes mellitus.

Methods: A cross sectional prospective study was conducted on 60 patients with type II diabetes mellitus. Serum Cystatin C and serum Creatinine were measured, and GFR was calculated using Hoek's and Cockcroft–Gault formulas. Patients were classified into normal (≥90 ml/min) and reduced (<90 ml/min) GFR groups. Chi square test was applied to assess associations with gender and duration of diabetes.

Results: Hoek's formula classified 76.7% of patients as having reduced GFR compared to 63.3% by Cockcroft–Gault. Gender did not significantly influence GFR classification ($p > 0.8$), while duration of diabetes showed a highly significant association with reduced GFR in both methods (Hoek: $\chi^2 = 15.27$, $p = 0.0005$; Cockcroft–Gault: $\chi^2 = 14.46$, $p = 0.0007$).

Conclusion: Serum Cystatin C provides a more sensitive measure of renal impairment than serum Creatinine, particularly in relation to disease duration. It may serve as a superior biomarker for early detection and monitoring of diabetic nephropathy.

Introduction

Diabetes mellitus is a group of metabolic disorders characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Persistent hyperglycemia is associated with long-term damage, dysfunction, and failure of various organs, particularly the kidneys, eyes, and nerves[1]. The burden of diabetic nephropathy is substantial, as it represents one of the leading causes of chronic kidney disease (CKD) worldwide[2]. Glomerular filtration rate (GFR) is considered the most reliable indicator of renal function. Traditionally, serum creatinine has been the most widely used endogenous marker for estimating GFR[3]. However, creatinine levels are influenced by several non-renal factors such as age, gender, muscle mass, and dietary intake, which may lead to inaccurate estimation of renal function[4]. The Cockcroft–Gault formula, developed to overcome some of these limitations, remains a common method for estimating GFR in clinical practice[5]. Despite this, creatinine-based equations may still overestimate renal function, particularly in patients with early diabetic nephropathy[6]. Cystatin C, a low-molecular-weight protein produced by all nucleated cells, has emerged as an alternative biomarker for GFR estimation. Unlike creatinine, its levels are less affected by muscle mass,

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age, or gender, making it a more sensitive marker of early renal impairment[7]. Several studies have demonstrated that serum Cystatin C correlates more closely with measured GFR and provides better diagnostic accuracy in detecting mild to moderate reductions in renal function compared to creatinine[8–10]. Given these considerations, the present study was undertaken to evaluate and compare GFR estimation using serum Cystatin C (Hoek's formula) and serum Creatinine (Cockcroft–Gault formula) in patients with type II diabetes mellitus. By analyzing demographic variables and duration of illness in relation to GFR classification, the study aims to highlight the potential role of Cystatin C as a superior marker for early detection of diabetic nephropathy.

Aims and Objectives

Aim:

To evaluate and compare the estimation of glomerular filtration rate (GFR) using serum Cystatin C (Hoek's formula) and serum Creatinine (Cockcroft–Gault formula) in patients with type II diabetes mellitus.

Objectives:

1. To determine the proportion of patients classified as having normal (≥90 ml/min) and reduced (<90 ml/min) GFR using serum Cystatin C and serum Creatinine.
2. To compare gender-wise differences in GFR classification between Hoek's and Cockcroft–Gault methods.
3. To assess the impact of duration of diabetes on GFR classification by both methods.
4. To evaluate the statistical significance of differences in classification outcomes between the two methods.
5. To highlight the utility of serum Cystatin C as an early marker of renal impairment in type II diabetes mellitus.

Materials and Methods

Present study is a cross-sectional prospective study conducted at tertiary care setting. Institutional ethics committee permission was taken prior to commencement of present study. 60 Participants fulfilling inclusion and exclusion criteria were enrolled. Study was explained to all participants and written informed consent was obtained from all.

Inclusion Criteria:

a. Patients diagnosed with type II diabetes mellitus within the last two years.

b. Normal baseline serum creatinine levels.

c. Age group: adults (>18 years).

Exclusion Criteria:

a. Type I diabetes mellitus.

b. Thyroid disorders.

c. Patients on long-term glucocorticoid therapy.

d. Pregnant females.

e. Chronic inflammatory diseases.

Procedure:

Detailed clinical history was recorded including age, gender, height, weight, and duration of diabetes. Blood samples were collected for estimation of:

a. **Serum Cystatin C** using turbidometric immunoassay[7].

b. **Serum Creatinine** using Modified Jaffe's reaction[11].

- GFR was calculated using:
  a. **Hoek's formula** (based on serum Cystatin C)[12].
  b. **Cockcroft–Gault formula** (based on serum Creatinine)[13].
- Patients were grouped into:
  a. **Normal GFR (≥90 ml/min)**
  b. **Reduced GFR (<90 ml/min)** separately for each method.

Statistical Analysis:

Data were expressed as mean ± SD and percentages. Chi-square test was applied to compare categorical variables (Normal vs Reduced GFR) across gender and duration of diabetes. A p-value <0.05 was considered

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statistically significant. Statistical analysis was performed using SPSS version 20.

Observation and Result

Table 1: Demographic Profile

Sr No	Variables	Number of cases n/ Mean	Percentage %/SD
1	**Age (Years)** Mean ± SD	51.1	6.9
2	**Gender n (%)** a. Male b. Female	38 22	63.3 % 36.7 %
3	**Height (cm)** Mean ± SD	155.9	4.7
4	**Weight (kg)** Mean ± SD	66.9	7.5
5	**Diabetes duration n (%)** a. newly diagnosed b. <1 year c. between 1–2 years	14 15 31	23.3 % 25 % 51.7 %

The study included 60 patients with type II diabetes mellitus. The mean age of participants was 51.1 ± 6.9 years, indicating a middle-aged cohort. Out of the total, 38 were males (63.3%) and 22 were females (36.7%), showing a male predominance. The average height was 155.9 ± 4.7 cm and mean weight was 66.9 ± 7.5 kg, reflecting a relatively uniform anthropometric profile. Regarding disease duration, 14 patients (23.3%) were newly diagnosed, 15 (25%) had diabetes for less than one year, and 31 (51.7%) had diabetes for one to two years. This distribution highlights that the majority of cases had diabetes for more than one year, which is relevant when assessing renal function decline.

Table 2: Gender-wise GFR Classification

Sr No	Gender	Normal GFR (≥90 ml/min) – Hoek	Reduced GFR (<90 ml/min) – Hoek	Normal GFR (≥90 ml/min) – CG	Reduced GFR (<90 ml/min) – CG
1	Male (n=38)	8 (21.1%)	30 (78.9%)	14 (36.8%)	24 (63.2%)
2	Female (n=22)	6 (27.3%)	16 (72.7%)	8 (36.4%)	14 (63.6%)
Total N (%)		14 (23.3%)	46 (76.7%)	22 (36.7%)	38 (63.3%)

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When GFR was estimated using Hoek's formula (Cystatin C), 78.9% of males and 72.7% of females were classified as having reduced GFR (<90 ml/min). In contrast, Cockcroft–Gault (Creatinine) classified fewer patients as reduced: 63.2% of males and 63.6% of females. Overall, Hoek identified 76.7% of the cohort as reduced compared to 63.3% by Cockcroft–Gault. This indicates that Cystatin C is more sensitive in detecting early renal impairment, particularly among males, where the difference between methods was more pronounced.

Table 3: Duration-wise GFR Classification

Sr No	Duration of Illness	Normal GFR (≥90 ml/min) – Hoek	Reduced GFR (<90 ml/min) – Hoek	Normal GFR (≥90 ml/min) – CG	Reduced GFR (<90 ml/min) – CG
1	Newly diagnosed (n=14)	10 (71.4%)	4 (28.6%)	11 (78.6%)	3 (21.4%)
2	< 1 year (n=15)	6 (40.0%)	9 (60.0%)	7 (46.7%)	8 (53.3%)
3	1–2 years (n=31)	4 (12.9%)	27 (87.1%)	6 (19.4%)	25 (80.6%)
Total N (%)		20 (33.3%)	40 (66.7%)	24 (40.0%)	36 (60.0%)

Duration of diabetes showed a clear relationship with GFR reduction. Among newly diagnosed patients, Hoek classified 28.6% as reduced, while Cockcroft–Gault classified only 21.4%. In patients with less than one year of diabetes, reduced GFR was detected in 60% by Hoek and 53.3% by Cockcroft–Gault. The most striking difference was seen in patients with one to two years of diabetes: Hoek classified 87.1% as reduced compared to 80.6% by Cockcroft–Gault. Overall, Hoek identified 66.7% of all patients as reduced versus 60% by Cockcroft–Gault. These findings emphasize that longer duration of diabetes is strongly associated with reduced renal function, and Cystatin C detects impairment earlier and in a greater proportion of patients.

Graph 1: Duration-wise GFR Classification

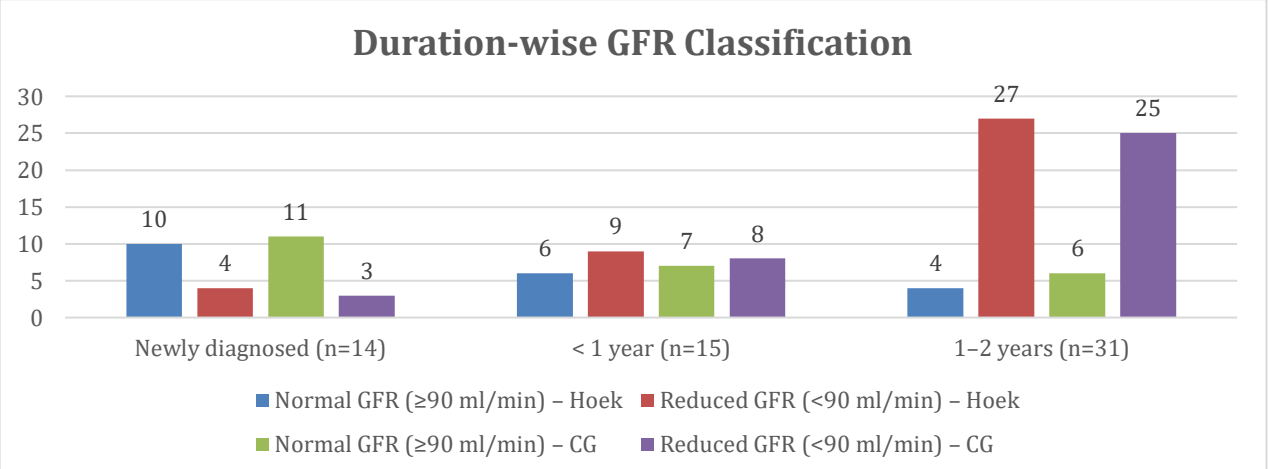

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Table 4: statistical Interpretation

Sr No	Table / Variable	Method	χ^2 Value	df	p-value	Significance
1	Gender vs GFR category	Hoek (Cystatin C)	0.054	1	0.816	NS
2	Gender vs GFR category	Cockcroft–Gault	0.000	1	1.000	NS
3	Duration vs GFR category	Hoek (Cystatin C)	15.27	2	0.0005	Significant
4	Duration vs GFR category	Cockcroft–Gault	14.46	2	0.0007	Significant

Chi-square testing confirmed these observations. Gender did not significantly influence GFR classification by either method (Hoek: $\chi^2 = 0.054$, $p = 0.816$; Cockcroft–Gault: $\chi^2 = 0.000$, $p = 1.000$). However, duration of diabetes was highly significant in both methods (Hoek: $\chi^2 = 15.27$, $p = 0.0005$; Cockcroft–Gault: $\chi^2 = 14.46$, $p = 0.0007$). This demonstrates that disease duration is a major determinant of renal impairment, and Cystatin C provides a more sensitive measure of decline compared to creatinine.

Discussion

The present study demonstrated that serum Cystatin C (Hoek's formula) classified a greater proportion of type II diabetes mellitus patients as having reduced GFR compared to serum Creatinine (Cockcroft–Gault formula). Specifically, 76.7% of patients were identified as having reduced GFR by Hoek's method, whereas only 63.3% were classified as reduced by Cockcroft–Gault. This suggests that Cystatin C is more sensitive in detecting early renal impairment, particularly in patients with longer duration of diabetes. These findings are consistent with the study by Hojs et al., who reported that serum Cystatin C had higher diagnostic accuracy than serum creatinine in distinguishing patients with mildly to moderately impaired kidney function, especially in diabetic cohorts[14]. Similarly, Rodrigues et al. observed that values obtained from Cockcroft–Gault differed significantly from measured creatinine clearance, often leading to overestimation of renal function[15]. In line with our results, Salgado et al. found that Cystatin C correlated better with measured GFR than creatinine, and was particularly useful in identifying early nephropathy in diabetic patients[16]. Another study by Perkins et al. highlighted that Cystatin C levels rise earlier than creatinine in the course of diabetic nephropathy, making it a more reliable marker for early detection[17]. The association between longer duration of diabetes and reduced GFR observed in our study is also supported by previous literature. A study by Shlipak et al. demonstrated that Cystatin C detected renal impairment earlier in patients with chronic conditions, including diabetes, compared to creatinine-based methods[18]. This reinforces the utility of Cystatin C in longitudinal monitoring of diabetic patients.

The superior sensitivity of Cystatin C in detecting reduced GFR can be explained by several mechanisms. Cystatin C is produced at a constant rate by all nucleated cells and freely filtered by the glomeruli. It is not secreted by renal tubules and is almost completely reabsorbed and catabolized in the proximal tubules, making its serum concentration a direct reflection of GFR[11]. In contrast, serum creatinine levels are influenced by muscle mass, diet, age, and gender, which may mask early declines in renal function[12]. This explains why creatinine-based formulas often overestimate GFR, particularly in patients with reduced muscle mass such as elderly individuals or females. Furthermore, hyperglycemia in diabetes induces glomerular hyperfiltration initially, followed by progressive glomerulosclerosis and tubular dysfunction. These changes may not immediately alter serum creatinine but are more sensitively captured by Cystatin C levels[13]. The earlier rise in Cystatin C during renal

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impairment reflects its independence from extrarenal factors and its closer correlation with true GFR decline[14].

Conclusion

The present study demonstrates that serum Cystatin C (Hoek's formula) identifies a higher proportion of type II diabetes mellitus patients with reduced GFR compared to serum Creatinine (Cockcroft–Gault formula). While gender did not significantly influence GFR classification, duration of diabetes showed a strong association with renal impairment. These findings highlight the superior sensitivity of Cystatin C in detecting early nephropathy and support its use as a reliable biomarker for monitoring renal function in diabetic patients.

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