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HbA1c's Role in eGFR Variations Among Young Diabetics: Insights from South Indian CKD Study

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Abstract :

Diabetes Mellitus (DM) is a leading cause of chronic kidney disease (CKD) worldwide, yet its prevalence among younger adults remains underexplored. This study aimed to investigate the relationship between HbA1c levels and kidney function, measured by eGFR, in young diabetic patients (20-40 years). A total of 191 participants were included, consisting of 107 males (56%) and 84 females (44%). HbA1c > 6.5% was measured using the immunoturbidimetric method on the Mindray BS-600 machine, and eGFR was calculated via the Cockcroft-Gault equation. Other parameters, such as fasting and postprandial glucose, urea, creatinine, and blood urea nitrogen (BUN), were also assessed.

The study found a negative correlation between HbA1c and eGFR, particularly in females (p = -0.126), suggesting a link between higher HbA1c and reduced kidney function. Females exhibited a higher prevalence of Stage 3 CKD (25%) compared to males (7%). Our findings revealed a decline in eGFR correlated with elevated HbA1c, suggesting early diabetic nephropathy linked to poor glycemic control. Males showed slightly elevated creatinine levels (1.07 mg/dL), indicating early kidney impairment. The correlation between HbA1c

and BUN was weak but notable, with p-values of 0.10 in males and 0.20 in females, suggesting impaired kidney function.

In conclusion, females had higher HbA1c levels (9.3 ± 1.94) than males (9.26 ± 1.99) and a greater prevalence of Stage 3 CKD, with eGFR decline linked to poor glycemic control. These findings underscore the need for early intervention in managing diabetes to prevent kidney impairment.

Keywords:

Diabetes Mellitus, eGFR, Chronic Kidney disease, Cockcroft-Gault equation, Blood Urea Nitrogen, HbA1c, Diabetic nephropathy.

Introduction:

Diabetes Mellitus is a worldwide condition characterized by elevated blood sugar levels, resulting from issues with insulin production, secretion, or effectiveness. In simpler terms, it involves problems with how the body manages glucose due to insulin-related factors (1). The International Diabetes Federation (IDF) estimates that in 2019, over 463 million people globally were affected by diabetes. The prevalence of this condition is on the rise, with projections suggesting that more than 700 million people will have diabetes by 2045 (2).

Diabetes Mellitus (DM), especially Type 2 diabetes, is the primary contributor to chronic kidney disease (CKD) in both developed and developing nations (3,4). Worldwide, over 50% of individuals with Type 2 Diabetes Mellitus(DM) go on to develop Chronic Kidney Disease (CKD) (5). Multiple factors of diabetes contribute to the elevated prevalence of chronic kidney disease (CKD) in India (6). The causes of chronic kidney disease (CKD) differ significantly across India. In regions of Andhra Pradesh, Odisha, and Goa, there are elevated rates of chronic kidney disease of unknown etiology, which is characterized by a gradual onset and slow progression of chronic interstitial nephropathy (7)

As kidney dysfunction becomes more common, estimating kidney function using formulas is increasingly integrated into clinical practice. The most commonly utilized formulas are the Cockcroft-Gault equation and the abbreviated Modification of Diet in Renal Disease (MDRD) equation (8). More than 50% of patients with advanced chronic kidney disease (CKD) are first diagnosed when their estimated glomerular filtration rate (eGFR) falls below 15 ml/min using Cockcroft-Gault equation (9).

Similarly, Blood Urea Nitrogen (BUN) and serum creatinine (sCr) levels are reliable indicators of kidney function because they reflect the efficiency of glomerular filtration. As kidney function declines, the levels of BUN and sCr increase since they are primarily excreted through the glomeruli and are not significantly reabsorbed or secreted by the kidneys, making them effective markers of the glomerular filtration rate (GFR)(10). Monitoring HbA1c variability may provide valuable insights into a patient's overall glycemic management and the risk of kidney complications (11).

Hence the objective of this study was to investigate the relationship between HbA1c levels and changes in kidney function, as measured by eGFR, in young adults with diabetes.

Materials and Methods:

This was a prospective cross-sectional study that was carried out at Sree Balaji Medical College and Hospitals in Chennai, South India, from August 2023 to August 2024. All diabetic patients aged 20 to 40 years who visited

Sree Balaji Medical College Hospital during the data collection period and consented to participate were included in the study. Only diabetic patients aged 20 to 40 years with a HbA1c level above 6.5% were included in the study. Individuals who were non-diabetic, smokers, alcohol consumers, or had endocrine disorders, genetic disorders, or were on steroid medication were excluded. Socio demographic factors such as age, sex, height, and weight were gathered using a questionnaire.

Biochemical Parameters:

Fasting blood glucose and postprandial blood glucose levels were measured using the glucose oxidase-peroxidase method. Serum urea, uric acid, and creatinine were assessed using the GLDH (Glutamate dehydrogenase) urease method, sarcosine oxidase method, and Uricase Peroxidase-antiperoxidase method, respectively, all on the Mindray BS-600 machine. HbA1c was determined using the immunoturbidimetric method on Mindray BS-600 machine. BUN was calculated with the formula BUN [mg/dL] = Urea [mg/dL] / 2.14. Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault equation: eGFR = (140 − age) × body weight / plasma creatinine × 72 (× 0.85 if female) mL/min.

Statistical analyses for the study were conducted using SPSS Statistics 26 software to ensure accurate data interpretation and results.

Ethics

This study was approved by the Institutional Ethics Committee in August 2023.

Reference range

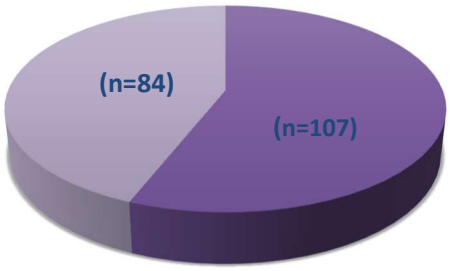
The normal values for HbA1c are less than 6.5%, fasting blood glucose should range from 70 to 99 mg/dL, and postprandial blood glucose should be under 140 mg/dL. A normal glomerular filtration rate (GFR) for adults was between 90 and 125 mL/min. Normal urea levels were between 12.84 and 42.8 mg/dL. Serum creatinine levels were considered normal at 0.9 to 1.3 mg/dL for males and 0.6 to 1.1 mg/dL for females. Uric acid levels are normal at 4.4 to 4.6 mg/dL for males and 2.3 to 6.6 mg/dL for females The normal. range for Blood Urea Nitrogen (BUN) was typically between 6 and 21 mg/dL.

Results

A total of 191 young diabetics participated in the study, comprising 107 males (56%) and 84 females (44%) (Fig 1).

Gender Distribution:

FIGURE 1 : Gender distribution of the study participants.



The results for all the laboratory tests are provided in Table 1. The HbA1c level indicated poor glycemic control, which is a risk factor for CKD. Elevated fasting (197.13 mg/dL) and postprandial glucose (275.08 mg/dL) levels further suggested potential metabolic dysregulation. Urea and creatinine levels are slightly elevated in males (34.16 mg/dL and 1.07 mg/dL, respectively). The eGFR was lower in males (85.13 mL/min), suggesting reduced kidney function, while females show a healthier eGFR of 111.90 mL/min. Elevated uric acid levels and blood urea nitrogen (BUN) in males (15.96 mg/dL) also raise concerns for CKD

Table 1 Laboratory parameters of the study participants.

Biochemical Parameters	Male (Mean ± SD)	Female (Mean ± SD)
HBA1C	9.26±1.99	9.3±1.94
Fasting Glucose	197.13±74.37	196.2±65.36
Postprandial Glucose	275.08±71.25	288.18±71.58
Urea	34.16±18.68	31.52±11.72
Creatinine	1.07±0.63	1.05±0.29
Uric Acid	5.07±1.58	5.48±1.64

eGFR	85.13±48.94	111.9±32.32
BUN	15.96±8.73	14.73±5.48

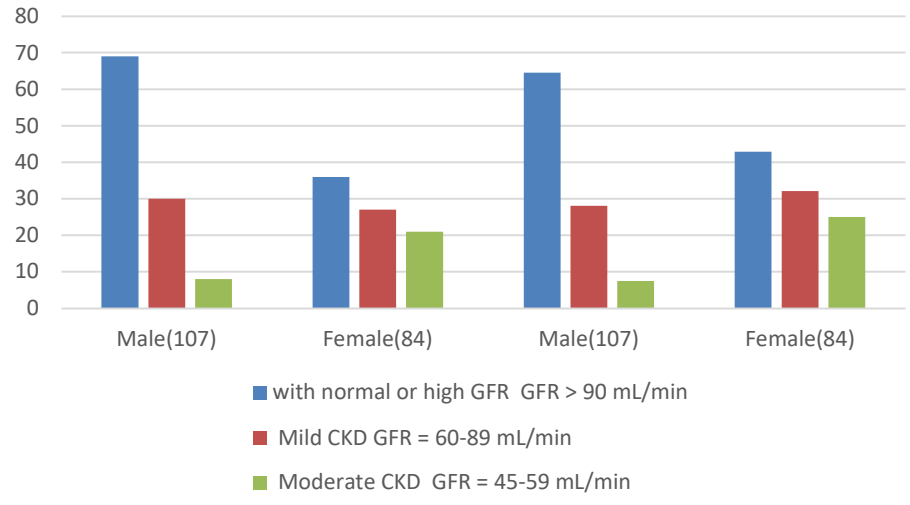
Stages of Chronic Kidney Disease:

Table 2 & Figure 2 outlines the distribution of chronic kidney disease (CKD) stages among male and female patients based on their estimated glomerular filtration rate (eGFR). In Stage 1, defined as having a normal or high eGFR (greater than 90 mL/min), there are 69 male patients (64%) and 36 female patients (43%). This indicates a significant proportion of both genders maintaining healthy kidney function. Stage 2 represents mild CKD, with 30 males (28%) and 27 females (32%) falling within an eGFR range of 60-89 mL/min. This suggests early signs of kidney impairment. In Stage 3, categorized as moderate CKD with eGFR values between 45-59 mL/min, 8 males (7%) and 21 females (25%) are affected, highlighting a greater prevalence of moderate CKD in females. None of the participants identified in Stage 4 and 5

Table 2 Stages of Chronic Kidney Disease Among the Study Participants

Stages of CKD	Description	eGFR (mL/min)	Male (n=107)	Female (n=84)	% Male	% Female
Stage 1	With normal or high GFR	GFR > 90	69	36	64%	43%
Stage 2	Mild CKD	GFR = 60-89	30	27	28%	32%
Stage 3	Moderate CKD	GFR = 45-59	8	21	7%	25%

Figure 2 Flowchart Showing the Stages of CKD



Prevalence of Chronic Kidney Disease:

Table 3 Pearlson Correlation of HbA1c with Other Parameters showing the Prevalence of CKD

Parameter	Male Correlation with HbA1c(p Value)	Female Correlation with HbA1c(p value)	Interpretation for CKD
Fasting	0.644	0.63	Moderate positive correlation; higher fasting levels may be associated with poorer glycemic control, potentially indicating increased CKD risk.
Postprandial (PP)	0.511	0.602	Moderate positive correlation; higher PP glucose levels could suggest increased risk of CKD.
Urea	0.107	0.205	Weak positive correlation; elevated urea levels may indicate reduced kidney function in individuals with high HbA1c.
Creatinine	0.021	-0.126	No significant correlation for males; slight negative correlation for females; suggests that high HbA1c may not strongly influence creatinine levels directly.
Uric Acid	-0.081	0.008	No significant correlation; the relationship between uric acid and HbA1c appears negligible.
eGFR	0.021	-0.126	No significant correlation for males; negative correlation for females suggests that higher HbA1c may relate to lower eGFR, indicating possible kidney impairment.
BUN	0.107	0.205	Weak positive correlation; higher BUN levels may indicate impaired kidney function related to poor glycemic control.

(Table 3) suggests that higher HbA1c levels are associated with certain markers of kidney function, which may indicate an increased risk for CKD in both male and female participants. This relationship highlights the

importance of managing blood glucose levels to potentially mitigate kidney-related complications.

Discussion:

In this cross-sectional study, decline in eGFR levels with elevated HbA1c indicated a potential deterioration in kidney function, suggesting early stages of diabetic nephropathy or kidney impairment associated with poor glycemic control.

In a similar study conducted by Bethany et al, it was found that diabetes is linked to a significantly faster decline in kidney function over a 26-year period in a community-based population. The study measured the annual expected decrease in eGFR among individuals without diabetes, those with undiagnosed diabetes, and those with diagnosed diabetes. These findings could be valuable for guiding future monitoring strategies and clinical trials(12).

According to the study conducted by federic et al, the higher HbA1c levels are a strong indicator of a decrease in eGFR, regardless of whether a person has diabetes or the stage of CKD they are in, showing a clear link that gets stronger as HbA1c levels rise(13)

In our study population, Stage 3 CKD was observed in 25% of participants, indicating a notable level of kidney impairment among them. However, only 7% of men were affected by Stage 3 CKD, suggesting that male participants had a lower prevalence.

The study by Ching et al. shows that in diabetic patients with stage 3–4 CKD, higher HbA1c levels are linked to an increased risk of negative health outcomes. However, this association is not observed in patients with stage 5 CKD(14)

In the study conducted by Taryn et al., it was found that the global prevalence of CKD is higher in women (14.6%) compared to men (12.8%), indicating that women are more commonly affected by CKD worldwide (15,16)

The multinational REVEAL-CKD study by Navdeep et al. suggests that there are significant opportunities to enhance the diagnosis of stage 3 CKD, especially among female patients, in countries like France, Germany, Italy, Japan, and the USA (17)

In our study, males showed slightly elevated creatinine levels, averaging 1.07 mg/dL, suggesting potential early signs of kidney impairment, which may indicate a risk of renal dysfunction in this group.

According to the study by Holtkamp, an initial rise in creatinine levels was found to predict a slower long-term decline in kidney function, suggesting it may indicate a more gradual progression of renal impairment (18,19).

A study conducted in California by Linda et al. found that elevated creatinine levels are linked to a higher risk of death, cardiovascular disease (CVD), and congestive heart failure (CHF), with this increased risk becoming evident even in the early stages of kidney disease (20)

In our study, a weak positive correlation was identified between higher BUN levels and impaired kidney function, with values of 0.107 for males and 0.205 for females. This suggests that elevated BUN levels may be linked to poor glycemic control.

A Chinese study by Jie Du et al. found that high levels of BUN (blood urea nitrogen) are linked to a greater risk of developing diabetes (DM) in Chinese adults (21).

The study conducted by Makiko Seki indicates that BUN is a key substance influencing calculated serum osmolality levels. In patients with advanced chronic kidney disease (CKD), both calculated serum osmolality and BUN levels rise simultaneously. Additionally, a recent study found that elevated BUN and calculated serum osmolality levels are independently linked to the development of CKD (22,23).

The study conducted by Mohammed Adem reported a significant prevalence of chronic kidney disease, affecting 31.5% of diabetic patients (24).

The study by Alemu et al. indicates that the occurrence of CKD among diabetic patients in Northwest Ethiopia is high and similar to findings from other low- and middle-income countries(25).

This Case control study reveals a concerning link between poor glycemic control and kidney impairment in younger diabetic patients, with evidence of early stages of diabetic nephropathy. Regular monitoring of kidney function is essential to prevent further progression and complications**.**

Limitations of the study:

Limitations include the cross-sectional design, which limits causal inference, and the small sample size. Improvements could involve longitudinal studies with larger populations to better assess kidney function and its progression over time.

Conclusion:

In conclusion, this study shows that females had a slightly higher HbA1c (9.3 ± 1.94) than males (9.26 ± 1.99). In Stage 3 CKD, categorized as moderate with eGFR values between 45-59 mL/min, 8 males (7%) and 21 females (25%) were affected, highlighting a greater prevalence of moderate CKD in females. None of the participants were identified in Stages 4 and 5. Additionally, elevated creatinine and BUN levels suggest potential early renal dysfunction. The correlation study emphasizes a significant relationship between poor glycemic control and kidney impairment, with a notable eGFR decline. Early intervention is crucial.

Abbreviations

CKD:Chronic kidney disease

DM:Diabetes mellitus

GFR:Glomerular filtration rate

eGFR:Estimated glomerular filtration rate

SPSS:Statistical package for social sciences

WHO:World Health Organization

MDRD:Modification of diet in renal disease

BUN: Blood Urea Nitrogen

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Conflict of interest disclosure

There is no Conflict of Interest.

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