VARIATIONS IN GLYCEMIC STATUS IN VARIOUS CHRONIC KIDNEY STAGES IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: As diagnostic tests to evaluate diabetes and identify the emergence of chronic diabetic problems, CBC (complete blood count) and HbA1c readings are employed. Numerous variables, including hemoglobin, the age of red blood cells (RBCs) in circulation, and the Hb glycation rate, influence HbA1c levels.

Aim: to evaluate the relationship between RBC, Hb, and HbA1c levels and the changes in glycemic status in different stages of chronic renal disease in individuals with type 2 diabetes.

Methods: 312 adults with type 2 diabetes mellitus (T2DM) were evaluated for the research. phases I–V of the Modification of Diet in Renal Diseases (MDRD) equation were used to determine the phases. Subjects in each stage had their RBS, HbA1c, and RBC count measured. The results were developed by statistical analysis of the collected data.

Results: The study's findings revealed that, out of 312 diagnosed study participants, 58.3% were men and 41.6% were women. Crucially, most of the participants with end-stage illnesses (stage V) had HbA1c levels between 4 and 7%. HbA1c and blood sugar irregularities were concerning signs of additional underlying conditions, such as renal anemia.

Conclusion: is that diabetes mellitus and hypertension, which also contribute to renal anemia, are the main causes of kidney disorders. In advanced stages of chronic kidney disease, the HbA1c test is not reliable due to low RBC counts, which result in a misleading glycated hemoglobin percentage. This is the study's clinical importance.

Keywords: Chronic kidney disease, Diabetic nephropathy, HbA1c, Renal anemia, Type 2 diabetes mellitus

INTRODUCTION

Chronic kidney disease, or CKD, is a progressive, long-term illness in which the kidneys get damaged and lose their ability to effectively filter blood. GFR (glomerular filtration rate), which measures how efficiently the kidneys filter waste and extra fluid from the blood in the body, is used to categorize chronic kidney disease into five phases. renal illnesses deteriorate and renal function decreases with increasing stages. Over time, these phases get worse. The kidneys can filter waste materials from the blood in the first three phases of chronic kidney disease. Dialysis may result from the kidneys' increased effort to filter blood in later stages (IV–V) and potential failure.[1]

When blood glucose (blood sugar) levels are very high, a disease known as diabetes develops. The inability of the body to respond to or create insulin and to maintain appropriate blood sugar levels are the hallmarks of diabetes. All age groups and both sexes are affected by diabetes. The majority of diabetes types are chronic and lifelong. Although diabetes is a leading cause of death and morbidity,

these consequences are not thought to be the direct result of the disease. 2 As CKD progresses, HRQoL (health-related quality of life) is greatly impacted and reduced. People with type 2 diabetes mellitus are more likely to experience worse mental and physical health effects than people without the disease.

An elevated risk of end-stage kidney disease (ESKD) is associated with about 40% of individuals with CKD and type 2 diabetes mellitus. The phrase "chronic kidney disease" refers to a large category of similar disorders that are typically associated with immune system dysfunction. Similar to etiologically distinct instances, similar clinical manifestations of kidney disorders, such as glomerulosclerosis and/or interstitial fibrosis, are observed.3

The majority of persons with ESKD worldwide also have chronic kidney disease, which is associated with significant mortality and morbidity rates in people with type 2 diabetes. In contrast to people with advanced kidney disease, those with type 2 diabetes mellitus and chronic kidney disease (CKD) have substantial residual cardiorenal mortality and morbidity despite current medications. Additionally, the risk of cardiovascular events and renal failure increases with the stage and severity of CKD illnesses that have the potential to develop into dialysis. High blood sugar in diabetics can harm kidney nephrons and blood arteries over time, impairing their ability to function effectively.

A lot of people with diabetes also have high blood pressure, which can harm their kidneys. Since high trans and intraglomerular hyperfiltration is the foundation of GFR, hypertension may exacerbate the development of CKD. 4 Glycemic variability, or GV, is more complex in people with CKD and type 2 diabetes. Additionally, in individuals with CKD whose estimated GFR (eGFR) is less than 60 mL/min/1.73 m2 in addition to T2DM, there is a higher chance of detecting faux hypoglycemia, which is low glycated Hb (HbA1c). Additionally, because of its impact on CKD patients, the HbA1c test, which measures ABG (average blood glucose) levels over the previous two to three months, has limits.

Red blood cell (RBC) survival periods shorten when eGFR declines, which lowers the observed HbA1c. This is explained by the significance of carefully interpreting HbA1c in individuals with CKD and T2DM. 5 Blood sugar levels are not the sole factor that determines HbA1c. Hb (hemoglobin) and RBC counts are two of the several confounding variables used to calculate HbA1c. The current study aims to evaluate GV (glycemic variability) in various phases of chronic kidney disease (CKD) in individuals with type 2 diabetes by measuring two parameters: the participants' blood sugar level and RBC/hemoglobin count, which may aid in detecting erroneous HbA1c readings.

MATERIAL AND METHODS

to evaluate how participants with type 2 diabetes mellitus differ in their glycemic status throughout different stages of chronic renal disease and how these differences relate to their RBC and Hb levels in connection to their HbA1c levels.

The research participants came from the Institute's outpatient department. Prior to participation, all individuals gave their written and verbal informed permission. According to WHO criteria 6, 312 participants with type 2 diabetes mellitus and chronic renal disease were evaluated for the study.

Participants had to be above 30 years old and of either gender. Hemodialysis patients were included in Stage V as well. Based on the KDOQI (National Kidney Foundation Kidney Disease Outcomes Quality Initiative) staging criteria, 156 subjects with I-V CKD and type 2 diabetes mellitus were divided into three stages: stage I included subjects with normal/high eGFR >90mL/min/1.73m2, stage II included subjects with eGFR of 60-89mL/min/1.73m2, stage III included subjects with eGFR of 30-59mL/min/1.73m2, stage IV included subjects with eGFR of 60-89 mL/min/1.73m2, and stage V

included subjects with eGFR <15mL/min/1.73m2.[7] The simplified modification of diet in renal disease (MDRD) research equation was used to determine the eGFR: GFR (mL/min/1.73 m2) = 175 × (Scr) –1.154 × (Age)–0.203 × (0.742 if female) × (1.212 if African American).[8]

At every visit, all individuals were routinely monitored for sociodemographic data, standard hematological and biochemical laboratory evaluations, and CKD problems. Participants who were newly diagnosed or on follow-up for chronic kidney disease (CKD) associated with hypertension and type 2 diabetes mellitus and who visited the Institute during the study period met the study's inclusion criteria. Both male and female subjects who were at least 30 years old were included. People under 30 years old, people with illnesses other than hypertension, type 2 diabetes, and chronic renal disease, women who are pregnant, smokers, people who have donated blood of any kind, women who are nursing, people who have had surgery within the last six months, menorrhea, heart failure, kidney stones, and urinary tract infections.

The questionnaire was used to hand collect the data on an organized and standardized proforma. Laboratory reports were the source of the information. Age, gender, weight, and test results were among the information acquired. Nearly 5 mL of intravenous blood was drawn from each participant for the blood examination. This blood was then split into two tubes, with 2 mL being drawn in a vial containing EDTA (ethylene diamine tetra acetic acid) to evaluate HbA1c, CBC (complete blood count), and other hematological parameters.

An additional 3 ml of blood was drawn in a simple tube devoid of anticoagulant in order to measure biochemical markers including creatinine and RBS (random blood sugar). During their visit, study participants' demographic information was collected, and a written questionnaire was used to collect their medical history. To assess the prevalence of CKD and the start of dialysis, MDRD was utilized.

Using the boronate affinity technique, the hospital laboratory determined the HbA1c levels as clinically required. Using an auto haematology analyser, RBC and Hemoglobin levels were measured as part of the CBC. Using a fully automated system pack, RBS was evaluated.

A reference chart for Breath Well-Being was used to determine the average blood glucose (avBG) levels. Ten WHO criteria, which state that HbA1c results greater than 7% are indicative of hyperglycemia, were adhered to for every test. A blood sugar level of more than 200 mg/dl was considered high. Males and females were found to have normal hemoglobin levels of 13.5–17.5 gm/dL and 12–16 gm/dL, respectively, and normal red blood cell counts of 4-5.9 million/mm3 and 3.8–5.2 million/mm3, respectively.

The statistical analysis of the collected data was conducted using the Statistical Package for the Social Sciences (SPSS) software version 24.0 (IBM Corp., Armonk, NY, USA) for the evaluation of descriptive measures, Student t-test, ANOVA (analysis of variance), Spearman correlation coefficient, and Chi-square test. The data were presented as frequency, percentages, mean, and standard deviation. The p-value of less than 0.05 was taken into account.

RESULTS

Subjects with type 2 diabetes mellitus were the focus of the current cross-sectional investigation, which sought to evaluate the differences in glycemic status throughout different chronic kidney stages and their relationship to RBC and Hb levels to their HbA1c values.

In this study, 312 adults with type 2 diabetes mellitus (T2DM) were evaluated. phases I–V of the Modification of Diet in Renal Diseases (MDRD) equation were used to determine the phases. For patients in each stage, RBC count, HnA1c, and RBS were measured.

The mean age of the research participants was similar for those in CKD stages I–V, according to the study results, for the stage-wise distribution of CKD with different parameters (p=0.47). In stage I CKD, RBCx1012/L levels were considerably higher; from stage I to V, they progressively declined (p=0.00). Additionally, there was a substantial decline in hemoglobin levels from stage I to stage V (p=0.00). considerable variation in HbA1c levels, which rose noticeably from stage I to stages II and III of CKD and fell from stage IV to stage V (p=0.01).

The difference between CKD stages I and V was statistically non-significant, according to RBS values (p=0.93). Compared to stage I, average blood glucose levels were greater in stages II and III, and they considerably dropped in stages IV and V (p=0.05) (Table 1).

With an r-value of 0.074, it was shown that RBS had a non-significantly negative connection with HbA1c when compared to other research parameters. With a p-value of less than 0.01 and an r-value of 0.268, RBC demonstrated a strong positive connection with HbA1c readings. Furthermore, hemoglobin levels showed a strong positive connection with the HbA1c value (Table 2), with an r-value of 0.376 and a p-value of less than 0.01. According to the stage-wise distribution of CKD in three HbA1c subgroups, Group I had a HbA1c of 4-7%.

Among the 214 patients, there were 4, 2, 22, 56, and 140 in phases I, II, III, IV, and V. The glycemic variability was 68.4%. There were 0, 2, 14, 42, and 28 participants in phases I, II, III, IV, and V—a total of 86 subjects—with a prevalence of glycemic variability of 27.4% in Group II, which had a HbA1c of 7–11%. Twelve participants with a glycemic variability of 3.6% were included in Group III, which included 0, 0, 4, 6, and 2 subjects in stages I, II, III, IV, and V. In CKD stages I, II, III, IV, and V, the corresponding numbers of individuals were 0, 0, 4, 6, 2, and 12. The percentages of individuals were as follows: 1.4% (n=2), 1.4% (n=2), 12.6% (n=40), 33.1% (n=104), and 51 (n=160) in total. Table 3.

DISCUSSION

Three hundred and twelve adults with type 2 diabetes mellitus (T2DM) were evaluated in this study. Following the dietary adjustment, phases I–V of the MDRD equation were established. RBC count, HnA1c, and RBS were measured for each stage's patients. For CKD stage-wise distribution with different parameters, the mean age of study participants was similar for i-V CKD stages (p=0.47).

Significantly higher RBCx1012/L levels were seen in stage I CKD, and these values progressively dropped from stage I to stage V (p=0.00). Additionally, hemoglobin levels revealed a substantial decline from stage I to stage V, with a p-value of 0.00. There was a notable change in HbA1c levels, which rose considerably from stage I to stages II and III of CKD and fell from stage IV to stage V (p=0.01).

RBS results revealed a p-value of 0.93 for the statistically non-significant difference between CKD stages I and V. Stages IV and V saw a substantial drop in average blood glucose levels (p=0.05), but stages II and III showed greater levels than stage I. The findings of Freedman BI et al. (2010) and Astor BC et al. (2006), who evaluated participants with CKD, type 2 DM, and hypertension using data similar to the current study, were in line with these results.

With an r-value of 0.074, the study's findings indicated that RBS had a non-significantly negative connection with HbA1c when compared to other study parameters. The r-value of 0.268 and the p-value of less than 0.01 indicated a strong positive connection between RBC and HbA1c level.

With an r-value of 0.376 and a p-value of less than 0.01, hemoglobin levels also showed a significant positive connection with the amount of HbA1c. These results concurred with those of Portolés J et

al. (2021) and Cristy AL et al. (2014), whose research found a similar association between HbA1c and many indices, including RBS, RBC, and Hb.

Regarding the stage-wise distribution of CKD in three subgroups based on HbA1c, it was also observed that Group I, which had a HbA1c of 4-7%, had 214 people with glycemic variability of 68.4% and 4, 2, 22, 56, and 140 participants in stages I, II, III, IV, and V together.

In Group II with HbA1c of 7-11%, there were 0, 2, 14, 42, and 28 subjects in stages I, II, III, IV, and V, and a total of 86 subjects with the prevalence of glycemic variability as 27.4%. Group III had 12 participants with a glycemic variability of 3.6%, including 0, 0, 4, 6, and 2 subjects in stages I, II, III, IV, and V. For CKD stages I, II, III, IV, and V, the corresponding numbers of individuals were 0, 0, 4, 6, 2, and 12. A total of 1.4% (n=2), 1.4% (n=2), 12.6% (n=40), 33.1% (n=104), and 51% (n=160) of the patients were present. These findings were consistent with research by Agarwal R13 in 2011 and Home P et al. in 2005, where the authors' stage-wise distribution of chronic kidney disease (CKD) in various HbA1c ranges was similar to the findings of this study.

CONCLUSIONS

Taking into account its limitations, the current study comes to the conclusion that renal anemia is a common consequence of diabetes mellitus and hypertension, which also cause kidney disorders. Because hemoglobin and red blood cell counts are low in the later stages of chronic kidney disease with type 2 diabetes, a low HbA1c level between 4% and 7% is observed. Since low RBC counts result in a misleading glycated hemoglobin percentage, the study's clinical importance is the non-reliability of the HbA1c test in patients with severe chronic kidney disease.

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Variables	Stage I	Stage II	Stage III	Stage IV	Stage V	p
Mean age (years)	50±3	47±2	51.4±10.7	54.6±10.9	53.1±12.4	0.47
RBCx10^{12}/L	3.92±0.79	3.86±0.40	3.35±0.70	3.09±0.58	2.70±0.47	**0.00**
Hb (gm/dl)	10.63±2.83	10.23±0.23	10.19±2.24	9.59±2.09	8.49±1.65	**0.00**
HbA1c (%)	6.73±0.03	7.3±1.3	7.41±2.58	6.63±1.49	5.41±0.62	**0.01**
RBS (mg/dl)	167.3±2.3	197.3±67.3	348.6±212.2	300.7±177.4	319.4±200.5	0.93
avBG (mg/dl)	170.3±9.3	205±73	186±90.0	159±54	145.1±51.0	**0.05**

Table 1: Stage-wise distribution of CKD with various parameters

S. No	HbA1c	Correlation coefficient (r)	p-value	Remarks
1.	**RBS**	**0.074**	>0.05	Negative correlation
2.	**RBC**	**0.268**	**<0.01**	Positive correlation
3.	**HB**	**0.376**	**<0.01**	Positive correlation

Table 2: Correlation of HbA1c to various study parameters

HbA1c	Stage I	Stage II	Stage III	Stage IV	Stage V	Total	Glycemic variability prevalence (%)
Group I (4-7)	4	2	22	56	130	214	68.4
Group II (7-11)	0	2	14	42	28	86	27.4
Group III (11-15)	0	0	4	6	2	12	3.6
Total	4	4	40	104	160	312	
%	1.2	1.2	12.6	33.1	51.0		

Table 3: Stage-wise distribution of CKD in three subgroups from HbA1c