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CHRONIC KIDNEY STAGES IN SUBJECTS WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: HbA1c readings and complete blood counts (CBCs) are employed as diagnostic tests to evaluate diabetes and identify the emergence of chronic diabetic problems. The Hb glycation rate, the age of red blood cells (RBCs) in the bloodstream, and/or hemoglobin are some of the variables that influence HbA1c levels.

Aim: In individuals with type 2 diabetes mellitus, the current study sought to evaluate the differences in glycemic status in different chronic kidney stages and their relationship to RBC, Hb, and HbA1c levels.

Methods: 312 adult participants with type 2 diabetes mellitus (T2DM) were evaluated for the study. RBS, HbA1c, and RBC count were measured for each stage's subjects. The stages were defined in accordance with the stages I–V of the Modification of Diet in the Renal Diseases (MDRD) equation. The results were developed through statistical analysis of the collected data.

Results: According to the study's findings, 58.3% of the 312 diagnosed participants were men and 41.6% were women. It was important to highlight that most individuals with end-stage illnesses (stage V) had HbA1c levels between 4 and 7%. Blood sugar and HbA1c variations were concerning signs of additional underlying problems, such as renal anemia.

Conclusion: The current study comes to the conclusion that diabetes mellitus and hypertension, which also contribute to renal anemia, are typically the causes of kidney disorders. Due to decreased hemoglobin and red blood cell counts, a low HbA1c level in the range of 4% to 7% is observed in the later stages of chronic renal disease with type 2 diabetes. Because low RBC counts result in a misleading glycated hemoglobin percentage, the HbA1c test is unreliable in advanced stages of CKD individuals, which is the study's clinical significance.

Keywords: Diabetic nephropathy, HbA1c, renal anemia, Type 2 diabetes, chronic kidney disease

INTRODUCTION

Chronic kidney disease, or CKD, is a long-term, progressive illness in which the kidneys are damaged to the point where they are unable to effectively filter blood. Based on GFR (glomerular filtration rate), which measures how successfully the kidneys filter waste and extra fluid from the body's circulation, chronic kidney disease is classified into five phases. Kidney illnesses deteriorate and kidney function declines as they progress. Over time, these phases get worse. The kidneys are able to filter waste from the blood in the first three stages of chronic kidney disease. Dialysis may be necessary in later stages (IV–V), when the kidneys must work harder to filter blood and may eventually fail.[1]

Blood glucose (blood sugar) levels that are too high are indicative of diabetes. The inability of the body to respond to or manufacture insulin and maintain appropriate blood sugar levels are the hallmarks of diabetes. Individuals of all ages and genders 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 direct consequences of the disease.[2]

As CKD progresses, HRQoL (health-related quality of life) is considerably impacted and reduced. People with type 2 diabetes mellitus are more likely to experience worse mental and physical health outcomes than people without the

disease. An increased risk of end-stage kidney disease (ESKD) is associated with about 40% of individuals with CKD and type 2 diabetes mellitus. The term "chronic kidney disease" refers to a broad category of related conditions that are typically associated with immune system dysfunction. Similar to the etiologically distinct situations, interstitial fibrosis and/or glomerulosclerosis are common clinical manifestations of kidney disorders.3

The majority of people with ESKD worldwide also have chronic kidney disease, which is associated with significant mortality, morbidity, and poor quality of life. In contrast to individuals with advanced kidney disease, those with type 2 diabetes mellitus and chronic kidney disease (CKD) have considerable residual cardiorenal mortality and morbidity despite current medications. The risk of cardiovascular events and renal failure increases with the severity and stage of CKD. conditions that could lead to dialysis. Diabetes-related elevated blood sugar can eventually harm kidney blood vessels and nephrons, 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 are the foundation of GFR, hypertension may contribute to the advancement of CKD.4 In individuals with T2DM and CKD, GV (glycemic variability) becomes more complex. Additionally, those with CKD and T2DM who have an eGFR (estimated GFR) of less than 60 mL/min/1.73 m2 are more likely to be diagnosed with faux hypoglycemia, which is low glycated Hb (HbA1c). Additionally, because of its perception in CKD people, the HbA1c test, which measures ABG (average blood glucose) levels over the previous two to three months, has limitations. Red blood cell (RBC) survival periods shorten as eGFR declines, resulting in a lower measured HbA1c. This is explained by the significance of carefully interpreting HbA1c in individuals with CKD and T2DM.5

HbA1c is not only governed by blood sugar levels alone. There are a variety of confounding factors utilized for assessing HbA1c including Hb (hemoglobin) and RBC counts. The present study focuses on assessing GV (glycemic variability) in different CKD stages in subjects with T2DM by capturing two parameters as RBC/hemoglobin count and blood sugar level in subjects which could help in identifying false HbA1c levels.

MATERIALS AND METHODS

In individuals with type 2 diabetes mellitus, the current cross-sectional study sought to evaluate the differences in glycemic status in different chronic kidney stages and their relationship to RBC and Hb levels to their HbA1c levels. The Institute's Outpatient Department provided the study participants. Prior to participation, each subject provided both written and verbal informed consent.

In accordance with WHO criteria6, the study evaluated 312 individuals with type 2 diabetes mellitus and chronic renal disease, including both male and female participants over 30. Hemodialysis patients were also included in Stage V. According to the KDOQI (National Kidney Foundation Kidney Disease Outcomes Quality Initiative) staging criteria, among 156 subjects with I–V CKD and type 2 diabetes mellitus, stage I included subjects with normal/high eGFR >90 mL/min/1.73m2, stage II as eGFR of 60–89 mL/min/1.73m2, stage III as eGFR of 30–59 mL/min/1.73m2, and stage V as eGFR <15 mL/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 testing, and evaluation of CKD sequelae. Participants with type 2 diabetes mellitus, hypertension, and a recent diagnosis of chronic kidney disease (CKD) who attended the Institute throughout the designated study period met the study's inclusion criteria. Included were subjects of both sexes who were at least 30 years old. Subjects with conditions other than hypertension, type 2 diabetes, and chronic kidney disease (CKD), those under 30, pregnant women, smokers, blood donors of any kind, surgery within the last six months, breastfeeding women, menorrhagia, heart failure, kidney stones, and UTIs were all excluded from the study.

The questionnaire was used to hand collect the data on a structured and standardized proforma. The information came from lab reports. Age, gender, weight, and laboratory results were among the information collected. In order to measure biochemical parameters, CBC (complete blood count), and other hematological parameters in addition to HbA1c, approximately 5 mL of intravenous blood was drawn from each subject and split into two tubes, with 2 mL being collected in a vial containing EDTA (ethylene diamine tetra acetic acid). To measure biochemical markers like creatinine and RBS (random blood sugar), an additional 3 milliliters of blood were drawn in a plain tube without an anticoagulant.

A printed questionnaire was used to collect research participants' demographic information and medical history during their visit. Dialysis initiation and the prevalence of CKD were assessed using MDRD. The hospital laboratory used the boronate affinity method to measure HbA1c values as suggested clinically. Auto Hematology Analyzer was used to measure RBC and Hb levels as part of the CBC. A completely automated system pack was used to evaluate RBS.

The Breathe well-being reference chart was used to measure average blood glucose (avBG) levels.Ten WHO criteria, which state that HbA1c readings greater than 7% are considered hyperglycemia, were adhered to for every test. High blood sugar was defined as RBS readings more than 200 mg/dl. Normal RBC counts for males and females were 4–5.9 million/mm3 and 3.8–5.2 million/mm3, respectively, and normal hemoglobin values were 13.5–17.5 gm/dL for males and 12–16 gm/dl for females.

Using SPSS (Statistical Package for the Social Sciences) software, the collected data was statistically analyzed using the Student t-test, ANOVA (analysis of variance), Chi-square test, and assessment of descriptive measures. The mean, standard deviation, frequency, and percentages were used to express the results. A p-value of less than 0.05 was taken into account.

RESULTS

In individuals with type 2 diabetes mellitus, the current cross-sectional study sought to evaluate the differences in glycemic status in different chronic kidney stages and their relationship to RBC and Hb levels to their HbA1c levels. 312 adult participants with type 2 diabetes mellitus (T2DM) were evaluated for the study. RBS, HnA1c, and RBC count were measured for each stage's individuals. The stages were determined using the modification of diet in the renal diseases (MDRD) equation stages I–V.

According to the study's findings, the mean age of the participants was similar for those in CKD stages i–V with p=0.47 for the stage-wise distribution of CKD with different parameters. Stage I CKD had significantly higher RBCx1012/L values, which gradually dropped from stage I to stage V (p=0.00). Additionally, hemoglobin levels considerably decreased from stage I to stage V (p=0.00). HbA1c values showed a significant difference, rising from stage I in stages II and III of CKD and falling in stages IV and V (p=0.01). RBS levels revealed a statistically insignificant difference (p=0.93) between stages I and V of CKD. In comparison to stage I, average blood glucose levels were higher in stages II and III and significantly lower in stages IV and V (p=0.05) (Table 1).

RBS demonstrated a non-significant negative connection to HbA1c with an r-value of 0.074 when it came to the correlation of HbA1c to different study parameters. With an r-value of 0.268 and a p-value of less than 0.01, RBC demonstrated a strong positive connection with HbA1c readings. Additionally, there was a substantial positive association between hemoglobin levels and the HbA1c value, with r-values of 0.376 and p<0.01, respectively (Table 2).

In Group I with HbA1c 4-7%, there were 4, 2, 22, 56, and 140 participants in stages I, II, III, IV, and V, totaling 214 subjects with glycemic variability of 68.4%, according to the stage-wise distribution of CKD in three subgroups from HbA1c. There were 0, 2, 14, 42, and 28 participants in phases I, II, III, IV, and V in Group II with HbA1c of 7–11%, and a total of 86 subjects with a prevalence of glycemic variability of 27.4%. Group III had 12 participants with glycemic variability of 3.6%, including 0, 0, 4, 6, and 2 subjects in stages I, II, III, IV, and V. There were 0, 0, 4, 6, 2, and 12 patients in CKD stages I, II, III, IV, and V, respectively. In all, there were 1.4% (n=2), 1.4% (n=2), 12.6% (n=40), 33.1% (n=104), and 51% (n=160) patients. (Table 3).

DISCUSSION

312 adult participants with type 2 diabetes mellitus (T2DM) were evaluated in this study. RBS, HnA1c, and RBC count were measured for each stage's individuals. The stages were determined using the modification of diet in the renal diseases (MDRD) equation stages I–V. The mean age of the study participants was similar for those in CKD stages i–V with p=0.47, according to the stage-wise distribution of CKD with different parameters. Stage I CKD had significantly higher RBCx1012/L values, which gradually dropped from stage I to stage V (p=0.00). Additionally, hemoglobin levels considerably decreased from stage I to stage V (p=0.00).HbA1c values showed a significant difference, rising from stage I in stages II and III of CKD and falling in stages IV and V (p=0.01). RBS levels revealed a statistically insignificant difference (p=0.93) between stages I and V of CKD. In comparison to stage I, average blood glucose levels were higher in stages II and III and significantly lower in stages IV and V (p=0.05). These findings were in line with those of Freedman BI et al. (2010) and Astor BC et al. (2006), who evaluated individuals with CKD, type 2 diabetes, and hypertension using data similar to the current study.

According to the study's findings, there was a non-significant negative connection between RBS and HbA1c with an r-value of 0.074. With an r-value of 0.268 and a p-value of less than 0.01, RBC demonstrated a strong positive connection with HbA1c readings. Additionally, there was a substantial positive association between hemoglobin levels and the HbA1c value, with r-values of 0.376 and p<0.01, respectively. These results were consistent with those of Portolés J et al. (2021) and Cristy AL et al. (2014), who observed similar correlations between HbA1c and several markers as RBS, RBC, and Hb.

Additionally, the stage-wise distribution of CKD in three subgroups based on HbA1c was observed. In Group I with HbA1c 4-7%, there were 4, 2, 22, 56, and 140 participants in stages I, II, III, IV, and V, totaling 214 subjects with glycemic variability of 68.4%. There were 0, 2, 14, 42, and 28 participants in phases I, II, III, IV, and V in Group II with HbA1c of 7–11%, and a total of 86 subjects with a prevalence of glycemic variability of 27.4%. Group III had 12 participants with glycemic variability of 3.6%, including 0, 0, 4, 6, and 2 subjects in stages I, II, III, IV, and V. There were 0, 0, 4, 6, 2, and 12 patients in CKD stages I, II, III, IV, and V, respectively. There were 1.4% (n=2), 1.4% (n=2), 12.6% (n=40), 33.1% (n=104), and 51% (n=160) patients in total. These results were consistent with the stage-wise distribution of CKD in various HbA1c ranges reported by the authors in the investigations of Agarwal R13 in 2011 and Home P et al.14 in 2005.

CONCLUSIONS

Taking into account its limitations, the current study comes to the conclusion that renal illnesses are typically caused by diabetes mellitus and hypertension, which also contribute to renal anemia. Due to decreased hemoglobin and red blood cell counts, a low HbA1c level in the range of 4% to 7% is observed in the later stages of chronic renal disease with type 2 diabetes. Because low RBC counts result in a misleading glycated hemoglobin percentage, the HbA1c test is unreliable in advanced stages of CKD individuals, which is the study's clinical significance.

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Variables	Stage I	Stage II	Stage III	Stage IV	Stage V	p-value
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

S. No	HbA1c	Stage I	Stage II	Stage III	Stage IV	Stage V	Total	Glycemic variability prevalence (%)
1.	**Group I (4-7)**	4	2	22	56	130	214	68.4
2.	**Group II (7-11)**	0	2	14	42	28	86	27.4
3.	**Group III (11-15)**	0	0	4	6	2	12	3.6
4.	**Total**	4	4	40	104	160	312	
5.	**%**	1.2	1.2	12.6	33.1	51.0		

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