Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL 9, ISSUE 4, 2018

Original Research Paper

GLYCEMIC STATUS IN CKD IN TYPE 2 DIABETES MELLITUS PATIENTS

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ABSTRACT

Background: Diagnostic tests for diabetes and the emergence of chronic diabetic problems include complete blood counts and HbA1c readings. Numerous variables, including hemoglobin, the age of red blood cells in the bloodstream, and the Hb glycation rate, influence HbA1c levels.

Aim: The purpose of this study was to evaluate the differences in glycemic status throughout different phases of chronic renal disease and how these differences relate to RBC, Hb, and HbA1c levels in individuals with type 2 diabetes.

Methods: 312 adult participants with type 2 diabetes mellitus (T2DM) were evaluated for the research. The phases were established in accordance with the renal diseases (MDRD) equation stages I–V, which call for dietary modifications. For each step, the individuals' RBS, HbA1c, and RBC count were measured. The data gathered were analyzed statistically to formulate the results.

Results: Out of the 312 diagnosed study participants, 41.6% were female and 58.3% were male. Importantly, the majority of people with end-stage illnesses (stage V) had HbA1c levels between 4 and 7%. Variations in blood sugar and HbA1c levels were concerning signs of other underlying conditions, such as renal anemia.

Conclusion: Due to reduced hemoglobin and red blood cell counts, a low HbA1c level in the range of 4% to 7% is observed in the latter stages of CKD with T2DM. Because low RBC counts result in a misleading glycated hemoglobin percentage, the HbA1c test is not reliable in patients with severe chronic kidney disease (CKD). This makes the study clinically significant.

Keywords: CKD, Diabetic nephropathy, HbA1c, Renal anemia, Type 2 diabetes mellitus

INTRODUCTION

Chronic kidney disease (CKD) is a chronic, long-term illness in which the kidneys are damaged to the point that they are unable to effectively filter blood. GFR (glomerular filtration rate), which measures how successfully the kidneys filter waste and extra fluid from the blood in the body, is used to categorize chronic kidney disease (CKD) into five phases. renal illnesses deteriorate and renal function decreases with increasing stages. Over time, these phases get worse. The kidneys can remove waste from the circulation in the early phases of chronic kidney disease (CKD I–III). Dialysis may result from the kidneys' increased effort to filter blood in later stages (IV–V) and potential failure. When blood glucose (blood sugar) levels are very high, a disease known as diabetes develops.[1]

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 increased risk of end-stage kidney disease (ESKD) is associated with about 40% of people with CKD and type 2 diabetes mellitus.

Chronic kidney disease (CKD) is a general term that refers to a collection of related disorders and is typically associated with immune system dysfunction. Interstitial fibrosis and/or glomerulosclerosis are common pathophysiological manifestations of kidney disorders. 3 CKD is associated with significant mortality, morbidity, and a poor quality of life in individuals with type 2 diabetes and accounts for individuals with ESKD worldwide. 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 those with CKD and T2DM. 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 indicators, such as the participants' blood sugar level and RBC/hemoglobin count, which may aid in detecting erroneous HbA1c readings.

MATERIALS AND METHODS

Assessing the differences in glycemic status throughout different stages of chronic renal disease and their relationship to RBC and Hb levels to their HbA1c levels in individuals with type 2 diabetes mellitus was the goal of the current cross-sectional investigation.. The research participants came from the Institute's outpatient department. Prior to participation, all individuals gave their written and verbal informed permission.

The study recruited participants of both sexes who were over 30 years old and evaluated 312 individuals with CKD and type 2 diabetes mellitus in accordance with WHO criteria6.

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. Participants under 30 years of age, those with conditions other than hypertension, type 2 diabetes, and chronic kidney disease,

women who were pregnant, smokers, had donated blood of any kind, had undergone surgery within the previous six months, were nursing, had menorrhagia, heart failure, kidney stones, or UTIs. Information was collected manually using a standardized and unified questionnaire. 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. In order to measure biochemical markers like creatinine and RBS (random blood sugar), an additional 3 milliliters of blood were drawn in a simple tube without an anticoagulant.

During their visit, study participants' demographic information was collected, and a written questionnaire was used to collect their medical history. Dialysis start and CKD prevalence were assessed using MDRD. The hospital laboratory used the boronate affinity technique to determine HbA1c readings as clinically advised. The Auto Hematology Analyzer was used to measure the 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 determine the average blood glucose (avBG) levels. 10 All tests were conducted in accordance with WHO recommendations, which state that hyperglycemia is defined as HbA1c levels more than 7%. High blood sugar was defined as RBS readings more than 200 mg/dl. Normal hemoglobin levels were defined as 12–16 g/dL for females and 13.5–17.5 g/dL for males and Male and female RBC counts were typically between 3.8 and 5.2 million/mm3 and 4-5.9 million/mm3, respectively.

The collected data was statistically evaluated using the Student t-test, ANOVA (analysis of variance), Spearman correlation coefficient, Chi-square test, and SPSS (Statistical Package for the Social Sciences) software version 24.0 (IBM Corp., Armonk, NY, USA) for evaluating

descriptive measures. The findings were presented as frequency, percentages, mean, and standard deviation. A p-value of less than 0.05 was taken into account.

RESULTS

Assessing the differences in glycemic status throughout different stages of chronic renal disease and their relationship to RBC and Hb levels to their HbA1c levels in individuals with type 2 diabetes mellitus was the goal of the current cross-sectional investigation. For the study, 312 adults with type 2 diabetes mellitus (T2DM) were assessed.

The phases were established in accordance with the renal diseases (MDRD) equation stages I–V, which call for dietary modifications. For each step, the individuals' RBS, HnA1c, and RBC count were measured.

According to the study findings, the mean age of the participants was similar for those in CKD stages I–V (p=0.47) for the stage-wise distribution of CKD with different parameters. Stage I CKD had substantially higher RBCx1012/L values, which progressively dropped from stage I to V (p=0.00). Additionally, hemoglobin levels considerably decreased from stage I to stage V (p=0.00).

HbA1c values showed a substantial difference, rising considerably from stage I to stages II and III of CKD and falling from stage IV to stage V (p=0.01). The difference between stages I and V of CKD was statistically non-significant, according to RBS values (p=0.93). In comparison to stage I, average blood glucose levels were higher in stages II and III and considerably lower 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. A substantial positive association between RBC and HbA1c readings was observed, with a p-value of less than 0.01 and an r-value of 0.268. Additionally, Table 2 showed a substantial positive association between hemoglobin levels and the HbA1c value, with r-values of 0.376 and $p<0.01$, respectively.

For the stage-wise distribution of CKD in three subgroups based on HbA1c, Group I with HbA1c 4-7% included 214 participants with glycemic variability of 68.4% and 4, 2, 22, 56, and 140 subjects in stages I, II, III, IV, and V. There were 86 participants with a prevalence of glycemic variability of 27.4% in Group II, which included 0, 2, 14, 42, and 28 subjects in stages I, II, III, IV, and V, and a HbA1c of 7–11%.

Group III consisted of 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. There were 0, 0, 4, 6, 2, and 12 patients in CKD stages I, II, III, IV, and V, respectively. The participants' respective percentages were 1.4% (n=2), 1.4% (n=2), 12.6% (n=40), 33.1% (n=104), and 51% (n=160). (Table 3).

DISCUSSION

312 adult participants with type 2 diabetes mellitus (T2DM) were evaluated in this study. The phases were established in accordance with the renal diseases (MDRD) equation stages I–V, which call for dietary modifications. For each step, the individuals' RBS, HnA1c, and RBC count were measured.

According to the stage-wise distribution of CKD with different parameters, the mean age of study participants was similar for those in stages I–V of CKD (p=0.47). Stage I CKD had

substantially higher RBCx1012/L values, which progressively dropped from stage I to V (p=0.00). Hemoglobin levels considerably decreased from stage I to stage V, with a p-value of 0.00. HbA1c values showed a substantial difference, rising considerably from stage I in stages II and III of CKD to stages IV and V (p=0.01). The difference between stages I and V of CKD was statistically non-significant, according to RBS values (p=0.93). Compared to stage I, average blood glucose levels were higher in stages II and III and considerably lower in stages IV and V (p=0.05).

These outcomes were in line with those of studies by Freedman BI et al.9 and Astor BC et al.10, in which the authors evaluated participants with type 2 DM, hypertension, and chronic kidney disease (CKD) using data similar to the current study.

According to the study's findings, RBS had a non-significantly negative connection (r-value of 0.074) with HbA1c when compared to other study parameters. A substantial positive association between RBC and HbA1c readings was observed, with a p-value of less than 0.01 and an r-value of 0.268. Also, with an r-value of 0.376 and a p-value of less than 0.01, hemoglobin levels showed a significant positive connection with the HbA1c value. These results concurred with those of Cristy AL et al. (2014) and Portolés J et al. (2011) in 2021, where the results of the current investigation were similar to the association of HbA1c to several indicators including RBS, RBC, and Hb that the authors reported in their studies. Additionally, the stage-wise distribution of CKD in three subgroups based on HbA1c was observed. In Group I, which had a HbA1c of 4-7%, there were 214 people with glycemic variability of 68.4% and 4, 2, 22, 56, and 140 participants in stages I, II, III, IV, and V. There were 86 participants with a prevalence of glycemic variability of 27.4% in Group II, which included 0, 2, 14, 42, and 28 subjects in stages I, II, III, IV, and V, and a HbA1c of 7–11%.

Group III consisted of 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. There were 0, 0, 4, 6, 2, and 12 patients in CKD stages I, II, III, IV, and V, respectively. The individuals were distributed as follows: 1.4% (n=2), 1.4% (n=2), 12.6% (n=40), 33.1% (n=104), and 51% (n=160). These results 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

Given its limitations, the current study comes to the conclusion that diabetes mellitus and hypertension, which also contribute to renal anemia, are the main causes of kidney disorders.

A low HbA1c level between 4% and 7% is observed in the latter stages of CKD with T2DM because to low hemoglobin and RBC counts. Because low RBC counts result in a misleading glycated hemoglobin percentage, the HbA1c test is not reliable in patients with severe chronic kidney disease (CKD). This makes the study clinically significant.

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Variables	Stage I	Stage II	Stage III	Stage IV	Stage V	p-value
Mean age (yr)	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

HbA1c	Correlation coefficient (r)	p-value	Remarks
RBS	**0.074**	>0.05	Negative correlation
RBC	**0.268**	**<0.01**	Positive correlation
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