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# Association of HbA1c Values with Cardiovascular Complication in Diabetic patients on Hemodialysis

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ORIGINAL ARTICLE

# Association of HbA1c Values with Cardiovascular Complication in Diabetic patients on Hemodialysis

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Abstract

*Background:* ***Diabetes is a long-term metabolic disease marked by elevated blood sugar values. People all around the globe suffer from it often, and those who have end-stage renal disease (ESRD) are more likely to have it.***

*Aim and objectives:* ***To examine the relationship between diabetic dialysis patients' HbA1c levels and cardiovascular events.***

*Patients and methods:* ***This prospective observational and analytical research was conducted on 60 diabetic patients on hemodialysis at the dialysis Unit of the National Institute of Urology and Nephrology, Egypt.***

*Results:* ***The mean HBA1C was statistically substantially more significant in the cases with cardiovascular complications as compared to the cases without cardiovascular complications. The prevalence of cases with uncontrolled diabetes was statistically substantially more significant in the cases with cardiovascular complications as compared to the cases without cardiovascular complications. The best cutoff point of HbA1C to differentiate the occurrence of cardiovascular complications was > 8.15 %, with 84.6 sensitivity and 614% specificity. The AUC was 0.709, with a statistically substantial value. The incidence of Myocardial infarction, PAD, and heart failure was statistically more significant in the cases with uncontrolled diabetes as compared to the cases with controlled diabetes.***

*Conclusion:* ***Cardiovascular complications up to death are frequent in diabetic patients on hemodialysis. Uncontrolled diabetes mellitus (represented by elevated HbA1C) is associated with a greater prevalence incidence of complications in diabetic patients on hemodialysis. Adequate and timely diagnosis and treatment of cardiovascular complications could improve the quality of life and postpone complications in these patients.***

*Keywords:* Cardiovascular Complication; ESRD; Hemodialysis

## 1. Introduction

Diabetes is a long-term metabolic disease marked by elevated blood sugar levels. It is a common condition among people worldwide and is particularly prevalent in those with end-stage renal disease (ESRD) who require dialysis management. The prevalence of diabetes in dialysis patients is estimated to be around 30-50%.[1]

Hemoglobin A1c (HbA1c) values are often used to assess diabetes patients' long-term blood glucose management. This test is conducted in a lab and measures the average blood glucose value during the previous two to three months.[2]

Studies have revealed that higher HbA1c values are associated with an elevated risk of cardiovascular conditions in diabetic patients. This is because when blood glucose levels are high over a prolonged period, it may harm neurons and blood vessels, leading to cardiovascular disease and other complications.[3]

However, despite the strong connection between HbA1c values and cardiovascular events in diabetic dialysis patients, it is crucial to remember that other factors, such as blood pressure, cholesterol, and body mass index, may also play a role. For example, uncontrolled hypertension and dyslipidemia are common comorbidities among dialysis patients with diabetes, which can further increase the risk of cardiovascular events.[4]

Therefore, it is essential for diabetic dialysis patients not only to monitor their HbA1c values closely but also to manage other risk factors in order to reduce their risk of complications. This may include taking medications to control blood pressure and cholesterol and altering one's lifestyle to include regular exercise and a balanced diet.[5]

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Diabetic dialysis patients should aim to achieve HbA1c values below 7%, as recommended by the American Diabetes Association, which is considered to be the target for reasonable glucose control. This can be achieved through lifestyle changes, medications, and close monitoring.[6]

This study examined the association between HbA1c values and cardiovascular events in diabetic dialysis patients.

## 2. Patients and methods

This prospective observational and analytical research was conducted on 60 diabetic patients on hemodialysis at the dialysis Unit of the National Institute of Urology and Nephrology, Egypt.

Inclusion Criteria: Diabetic dialysis patients (patients with both diabetes and end-stage renal illness requiring dialysis treatment), patients who have undergone at least one HbA1c test within the past year, patients who have complete data on demographic information, medical history, and laboratory results and patients with dialysis adequacy (KT/V 1.2)

Exclusion criteria: Patients with secondary causes of diabetes, such as pancreatitis or cystic fibrosis; Patients with Liver cell failure; Patients unable to provide informed consent; Patients who have not undergone an HbA1c test within the past year; and Patients with missing or incomplete data on demographic information, medical history, and laboratory results.

Sample size: The sample size was determined using STATCALC, taking into account the following assumptions, based on research conducted by Sturm et al.,[7] Epi Info - A two-sided confidence level of 95%, an 80% power, and a 5% α error. 53 was the final maximum sample size that could be obtained from the Epi-Info output. In order to account for potential incidences of dropout during follow-up, the sample size was raised to 60 individuals.

Diagnosis of diabetes: The patient had previously established a diagnosis of T2DM as per the American Diabetes Association(ADA).[8] The diagnosis was made using the plasma glucose standards, which included HbA1C > 6.5%, fasting blood glucose ≥ 126 mg/dl, or 2-hour postprandial blood glucose ≥ 200 mg/dl on a 75-g oral glucose tolerance test.

Sampling method: The cases were selected by random sampling.

Ethical consideration: The Al-Azhar University Faculty of Medicine's local research committee accepted the study's overall concept. Privacy and confidentiality were upheld at every stage of the research. Patients could leave the research at any moment and would not face any repercussions. There was no alternative use for the collected data. Before enrolling in the research, all participants provided written informed permission that detailed the purpose of the investigation and the procedures that were initiated.

methods

Every sufferer endured the following: Complete history taking, full clinical examination, laboratory investigations, and radiology.

Samples collection and preparation: Blood samples were taken, and the standard protocols for venipuncture sample collection were scrupulously adhered to. Using a sterile venipuncture, ten milliliters of venous blood were taken from each participant in the research. One milliliter was given into EDTA blood (CBC) for the complete blood count. Two milliliters were added to a citrated tube to measure the erythrocyte sedimentation rate (ESR). After centrifuging the remaining volume for the serum preparation for 15 minutes at 3000 rpm, the tube was left plain for clotting. The Hitachi 912 auto-analyzer (Roche Diagnostics GmbH, Mannheim, USA, D-68298) was used to measure the serum triglyceride, total cholesterol, and fasting plasma glucose using colorimetric methods. Phosphotungestic acid and magnesium ions were used to precipitate all lipoproteins except for the HDL fraction found in the supernatant and analyzed using an auto-analyzer to determine HDL-C. HbA1c was determined by cation-exchange HPLC using a D-10 hemoglobin testing system by a kit from Bio-Rad, California, USA.

Radiology: Abdominal sonography, emphasizing the kidneys.

Ankle-brachial index (ABI): A single, skilled examiner used an 8 MHz portable Doppler and a sphygmomanometer with a cuff appropriate for the limbs' circumference to assess the ankle-brachial index. The ratio of the highest SBP recorded in the arms (brachial artery) to the maximum SBP measured at the ankle (posterior tibial and dorsalis pedis arteries) was used to calculate the ABI for each leg.

Classification: The American College of Cardiology/American Heart Association (ACC/AHA)[9] standards provide the basis for the test's methodology and the ABI categorization. ABI values in the range of 0.91 to 1.39 were regarded as typical.

Follow-up and Outcomes: The cases were followed up during the length of hospital admission and followed up at one month and six months. Acute myocardial infarction, identified by troponin I [cTnI] >1.5 µg/l in addition to symptoms or evidence from an ECG. Heart failure exacerbations (cTnI >0.11 with radiological evidence or recorded clinical symptoms). Determination of PAD: Values ≤ 0.90 were considered compatible with PAD. Angiographic lesion (< 50% obstruction). Cerebrovascular accidents. Mortality related to

cardiac events. The term "CV mortality" referred to a composite of deaths from myocardial infarction, heart failure, cardiogenic shock, cerebrovascular events, and aortic illnesses, as well as sudden deaths in which non-cardiac deaths could not be ruled out.[10]

## 3. Results

There were 45% females and 55% males. The median age of the cases was 51.58 ± 7.76 years with range between 38 and 65 years (Table 1)

*Table 1. Demographic data in the research cases*

| ITEMS | STUDY CASES N= 60 | |
|---|---|---|
| | Number | Percent (%) |
| AGE (YEARS) | | |
| MEAN ± SD | 51.58 ± 7.76 | |
| MEDIAN (RANGE) | 51 (38- 65) | |
| SEX | | |
| FEMALES | 27 | 45 |
| MALES | 33 | 55 |

Categorical data presented as Number (%), Continuous data are presented as mean ± SD/ median (Min-Max)

The incidence of cardiovascular complications was 43.3%. the cardiovascular complications included Myocardial infarction in 23.3 %, significant angiographic lesion (> 50%) in 18.3%, PAD in 28.3 %, Cerebrovascular accidents in 20 %, heart failure in 15% and cardiovascular related mortality in 15% (Table 2).

*Table 2. Incidence of Cardiovascular Complication in the cases of the study*

| ITEMS | STUDY CASES N= 60 | |
|---|---|---|
| | Number | Percent (%) |
| CARDIOVASCULAR COMPLICATION | | |
| PRESENT | 26 | 43.3 |
| ABSENT | 34 | 56.7 |
| TYPE OF CARDIOVASCULAR COMPLICATION | | |
| MYOCARDIAL INFARCTION | 14 | 23.3 |
| SIGNIFICANT ANGIOGRAPHIC LESION > 50% | 11 | 18.3 |
| PAD | 17 | 28.3 |
| CEREBROVASCULAR ACCIDENTS | 12 | 20 |
| HEART FAILURE | 9 | 15 |
| CARDIOVASCULAR RELATED MORTALITY | 9 | 15 |

Categorical data presented as Number (%)

The median age of the cases with cardiovascular complications was statistically substantially greater as compared with the cases with no cardiovascular complications (p=0.002). There was no statistical substantial variation in the sex distribution or the BMI. Moreover, there was no statistical substantial variation between the cases with and without cardiovascular complications regarding the percentage of cases with HTN, smoking and dyslipidaemia (Table 3).

*Table 3. Relation between cardiovascular complication and demographic data and other risk factors*

| VARIABLES | CARDIOVASCULAR COMPLICATION (N= 26) | NO CARDIOVASCULAR COMPLICATION (N= 34) | P-VALUE |
|---|---|---|---|
| AGE | 55.04 ± 7.35 | 48.94 ± 7.09 | 0.002* |
| SEX | | | |
| MALES | 13 (50%) | 20 (58.8%) | 0.496 |
| FEMALES | 13 (50%) | 14 (41.2%) | |
| BMI | 32.98 3.12 | 31.94 3.94 | 0.273 |
| HYPERTENSION | 18 (69.2%) | 24 (70.7%) | 0.909 |
| SMOKERS | 7 (26.9%) | 15 (44.1%) | 0.141 |
| DYSLIPIDEMIA | 18 (69.2%) | 21 (61.8%) | 0.548 |

*: Statistically significant (p< 0.05)

The dialysis duration was statistically substantially longer in the cases with cardiovascular complication as compared to the cases with no cardiovascular complication. Otherwise, the serum creatinine level, GFR and Kt/V showed no statistically substantial variation between the two groups (Table 4).

*Table 4. Relation between the cardiovascular complication and kidney functions and dialysis criteria*

| VARIABLES | CARDIOVASCULAR COMPLICATION (N= 26) | NO CARDIOVASCULAR COMPLICATION (N= 34) | P-VALUE |
|---|---|---|---|
| DURATION OF DIALYSIS (YEARS) | 10 (3 – 15) | 7 (2 – 15) | 0.005* |
| CREATININE (MG/DL) | 2.3 (1.6 – 6.8) | 2.9 (1.5 – 7.8) | 0.370 |
| GFR (ML/MIN/1.73 $M^2$) | 10.81 ± 2.56 | 10.21 ± 2.88 | 0.404 |
| KT/V | 1.37 ± 0.14 | 1.37 ± 0.11 | 0.539 |

*: Statistically significant (p< 0.05)

The median HBA1C was statistical substantially greater in the cases with cardiovascular complications as compared to the cases without cardiovascular complications (p = 0.010). The prevalence of cases with uncontrolled diabetes was statistical substantially greater in the cases with cardiovascular complications as compared to the cases without cardiovascular complications (p = 0.002). (Table 5)

*Table 5. Relation between the cardiovascular complication and HBA1C and the degree of diabetes control*

| VARIABLES | CARDIOVASCULAR COMPLICATION (N= 26) | NO CARDIOVASCULAR COMPLICATION (N= 34) | P-VALUE |
|---|---|---|---|
| HBA1C (%) | 8.43 ± 1.58 | 7.25 ± 1.79 | 0.010* |
| GLYCEMIC CONTROL | | | |
| CONTROLLED | 3 (11.5%) | 17 (50%) | 0.002* |
| UNCONTROLLED | 23 (88.5%) | 17 (50%) | |

*: Statistically significant (p< 0.05)

The mean ejection fraction was statistically significantly lower in the cases with cardiovascular complications as compared to the cases without cardiovascular complications (p =

0.035). Also, the prevalence of cases with ejection fraction < 40% was statistically significantly higher in the cases with cardiovascular complications as compared to the cases without cardiovascular complications (p = 0.033). Moreover, the prevalence of cases with mild hypokinesia and severe hypokinesia was statistically significantly higher in the cases with cardiovascular complications as compared to the cases without cardiovascular complications (p = 0.047) (Table 6).

*Table 6. Relation between the cardiovascular complication and ejection fraction and the degree of diabetes control*

| VARIABLES | CARDIOVASCULAR COMPLICATION (N= 26) | NO CARDIOVASCULAR COMPLICATION (N= 34) | P-VALUE |
|---|---|---|---|
| EJECTION FRACTION (%) | 45.04 ± 9.14 | 50.18 ± 9.25 | 0.035* |
| EJECTION FRACTION CATEGORIES | | | |
| EF < 40% | 9 (34.6%) | 4 (11.8%) | 0.033* |
| EF ≥ 40% | 17 (65.4%) | 30 (88.2%) | |
| HYPOKINESIA OF THE WALL | | | |
| NORMOKINESIA | 16 (61.5%) | 29 (85.3%) | 0.047* |
| MILD HYPOKINESIA | 7 (26.9%) | 5 (14.7%) | |
| SEVERE HYPOKINESIA | 3 (11.5%) | 0 (0%) | |

*: Statistically significant (p< 0.05)

The best cutoff point of HbA1C to differentiate the occurrence of the cardiovascular complications was > 8.15 % with 84.6 % sensitivity and 61.4% specificity. The AUC was 0.709 with a statistically significant value (p= 0.006) (Table 7)

*Table 7. Predictive value of HbA1C in prediction of cardiovascular complications*

| | HBA1C (%) |
|---|---|
| AUC | 0.709 |
| CUT OFF POINT | > 8.15 |
| SENSITIVITY | 84.6 % |
| SPECIFICITY | 61.4 % |
| PPV | 67.3 % |
| NPV | 78.6 % |
| ACCURACY | 76.2 % |
| P | 0.006* |

AUC: Area under curve, PPV: positive predictive value, NPV: Negative predictive value

Figure 1 showed that the incidence of Myocardial infarction, PAD and heart failure were statistically significantly higher in the cases with uncontrolled diabetes as compared to the cases with controlled diabetes. Moreover, the incidence of Angiographic lesion (< 50% obstruction), Cerebrovascular accidents and CV related mortality were higher in the cases with uncontrolled diabetes as compared to the cases with controlled diabetes, but it didn't reach a statistically significant value.

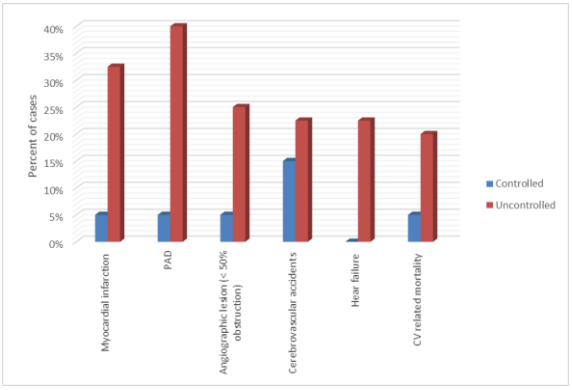


Figure 1. Relation between the degree of diabetic control and the incidence of individual cardiovascular complications

## 4. Discussion

The current study included 60 diabetic cases on hemodialysis. Our results showed that the median age of the studied cases was 51.58 ± 7.76 years, ranging between 38 and 65 years. 45% were females, and 55% were males.

Research by Mukherjee T et al.[11] noted similar distributions of age and gender. The finding that ESRD is more common in this group might help explain this.

The present study revealed that the incidence of cardiovascular complications was 43.3%, including 23.3 % had Myocardial infarction, 18.3% had significant angiographic lesions of more than 50%, 28.3 %PAD, 20 % had Cerebrovascular accidents, 15% had heart failure and 15%. she had cardiovascular-related mortality.

Similarly, our findings, in line with Sturm et al.[7] who, revealed that the incidence of cardiovascular complications among diabetic patients on hemodialysis was 48.7% (38/78(cases.

Our results showed that the duration of dialysis was statistically substantially longer in the cases with cardiovascular complications compared to those with no cardiovascular complications. Otherwise, the serum creatinine level, GFR, and Kt/V showed no statistically substantial variation between the two groups. We found that the median age of the cases with cardiovascular complications was statistically more significant than those without cardiovascular complications (p=0.002). At the same time, there was no statistically substantial variation in the sex distribution or the BMI.

The present study agrees with Aljarid et al.[12], who revealed that the group with cardiovascular problems was characterized by advanced age (61.67 years vs. 58.05 years in the other group) and that there was a substantial age disparity (p = 0.048) between the two groups.

This research found that the mean HBA1C was statistically more significant in cases with cardiovascular complications than those without cardiovascular complications (p = 0.010). Also, our results revealed that the prevalence of cases with uncontrolled diabetes was statistically substantially more significant in the cases with cardiovascular complications than in the cases without cardiovascular complications (p = 0.002).

Similarly, our findings were in line with Rhee et al.[13], who revealed that in an extensive prospective investigation of the connection between glycemic control and cardiovascular results in a cohort of occurrence US patients on hemodialysis with DM, greater levels of HbA1c were positively linked with more excellent rates of MI and cardiovascular mortality, but not with the rates of stroke, PAD, or all-cause mortality. Similarly, an examination of data from the Dialysis Outcomes and Practice Patterns Study of patients undergoing hemodialysis with diabetes mellitus showed that mortality increased at lower and greater levels as HbA1c increased from 7% to 7.9%. The hemodialysis patients were the subject of the investigation.[14]

Our results demonstrated that the best cutoff point of HbA1C to differentiate the occurrence of cardiovascular complications was > 8.15 %, with 84.6 sensitivity and 614% specificity. The AUC was 0.709, with a statistically substantial value (p= 0.006). We found that the incidence of Myocardial infarction, PAD, and heart failure was statistically substantially more significant in the cases with uncontrolled diabetes than in the cases with controlled diabetes.

Also, our results are consistent with Ricks et al.[15], who revealed that in diabetic MHD patients, a time-averaged A1C of ≥8% or a time-averaged blood glucose of ≥200 mg/dL seems to be associated with increased all-cause and cardiovascular deaths. This was likewise in the same vein as Salem et al.[16], who revealed that the prevalence of CVD was strongly positively correlated with HbA1c.

Our results showed that the incidence of Myocardial infarction, PAD, and heart failure were statistically significantly higher in the cases with uncontrolled diabetes as compared to the cases with controlled diabetes. Moreover, we found that the incidence of Angiographic lesions (< 50% obstruction), Cerebrovascular accidents, and CV-related mortality were higher in the cases with uncontrolled diabetes as compared to the cases with controlled diabetes, but it did not reach a statistically significant value.

Also, our findings are in line with those of NeitherOkada et al.[17]. Neither HbA1c levels nor Glycated albumin levels at the initiation of dialysis or on chronic dialysis were associated with all-cause mortality, CV mortality, or the development of CV diseases in diabetic ESRD patients. However, poor glycemic control, as reflected by higher GA levels, may be associated with the development of CV diseases.

### *4. Conclusion*

Cardiovascular complications up to death are frequent in diabetic patients on hemodialysis. Uncontrolled diabetes mellitus (represented by elevated HbA1C) is associated with a greater prevalence of complications in diabetic patients on hemodialysis. Adequate and timely diagnosis and treatment of cardiovascular complications could improve the quality of life and postpone complications in these patients.

## Disclosure

The authors have no financial interest to declare in relation to the content of this article.

## Authorship

All authors have a substantial contribution to the article

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## Conflicts of interest

There are no conflicts of interest.

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