Original Article

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Impact of Hypoglycaemia on Heart Rate in Diabetic versus Non Diabetic Patients on Haemodialysis: A Cross-sectional Study

Internal Medicine Section

CHARAN BALE[1], ATUL SAJGURE[2], SHREEHARSH GODBOLE[3]

ABSTRACT

Introduction: Patients with Chronic Kidney Disease (CKD) on maintenance Haemodialysis (HD) are at risk of hypoglycaemia during HD. This is especially important in patients with diabetes mellitus. Patients with CKD are also known to have heart rate variability during HD.

Aim: This study aims to study the impact of hypoglycaemia on heart rate in diabetic versus non diabetic patients undergoing maintainence HD.

Materials and Methods: This was a cross-sectional study done at a tertiary care centre in Western India from July 2022 to October 2024. A total of 50 patients of CKD on maintenance HD were enrolled. They were monitored for two consecutive HD sessions, each of four hours. Participants were divided into two groups of 25 participants each- 'diabetic group', having patients with diabetes mellitus, and 'non diabetic group', comprising of patients without diabetes mellitus. Continuous blood glucose was monitored along with heart rate for the time on HD. Hypoglycaemia was checked for association with heart rate variability at the time of the hypoglycaemic episode.

Results: Hypoglycaemia was seen in 7 (28%) of the diabetic group, and in 2 (8%) of non diabetic group (p=0.0657). All hypoglycaemic episodes were asymptomatic. Patients with diabetes have a higher heart rate during a hypoglycaemic event, compared to non diabetic patients (p=0.0002).

Conclusion: Hypoglycaemia was more common in patients with diabetes with CKD on HD, though not significant. This hypoglycaemia was also associated with a higher heart rate in patients with diabetes. Hypoglycaemia was also seen in patients not having diabetes mellitus. The study emphasises the importance of monitoring of blood sugar levels along with heart rate variability in patients of CKD during HD.

Keywords: Blood glucose, Diabetes mellitus, Renal dialysis

INTRODUCTION

Diabetic Kidney Disease (DKD) is now the leading cause of CKD in many countries [1]. Patients with diabetes and CKD on maintenance HD have increased risk of morbidity and premature mortality [1]. Patients with CKD on maintenance HD are at increased risk and more vulnerable to hypoglycaemic episodes [2]. HD can cause a significant decrease in blood sugar levels, both in patients who have diabetes mellitus and those who do not [3]. In patients with CKD, defective counter-regulatory mechanisms reduced renal gluconeogenesis and hypoglycaemia unawareness might result in frequent asymptomatic hypoglycaemic events [2]. With the advent of Continuous Glucose Monitoring (CGM), it is now possible to monitor the glycaemic status with better precision in patients with CKD on maintenance HD [3].

Patients with CKD on maintenance HD often have autonomic nervous system dysfunction [4]. This can lead to cardiac death in HD patients [5]. Baroreceptor sensitivity is a measure of the function of the autonomic nervous system [6]. Activation of the sympathetic nervous system leads to tachycardia and activation of parasympathetic nervous system leads to bradycardia [7]. Thus heart rate can be used to assess the autonomic nervous system.

Previous studies have been done by measuring the heart rate during hypoglycaemia in patients with diabetes mellitus [8,9], or measuring the Resting Heart Rate (RHR) in patients on HD [10]; but a study measuring the association of heart rate during hypoglycaemia in patients of diabetes mellitus on HD was lacking. The present study aims to fill this gap, by assessing how hypoglycaemic episodes are associated with heart rate in patients of CKD undergoing maintenance HD.

MATERIALS AND METHODS

This was a cross-sectional study done at a tertiary care centre in Western India from July 2022 to October 2024. This study was approved by the Institutional Ethics Committee (Research Protocol No. IESC/S.SP/11/2022). A total of 50 patients of CKD on maintenance HD were enrolled. The study participants were monitored for two consecutive HD sessions, each session consisting of four hours.

A convenience sample of 50 participants was included. Study participants were divided into two groups- 'diabetic group', comprising of patients with diabetes mellitus, and 'non diabetic group', comprising of patients without diabetes mellitus, each arm had 25 participants. Continuous blood glucose was checked for the amount of time the patients were on HD and the heart rate was monitored using a Holter machine.

Study Procedure

Although there is no universally accepted definition of hypoglycaemia, for the purposes of this study, it was defined as a blood glucose level less than 80 mg/dL, as it is known that the first response of the body to decreasing blood glucose levels, that is, the inhibition of insulin secretion by pancreatic β cells starts at this level [11]. Bradycardia was defined as <60 beats per minute [12] and tachycardia was defined as >90 beats per minute [13].

In the present study, continuous blood glucose was monitored for the amount of time the patient was on HD. Hypoglycaemia was checked for association with heart rate changes at the time of the hypoglycaemic episode. The most popular technique used for CGM systems relies on the glucose oxidation reaction [14]. For the study, FreeStyle Libre Pro (Abbott Inc.) was used.

The patient was also monitored for heart rate for the same time using a Holter machine. The Holter machine is a portable battery operated device that connects to the patient with bipolar electrodes and provides recordings from up to 12 electrocardiographic leads [15]. A TLC5000 Holter Monitor (Contec Co., Ltd.,) was used in this study.

The parameter Kt/V is a measurement of the efficacy of a HD session. It identifies the effective removal of a specific solute (clearance K) resulting from a given treatment (characterised by time t) in a given patient (with a specific volume of distribution V for the solute considered). Operationally, Kt/V is a dimensionless number [16].

STATISTICAL ANALYSIS

The IBM Statistical Package for the Social Sciences (SPSS) Statistics software was used for statistical analysis. The Chi-square test was used for the non continuous variables. The unpaired t-test was used for continuous variables. $p<0.05$ was considered significant.

RESULTS

A total of 50 patients of CKD on maintenance HD were enrolled. They were divided into two groups- 'Diabetic Group' and 'Non diabetic Group', 25 participants in each group. The demographic data is described in [Table/Fig-1]. The mean age of the study population was 52.7±12.21 years. All the participants had hypertension, five (10%) had ischemic heart disease, 3 (6%) had a history of cerebrovascular accident, and one (2%) had a ventricular septal defect [Table/Fig-1].

Parameter	Value
Age	52.7±12.21 years
Gender	
Male	27 (54%)
Female	23 (46%)
Access	
Cuffed tunnelled catheter	43 (86%)
Arteriovenous (AV) Fistula	7 (14%)
Vintage	5.82±5.00 months
Kt/V	1.38±0.19
Diabetes	25 (50%)
Insulin	23 (46%)
Oral Hypoglycaemic Agents (OHA)	2 (4%)
Non Diabetes	25 (50%)
Hypertension	50 (100%)
No. of antihypertensives	
1	10 (20%)
2	26 (52%)
3	12 (24%)
4	2 (8%)
Co-morbidities	
Ischemic Heart Disease (IHD)	5 (10%)
Cerebrovascular Accident (CVA)	3 (6%)
Ventricular Septal Defect (VSD)	1 (2%)

[Table/Fig-1]: Demographic data of study cohort (n=50).

Diabetic patients: The cohort with diabetes had 16 (64%) males average age was 57.36±10.30 years. The mean HD vintage of the paticipants was 5.6±3.98 months, and kt/V was 1.35±0.17. The mean urea was 96.92±33.37279 mg/dL, mean creatinine was 6.012±1.62089 mg/dL, mean Na was 137.64±4.872371 meq/dL and mean K was 4.3528±0.676686 meq/dL [Table/Fig-2]. Cuffed tunnelled catheter was the HD access in 22 (88%) patients, while the remaining three (12%) had arteriovenous fistula. Of these 25 diabetics, 23 (92%) patients were on Insulin, hypoglycaemia was observed in 7 (28%) patients, average blood sugar level was 122.3±51.61 mg/dL. Heart rate changes as tachycardia were observed in 16 (64%) patients. No bradycardia was recorded in the cohort. The mean heart rate was 89.04±11.40 beats per minute. The mean heart rate in those having hypoglycaemia was 90.22±12.42 beats per minute [Table/Fig-3].

Parameter	Diabetes group	Non-diabetes group	p-value
Age (years)	57.36±10.30	48.04±12.38	0.0057
Vintage (months)	5.6±3.98	6.04±5.91	0.7593
Kt/V	1.35±0.17	1.41±0.21	0.3183
Urea (mg/dL)	96.92±33.37	106.6±39.84	0.3564
Creatinine (mg/dL)	6.01±1.62	8.36±3.51	0.0039
Na (mmol//L)	137.64±4.87	135.64±5.50	0.1802
K (mmol/L)	4.35±0.67	4.50±0.73	0.4380

[Table/Fig-2]: Descriptive data of both the groups.

Parameter	Diabetes group	Non-diabetes group	p-value
Hypoglycaemia N (%)	7 (28%)	2 (8%)	0.0657
BSL (mg/dL)	122.3±51.61	113.8±20.28	0.4473
Heart Rate changes (tachycardia) N (%)	16 (64%)	7 (28%)	0.0080
Heart Rate (beats per minute)	89.04±11.40	87.92±11.65	0.7328
Heart Rate+Hypoglycaemia (beats per minute)	90.22±12.42	78.66±7.02	0.0002

[Table/Fig-3]: Hypoglycaemia and heart rate in diabetic group and non diabetic group.

Non diabetic patients: The cohort of non diabetic group consisted had 11 (44%) males with mean age of 48.04±12.38 years. The average HD vintage of the participants was 6.04±5.91 months, and kt/V was 1.41±0.21. The mean urea was 106.6±39.84763 mg/dL, mean creatinine was 8.3608±3.514631 mg/dL, mean Na was 135.64±5.506663 meq/dL and mean K was 4.5096±0.739687 meq/dL. One (4%) each had ischemic heart disease and history of cerebrovascular accident. Cuffed tunnelled catheter was the HD access in 21 (84%) patients, while four (16%) had arteriovenous fistula [Table/Fig-2]. Hypoglycaemia was observed in two (8%) patients. The average blood sugar level was 113.8±20.28 mg/dL. Heart rate changes were observed in 7 (28%) patients, all being tachycardia. The mean heart rate was 87.92±11.65 beats per minute. The mean heart rate in those having hypoglycaemia was 78.66±7.02 beats per minute [Table/Fig-3].

Significantly more number of patients exhibited tachycardia during hypoglycaemic episodes in the diabetic group when compared to the non diabetic group (p=0.008) [Table/Fig-3].

DISCUSSION

In the present study, hypoglycaemia was seen in 28% of the diabetic group, while 8% of those in the non diabetic group had hypoglycaemia (p=0.0657). All the patients who had hypoglycaemia in the study were asymptomatic at the time of the hypoglycaemic episode. Asymptomatic hypoglycaemia has its own implications, being associated with increased cardiovascular events and mortality. Impaired counter regulatory mechanisms and hypoglycaemia unawareness are the main causes for severe hypoglycaemia. Hypoglycaemia has also been found to be common in patients with diabetes mellitus, compared to those who do not have diabetes mellitus [17].

In a study conducted by Gai M et al., on 12 patients, the intradialytic glucose showed a decreasing trend after starting dialysis, with values falling below dialysate glucose concentration for most (87%) of the dialysis session. Lowest average glucose was 79 (45-138) mg/dL after a median of 200 (135-230) minutes. Two patients developed hypoglycaemia during HD and both were asymptomatic. After dialysis, the mean peak value of blood glucose was 187±47 mg/dL reaching after a mean time of 152.73±35 minutes [18]. In the present study, hypoglycaemia was seen in 7 (28%) of the diabetic group, while 2 (8%) of those in the non diabetic group had hypoglycaemia (p=0.0657). All the patients who had hypoglycaemia in the study were asymptomatic at the time of the hypoglycaemic episode. In a single centre study conducted by Gungon MCH,

Cunanan EC on 75 patients of CKD on maintenance HD, the prevalence of hypoglycaemia was 12%. The researchers measured predialysis and hourly intradialytic serum glucose levels. They concluded that there is an increased rate of hypoglycaemia with old age (p=0.0028) and hospitalised patients (p=0.001). They also identified presence of coronary artery disease and frequency of HD as the predictors of hypoglycaemia in their study [19]. In the present study, the prevalence of hypoglycaemia was greater in the diabetic group 7 (28%). The cohort of the diabetic group (57.36±10.30 years) was older than the non diabetic group (48.04±12.38 years) and this was significant (p=0.0057).

The absence of bradycardia in the present study could be because excessive sympathetic nervous system activation that is prevalent in patients of CKD [20]. When hypoglycaemia does occur, the difference in the mean heart rates in the two groups of the present study assumes significance. Patients with diabetes had a higher heart rate during a hypoglycaemic event, compared to non diabetic patients. Patients with diabetes may have sympathetic overactivity along with vagal impairment and increased activation of the Renin-Angiotensin-Aldosterone (RAA) system [21]. Thus, patients with diabetes may have excessive sympathetic nervous system activation, making them prone for a higher heart rate.

Tsai M et al., conducted a cohort study investigating the relationship between RHR and End-Stage Renal Disease (ESRD) risk. The study analysed data from 476,347 Taiwanese adults, of which 2504 participants had ESRD. Participants with a higher RHR (>80 bpm) had a higher prevalence of proteinuria, had a lower eGFR and a higher likelihood of developing CKD. The RHR and CKD had a J shaped risk relationship. All cause mortality and cardiovascular mortality also increased with increasing RHR [10]. In the present study, tachycardia was seen in 16 (64%) diabetic patients, while in non diabetics, tachycardia was seen in 7 (28%) patients (p=0.0080). Bradycardia was not seen in any of the patients. In a study by Andersen A et al., assessed the effect of hypoglycaemia on cardiac rhythm and cardiac repolarisation in 21 insulin-treated patients with type 2 diabetes and compared it with 21 matched controls without diabetes. The baseline heart rate in patients with diabetes was 67.1±10.7 beats per minute and was 60.0±9.6 in the control group (p=0.027). Hypoglycaemia was induced by insulin using a clamp procedure, and electrocardiographic monitoring was done throughout the period. A marked increase in heart rate was observed in both groups during hypoglycaemia compared to the fasting glucose values (p=<0.0001) [8]. Similarly, in this study also tachycardia was seen during hypoglycaemic episodes. The heart rate in diabetic patients during hypoglycaemias was significantly higher than the non diabetic patient (p=0.0002).

Chow E et al., conducted a study to evaluate the risk of arrhythmias during hypoglycaemia. A total of 25 patients with type 2 diabetes underwent simultaneous continuous interstitial glucose and ambulatory electrocardiogram monitoring for five days. The heart rate during hypoglycaemia was 76±12 beats per minute, while the heart rate when hypoglycaemia was not present was 73±11 beats per minute (p=0.51). However, the study did show an increase in arrhythmias that was coincident with hypoglycaemic periods [9]. In the present study, the heart rate at the time of hypoglycaemia in diabetic patients was 90.22±12.42 beats per minute, while that in non diabetics was 78.66±7.02 beats per minute (p=0.0002). This was a significant finding. However, no symptoms were observed in any of the patients during the hypoglycaemic episode.

The present study suggests that blood glucose levels fluctuate during HD. This phenomenon was observed regardless of diabetes mellitus, though it is commoner in patients having diabetes. The heart rate was also higher in these patients. Although these findings are preliminary, they suggest the need for a combined monitoring of blood glucose levels along with heart rate. This may have implications in cardiovascular morbidity and mortality.

Limitation(s)

The present study was conducted in a single centre. The sample size is relatively small, which limits the statistical power. The study findings need to be confirmed in a multicentre trial. Excessive ultrafiltration increases heart rate. The interdialytic weight gain, the main determinant of ultrafiltration rate, has seasonal as well as individual variations. Variations in diet, including food consumed during dialysis, may confound the blood glucose levels. Such confounding factors like ultrafiltration rate and differences in dietary intake need to be eliminated in a larger study in more controlled conditions.

CONCLUSION(S)

The study shows that hypoglycaemia is more common in patients with diabetes with CKD on HD compared to patients not having diabetes however the difference was not statistically significant. Hypoglycaemia was also seen in patients not having diabetes mellitus. Patients with diabetes had significantly higher mean heart rate during hypoglycaemia, compared to patients without diabetes. The study emphasises the importance of monitoring of blood glucose levels along with heart rate in patients of CKD during HD.

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PARTICULARS OF CONTRIBUTORS:
1. Professor, Department of Nephrology, Dr. D. Y. Patil Medical College, Pune, Maharashtra, India.
2. Professor, Department of Nephrology, Dr. D. Y. Patil Medical College, Pune, Maharashtra, India.
3. Resident, Department of Nephrology, Dr. D. Y. Patil Medical College, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Shreeharsh Godbole,
Resident, Department of Nephrology, Dr. D. Y. Patil Medical College,
Sant Tukaram Nagar, Pimpri, Pune-411018, Maharashtra, India.
E-mail: shreeharshgodbole@gmail.com

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