Original Research

# Hypoglycemia in Patients with Type-2 Diabetes Mellitus Nephropathy

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**ABSTRACT**

*Objective:* To find out the frequency of hypoglycemia in Type-2 Diabetics having nephropathy

*Methodology:* This cross-sectional observational study was carried out in Medical Teaching Institute Khyber Teaching Hospital Department of Medicine, from August 21, 2020, to January 21, 2021. Two-hundred and eighty-one (281) patients with Type 2 diabetic nephropathy were observed in due course and were subjected to detailed history and examination. A sample of 5 ml venous blood was obtained from the patients to measure blood glucose levels to detect hypoglycemia. Experienced pathologists analyzed all investigations.

*Results:* The mean ± Standard deviation (SD) of age in this study was 60± 10.26 years. Female patients outnumbered males in this study. Hypoglycemia was reported in 21% of patients while 79% did not have hypoglycemia.

*Conclusion:* Type-2 diabetics having nephropathy are prone to hypoglycemia. These patients should be carefully observed for clinical and biochemical features of hypoglycemia.

**KEYWORDS**: Type-2 Diabetes, Nephropathy, Hypoglycemia

## INTRODUCTION

Diabetes mellitus (DM) is a protean of metabolic afflictions either due to malfunctions in insulin's secretions, actions, or both.[1] About 40% of newly developing instances of the end- stage renal disease reported each year are caused by diabetic nephropathy.[2] Presence of persistent albuminuria, gradual glomerular filtration rate decline, and blood pressure increase are its defining features.[3] Defect in the counter-regulation of glucose is a significant cornerstone to the development of there is a modest impairment of the regulation of glucose. Presence of chronic kidney disease hypoglycemic events in Type I diabetics in contrast to Type 2

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Diabetics (T2DM), where (CKD) is an additional risk factor for patients who have diabetes. A study conducted by Yun et al.; documented baseline microalbuminuria over ten years of follow-up. This feature was described as an independent risk factor for the development of severe hypoglycemia in T2DM patients with the renal function that appeared to be normal or only slightly impaired. Regardless of whether they were getting insulin, this finding was documented.[4] Another study showed 19.1% of patients with diabetes and nephropathy had experienced one episode of hypoglycemia over follow-up.[5]

The objective of this research is to determine the biochemical evidence of hypoglycemia among patients of T2DM having diabetic nephropathy. Owing to the increased burden of DM in our population and fatality related to CKD, patients with CKD need their diabetes to be managed effectively to prevent disease progression.

## METHODOLOGY

This cross-sectional observational study was carried out in the Department of Medicine, Khyber Teaching Hospital Peshawar from August 21, 2020, to January 21, 2021. Open EPI's sample size calculator (http://openepi.com) was used to determine the sample size, taking the population of Peshawar as 4 million and 95% as the confidence level and prevalence of hypoglycemia (24%) in

diabetics having kidney disease.[6] The sample size is calculated to be 281.[3] The sampling was done by convenience-based probability sampling. Patients, including both genders, aged between 18- 70 years with the minimum disease (T2DM) 5 years and diabetic nephropathy, as per operational definitions, diagnosed during the last 6 months of study onset were included in this study. Patients were listed as exclusion criteria having concomitant liver diseases, malignancies, or who received oral or IV glucose before presentation to the Medical OPD. All these eligible patients were already enrolled in the diabetic registry of the ward. They were diagnosed as having diabetic nephropathy during the last 6 months based on persistent albuminuria (>300 mg/d or >200 μg/min), progressive decline in the glomerular filtration rate (GFR), and hypertension[7]. These patients were brought to Medical OPD for a routine checkup in a fasting state to minimize the confounding bias of drug-induced hypoglycemia. Their blood glucose level was checked at 8 AM to minimize the confounders.

After receiving an endorsement from the hospital IREB (Institutional Research and Ethical Board), the study was carried out (Ref. No. 838/ADR/KMC Dated 23-4-2020). All patients with type-2 DM, according to the operational definition and having diabetic nephropathy with six months minimum duration and meeting the inclusion criteria were included. Written informed consent was acquired from the patient or close relative in Urdu. The patients were subjected to history, and clinical examination, and variable, like age, name, and gender, was recorded on a pre-designed validated questionnaire. Exclusion criteria (like concomitant liver diseases, malignancies, and a recent (last week) episode of hypoglycemia) were closely adhered to prevent confounders and bias in the study's findings. Experienced pathologists conducted laboratory investigations on 5ml of venous blood obtained from all patients to measure blood glucose levels. A blood glucose level ≤ 70 mg/dl will be considered hypoglycemia.

***Statistical analysis:*** The SPSS version 20 software was utilized to analyze various data variables. Mean, median, mode, and SD was calculated for quantitative variables like age, diabetes duration, duration of Diabetic nephropathy, and blood glucose level. For categorical variables such as gender and hypoglycemia, percentages and frequencies were determined. Effect modifiers like age, DM duration of diabetic nephropathy, and gender were addressed through stratification. Pearson's chi-square test was used to test the relationship between the variables, and p <0.05 was taken as significant to either accept or reject the null hypothesis.

## RESULTS

This study analyzes age distribution among 281 patients. Patients' ages ranged from 30 to 45 years for 96 (34%) and from 46 to 70 years for 185 (66%) patients. The SD was 10.26, and the mean age was 60. The distribution of gender among 281 patients was recorded: 87 (31%) males and 194(69%) females. The analysis of the duration of diabetes among 281 patients showed 79(28%) patients having diabetes duration < 12 years and 202(72%) patients having a duration of diabetes >12 years. The mean duration of diabetes was 12 years with SD ± 10.51. The mean fasting blood glucose level was 99 mg% with SD ± 10.5 mg%. The data analyzed the duration of diabetic nephropathy among 281 patients as 93(33%) patients had a duration of diabetic nephropathy < 1 year and 188(67%) patients had a duration of diabetic nephropathy > one year.

| Table 1: Demographic variables of study participants | | | |
|---|---|---|---|
| **Demographics Characteristics** | | | |
| **Variables** | **Groups** | **Frequency** | **Percentage (%)** |
| Age | 30-45 years | 96 | 34 |
| | 46-70 years | 185 | 66 |
| Gender | Male | 87 | 31 |
| | Female | 194 | 69 |
| Duration of diabetes | <12years | 79 | 28 |
| | >12 years | 202 | 72 |
| Duration of diabetic nephropathy | < 1 year | 93 | 33 |
| | >1 year | 188 | 67 |

P value ≤ 0.05 is considered significant

**Table 2: Correlation of hypoglycemia with different demographics of study participants**

| Variables | Group | HYPOGLYCEMIA | | | | Statistics | |
|---|---|---|---|---|---|---|---|
| | | Yes | | No | | Chi-Square (df) | P-value |
| | | N | % | N | % | | |
| Age in years | 30-45 | 20 | 20.8 | 76 | 79.2 | 0.002 | 0.961 |
| | 46-70 | 39 | 21.1 | 146 | 78.9 | | |
| Gender | Male | 18 | 20.7 | 69 | 79.3 | 0.007 | 0.933 |
| | Female | 41 | 21.1 | 153 | 78.9 | | |
| Duration of diabetes | <12 years | 17 | 21.5 | 62 | 78.5 | 0.018 | 0.893 |
| | >12 years | 42 | 20.8 | 160 | 79.2 | | |
| Duration of diabetic nephropathy | < 1year | 19 | 20.4 | 74 | 79.6 | 0.027 | 0.870 |
| | >1 year | 40 | 21.3 | 148 | 78.7 | | |

P value ≤ 0.05 is considered significant

The mean± SD duration of diabetic nephropathy was 4± 3.91yrs.. The frequency of hypoglycemia among 281 patients was reported as 59(21%) patients had hypoglycemia while 222(79%) patients didn't Stratification of hypoglycemia with various variables like age, duration of DM, duration of diabetic nephropathy, and gender are represented in Tables No. 1, 2, and 3 respectively.

## DISCUSSION

Diabetes mellitus is a pinnacle of metabolic ailments characterized by chronic hyperglycemia either due to malfunctions in insulin's action, secretion, or both.[6] Metabolic abnormalities in carbohydrates, proteins, and lipids mainly result from defects in insulin regulation. Diabetics from the type-2 group during the initial years of the disease are relatively asymptomatic compared to those with type 1 Diabetes.[7] Patients with uncontrolled diabetes may be more susceptible to stupor or coma. Death may be the ultimate consequence either due to ketoacidosis or non-ketotic hyperosmolar coma resulting from ineffective treatment.[8] Approximately 85% of the diabetic population is obese, a prime factor behind insulin resistance. In contrast, diabetic nephropathy accounts for 40% of all new end-stage renal disease development cases recorded annually.[9] This study recorded the mean age as 60 years with SD ± 10.26. 87(31%) patients

were male and 194(69%) patients were female. More than 59(21%) patients had hypoglycemia, while 222(79%) patients didn't. Unfortunately, Diabetes is too common in our society. Poor glycemic status, early age onset, late diagnosis, and co-morbid may be the contributory factors accordingly. Similar findings were reported in another study by Chu YW et al., where 19.18% of patients experienced at least one episode of hypoglycemia a year before initiating dialysis.[8] Higher scores of adapted Diabetes Complications Severity Index (aDCSI) were linked to repeated hypoglycemia in advanced diabetic kidney disease (DKD) patients (p-value < 0.001). Hypoglycemic events after dialysis have a profound impact on subsequent severe hypoglycemic episodes and mortality rates. One hypoglycemic episode was associated with a 15% increased risk of death and a 2.3-fold increased risk of recurrent profound hypoglycemia compared to those who had none. Two or more episodes were associated with a 3.9-fold increased risk of severe hypoglycemia and a 19% increased chance of death. However, the risk of myocardial infarction (MI) after dialysis was not correlated with prior severe hypoglycemia.[10]

Another study by Aghaali M et al., revealed similar findings, reporting that 38% of patients receiving glibenclamide medication and 32% of patients receiving insulin therapy experienced a minimum of one hypoglycemia incident.[11] Similar findings were found in a different study by Moen MF et al., which showed that individuals with CKD had a greater incidence of hypoglycemia than those without CKD.[12] Patients with diabetes experienced rates of CKD of 10.72 versus 5.33 /100 patient months while patients without diabetes experienced rates of 3.46 versus 2.23 / 100 patient months, respectively. At all degrees of hypoglycemia, the risks of 1-day mortality increased but attenuated in CKD patients compared to controls. Adjusted odds ratios (OR) for 1-day mortality from outpatient (OPD) records of patients with CKD were 13.28, 7.36, and 4.34, respectively, while OR for 1-day mortality from outpatient data of patients without CKD were 7.36, 4.34, and 60.[12]

The main limitation of this study is the single-centered data and cross-section nature of the study. The number of previous hypoglycemic events and clinical manifestations of previously documented hypoglycemia was also not reported in this study. Large multi-centered prospective cohorts are needed

for the generalization of these findings.

## CONCLUSION

Patients with type 2 diabetes mellitus having nephropathy experienced hypoglycemia at the frequency of 21% in this study. Among these patients, diabetic nephropathy was found to be predicted by older age, duration with DM since diagnosis, poor glycemic control, and non-adherence to diet, exercise, and medication.

*Conflict of Interest:* None
*Grant Support and Financial Disclosures:* None

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| **Author's Contribution** | |
| --- | --- |
| **Faheem ur Rahman** | Study design, data collection, manuscript writing, data analysis |
| **Iqbal Haider** | Conceived and designed the study, supervise overall research work data analysis, critical revision of the manuscript for important intellectual content. |
| **Sumayya Rahman** | Study design, data collection, drafted and edited the manuscript |
| **Nayab Munib** | Study design, data collection drafted and edited the manuscript |
| **Wazir Mohammad** | Study design, data collection, revised and approved the article |
| All authors gave final approval for the manuscript to be published and responsible for integrity of research work | |