

Risk Factors of Hypoglycemia Among Type 2 Diabetics Admitted in a Tertiary Care Hospital of Rawalpindi

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ABSTRACT

Objective: To determine risk factors associated with hypoglycemia among hospitalized patients with type 2 diabetes mellitus admitted in a tertiary care hospital of Rawalpindi.

Study Design: Case-control study.

Place and Duration of Study: Combined Military Hospital Rawalpindi, Pakistan, from Sep 2023 to Aug 2024.

Methodology: A total of 300 patients participated in the study. They were divided into two groups: Group-A (Hypoglycemia group, n=150) and Group-B (non-hypoglycemia group, n=150). Inclusion criteria were patients of at least 18 years of age with type 2 diabetes mellitus admitted in hospital for three or more days. Exclusion criteria included type 1 diabetes, gestational diabetes, and diabetic emergencies. Demographics, clinical, treatment related and nutritional variables were assessed using a structured data collection protocol to identify the risk factors.

Results: Among 300 patients (150 Group-A; 150 Group-B), baseline age, Body Mass Index, glycosylated hemoglobin (HbA1c), and creatinine were comparable. Multivariate analysis identified four independent predictors of hypoglycemia: ICU admission (AOR 6.68, 95% CI 1.89–23.65, $p=0.003$), diabetic foot (AOR 7.98, 95% CI 3.14–20.28, $p<0.001$), infection on admission (AOR 3.54, 95% CI 1.85–6.78, $p<0.001$), and NPO status (AOR 14.16, 95% CI 3.94–50.90, $p<0.001$).

Conclusion: Risk factors of hypoglycemia among admitted patients of diabetes mellitus emphasizes the need for monitoring high-risk patients to improve clinical outcomes.

Keywords: Diabetic Foot, Diabetes Mellitus, Hypoglycemia, Infection, Risk Factors, Tertiary Healthcare.

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INTRODUCTION

Diabetes mellitus is an important health concern worldwide, affecting over 537 million adults, with type 2 diabetes mellitus comprising 90% of the cases. The International Diabetes Federation says that this number will likely rise to 783 million by 2045.¹ Pakistan now ranks third in the world with almost 33 million adults living with diabetes.² This number is increasing and estimates to be 60 million by 2045.¹

With rising diabetes cases, attention must focus on life-threatening complications like hypoglycemia, especially in hospitalized patients. It is associated with increased risk of mortality, cardiovascular events, and longer hospital stays.³ A U.S. based study by McCoy *et al.* stated that 7.1 events of hypoglycemia per 1,000 person-years occurred in 2020.⁴ Another study by Vikas *et al.* reported prevalence rates of 15%.⁵ In Pakistan, a 2022 study from Karachi reported that 12.3% of hospitalized diabetic patients developed hypoglycemia during admission.⁶ Another study from

Kohat in 2024 by Usman *et al.* reported a 28% hypoglycemia rate among hospitalized type 2 diabetics.⁷

Hypoglycemia is a preventable complication. Previous studies reported that one-third of diabetic patients exhibit risk factors including advanced age, renal impairment, intensive insulin therapy, comorbidities, and poor nutritional intake which are associated with hypoglycemia.^{8,9}

Most studies are based on populations in high-income countries with different clinical protocols and patient profiles. However, data on admitted hypoglycemia patients in Pakistan remains sparse, especially regarding its risk factors. Considering the rising diabetes burden and local healthcare challenges, this study assessed clinical, therapeutic, and nutritional risk factors for hypoglycemia in hospitalized T2DM patients at a tertiary hospital in Rawalpindi.

METHODOLOGY

This case-control study was carried out at the Combined Military Hospital (CMH) Rawalpindi, Pakistan, from September 2023 to August 2024, after

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approval by the Hospital Ethical Review Committee (certificate number 818).

Inclusion Criteria: Patients of either gender, with type 2 diabetes who were hospitalized for at least three days and who were at least 18 years of age were included.

Exclusion Criteria: Patients with type 1 diabetes, gestational diabetes, diabetic ketoacidosis (DKA), or hyperosmolar hyperglycemic state (HHS) were excluded.

Sample size was calculated using OpenEpi online calculator, assuming an exposure rate of 30% of risk factors in controls, and an odds ratio of 2.0 for their association with hypoglycemia. It was estimated that a total of 284 participants (142 cases and 142 controls) were needed to detect significant associations between risk factors and hypoglycemia.¹⁰ We included 150 patients in each group.

Data was collected prospectively using non-probability consecutive sampling. Informed consent was taken from all participants before data collection. Patients with type 2 diabetes that were admitted during study period were 2340. Among them, patients were reviewed based on inclusion criteria. Patients were divided into two groups. Group-A (n=150) was taken as Case-Group and consisted of patients who had at least one episode of hypoglycemia during admission, which is defined as blood glucose levels below 70 mg/dL (3.9 mmol/L). Patients who did not develop hypoglycemia during their hospital and whose blood glucose levels were equal or greater than 70 mg/dL (3.9 mmol/L) made up to the Group-B (n=150) which is the Control-Group. Both groups were selected using non-probability consecutive sampling during the same admission window to ensure consistent inclusion of eligible patients. A step-by-step representation is illustrated in **Error! Reference source not found..**

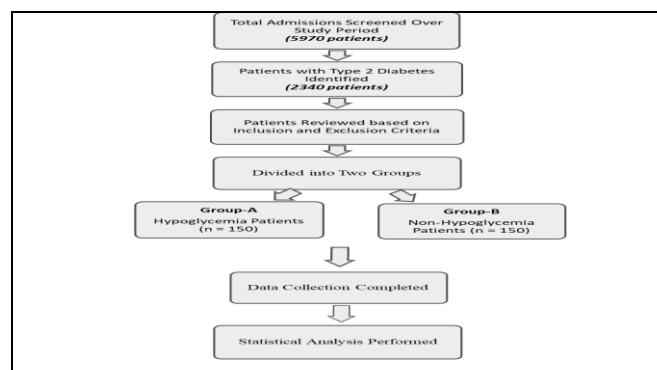


Figure-1 Patient Flow Diagram (n=300)

Data collected included demographics such as age, gender, Body Mass Index (BMI), and occupation; comorbidities including macro-vascular complications (e.g., diabetic foot, ischemic heart disease, stroke) and microvascular complications (e.g., retinopathy, nephropathy, neuropathy); hospital data including length of hospital stay, admission diagnosis, and hospital complications (e.g., infections, ICU admission); diabetic treatment encompassing oral hypoglycemic agents (specific agents to be detailed) and insulin therapy (mixed, basal, or regular insulin); laboratory tests including Hemoglobin A1c (HbA1c) and serum creatinine levels; and nutritional therapy used (oral, tube feeding [nasogastric or percutaneous endoscopic gastrostomy [PEG], or nil per mouth [NPO]).

Data analysis was done using Statistical Package for the Social Sciences (SPSS) version 23. Categorical data was summarized as frequencies or percentages while quantitative data as Mean±SD or median (interquartile range [IQR]). Normality was assessed and appropriate parametric or non-parametric tests were applied accordingly. The Independent t-test was used to compare means between the case and Group-B. Mann-Whitney U test was used for the non-parametric data. Chi-square test was performed to find association between categorical variables and hypoglycemia.

Univariate logistic regression was first applied to evaluate each factor separately. Subsequently, multivariate logistic regression was applied to identify independent predictors of hypoglycemia after adjusting for other risk factors. The results were presented as unadjusted odds ratios (UOR) from univariate analysis and adjusted odds ratios (AOR) from multivariate analysis, each with 95% confidence intervals (CIs). A *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 300 patients were included, with 150 in each group. Median age (67 vs. 68 years, *p*=0.550), mean BMI (29.91±3.4 vs. 29.92 ± 3.5 kg/m², *p* = 0.987), HbA1c (8.9±1.77% vs. 9.0±1.76%, *p*=0.888), and creatinine (89 vs. 89 μmol/L, *p*=0.826) were comparable, indicating well-balanced baseline characteristics Table-I.

Among diabetes-related complications, diabetic foot was statistically significant and more common in Group-A (16% vs. 4.7%; UOR 3.89, *p*=0.002).

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Malignancy was more frequent in Group-B (34.7% vs. 21.3%; UOR 0.51, $p=0.014$). Amputation was slightly higher in Group-A but not statistically significant. Other complications, including neuropathy, nephropathy, retinopathy, stroke, and ischemic heart disease, showed no meaningful difference.

Table-I: Baseline Demographic and Clinical Characteristics of Study Participants (n=300)

Factor		Group-A (n=150)	Group-B (n=150)	p-value
Gender	Male	89(59.3%)	85(56.7%)	0.726
	Female	61(40.7%)	65(43.3%)	
Age in years, median (IQR)		67(21)	68(20)	0.550
BMI (kg/m ²), Mean±SD		29.91±3.4	29.92±3.5	0.987
HbA1c %, Mean ± SD		8.9±1.77	9.0±1.76	0.888
Creatinine µmol/L, median (IQR)		89(25)	89(25)	0.826

BMI = Body mass index; HbA1c = Glycated hemoglobin; SD = Standard deviation; IQR = Interquartile range

Regarding admission diagnoses, infection was significantly higher in Group-A (28.7% vs. 16%; UOR 2.11, $p=0.012$), highlighting its role as a major driver of hospitalization. Nonspecific causes were more frequent in Group-B (40.7% vs. 27.3%; UOR 0.55, $p=0.020$). Cardiovascular, neurological, pulmonary, and malignancy-related admissions did not differ significantly.

Hospital-acquired infections such as cellulitis, UTI, pneumonia, and sepsis were similar between groups, but ICU admission was markedly higher in Group-A (18.7% vs. 4.7%; UOR 4.69, $p<0.001$), reflecting more severe clinical deterioration in this group. Table-II.

Table-II: Complications at Baseline, Admission Characteristics, and In-Hospital Outcomes across Groups (n=300)

Factor	Study Parameter		Univariate logistic regression		
	Group-A (n=150) n (%)	Group-B (n=150) n (%)	Unadjusted OR	p-value	95% CI UOR
Presence of DM complications					
-Diabetic Foot	24(16)	7(4.7)	3.891	0.002	1.622 – 9.337
-Amputation	14(9.3)	6(4)	2.471	0.103	0.923– 6.614
-Malignancy	32 (21.3)	52 (34.7)	0.511	0.014	0.305– 0.856
Diagnosis on Admission					
-Infection	43 (28.7)	24 (16)	2.110	0.012	1.203– 3.701
Hospital Complications					
-ICU admission	28(18.7)	7(4.7)	4.689	<0.001	1.949– 11.110

DM = Diabetes mellitus; OR = Odds ratio; CI = Confidence interval; UOR = Unadjusted odds ratio; ICU = Intensive care unit

Table-III shows that insulin use was common between both groups (90% vs. 82%, $p=0.092$), but there was no significant difference in type of regimen. Use of oral hypoglycemic was a little higher in Group-B (17.3% vs. 10%), and yet not statistically significant

($p=0.092$). Nutritional therapy showed that Group-A had a significantly higher percentage of NPO status (14% vs. 2%; UOR 7.98, 95% CI 2.33–27.36, $p<0.001$) and tube feeding (14% vs. 6%; UOR 2.55, 95% CI 1.13–5.77, $p=0.033$). Oral feeding was predominant in Group-B (92% vs. 72%, $p<0.001$).

Table-III: Treatment Modalities and Nutritional Support in both Study Groups (n=300)

Factor	Study Parameter		Univariate logistic regression		
	Group-A (n=150) n (%)	Group-B (n=150) n (%)	Unadjusted OR	p-value	95% CI UOR
Treatment Modalities					
Insulin use	135 (90)	124 (82)	1.887	0.092	0.955– 3.727
-Regular	39 (26)	35 (23.3)	1.154	0.688	0.628– 1.953
-Mixed	54 (36)	58 (38.7)	0.892	0.720	0.559– 1.425
-Basal Bolus	42 (28)	31 (20.7)	1.493	0.178	0.877– 2.542
-OHA use	15 (10)	26 (17.3)	0.530	0.092	0.268 – 1.047
Nutritional therapy					
-Oral	95 (63.3)	138 (92)	0.150	<0.001	0.076– 0.296
-NG/PEG tube	21 (14)	9 (6)	2.550	0.033	1.127– 5.771
-NPO	21 (14)	3 (2)	7.977	<0.001	2.325– 27.362

OR = Odds ratio; CI = Confidence interval; UOR = Unadjusted odds ratio; OHA = Oral hypoglycemic agent; NG = Nasogastric; PEG = Percutaneous endoscopic gastrostomy; NPO = Nil per oral

Multivariate analysis confirmed four independent predictors strongly associated with Group-A. These included ICU admission (AOR 6.68, 95% CI 1.89–23.65, $p=0.003$), diabetic foot (AOR 7.98, 95% CI 3.14–20.28, $p<0.001$), infection on admission (AOR 3.54, 95% CI 1.85–6.78, $p<0.001$), and NPO status (AOR 14.16, 95% CI 3.94–50.90, $p<0.001$) as shown in Table-IV. These variables show more severe illness and poorer prognosis, emphasizing the importance of early identification and targeted interventions in such high-risk patients.

Table-IV: Independent Predictors of Hypoglycemia (n=150)

Factor	Univariate logistic regression			Multivariate logistic regression		
	Unadjusted OR	95% CI UOR	p-value	Adjusted OR	95% CI AOR	p-value
ICU Admission	4.689	1.949– 11.110	<0.001	6.679	1.886 – 23.649	0.003
Diabetic Foot	3.891	1.622 – 9.337	0.002	7.979	3.139 – 20.281	<0.001
Infection on Admission	2.110	1.203– 3.701	0.012	3.537	1.846 – 6.776	<0.001
NPO	7.977	2.325– 27.362	<0.001	14.161	3.940 – 50.897	<0.001

OR = Odds ratio; CI = Confidence interval; UOR = Unadjusted odds ratio; AOR = Adjusted odds ratio; ICU = Intensive care unit; NPO = Nil per oral

DISCUSSION

In this case-control study, many independent risk factors of hypoglycemia among hospitalized patients with type 2 diabetes mellitus were recognized, which comprises of ICU admission, diabetic foot, infection on admission, and nil per oral (NPO) status. These results will guide us identifying patients who are at risk of hypoglycemia.

ICU admission was found to be a strong independent risk factor (AOR 6.68, 95% CI 1.89–23.65). Bagshaw *et al.* reported that incidence of ICU patients who experienced hypoglycemia within 24 hours was 13.8%, and among those who experienced hypoglycemia had double mortality rate.⁹ Our results showed that 18.7% of ICU admissions had hypoglycemia. This highlights the significance of glycemic target maintenance and constant monitoring in ICU patients.

The occurrence of diabetic foot was another significant risk factor (AOR 7.98, 95% CI 3.14–20.28). Salehi *et al.* reported 21.8% of patients who experienced hypoglycemia prior to amputation, which was increased to 36.4% postoperatively.¹⁰ In our study, 16% of the patients having diabetic foot as a complication developed hypoglycemia. This points out that patients with diabetic foot may require careful glycemic modifications, mainly around surgical interventions.

Infection at the time of admission was also strongly associated with hypoglycemia in our study (AOR 3.54, 95% CI 1.85–6.78). Pratiwi *et al.* had demonstrated in an Indonesian study that admissions which were related to infections significantly elevated the odds of hypoglycemia, with an OR of 2.11 and $p=0.012$.¹¹ With an AOR of 3.54, our results are consistent with this study and demonstrate relevance, especially in developing nations where infections are a major cause of hospitalization.

In our study, NPO status was the most significant risk factor (AOR 14.16, 95% CI 3.94–50.90). Patients who were NPO orders had a higher risk of hypoglycemia, with an OR of 1.9, according to Li *et al.*¹² Furthermore, our univariate analysis revealed that NG/PEG feeding also increased the odds of hypoglycemia with a UOR of 2.5. This is in line with the meta-analysis conducted by Valero *et al.*, which found enteral feeding to be a significant risk factor for hypoglycemia in hospitalized diabetic patients with an OR of 1.75.¹³ The significance of regular blood glucose monitoring during altered feeding schedules is stressed by these findings.

Despite being 90% of hypoglycemia cases, insulin use did not remain significant in multivariate analysis. This could be because insulin therapy is almost universal in both groups, but prior research indicates a strong correlation of insulin and hypoglycemia. Around 36–43.5% of Pakistani T2DM patients receiving insulin had hypoglycemia, according to

Shabbir *et al.* and Javed *et al.*^{14,15} After moving from premixed insulin to a basal bolus regimen, Malik *et al.* also demonstrated a 30% decrease in hypoglycemia, indicating that insulin formulation and regimen are important factors.¹⁶ These findings are also supported by international data, which show that insulin therapy is linked to a 2.5-fold higher risk of hypoglycemia than other antidiabetic treatments as evident in a study by Seaquist *et al.*¹⁷

Our overall findings regarding the risk factors were also consistent with evidence from around the world. Approximately 12.5% of hospitalized T2DM patients experienced inpatient hypoglycemia, according to a multicenter study conducted in Spain by González *et al.*¹⁸ This condition was significantly related with infection, insulin therapy, and changed dietary intake.

This study provides valued understandings of the risk factors for hypoglycemia in hospitalized type 2 diabetic patients and suggests that interventions, like cautious monitoring of patients in the ICU, with diabetic foot complication, infection on admission, and modified nutritional management, could help reduce the incidence of hypoglycemia.

LIMITATIONS OF THE STUDY

Limitation of this study includes its single center setting, which may limit the diversity of the findings data. Future research should be done to explore interventions and management strategies to prevent hypoglycemia in this high risk population.

CONCLUSION

We found that factors which significantly increase the risk of hypoglycemia include Intensive care unit admission, presence of diabetic foot as complication, infection at admission and NPO status. The findings suggest the importance of rigorous monitoring and management options for high risk patients. The incidence of hypoglycemia can be reduced by addressing these risk factors which will ultimately improve overall clinical outcomes for hospitalized type 2 diabetic patients.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

MSS & FAS: Conception, study design, drafting the manuscript, approval of the final version to be published.

IK & FR: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

SA & AA: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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