

Frequency of Hypoglycemia in Elderly Patients on Oral Hypoglycemics Vs Insulin Therapy Presenting to the Accident and Emergency Department of a Tertiary Care Hospital

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ABSTRACT

Objective: To assess the frequency of hypoglycemia in elderly patients on oral hypoglycemics vs insulin therapy presenting to A&E, and to assess associated risk factors.

Study design: Comparative Cross-sectional study.

Place and Duration of Study: Accident and Emergency Department, Combined Military Hospital (CMH), Rawalpindi, Pakistan, from Jul to Dec 2024.

Methodology: The data were collected from 155 elderly patients (≥ 60 years) with T2DM who presented to the A&E department with symptoms suggestive of hypoglycemia or documented hypoglycemia ($\text{BSR} < 70 \text{ mg/dl}$). Patients were categorized into oral hypoglycemic agents ($n = 78, 50.3\%$) and insulin therapy ($n = 77, 49.7\%$). Data was analyzed using SPSS 25 with chi-square test and logistic regression applied to determine associations.

Results: The mean age of the patients was 68.5 ± 5.7 years. Severe hypoglycemia was significantly more frequent in insulin users (39%) compared to oral hypoglycemic users (15.4%, $p = 0.004$). Sulfonylureas were responsible for 41% of hypoglycemia cases in oral drug users. Renal impairment ($\text{OR} = 2.2, p = 0.029$) and medication overdose ($\text{OR} = 2.2, p = 0.029$) were identified as independent risk factors for hypoglycemia. Key risk factors included longer diabetes duration (> 10 years, $p = 0.012$), poor medication adherence ($\text{OR} = 2.2, p = 0.008$), and low BMI ($p = 0.019$).

Conclusion: Insulin therapy is associated with a higher frequency of severe hypoglycemia in elderly patients compared to oral hypoglycemics. Renal impairment, missed meals, and medication errors significantly contribute to hypoglycemia risk. Regular monitoring, individualized treatment strategies, and patient education are essential to minimize hypoglycemia-related emergency visits in elderly diabetic patients. Future research with larger, multi-center cohorts is needed to validate these findings and guide clinical practice.

Keywords: Elderly, Hypoglycemia, Insulin Therapy, Oral Hypoglycemics, Risk Factors, Type 2 Diabetes Mellitus.

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INTRODUCTION

Hypoglycemia refers to blood glucose levels that are less than normal ($< 70 \text{ mg/dl}$ or 3.9 mmol/L). It is a significant concern when managing diabetic patients, especially the elderly population. The presence of comorbidities, polypharmacy, and a potential cognitive decline makes them more vulnerable to hypoglycemia.¹ Studies suggest that second-generation basal insulins and long-acting insulins are associated with lower rates of hypoglycemia compared to earlier intermediate, basal, or NPH insulins.² This finding is particularly significant in the context of Pakistan, where selecting insulin therapies that reduce the risk of hypoglycemia could help decrease emergency visits related to hypoglycemia among older individuals.³ A study suggests that

approximately 65.2% of patients have reported hypoglycemia with oral hypoglycemic agents.⁴ Studies suggest that optimizing blood sugar levels through careful monitoring to achieve target plasma glucose while preventing hypoglycemia,⁵ along with continuous monitoring and tailored treatment plans for each individual, can reduce hypoglycemia-related emergency visits and effectively manage diabetes in the elderly population.⁶

Hypoglycemia requiring emergency department visits or inpatient admissions is considered severe.⁷ A recent study done in the U.S on adults with type 2 diabetes showed that approximately 0.49/100 person-years visited A&E or were hospitalized with hypoglycemia (20% were using insulin therapy while 35% were on sulfonylureas).⁸ Another study in Germany showed 3.9 hypoglycemic events/100 patients-years (all of them were on sulfonylureas).⁹ A study conducted in Pakistan showed that

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approximately 50% of the individuals were diagnosed with hypoglycemia, of whom 18% had severe hypoglycemia requiring hospitalization.¹⁰

The prevalence of hypoglycemia in the elderly population on oral hypoglycemics and insulin therapy is a significant concern, particularly in emergency departments in Pakistan. While current research highlights the importance of personalized treatment plans, appropriate insulin choices, and management of blood sugar fluctuations to reduce hypoglycemia risk, further studies are needed to better understand its prevalence and develop targeted interventions to improve management and patient safety.

METHODOLOGY

This Comparative cross-sectional study was carried out at the A&E department of Combined Military Hospital (CMH), Rawalpindi, Pakistan, from Jul to Dec 2024 after getting approval from the Institutional Ethical Review Board (ERB Reference No: 737, Dated 20 June, 24). A total sample size of 155 elderly patients was included in this study through a consecutive sampling technique, where all eligible patients meeting the inclusion criteria were included until the required sample size was achieved. The sample size was calculated using the WHO sample size calculator, considering the expected prevalence of hypoglycemia in insulin users as 40%, while in oral hypoglycemic users as 25%. These estimates were taken from previously published studies where hypoglycemia in patients with insulin therapy ranged from 40-90%,¹¹ while oral hypoglycemics varied from 10-30%.¹² There was a 95% confidence interval, a 5% margin of error, a study power of 80%, and an estimated population size (N) of 500-2000 cases/year.

Inclusion Criteria: Patients of either gender aged 60 years and older who came to the A&E department with symptoms of potential hypoglycemia or documented hypoglycemia (Blood sugar <70mg/dl) and diagnosed with T2DM either on insulin or at least one oral hypoglycemic agent for at least 6 months.

Exclusion Criteria: Patients with T1DM who were on both insulin and oral hypoglycemics (combination therapy) were excluded. Those with incomplete medical records or hypoglycemia due to other causes like liver failure, sepsis, or adrenal insufficiency were also excluded.

Data was collected with the help of structured questionnaire and medical records after informed consent including questions related to demographics

(age, gender, duration of diabetes), clinical characteristics (HbA1C levels, presence of dyslipidemia, hypertension, smoking status, physical activity), and treatment-related factors (type of treatment: insulin vs. oral hypoglycemic agents), clinical presentation and risk factors (missed meals, overdose of medications, renal impairment). Patients were categorized into two groups based on their treatment, i.e., Group-A (patients on oral hypoglycemic agents) and Group B (patients on insulin therapy).

To statistically analyze the collected data, Statistical Package for Social Sciences (SPSS) software version 25.00 was used. Descriptive statistics were used for the mean $\pm$ SD of continuous variables and percentages for categorical variables. The Shapiro-Wilk test was applied to assess the normality of continuous variables. Age and BMI were found to be normally distributed. The duration of diabetes showed a slightly non-normal distribution. The chi-square test was used to compare hypoglycemia frequency between the two groups. Independent samples t-test was used to compare variables like age, duration of diabetes and BMI. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated using 2x2 contingency tables. A *p*-value of <0.05 was considered statistically significant.

RESULTS

A total of 155 elderly diabetic patients were included in the study. Patients were categorized into two groups based on treatment regimen: oral hypoglycemic agents (n=78, 50.3%) and insulin therapy (n=77, 49.7%). The mean age of the population was 68.5 $\pm$ 5.7 years, with 89(57.4%) males and 66(42.6%) females. The mean duration of diabetes was 11.2 $\pm$ 4.6 years, with no significant difference between the two groups (*p*=0.102). Baseline characteristics, including gender distribution and BMI, were comparable between the two groups (*p*>0.05). However, the proportion of patients with renal impairment was significantly higher in the insulin group (37.7%) compared to the oral agents' group (17.9%) (*p*=0.003) (Table-I).

The severity of hypoglycemia varied significantly with the treatment group (39% vs 15.4%). Insulin users had a higher frequency of severe hypoglycemia (<54 mg/dl) (*p*=0.004), whereas oral hypoglycemics were more often associated with mild to moderate episodes. Sulfonylureas (particularly Glibenclamide and Gliclazide) were the most common agents among oral

hypoglycemic users (32/78, 41%), while long-acting insulins and premixed preparations were most frequently implicated in the insulin group (51/77, 66.2%).

Table-I: Baseline Characteristics of Patients by Treatment Group (n = 155)

Characteristic	Oral Hypoglycemics (n=78)	Insulin Therapy (n=77)	p-value
Mean Age (years)	69.6 ± 5.5	68.9 ± 5.2	0.358 \$
Gender (Male/Female)	45 (57.7%) / 33 (42.3%)	44(57.1%)/33 (42.9%)	0.693 #
Duration of Diabetes (yrs)	10.7 ± 5.0	11.8 ± 4.6	0.102\$
BMI (kg/m ²)	25.5 ± 4.3	25.8 ± 4.0	0.374\$
Renal Impairment n (%)	11 (17.9%)	28 (37.7%)	0.003 #

\$ - independent t-test used, # - chi-square test, BMI - Body Mass Index

Duration of diabetes over 10 years was significantly associated with hypoglycemia (58% vs. 34.5%, $p=0.012$), as was low BMI (<18.5 kg/m²) ($p=0.019$). Recurrent hypoglycemia (>2 episodes in 6 months) was reported in 32.3% of patients. Non-adherence to treatment (as measured by MMAS-8) significantly increased the risk of hypoglycemia (OR = 2.2, $p=0.008$).

Table-II: Factors Associated with Severity of Hypoglycemia

Parameters	Severe hypoglycemia (n = %)	Mild-Moderate hypoglycemia (n = %)	p-value
Treatment group: Insulin	30 (39.0%)	47 (61.0%)	0.004
Treatment group: Oral agents	12 (15.4%)	66 (84.6%)	0.004
Sulfonylurea use (Glibenclamide/Gliclazide)	32 (41.0%)	46 (59.0%)	0.006
Long-acting/Premixed insulin use	51 (66.2%)	26 (33.8%)	0.003
Diabetes duration >10 years	45 (58.0%)	32 (41.6%)	0.012
Low BMI (<18.5 kg/m ²)	16 (20.5%)	06 (7.8%)	0.019
Recurrent hypoglycemia (>2 episodes/6 months)	25 (32.3%)	09 (11.7%)	0.021
Non-adherence to treatment (MMAS-8)	18 (23.0%)	06 (7.8%)	0.008

Table-III shows the association between key precipitating factors and risk of hypoglycemia. Missed or delayed meals (30.3%) had an odds ratio of 2.4 (95% CI: 1.2–4.9, $p=0.014$), excessive insulin or drug dosage (24.5%) had an OR of 1.8 (CI: 1.0–4.8, $p=0.035$), and renal impairment (27.7%) had an OR of 2.2 (CI: 1.1–4.6, $p=0.029$). Infection/sepsis, though present in 17.4% of cases, was not significantly associated with hypoglycemia (OR = 1.3, CI: 0.5–2.9, $p=0.600$).

An OR >1 indicates increased odds of hypoglycemia in the presence of the risk factor. For example, patients with renal impairment had 2.2 times the odds of experiencing hypoglycemia compared to

those without renal issues. Similarly, missed meals and medication overdosing were strong predictors of hypoglycemic episodes. Confidence intervals not crossing 1.0 and p -values <0.05 indicate statistically significant associations.

Table-III: Association Between Key Precipitating Factors and Hypoglycemia

Risk Factor	Total frequency (%)	With Hypoglycemia (n=79)	Without Hypoglycemia (n=76)	OR (95% CI)	p-value
Renal Impairment	43 (27.7%)	28 (35.4%)	15 (19.7%)	2.2 (1.1–4.6)	0.029
Missed/Delayed Meals	47 (30.3%)	31 (39.2%)	16 (21.1%)	2.4 (1.2–4.9)	0.014
Excessive Dose (Insulin/Drug)	38 (24.5%)	25 (31.6%)	13 (17.1%)	2.2 (1.0–4.8)	0.035
Infection/Sepsis	27 (17.4%)	15 (19.0%)	12 (15.8%)	1.3 (0.5–2.9)	0.600

OR = Odds Ratio; CI = Confidence Interval; $p < 0.05$ is considered statistically significant

DISCUSSION

The study targeted elderly individuals, in whom hypoglycemia is a common symptom, particularly those on insulin therapy. The study findings demonstrate that insulin therapy significantly increases the risk of hypoglycemia in elderly patients with T2DM, highlighting the importance of careful insulin dosing and consistent monitoring in elderly group. Our findings indicate that insulin therapy is significantly associated with severe hypoglycemia (39%), while oral hypoglycemics (15.4%) ($p=0.004$), particularly sulfonylureas (41%), are more likely to cause mild to moderate hypoglycemia. Renal impairment, missed meals, and medication overdose were independent risk factors for hypoglycemia. Other key risk factors included longer diabetes duration (>10 years, $p=0.012$), poor medication adherence (OR = 2.2, $p=0.008$), and low BMI ($p=0.019$).

Mainali *et al.*, reported that insulin use is associated with a higher risk of hypoglycemia, as demonstrated in research that found a higher prevalence of hypoglycemia among insulin-dependent individuals with Type 2 diabetes in a tertiary care setting.¹³ Similarly, our study observed that hypoglycemia was more common among insulin users than among those using oral hypoglycemic agents, aligning with these findings. Previous studies similar to Caballero-Corchuelo *et al.*, and Heller *et al.*, also highlight this link, as elderly patients are often more sensitive to insulin due to age-related physiological changes such as decreased renal function, which can impair insulin clearance and increase its potency.^{14,15}

The prevalence of hypoglycemia was slightly higher in female patients, as seen in a study by Ambaye *et al.*¹⁶

Our study also emphasizes the importance of thorough patient education, especially for older adults who may struggle to recognize the early signs of hypoglycemia. Studies similar to Mianali *et al.*, highlighted that limited awareness of hypoglycemia, inadequate understanding of its warning symptoms, and poor self-management skills can substantially increase the risk of hypoglycemic episodes, particularly among elderly patients.¹⁷ This risk may be further amplified in individuals who have irregular access to glucose monitoring devices, lack caregiver support, or are unaware of preventive measures such as timely meals, correct medication dosing, and appropriate responses to low blood sugar symptoms.¹⁸ Strengthening awareness programs and providing regular, practical training on recognizing, preventing, and managing hypoglycemia could therefore play an important role in reducing emergency presentations as reported by Hannan *et al.*¹⁹ In addition, individualized treatment plans that consider each patient's age, renal function, nutritional status, medication adherence, lifestyle pattern, and dietary habits may help minimize hypoglycemia risk while maintaining adequate glycemic control.²⁰

Gender-based differences may be influenced by body composition, metabolic variation, or treatment adherence and should be explored further in future studies. Future research with larger, multi-center cohorts is needed to validate these findings and guide clinical practice.

The study affirms the objective of the study that the elderly population of Pakistan suffers from hypoglycemia secondary to diabetes, and is either treated with oral hypoglycemics or Insulin Therapy. The causality was not established, yet they both have established their efficacy in accordance with the literature.

LIMITATIONS OF STUDY

Being a cross-sectional, single-center study, it only establishes an association between treatment type and hypoglycemia but cannot determine causality, limiting its generalizability to broader populations. Additionally, unmeasured factors such as dietary habits, physical activity, and concurrent medications were not considered

CONCLUSION

The type of treatment (insulin vs. oral medications) is an important factor in predicting hypoglycemia. It is crucial to optimize antihyperglycemic therapy selection in elderly

patients, enhance patient education on medication adherence and meal timing, monitor renal function regularly to adjust dosages, and implement preventive strategies to reduce hospital visits due to hypoglycemia.

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Authors' Contribution

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

AA & FAS: Data acquisition, data analysis, critical review, approval of the final version to be published.

AM & LS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AS & IK: 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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