Section: Miscellaneous

Original Research Article

MEDICATION ASSOCIATED SEVERE HYPOGLYCEMIA IN PATIENTS WITH DIABETES MELLITUS: A CROSS-SECTIONAL ANALYSIS

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Received : 09/05/2025
Received in revised form : 01/07/2025
Accepted : 18/07/2025

Keywords:
hypoglycemic, Diabetes Mellitus, Elucidate, cross-sectional study, insulin.

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DOI: 10.47009/jamp.2025.7.4.115

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (4); 611-618

ABSTRACT

Background: Aim: To elucidate the association of medication-associated severe hypoglycemia in individuals with diabetes mellitus. **Materials and Methods:** The research was employing a cross-sectional study design to elucidate association of medication-associated severe hypoglycemia in patients with diabetes mellitus and to identify symptomatology and contributing factors. Study duration between jan 1st 2024 to 30 jan 2025. **Result:** Elucidate the association of medication associated severe hypoglycemia in individuals with diabetes mellitus has been calculated and tabulated. **Conclusion: We find that** emphasize the multifactorial nature of severe hypoglycemia in diabetes and the necessity for careful therapeutic decision- making, regular monitoring of renal function, and targeted patient education to reduce the risk of hypoglycemic episodes and improve clinical outcomes.

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic condition characterized by sustained hyperglycemia resulting from defective insulin production, insulin action, or both.[1] The worldwide incidence of diabetes is increasing, with around 537 million individuals impacted globally in 2021, projected to escalate to 783 million by 2045.[2] Effective glycemic control is crucial in diabetes care to avert complications like nephropathy, neuropathy, retinopathy, and cardiovascular illnesses. Nevertheless, attaining appropriate glycemic objectives often correlates with a heightened risk of hypoglycemia, a significant unfavorable impact of diabetes management.[3,4]

Severe hypoglycemia, a condition requiring external intervention for recovery, poses a significant risk to patients with diabetes.[5] It may result in cognitive impairment, seizures, cardiovascular incidents, falls, coma, and even death (Desouza et al., 2010).

Hypoglycemia is a prevalent issue among individuals with type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and metabolic syndrome. Aggressive glycemic management, either insulin or oral hypoglycemic medications like sulfonylureas, is a significant predictor of hypoglycemia. Hypoglycemia episodes can make it hard for people with diabetes to control their blood sugar levels in the short and long term. They can also make it harder for them to think and move during episodes. Pathophysiologically, these occurrences may impair glucose counter-regulation and result in hypoglycemia unawareness, possibly causing repeated episodes, lasting morbidity, and even mortality.[6]

Increased awareness, education, and resource distribution can prevent severe hypoglycemia incidents, despite their prevalence and high cost. The American Diabetes Association (ADA) Standard of Diabetes Care-2024 highlights the heightened incidence of hypoglycemia in individuals receiving intensive insulin treatment, including several daily injections, continuous subcutaneous insulin infusion, or automated insulin delivery devices. Individuals administered basal insulin precede those receiving sulfonylureas or meglitinides. The concurrent administration of insulin and sulfonylureas significantly increases the risk.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Antidiabetic agents, especially insulin and sulfonylureas, are the primary causes of severe hypoglycemia.[7] There is a big risk of hypoglycemia with insulin treatment, which is necessary for people with type 1 diabetes and many people with type 2 diabetes.[8]

Alternative glucose-lowering drugs, such as DPP-4 inhibitors, GLP-1 RAs, and SGLT-2 inhibitors, have a lower risk of hypoglycemia when used alone.[1] When used in conjunction with insulin or sulfonylureas, they may induce hypoglycemia episodes, especially in patients with renal impairment, hepatic dysfunction, or those on polypharmacy.[9]

Recognizing this research gap, this work commences a thorough descriptive analytical investigation using a cross-sectional methodology. We concentrate on established diabetic patients exhibiting severe hypoglycemia in the emergency department of the Department of Medicine at Baba Raghav Das Medical College in Gorakhpur, Uttar Pradesh, India. Employing successive sampling guarantees the acquisition of a representative sample.

The major objective of our research is to elucidate the range of medication- induced hypoglycemia in individuals of Indian descent. We aim to provide significant insights into the prevalence and correlation of severe hypoglycemia in diabetics using diverse drugs. This includes those using premix insulin, basal- bolus multiple daily injections (MDI) insulin, basal insulin, sulfonylureas, meglitinides, or a combination of sulfonylureas with insulin, as well as a combination of sulfonylureas with DPP-4 inhibitors.

This research seeks to evaluate the incidence and risk factors of severe hypoglycemia in individuals with diabetes mellitus, emphasizing its correlation with several classes of antidiabetic medicines. The goal is to look at the demographic and clinical traits of people who are affected, figure out how they usually take their medications, and see how severe hypoglycemia affects patient outcomes. The study uses a cross-sectional analysis to look at the link between antidiabetic drugs and severe hypoglycemia in order to come up with safer ways to treat diabetes. The results will provide critical insights into the need for individualized treatment, patient education, and focused interventions to avert severe hypoglycemia in high-risk groups.

MATERIALS AND METHODS

The research was employing a cross-sectional study design to elucidate association of medication-associated severe hypoglycemia in patients with diabetes mellitus and to identify symptomatology and contributing factors. Study duration between jan 1st 2024 to 30 jan 2025.

Sampling Methodology

The study was target known diabetic patients presenting with severe hypoglycemia at the emergency department (ED) of the Department of Medicine, Baba Raghav Das (BRD) Medical College in Gorakhpur, Uttar Pradesh, India. Consecutive sampling was utilized to ensure the recruitment of a representative sample.

Data Collection Process

Data was collected through structured interviews, medical record reviews, and relevant clinical assessments. Information on medication regimens, frequency and symptoms of severe hypoglycemia episodes, and potential risk factors was systematically gathered.

Written informed consent was taken in the local language from all study subjects. Variables of interest include medication type (insulin, sulfonylureas, meglitinides, and combinations), dosage, and frequency of severe hypoglycemia episodes, symptoms accompanying episodes, patient comorbidities, and history of hypoglycemic events.

Each participant were undergo a comprehensive evaluation encompassing age, gender, education status, history of glycemic control, duration of diabetes, type of diabetes, diabetic medication, physical examination, systemic examination & relevant investigations (including HbA1C, RBS, LFT, KFT) Venous blood samples were collected in EDTA and serum separator vials, sent to the Central Pathology Lab at Nehru Chikitsalay, BRD Medical College, Gorakhpur, and processed using an automatic analyzer for HbA1C and other markers.

Inclusion Criteria

1. Age ≥ 18 years.
2. Individuals who have provided written informed consent.
3. Patients with diagnosis of Diabetes Mellitus (DM).
4. Presentation with severe hypoglycemia as per the categorization defined by the American Diabetes Association (ADA) guidelines in 2024.

Exclusion Criteria

1. Age less than 18 years
2. Individuals who have not given consent for participation
3. Pregnant women.
4. Terminal ill patients.

Sample Size Calculation

As per Hamdy O., Srinivasan V.A.R., Snow K.J. Hypoglycemia, https://emedicine.medscape.com/article/122122-overview#a6, the true prevalence of hypoglycemia, with blood sugar levels below 50 mg/dL, is generally 5-10% of people presenting with symptoms suggestive of hypoglycemia. We calculated the sample size assuming prevalence of 10%.

The formula used is:

$n = Z^2 \cdot P \cdot (1-P) / d^2$ where:

n is the sample size,

Z is the Z statistic for a 95% level of confidence (1.96), P is the expected prevalence or proportion, d is the precision. For this study:

The calculated sample size for this study is 139.

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To account for potential data loss or exclusion due to incomplete responses or lab errors, a final sample size of 142 was targeted.

Statistical Analysis

Participant data was meticulously recorded in a Microsoft® Excel spreadsheet (Microsoft® Corp., Redmond, WA).

Statistical analyses, including frequency distributions, chi-square tests, and logistic regression, was employed to assess associations between medication use and severe hypoglycemia, symptomatology, and potential risk factors. Further analysis was performed by Partial Least Squares-Structural Equation Modeling (PLS-SEM) test.

RESULTS

Table 1: Age-wise Distribution of Diabetic Patients with Severe Hypoglycemia

		n	%
Age	≤40 years	5	3.52
	41-50 years	22	15.49
	51-60 years	43	30.28
	61-70 years	46	32.39
	>70 years	26	18.31
	Total	142	100.00

Table 1 shows that severe hypoglycemia was most common in the 61–70 years group 46 (32.39%), followed by 51–60 years 43 (30.28%), and >70 years 26 (18.31%). Fewer cases were seen in 41–50 years 22 (15.49%) and ≤40 years 5 (3.52%), indicating higher risk in older age groups.

Table 2: Demographic and lifestyle characteristics of patients with severe hypoglycemia

		n	%
Gender	Male	99	69.72
	Female	43	30.28
Education level	Non Graduate	104	73.24
	Graduate	38	26.76
Tobacco	Yes	42	29.58
	No	100	70.42
Smoking	Yes	23	16.20
	No	119	83.80
Alcoholic	Yes	11	7.75
	No	131	92.25

Table 2 presents the demographic and lifestyle characteristics of patients who experienced severe hypoglycemia. A significant majority of patients were male (99, 69.72%), while females accounted for 43 cases (30.28%), indicating a higher prevalence of severe hypoglycemia among men in this cohort.

Regarding educational status, most patients (104, 73.24%) were non-graduates, suggesting a potential link between lower education levels and increased vulnerability to severe hypoglycemic episodes, possibly due to limited health literacy or suboptimal self-management practices.

In terms of lifestyle factors, tobacco use was reported in 42 patients (29.58%), and smoking in 23 patients (16.20%), both of which are known to worsen glycemic control and complicate diabetic management. Alcohol consumption was relatively low, with only 11 patients (7.75%) identifying as alcohol users.

Table 3: Distribution of chronic comorbid illnesses among diabetic patients with severe hypoglycemia

		n	%
History of chronic illness	HTN	62	43.66
	CKD	23	16.20
	CAD ACS	9	6.34
	COPD	5	3.52
	CLD	1	0.70
	CAD	10	7.04
	CVA	11	7.74
	Hypothyroidism	6	4.23
	Nephrotic Syndrome	1	0.70
	Pulm TB	3	2.11
	Osteoarthritis	1	0.70
	DCMP	1	0.70

Table 3 outlines the distribution of chronic comorbid illnesses among diabetic patients who experienced severe hypoglycemia. The most prevalent comorbidity was hypertension (HTN), observed in 62 patients (43.66%), indicating a high co- occurrence with hypoglycemia in this population. Chronic kidney disease (CKD) was the second most common, affecting 23 patients (16.20%), which is clinically

ISSN (O): 2687-5365; ISSN (P): 2753-6556

significant given the altered drug metabolism and increased risk of hypoglycemia in renal impairment. Other notable comorbidities included coronary artery disease (CAD and ACS) in 19 patients (13.38%), and cerebrovascular accidents (CVA and ischemic CVA) in 11 patients (7.74%), reflecting the cardiovascular vulnerability of this population. Less frequent conditions included chronic obstructive pulmonary disease (COPD) (3.52%), hypothyroidism (4.23%), and pulmonary tuberculosis (2.11%). Rare comorbidities such as chronic liver disease (CLD), nephrotic syndrome, osteoarthritis, and dilated cardiomyopathy (DCMP) were each observed in just one patient (0.70%).

Table 4: Distribution of patients based on the duration of diabetes

		n	%
Durationof the disease	≤1 years	31	21.83
	1-2 years	14	9.86
	2-5 years	34	23.94
	5-10 years	37	26.06
	>10 years	26	18.31

Table 4 shows the distribution of patients based on the duration of diabetes. The highest proportion had diabetes for 5–10 years [37 (26.06%)], followed by 2–5 years [34 (23.94%)] and ≤1 year [31 (21.83%)]. A smaller proportion had the disease for more than 10 years [26 (18.31%)] and 1–2 years [14 (9.86%)]. This suggests that severe hypoglycemia occurred across all durations, but was slightly more common in those with a moderate disease duration (5–10 years).

Table 5: Distribution of anti-diabetic treatment regimens among patients who experienced severe hypoglycemia

Standardized Treatment	n	
Glimepride 2 mg + Metformin 500 Mg	45	31.94
Glimepride 1 mg + Metformin 500 Mg	41	28.47
Gliclazide 80 mg + Metformin 500 Mg	12	8.33
Inj. Basalog	12	8.33
Insulin 30/70	11	7.63
Inj. Insulin R	5	3.47
Glimepride + Metformin + Pioglitazone	3	2.08
Gliclazide 60 mg + Metformin 500 MG	4	2.77
Glimepride + Metformin + Dapagliflozin	2	1.39
Glimepride + Metformin + Linagliptin	2	1.39
Glipizide Combination	1	0.69
Gliclazide 30 mg + Metformin 500 Mg	1	0.69
Glimepride 2 mg+Metformin 1000 Mg	1	0.69
Glimepride + Metformin + Voglibose	1	0.69
Glimepride + Metformin + Vildagliptin	1	0.69

Table 5 shows the distribution of anti-diabetic treatment regimens among patients who experienced severe hypoglycemia. It highlights that the most common combination associated with hypoglycemic episodes was Glimepiride 2 mg + Metformin 500 mg, accounting for 31.94% of the cases. This was followed by Glimepiride 1 mg + Metformin 500 mg at 28.47%, indicating that sulfonylurea-based combinations—especially with Glimepiride—were prominently involved.

Insulin use was also noted among the patients: Basalog (insulin glargine) and Insulin 30/70 were each responsible for around 8.33% and 7.63%, respectively, while Regular insulin (Insulin R) contributed to 3.47% of cases. Other combinations involving agents like Pioglitazone, Dapagliflozin, Linagliptin, Voglibose, and different forms of Gliclazide appeared less frequently but still played a role.

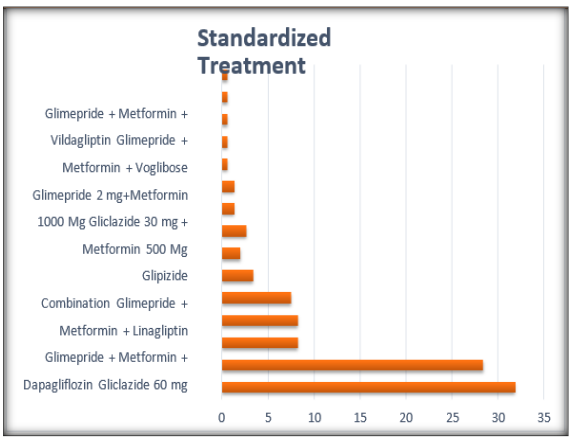

Figure 5: Distribution of anti-diabetic treatment regimens among patients who experienced severe hypoglycemia

Table 6: Distribution of patients based on the type of anti-diabetic medication regimens associated with severe hypoglycemia

Medication type	n	%
Sulfonylurea/Metformin	93	65.49
Insulin	26	18.31

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Sulfonylurea/Metformin/DPP 4 Inhibitor	7	4.93
Sulfonylurea/Metformin/SGLT 2 Inhibitor	4	2.81
Sulfonylurea/Metformin/Thiazolidineone	3	2.11
Insulin + DPP 4 Inhibitor	2	1.41
Sulfonylurea/DPP 4 Inhibitor	2	1.4
Sulfonylurea/Metformin/Glucosidase Inhibitor	2	1.41
Metformin/DPP 4 Inhibitor	1	0.7
Metformin/DPP 4 Inhibitor/SGLT 2 Inhibitor	1	0.7
Metformin/SGLT2 Inhibitors	1	0.7

Table 6 showsthe distribution of patients based on the type of anti-diabetic medication regimens associated with severe hypoglycemia. The most frequently observed regimen was the combination of Sulfonylurea and Metformin, seen in 93 patients (65.49%), indicating a strong association between sulfonylurea-based therapy and the risk of severe hypoglycemic events. Insulin alone was responsible for 26 cases (18.31%), reinforcing the known hypoglycemia risk linked to insulin therapy.

Combination regimens involving Sulfonylurea, Metformin, and DPP-4 inhibitors were identified in 7 patients (4.93%), while Sulfonylurea, Metformin, and SGLT-2 inhibitors were used by 4 patients (2.81%). Regimens including Sulfonylurea, Metformin, and Thiazolidinediones accounted for 3 cases (2.11%). Less common combinations such as Insulin + DPP-4 inhibitor (2 patients, 1.41%), Sulfonylurea + DPP-4 inhibitor (2 patients, 1.41%), and Sulfonylurea, Metformin + α- glucosidase inhibitor (2 patients, 1.41%) were also noted.

Additionally, single cases were reported for combinations like Metformin + DPP- 4 inhibitor (1 patient, 0.70%), Metformin + DPP-4 inhibitor + SGLT-2 inhibitor (1 patient, 0.70%), and Metformin + SGLT-2 inhibitors (1 patient, 0.70%).

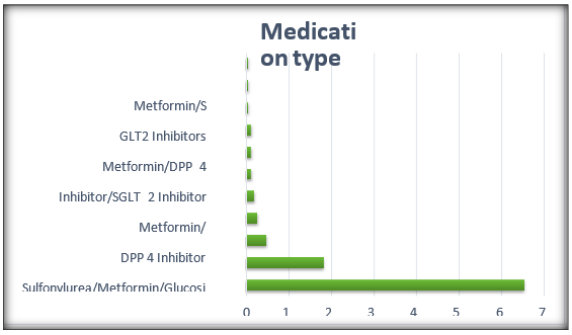

Figure 6: Distribution of patients based on the type of anti-diabetic medication regimens associated with severe hypoglycemia

Table 7: Distribution of insulin categories used among patients with severe hypoglycemia

Insulin Category	n	%
Basal	13	46.43
Insulin 30/70	8	28.57
Insulin R	7	25.0

Table 7 shows the distribution of insulin categories used among patients who experienced severe hypoglycemia. The most commonly used insulin type in these patients was basal insulin, specifically long-acting formulations like insulin glargine (e.g., Basalog), reported in 13 patients (46.43%). This was followed by premixed insulin (Insulin 30/70), used by 8 patients (28.57%), and short-acting insulin (Insulin R), which was associated with 7 cases (25.0%).

Table 8: History and Frequency of Hypoglycemic Episodes in the Study Population

		n	%
Previous history of hypoglycemia	Yes	75	52.82
	No	67	47.18
Past history of Severe hypoglycemia (n=75)	Yes	23	30.67
	No	52	69.33
Number of hypoglycemia episodes in last one month	1	28	19.72
	2	5	3.52
	No	109	76.76

Table 8 describes the history and frequency of hypoglycemic episodes among the study population. Out of the total participants, 75 patients (52.82%) reported a previous history of hypoglycemia, while 67 patients (47.18%) had no such history. Among those with a history of hypoglycemia (n = 75), 23 patients (30.67%) had experienced severe hypoglycemia in the past, whereas 52 patients (69.33%) had not reported any severe episodes previously.

When asked about hypoglycemic episodes in the last one month, 28 patients (19.72%) had experienced one episode, and 5 patients (3.52%) had experienced two episodes, while the majority, 109 patients (76.76%), reported no episodes during that time.

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Table 9: Descriptive statistics of various clinical and biochemical parameters among patients with severe hypoglycemia

	Mean	Median	Std. Deviation	Minimum	Maximum	Percentiles	
						25	75
Duration of treatment	6.57	5.00	6.11	0.08	35.00	1.88	10.00
RBS upon reporting	42.47	42.00	8.86	20.00	61.00	37.00	47.25
Duration of Hypoglycemia (symptoms) from onset	5.60	6.00	1.22	3.00	8.00	5.00	6.25
Total bilirubin	0.59	0.41	0.60	0.09	4.70	0.31	0.65
SGOT	65.65	43.00	88.00	14.00	647.00	34.00	64.00
SGPT	42.87	29.00	45.11	8.00	280.00	21.00	45.25
S. creatinine	2.41	1.30	2.88	0.45	22.65	0.91	2.63
serum urea	63.15	43.50	51.11	13.00	257.00	30.75	76.50
HbA1c	6.80	6.50	1.56	3.10	11.70	5.78	7.60

Table 9 shows the descriptive statistics of various clinical and biochemical parameters among patients with severe hypoglycemia.

The mean duration of treatment was 6.57 years, with a wide range from 0.08 to 35 years, suggesting varied disease chronicity. The median was 5.00 years, and 75% of patients were on treatment for ≤10 years.

Random blood sugar (RBS) at presentation had a mean of 42.47 mg/dL, reflecting a critically low [20.0 mg/dL] glucose level during the hypoglycemic event. The average duration of hypoglycemic symptoms from onset was 5.60 hours, with most cases ranging between 3 and 8 hours.

Total bilirubin was generally within normal range (mean 0.59 mg/dL), indicating minimal hepatic dysfunction in most.

Liver enzymes (SGOT: mean 65.65 U/L, SGPT: mean 42.87 U/L) showed high variability with some elevated values, suggesting hepatic stress in a few patients. Serum creatinine (mean 2.41 mg/dL) and serum urea (mean 63.15 mg/dL) were raised in many patients, indicating a significant presence of renal dysfunction, which is a known risk factor for hypoglycemia.

The mean HbA1c was 6.80%, suggesting that despite severe hypoglycemia, many patients had relatively tight glycemic control, possibly increasing the risk of such events.

Table 10: Comparison of mean age between patients on insulin treatment and those on oral drug therapy

	Insulin Treatment		Drug Treatment		t	p- Value
	Mean	±SD	Mean	±SD		
Age (years)	56.82	10.03	63.31	11.00	-2.841	0.005

Table 10 shows a comparison of mean age between patients on insulin treatment and those on oral drug therapy. The mean age of patients on insulin was 56.82 ± 10.03 years, while it was 63.31 ± 11.00 years in those on drug treatment. The t- value = -2.841 and p-value = 0.005, indicating a statistically significant difference in age between the two groups.

Table 11: Association between gender and type of diabetes treatment (insulin vs. drug therapy) among patients with severe hypoglycemia

Gender	Insulin Treatment		Drug Treatment		Chi sq.	p- Value
	n	%	n	%		
Male	**22**	**78.57**	**77**	**67.54**	0.83	0.364
Female	**6**	**21.43**	37	**32.46**		

Table 11 shows the association between gender and type of diabetes treatment (insulin vs. drug therapy) among patients with severe hypoglycemia. Among those on insulin, 22 (78.57%) were male and 6 (21.43%) were female. In the drug treatment group, 77 (67.54%) were male and 37 (32.46%) were female. The Chi- square value is 0.83 with a p-value of 0.364, indicating that the difference is not statistically significant.

Table 12: Comparison of biochemical parameters between patients on insulin treatment and those on oral drug therapy for diabetes

	Insulin Treatment		Drug Treatment		t	p- Value
	Mean	±SD	Mean	±SD		
RBS	41.71	6.57	42.66	9.37	-0.505	0.615
Total bilirubin	0.48	0.43	0.62	0.64	-1.084	0.280

ISSN (O): 2687-5365; ISSN (P): 2753-6556

SGOT	77.79	129.71	62.68	74.82	0.813	0.418
SGPT	46.29	58.55	42.03	41.43	0.446	0.656
S. creatinine	4.17	4.95	1.98	1.89	3.772	0.000
serum urea	87.07	59.91	57.28	47.17	2.832	0.005
HbA1c	7.88	1.93	6.54	1.33	4.325	0.000

Table 12 shows the comparison of biochemical parameters between patients on insulin treatment and those on oral drug therapy for diabetes.

Random Blood Sugar (RBS) at the time of reporting was similar between the groups (41.71 ± 6.57 vs. 42.66 ± 9.37, p = 0.615), showing no significant difference.

Liver function markers (total bilirubin, SGOT, SGPT) also showed no significant differences between the groups (p-values > 0.05), though SGOT was numerically higher in the insulin group.

Serum creatinine was significantly higher in the insulin group (4.17 ± 4.95 vs. 1.98 ± 1.89, p < 0.001), indicating more prevalent renal dysfunction among insulin users.

Serum urea was also significantly elevated in the insulin group (87.07 ± 59.91 vs. 57.28 ± 47.17, p = 0.005), supporting the same inference.

HbA1c levels were significantly higher in the insulin group (7.88 ± 1.93) compared to the drug group (6.54 ± 1.33, p < 0.001), indicating poorer long-term glycemic control among those requiring insulin.

These findings suggest that patient with renal dysfunction and higher hba1c were mainly put on insulin, explaining their increased risk of severe hypoglycemia.

DISCUSSION

Our cross-sectional analysis highlights the significant burden of severe hypoglycemia in individuals with diabetes mellitus, aligning with global findings but adding critical nuances from the Indian context. The observation that nearly one-third of patients had diabetes duration of less than 5 years underscores that severe hypoglycemia is not exclusive to long-standing disease but can occur early in the diabetes course, particularly with intensive glycemic control strategies.

Our study reinforces the well-documented association of sulfonylureas, particularly glimepiride, and insulin regimens with severe hypoglycemia. Notably, glimepiride combined with metformin emerged as the most frequent drug regimen linked to these episodes, emphasizing the need for careful drug selection, especially in elderly patients and those with comorbidities. Several international studies, including Holstein et al. (2012) and Hsu et al. (2013), have similarly highlighted glimepiride as a potent contributor to hypoglycemia, even more so than other sulfonylureas like glibenclamide.[10,11] Our data corroborate these findings, underscoring the need to re-evaluate sulfonylurea-based regimens in high-risk populations.

Insulin therapy accounted for nearly 18% of severe hypoglycemia cases in our cohort, with basal insulin regimens being the most implicated. This aligns with observations by Rosentock et al. (2024) and Geller et al. (2014), who demonstrated increased hypoglycemia risk with basal-bolus regimens, particularly in individuals with compromised renal function or multimorbidity.[12,13] Our study's finding of significantly higher serum creatinine and urea levels in insulin users further reinforces the interplay between renal dysfunction and hypoglycemia risk.

A noteworthy finding was that over half of the patients had a previous history of hypoglycemia, with nearly one-third experiencing recurrent severe episodes. This pattern mirrors global data from Yuni et al. (2023) and Chantzara et al. (2022), highlighting prior hypoglycemia as a strong predictor of future events.[14,15] Hypoglycemia-associated autonomic failure (HAAF) and impaired awareness of hypoglycemia symptoms likely contribute to this cycle, as suggested by Cryer et al. (2010).[4]

Interestingly, although tight glycemic control (mean HbA1c of 6.8%) was observed in our cohort, it paradoxically increased the risk of hypoglycemia, particularly in older adults with multiple comorbidities. This supports the need for individualized glycemic targets, especially in those with limited life expectancy or significant cardiovascular or renal disease.

Collectively, these finding highlight the multifactorial nature of severe hypoglycemia in diabetes. While medication choice plays a critical role, patient- level factors like age, socioeconomic status, renal function, and previous hypoglycemia history are equally important in risk stratification. This underscores the need for individualized, patient-centered treatment plans that balance glycemic targets with safety considerations.

Finally, our data have direct implications for clinical practice and policy. Structured diabetes education programs, routine renal function monitoring, and early adoption of safer antidiabetic alternatives are crucial. Health systems must prioritize access to glucagon, integrate structured discharge protocols, and ensure caregiver training to reduce emergency readmissions and improve patient outcomes.

CONCLUSION

This cross-sectional study underscores the significant burden of severe hypoglycemia among individuals with diabetes mellitus, particularly in older adults and those with comorbidities such as chronic kidney disease and cardiovascular disease. The findings demonstrate that sulfonylurea-based regimens—especially glimepiride in combination with metformin—and insulin therapies, notably basal

ISSN (O): 2687-5365; ISSN (P): 2753-6556

insulin, are the most frequently implicated in severe hypoglycemic episodes.

Notably, a substantial proportion of patients presented with recurrent severe hypoglycemia, and a previous history of hypoglycemia emerged as a strong predictor of future events. Furthermore, tight glycemic control (as indicated by low mean HbA1c) was associated with an increased risk of severe hypoglycemia, highlighting the importance of individualized treatment targets that account for patient-specific risk factors.

The complete absence of glucagon prescription or administration at discharge points to a critical gap in emergency hypoglycemia management and underscores the need for structured discharge protocols that incorporate education on glucagon use and access.

Overall, these findings emphasize the multifactorial nature of severe hypoglycemia in diabetes and the necessity for careful therapeutic decision- making, regular monitoring of renal function, and targeted patient education to reduce the risk of hypoglycemic episodes and improve clinical outcomes.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556