ORIGINAL ARTICLE

Hypoglycemia in hospitalized patients: A sleeping monster

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ABSTRACT

Objective: *This study describes the incidence and clinical profile of hypoglycemia (including mild, moderate, severe, and recurrent) and its correlation with the time of the day, duration of diabetes mellitus (DM), administration of insulin/oral hypoglycemic agents (OHAs) and diagnosis at admission in hospitalized adult patients.* **Materials and Methods:** *This retrospective, observational study analyzed the data of hospitalized patients with episode(s) of hypoglycemia. For each patient, clinical profiles such as age, gender, antidiabetic therapy, timing of hypoglycemic event, duration of diabetes, working diagnosis, place of hypoglycemia, dietary changes, and mode of corrective action were studied.* **Results:** *Of 100 patients with a mean ± standard deviation age of 62.72 ± 3.54 years, hypoglycemia was the most common among those aged 61–90 years. There were 134 hypoglycemic events and mild hypoglycemia was the most common (72.39% vs. moderate 21.64% and severe 5.97%). There were 59 (44%) events of recurrent hypoglycemia. Hypoglycemic events were maximum during 4:00 am–7:59 am (34%). Longer duration of DM (>15 years, 42%) and insulin therapy were the high-risk factors. There was a statistically significant association between hypoglycemia and duration of diabetes ($P < 0.0133$), insulin therapy ($P < 0.0001$), OHA ($P < 0.0192$), and a combination of insulin and OHA ($P < 0.0059$) within 24 h before the event but not with the incidence and dietary changes.* **Conclusion:** *Patients above 60 years were the most vulnerable population for hypoglycemia, especially during the early hours of the day. Patients who had diabetes for >15 years, on insulin therapy, and those with pulmonary and renal diseases were the most vulnerable to overall and recurrent hypoglycemic events, respectively.*

Key Words: *Diabetes mellitus, hospitalized patients, hypoglycemia, insulin therapy, oral hypoglycemic agents*

Introduction

The treatment goal of diabetes mellitus (DM) is achieving and maintaining a normal blood glucose level, thereby reducing disease-associated complications; managing hyperglycemia is the aim, but on the flipside, it results in hypoglycemia, a common unpredictable and potentially avoidable consequence of diabetes treatment, which can be fatal, if unrecognized and unattended.

The incidence of hypoglycemia varies due to inconsistencies in the definition used, the age of the populations studied, and the treatment modalities implicated. In a retrospective population-based study from the United States of America on 19,932 Medicaid patients, aged ≥65 years, the incidence of serious hypoglycemia was 1.23 episodes per 100 person-years for patients treated with sulfonylureas and 2.76 episodes per 100 person-years in those treated with insulin.[1] Incidence of severe hypoglycemia (blood glucose <50 mg/dL) cited in the literature varied between 7% and 35%.[2-5] The incidence of hypoglycemia is likely to be higher in older population than younger people.[1]

A high incidence of hypoglycemia in hospitalized patients with DM has been reported.[6] At least one episode of hypoglycemia is reported in 7%–10% of hospitalized

Access this article online	
Quick Response Code	Website: www.mjmsr.net
	DOI: 10.4103/mjmsr.mjmsr_81_23

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How to cite this article: Kuragayala SD, Nayak S, Khatib K. Hypoglycemia in hospitalized patients: A sleeping monster. Muller J Med Sci Res 2024;15:5-11.

Submitted: 01-Nov-2023 **Accepted:** 24-Apr-2024
Published: 06-Aug-2024

patients.[7] DM (~8% of hospital admissions) is one of the major risk factors, and hypoglycemia can prolong hospital stay and mortality.[8] Factors associated with the risk of hypoglycemia in older patients include low social status, long duration of DM, malnutrition, poly-pharmacy, diet, eating disorders, glycated hemoglobin (HbA1c) level, cognitive and functional disorders, kidney failure, falls, stroke, cancer, and cardiovascular diseases.

Glycemic control in hospitalized patients is crucial as both hyperglycemia and hypoglycemia are associated with a prolonged hospital stay, increased cost, morbidity, and mortality. Adequate and appropriate blood glucose control is necessary in hospitalized patients to prevent these adverse events.[3]

Real-life data on hypoglycemia in hospitalized patients is limited, countable from India, as most of the published literature on this topic are review articles. At this backdrop, we report real-life data that evaluated the risk factors, the role of DM and antidiabetic medications, and the burden of comorbidities associated with hypoglycemia in hospitalized patients.

Materials and Methods

This retrospective, observational study was conducted by the Department of Critical Care Medicine of a tertiary care hospital after obtaining approval from the Institutional Ethics Committee (IEC). Being a retrospective study, informed consent was waived off by the IEC. Data obtained between September 2018 and April 2019 from the electronic medical records of the patients from all inpatient wards, who experienced hypoglycemia during their stay in the hospital was analyzed. The objectives of the study were to determine the incidence of hypoglycemic events in the hospitalized patients, assess the relationship between antidiabetic medication (insulin, oral hypoglycemic agents (OHAs), and combination of insulin/OHA), the most likely time of the occurrence, diagnosis at the time of hospitalization, duration of DM, and correlate the burden of comorbidities and occurrence of hypoglycemia.

Patients of both genders with documented hypoglycemia were included. Random blood sugar (RBS) assessed by capillary blood samples obtained from the fingerstick method was analyzed by a glucometer (OneTouch SureStep®, MediSenseOptium®, and OptiumXceed®).[9] RBS levels between 54–49 mg/dL, 40–53 mg/dL, and <40 mg/dL were considered to be mild, moderate, and severe hypoglycemia. Data collection comprised relevant factors considered to be associated with hypoglycemic events. Demographic data, details of hypoglycemic events (type, time of occurrence, course, time taken for correction, and modality of corrective treatment), diabetic status and history, and incidence of hypoglycemia preceded by administration of insulin therapy or OHA within 24 h of the event. Corrective measures included oral or intravenous (IV) dextrose, depending on the severity of hypoglycemia.

Statistical analysis

We followed a convenient sampling method; the records that had complete details were considered for analysis. Statistical analysis was done using the software SAS Version 9.4 (Statistical Analysis System by y SAS Institute 00 SAS Campus Drive Cary, NC 27513-2414, USA). Descriptive statistics, i.e., percentages and distributions were used for hypoglycemic events and timelines. The risk estimate was assessed using odds ratio. An odds ratio value of >1 was taken as a consideration for estimating hypoglycemic incidence among all hospitalized patients. The relationship between two variables was assessed using rank correlation test and Chi-square test. $P < 0.05$ was taken as statistically significant, and the data were represented in the form of tables and graphs.

Results

A total of 100 patients (males: n = 76, 76%) who met the selection criteria with a mean ± standard deviation age 62.72 years ± 3.54 (range of 0–90 years) were included. All were diagnosed to have DM. There were 134 hypoglycemic events. Hypoglycemic episodes were more frequent among those aged >61 years–90 years, and recurrent hypoglycemia among those aged <60 years. The severity of hypoglycemic events among all age groups is shown in Figure 1.

Postsurgical patients (37%) had a higher incidence of hypoglycemia than those with a medical diagnosis (35%). Hypoglycemia was reported more from the wards (98%), and only 2% were from the intensive care unit (ICU) setting.

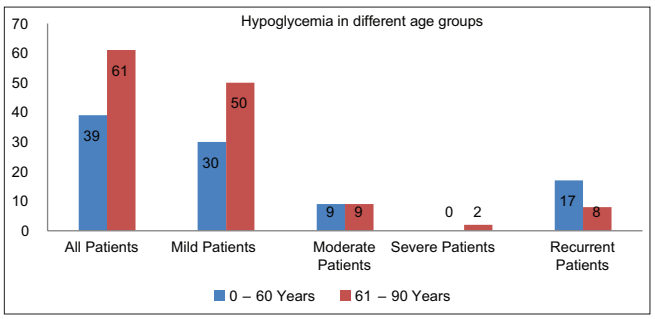

Figure 1: Age distribution and severity of hypoglycemia

Of the 134 hypoglycemic events, 97 (72.39%) were mild, 29 (21.64%) moderate, and eight (5.97%) were severe events; 59 (44%) were recurrent hypoglycemic events. All events occurred in those with DM (type 2 *n* = 85, 85%; type 1 *n* = 15, 15%). Patients who had a longer duration of diabetes >15 years (*n* = 42, 42%) were more susceptible to hypoglycemia [Table 1]. Surgical patients (events = 70, 52.24% vs. medical patients events = 64, 47.76%) had more hypoglycemic events.

Hypoglycemic events were reported the maximum between 4:00 am and 7:59 am (*n* = 45, 34%), followed by 4 pm to 7:59 pm (*n* = 36, 27%) [Table 2]. Incidence of recurrent hypoglycemia events was also observed more during the 4:00 am to 7:59 am timeline. The correction time period of 0:15:00 h (*n* = 42 events, 31%), 0:20:00 (*n* = 19, 14%), 0:30:00 (*n* = 25, 19%), and 1:00:00 h (*n* = 10, 7%) was most frequent of all time points [Supplementary Table 1].

Seventy-nine (59%) hypoglycemic events were treated with oral glucose, 46 (34.32%) with IV dextrose, and nine (6.7%) with a combination of both.

There was a statistically significant association between the medical/surgical status of the patients and the occurrence of hypoglycemic events (χ^2 = 5.4678 *P* = 0.01937) [Supplementary Table 2]. Medical patients were more susceptible to hypoglycemia events than surgical patients. However, the incidences of severe hypoglycemia events were more in surgical patients. Furthermore, the incidence of recurrent hypoglycemia was higher in medical patients than in surgical patients.

Approximately 50% of the incidence of hypoglycemia was associated with cardiac (18%), lung (15%), and endocrine diseases (14%). Hypoglycemic episodes were more in those with lung disease (23/134, 17%), followed by cancer, cardiac and endocrine disorders (21 each, 15.67%), and renal disease (18, 13.43%). Recurrent hypoglycemia was highest in patients with renal diseases followed by those with lung diseases [Table 3].

Insulin therapy (61%) followed by OHA (17%) and their combination (14%) were one of the risk factors for hypoglycemia; eight had no medication history. Of 134 hypoglycemic events, 84 (64.93%) were associated

Table 1: Duration of diabetes mellitus and severity of hypoglycemia

Duration of DM (year)	*n*	Hypoglycemia			
		Mild, *n* (%)	Moderate, *n* (%)	Severe, *n* (%)	Recurrent, *n* (%)
<1	5	5 (6.25)	0	0	1 (4)
1–5	4	4 (5)	0	0	1 (4)
5–10	13	8 (10)	5 (27.78)	0	8 (32)
10–15	34	31 (38.75)	3 (16.67)	0	6 (24)
<15	42	30 (37.5)	10 (55.56)	2 (100)	9 (36)
NA	2	2 (2.5)	0	0	0
Total	100	80	18	2	25

NA=Not available; DM=Diabetes mellitus

Table 2: Hypoglycemia events based on timeline

Timeline (HH:MM)	All events	Hypoglycemic events			
		Mild, *n* (%)	Moderate, *n* (%)	Severe, *n* (%)	Recurrent, *n* (%)
00:00–03:59	16 (12)	9 (9.28)	5 (17.24)	2 (25)	8 (13.56)
04:00–07:59	45 (33.6)	31 (31.96)	12 (41.38)	2 (25)	18 (30.51)
08:00–11:59	3 (2.24)	2 (2.06)	0	1 (12.5)	3 (5.08)
12:00–15:59	20 (15)	15 (15.46)	4 (13.8)	1 (12.5)	9 (15.25)
16:00–19:59	36 (26.87)	27 (27.84)	7 (24.14)	2 (25)	14 (23.73)
20:00–23:59	14 (10.45)	13 (13.40)	1 (3.45)	0	7 (11.86)
Total	134	97	29	08	59

Table 3: Hypoglycemic events and reason for hospitalization (primary organ system affected at the time of hospitalization – odds ratio estimate)

Primary organ system affected at the time of hospitalization	OR estimate with 95% CI as compared to the hypoglycemic events				
	All events	Mild	Moderate	Severe	Recurrent events
Malignancy	1.070 (0.48–2.40)	0.538 (0.19–1.50)	1.091 (0.25–4.79)	1.000 (0.03–39.64)	1.592 (0.53–4.80)
Cardiac diseases	0.493 (0.22–1.12)	0.752 (0.31–1.83)	0.024 (0.001–0.41)	N/A	0.640 (0.15–2.78)
Endocrine diseases	0.944 (0.42–2.12)	1.698 (0.68–4.24)	0.240 (0.03–2.08)	1.000 (0.03–39.64)	0.511 (0.16–1.61)
Gastrointestinal diseases	0.694 (0.25–1.94)	1.010 (0.32–3.15)	1.488 (0.12–18.16)	N/A	0.055 (0.01–0.40)
Musculoskeletal diseases	1.046 (0.32–3.38)	2.971 (0.83–10.62)	N/A	N/A	0.479 (0.08–2.81)
Pulmonary diseases	2.623 (1.19–5.79)	0.847 (0.28–2.52)	2.586 (0.66–10.17)	2.267 (0.13–39.61)	4.140 (1.35–12.68)
Renal diseases	1.116 (0.47–2.64)	1.317 (0.49–3.53)	N/A	0.219 (0.02–3.27)	5.344 (1.28–22.31)

If the OR estimate is equal to 1 there is no effect. If the OR estimate is <1 then the parameter is less likely to have an effect on the incidence of hypoglycemia. If the OR estimate is >1 then the parameter is more likely to have an effect on the incidence of hypoglycemia. N/A=Not applicable; OR=Odds ratio; CI=Confidence interval

with insulin therapy within the preceding 24 h of hypoglycemia followed by OHAs (*n* = 22, 16.42%) and combined insulin and OHA therapy (*n* = 1612%); in nine (6.72%) events, there was no medication history within preceding 24 h of hypoglycemia other than insulin/OHAs.

The impact of patient's antiglycemic medication intake within 24 h of the hypoglycemic event on the incidence of hypoglycemia was assessed using odd's ratio estimate. The incidence of hypoglycemia and recurrent hypoglycemia was highest with insulin administered 24 h before the event [Table 4].

Table 5 shows the rank correlation between Insulin/OHA intake within 24 h of the hypoglycemic event and medications (Insulin/OHAs).

It was observed that insulin intake within the preceding 24 h of the hypoglycemia event significantly affects the incidence of hypoglycemia in hospitalized patients. Among all categories of hypoglycemia, the incidence of severe hypoglycemia events was more in patients who were not on any treatment 24 h before the event.

We reviewed diet change, if any, within the preceding 24 h of hypoglycemia. There was no change in diet in 92% of patients. There was a statistically significant association between hypoglycemia and duration of diabetes ($P < 0.0133$), insulin therapy ($P < 0.0001$), OHA ($P < 0.0192$), and combined insulin/OHA ($P < 0.0059$) intake within 24 h of the event. However, there was no statistically significant association between the incidence of hypoglycemia and the age of the patient as well as dietary changes in the preceding 24 h.

Discussion

Hypoglycemia in hospitalized patients is commonly seen in diabetic patients but not uncommon in nondiabetics, and though a common event in clinical practice, there are less data. It is reportedly common among type 1 diabetic patients,[10,11] Sick patients and those who are on tight glycemic control (45%).[12]

Hypoglycemia in hospitalized patients is more frequent than reported; Tracy *et al*.[13] have reported 7895 unique hypoglycemic events at a cutoff <70 mg/dL in 3819 patients, who were primarily adult, female, and White patients. Unlike ours, where all patients had DM, there were only 58.7% diabetics in the study by Tracy *et al*.[13]

Considering a cutoff of <70 mg/dL, the prevalence of hypoglycemia was higher in those who were treated in ICU (10.1%) than in non-ICU setups (3.5%).[14] A pooled analysis of 31,970 patients has revealed that at a cutoff of <70 mg/dL, one episode of hypoglycemia was reported in 10.5%.[15] Different cutoffs have been used by different authors to define severe hypoglycemia; with ≤50 mg/dL by Turchin *et al*.,[2] the prevalence was 7.7% in the wards, ≤40 mg by Krinsley and Grover[16] the prevalence in ICU was 1.9%. In our study, with RBS ≤40 mg/dL as severe hypoglycemia, the incidence of hypoglycemia was more in non-ICU setting (98%) than the medical ICU setting (2%). Similar observations were reported by Varghese *et al*., (2007)[3] wherein too, hypoglycemic episodes were more frequent in non-ICU settings and ~1/4th of all episodes (23.8%) were reported from the ICU setting. The reason for the lower incidence of hypoglycemia is continuous monitoring of patients in ICU prevents development of hypoglycemic events. Place of occurrence of hypoglycemia is one of the factors

Table 4: Hypoglycemia events and patient's insulin/oral hypoglycemic administration within 24 h - odds ratio estimate

Insulin/OHA administration within 24 h	OR estimate with 95% CI as compared to the hypoglycemia events				
	All	Mild	Moderate	Severe	Recurrent
Insulin	2.512 (1.34–4.72)	1.943 (0.95–3.98)	16.927 (2.51–114.37)	0.300 (0.02–5.58)	5.154 (1.73–15.34)
OHA	0.505 (0.23–1.13)	0.752 (0.31–1.80)	0.122 (0.01–1.22)	N/A	0.116 (0.03–0.45)
Both	0.755 (0.31–1.87)	0.809 (0.28–2.32)	0.089 (0.01–0.92)	1.000 (0.03–39.64)	1.230 (0.21–7.15)
Nil	0.302 (0.09–1.10)	0.358 (0.10–1.28)	N/A	9.003 (0.16–509.85)	0.201 (0.02–2.44)

If the OR estimate is equal to 1 there is no effect. If the OR estimate is <1 then the parameter is less likely to have an effect on the incidence of hypoglycemia. If the OR estimate is >1 then the parameter is more likely to have an effect on incidence of hypoglycemia. N/A=Not applicable; OR=Odds ratio; CI=Confidence interval; OHA=Oral hypoglycemic

Table 5: Hypoglycemia events and patient's insulin/oral hypoglycemic administration within 24 h rank correlation

Patient's insulin/OHA administration within 24 h	Correlation coefficient values as compared to the hypoglycemia events				
	All	Mild	Moderate	Severe	Recurrent
Insulin	−0.24879	−0.18654	−0.41891	0.31686	−0.40737
OHA	0.16064	0.07309	0.15629	N/A	0.42960
Both	0.05184	0.03592	0.40091	N/A	−0.04162
Nil	0.16943	0.18404	N/A	−0.41487	0.18447

N/A=Not applicable; OHA=Oral hypoglycemic

influencing the outcome; worse outcome in those treated in wards than in ICU. Spontaneous hypoglycemia is associated with worse outcomes.[17]

Age and gender have a direct relationship with the development of hypoglycemia. There was a male preponderance (76%), and recurrent hypoglycemia was frequent in patients aged <60 years (17% vs. 8% in those >60 years) in our study; patients above 60 years had a greater risk of developing hypoglycemia in general and had more hypoglycemic episodes. A prospective study of 3810 patients in a primary care has reported similar observation as ours, with older patients (≥70 years) developing more hypoglycemic episodes than younger (<60 years) (12.8% vs. 9.0%, $P < 0.01$).[3] Akirov *et al*.[18] have too noted male preponderance (51%) and report that hypoglycemia is more common in old age (median age 70 years), in a patient pool of 33,675. Similar observations were reported by Ikeda *et al*.,[19] from a population of 166,806 patients (males 62.1%; age 66.2 ± 11.8 years). Despite being less common, regardless of the age group, rates of hypoglycemia were greater in women than in men ($P < 0.001$).[20]

Incidentally, all our patients were diagnosed to have DM. Similar observations were reported by Akirov *et al*.,[18] that of 4727 patients, 86% had preexisting DM.

Generally, medical patients are more susceptible to hypoglycemia events than surgical patients, but in our study, 37% postsurgical patients (vs. 35% medical) developed hypoglycemia. Severe hypoglycemic events were also more in surgical patients (52.44% vs. medical 47.76%). The incidence of recurrent hypoglycemia was more in medical patients. However, in contrast, few studies observed a higher incidence of hypoglycemia in the nonsurgical departments.[6]

Presence of comorbidities is a risk factor for developing hypoglycemia in hospitalized patients; those with cardiac, lung, renal, and endocrine diseases are at a higher risk of developing hypoglycemia. Recurrent hypoglycemia is common among those with renal diseases and lung diseases. Fischer *et al*.[21] have observed that renal diseases and the occurrence of hypoglycemia are common acquaintances, and the latter is mostly iatrogenic. Merrill and Dungan[22] have reported that hypoglycemia at a cutoff of <70 mg/dL is less frequent in those with heart failure than those without. Dendy *et al*.,[23] too noted the presence of renal diseases, cardiac diseases (congestive heart failure), insulin use, previous episodes of hypoglycemia, sepsis, and type 1 DM as risk factors for development of hypoglycemia in hospitalized patients. In our study, ~3/4th of events were mild (72.39%); our result indicates the possibility of occurrence of severe hypoglycemia though less common (5.97%), can be expected in hospitalized patients even if they are under continuous surveillance.

Our study indicates that recurrent hypoglycemic events are common (44%) and frequent in those with DM; duration of DM and surgery are influencing factors, longer the duration (>15 years, 42%), higher is the susceptibility to hypoglycemia.

Nocturnal hypoglycemia is more common,[24] in type 2 DM, treated with insulin, in most of the cases being asymptomatic, prolonged, particularly in those discharged from ICU and tends to occur within 24 h.[25] It is observed that the peak periods of hypoglycemia are 00:00 am–2:00 am, 22:00 pm–23:59 pm, 2:00 am–4:00 am, 8:00 am–10:00 am, and 10:00 am–12:00 pm.[6] We observed that most of the hypoglycemia events were reported between the timelines of 4:00 am–7:59 am, 16:00 pm–19:59 pm, 12:00 pm–15:59 pm, and 00:00 am–03:59 am, most frequent during early morning hours 4:00 am to 7:59 am (34%) followed by 4 pm–7:59 pm (27%). Recurrent hypoglycemia also followed a similar pattern. Late recognition of nocturnal hypoglycemia is a concern in non-ICU settings.

Mild hypoglycemic events were treated with oral glucose (79%); moderate-to-severe events were treated either with IV dextrose or a combination of both. The correction time period of 0:15:00 h (31%), 0:20:00 (14%), and 0:30:00 (19%) was most frequent of all time points. The time taken for corrective medical action after hypoglycemia events was 0:15:00 h (31%), 0:20:00 h (14%), 0:30:00 h (19%), and 1:00:00 h (7%).

Timely intervention can avert fatal outcomes in hypoglycemia in hospitalized patients; Kana Kadayakkara *et al*.[26] have reported that at a cutoff of ≤ 50 mg/dL for severe hypoglycemia, intervention reduced the incidence from 9.6% to 5.6%, and inpatient mortality rate from 4.1% to 0%, with a significant reduction in 30-day mortality rate (9.8%–3.8%) in hospitalized patients with hypoglycemia, but in diabetic patients, there was no significant difference in mortality and 30-day readmission rate.

Antidiabetic medication is a double-edged sword as these drugs themselves can cause hypoglycemia. Hypoglycemic patients are more likely to have diabetes and receive insulin therapy. As noted by Akirov *et al*.,[18] 14% of their study population as

treated with insulin during the hospitalization. Boucai *et al*.[15] described that the patients with diabetes, who were treated with insulin experienced higher rates of hypoglycemia compared with those not treated with insulin (23.7% [1447/6097 patients] vs. 7.4% [1902/25,873], $P = 0.001$).[15] It is also reported that patients on insulin therapy without concurrent OHAs are significantly associated with having one or more hypoglycemic events in the hospital ($P < 0.001$).[27] In our study, insulin therapy (61%), OHA (17%), and their combination (14%) proved to be the risk factor for hypoglycemia. However, eight patients without medication history also developed hypoglycemia, the reason for the same was not available.

In our study, the incidence of hypoglycemia and recurrent hypoglycemia was highest with insulin administered 24 h before the event, but the incidence of severe hypoglycemia events was more in patients who were not on any treatment 24 h before the event. This unique observation needs further investigation as we are unable to explain this finding.

The role of diet in the development of hypoglycemia was insignificant as there was no significant change in the diet of the patients (92%) within the preceding 24 h of hypoglycemia in our study. There was a statistically significant association between hypoglycemia and duration of diabetes ($P < 0.0133$) and antidiabetic therapy; insulin therapy ($P < 0.0001$), OHA ($P < 0.0192$), and combined insulin/OHA ($P < 0.0059$) intake within 24 h of the event were significant risk factors for developing hypoglycemia.

Similar to our study, Lee *et al*.[28] have reported an association of hypoglycemia with older age and premixed insulins in their study population of 3031 patients of whom 379 reported at least one episode of hypoglycemia in their retrospective study. Unlike our study, there was a female preponderance (60.4%). Extensive literature search yielded only one relevant article based on single-center experiences from India on this topic, which reported the incidence of hypoglycemia in type 2 DM patients to be 12.36% at a cutoff of <70 mg/dL (general RBS) and 30% were asymptomatic. In contrast to our study, it reported a female preponderance (60.8%). Premixed, fixed-dose insulin was administered to 72.5% of patients.[29]

Understanding the precipitating factors for hypoglycemia in hospitalized patients is essential to prevent future episodes. Literature has innumerable review articles on this topic; clinical trials and meta-analyses have focused on antidiabetic-induced hypoglycemia and compared the same between different agents. A systematic study on this topic is significantly limited compared to the prevalence of hypoglycemic events in hospitalized patients.

Limitations

We accept that being a single center, retrospective study with a small sample size of diabetic patients, a major limitation, stops us short of making any concrete conclusions, and also the results cannot be generalized. We considered only glucometer-assessed blood sugar values and did not compare other laboratory parameters. Power-based outcome assessment would have been more helpful in arriving at a meaningful decision. We did not capture details of sociodemography, iatrogenic hypoglycemia, previous diabetic status based on HbA1c, or previous hypoglycemic episodes in the recent past. We have not compared the doses of insulin (older vs. newer), OHAs received by the patients, and correlated with the severity of hypoglycemia. Inclusion of nondiabetic patients, assessing mortality rate, length of hospital stay, and long-term outcome in terms of 30-day mortality rate, and re-admission rate would have been more helpful. There is a need for prospective studies with well-designed protocol in our population using standard validated logistic models.[30] Prevention of hypoglycemia needs to be prioritized and structured interventions be applied.

Conclusion

There is a higher incidence of hypoglycemic events in diabetic patients particularly nocturnal hypoglycemia between 04:00 am and 07:59 am. Antidiabetic drugs, particularly insulin, are associated with the development of hypoglycemia. Cardiac, lung, and endocrine diseases can precipitate hypoglycemia in hospitalized patients. Hypoglycemia, particularly severe hypoglycemia is more common in postsurgical patients, whereas recurrent hypoglycemia is more in medical patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Abdelhafiz AH, Rodríguez Mañas L, Morley JE, Sinclair AJ. Hypoglycemia in older people – A less well recognized risk factor for frailty. Aging Dis 2015;6:156-67.
2. Turchin A, Matheny ME, Shubina M, Scanlon JV, Greenwood B, Pendergrass ML. Hypoglycemia and clinical outcomes in patients with diabetes hospitalized in the general ward. Diabetes Care 2009;32:1153-7.
3. Varghese P, Gleason V, Sorokin R, Senholzi C, Jabbour S,

Gottlieb JE. Hypoglycemia in hospitalized patients treated with antihyperglycemic agents. J Hosp Med 2007;2:234-40.

4. Deusenberry CM, Coley KC, Korytkowski MT, Donihi AC. Hypoglycemia in hospitalized patients treated with sulfonylureas. Pharmacotherapy 2012;32:613-7.
5. Farrokhi F, Klindukhova O, Chandra P, Peng L, Smiley D, Newton C, *et al.* Risk factors for inpatient hypoglycemia during subcutaneous insulin therapy in non-critically ill patients with type 2 diabetes. J Diabetes Sci Technol 2012;6:1022-9.
6. Yang CM, Ma YI, Kang J, Jia Z, Wang YY, Ma HY, *et al*. Time and department distribution of hypoglycemia occurrences in hospitalized diabetic patients. Int J Nurs Sci 2015;2:263-7.
7. Garg R, Hurwitz S, Turchin A, Trivedi A. Hypoglycemia, with or without insulin therapy, is associated with increased mortality among hospitalized patients. Diabetes Care 2013;36:1107-10.
8. McEwan P, Larsen Thorsted B, Wolden M, Jacobsen J, Evans M. Healthcare resource implications of hypoglycemia-related hospital admissions and inpatient hypoglycemia: Retrospective record-linked cohort studies in England. BMJ Open Diabetes Res Care 2015;3:e000057.
9. Gama M, Cruzeta CF, Ossowski AC, Bay MR, Michaelis MM. Detection accuracy of three glucose meters estimated by capillary blood glucose measurements compared with venous blood evaluated by the diabetes unit of the Hospital Evang and eacute; lico de Curitiba, Brazil. Res Rep Endocr Disord 2012;2:1-9.
10. Cryer PE. The barrier of hypoglycemia in diabetes. Diabetes 2008;57:3169-76.
11. Donnelly LA, Morris AD, Frier BM, Ellis JD, Donnan PT, Durrant R, *et al.* Frequency and predictors of hypoglycaemia in Type 1 and insulin-treated Type 2 diabetes: A population-based study. Diabet Med 2005;22:749-55.
12. NICE-SUGAR Study Investigators, Finfer S, Liu B, Chittock DR, Norton R, Myburgh JA, *et al.* Hypoglycemia and risk of death in critically ill patients. N Engl J Med 2012;367:1108-18.
13. Tracy MF, Manchester C, Mathiason MA, Wood J, Moore A. Adherence to a hypoglycemia protocol in hospitalized patients: A retrospective analysis. Nurs Res 2021;70:15-23.
14. Cook CB, Kongable GL, Potter DJ, Abad VJ, Leija DE, Anderson M. Inpatient glucose control: A glycemic survey of 126 U.S. hospitals. J Hosp Med 2009;4:E7-14.
15. Boucai L, Southern WN, Zonszein J. Hypoglycemia-associated mortality is not drug-associated but linked to comorbidities. Am J Med 2011;124:1028-35.
16. Krinsley JS, Grover A. Severe hypoglycemia in critically ill patients: Risk factors and outcomes. Crit Care Med 2007;35:2262-7.
17. Carey M, Boucai L, Zonszein J. Impact of hypoglycemia in hospitalized patients. Curr Diab Rep 2013;13:107-13.
18. Akirov A, Grossman A, Shochat T, Shimon I. Mortality among hospitalized patients with hypoglycemia: Insulin related and noninsulin related. J Clin Endocrinol Metab 2017;102:416-24.
19. Ikeda Y, Kubo T, Oda E, Abe M, Tokita S. Incidence rate and patient characteristics of severe hypoglycemia in treated type 2 diabetes mellitus patients in Japan: Retrospective diagnosis procedure combination database analysis. J Diabetes Investig 2018;9:925-36.
20. Quilliam BJ, Simeone JC, Ozbay AB, Kogut SJ. The incidence and costs of hypoglycemia in type 2 diabetes. Am J Manag Care 2011;17:673-80.
21. Fischer KF, Lees JA, Newman JH. Hypoglycemia in hospitalized patients. Causes and outcomes. N Engl J Med 1986;315:1245-50.
22. Merrill JD, Dungan KM. Hypoglycaemia in hospitalized patients with or without heart failure. Diabetes Obes Metab 2018;20:2472-6.
23. Dendy JA, Chockalingam V, Tirumalasetty NN, Dornelles A, Blonde L, Bolton PM, *et al.* Identifying risk factors for severe hypoglycemia in hospitalized patients with diabetes. Endocr Pract 2014;20:1051-6.
24. Amiel SA. Hypoglycemia at night: A cause for alarm? Diabetes Technol Ther 2012;14:99-100.
25. Ali Abdelhamid Y, Bernjak A, Phillips LK, Summers MJ, Weinel LM, Lange K, *et al*. Nocturnal hypoglycemia in patients with diabetes discharged from ICUs: A prospective two-center cohort study. Crit Care Med 2021;49:636-49.
26. Kana Kadayakkara D, Balasubramanian P, Araque KA, Davis K, Javed F, Niaki P, *et al.* Correction: Multidisciplinary strategies to treat severe hypoglycemia in hospitalized patients with diabetes mellitus reduce inpatient mortality rate: Experience from an academic community hospital. PLoS One 2019;14:e0222475.
27. Ghazi A, Landerman L, Lien L, Colon Emeric C. Impact of race on the incidence of hypoglycaemia in hospitalized older adults with type 2 diabetes. Clin Diabetes 2013;31:66-72.
28. Lee J, Kim TM, Kim H, Lee SH, Cho JH, Lee H, *et al.* Differences in clinical outcomes between patients with and without hypoglycemia during hospitalization: A retrospective study using real-world evidence. Diabetes Metab J 2020;44:555-65.
29. Vikas PV, Chandrakumar A, Dilip C, Suriyaprakash TN, Thomas L, Surendran R. Incidence and risk factors of hypoglycemia among type 2 diabetic patients in a South Indian hospital. Diabetes Metab Syndr 2016;10:S22-5.
30. Elbaz M, Nashashibi J, Kushnir S, Leibovici L. Predicting hypoglycemia in hospitalized patients with diabetes: A derivation and validation study. Diabetes Res Clin Pract 2021;171:108611.

Supplementary Table 1: Time taken for corrective medical treatment (oral, intravenous, and mixed)

Time taken (HH:MM:SS)	Events, *n* (%)
0:10:00	4 (2.99)
0:15:00	42 (31.34)
0:20:00	19 (14.18)
0:25:00	7 (5.22)
0:30:00	25 (18.66)
0:35:00	4 (2.99)
0:40:00	3 (2.24)
0:45:00	7 (5.22)
0:50:00	4 (2.99)
0:56:00	1 (0.75)
1:00:00	10 (7.46)
1:15:00	2 (1.49)
1:30:00	1 (0.75)
1:45:00	1 (0.75)
2:00:00	4 (2.99)
Total	134 (100.00)

Supplementary Table 2: Hypoglycemia events and medical/surgical status – odds ratio estimate

Medical/ surgical status	OR estimate with 95% CI as compared to the hypoglycemia events				
	All	Mild	Moderate	Severe	Recurrent
Medical	1.573 (0.87–2.84)	0.884 (0.44–1.78)	6.259 (1.43–27.42)	0.333 (0.03–4.22)	3.859 (1.51–9.87)
Surgical	0.636 (0.35–1.15)	1.131 (0.56–2.28)	0.160 (0.04–0.70)	3.000 (0.24–37.93)	0.259 (0.10–0.66)

If the OR estimate is equal 1 there is no effect, If the odds ratio estimate is <1 then the parameter is less likely to have an effect on the incidence of hypoglycemia. If the or estimate is >1, then the parameter is more likely to have an effect on the incidence of hypoglycemia. OR=Odds ratio; CI=Confidence interval