# Annual Trend in Hypoglycemia Emergency Cases in Oman: A Single Center Retrospective Study

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## *Abstract*

***Objective:*** To estimate the incidence and trends of hypoglycemia cases admitted to the emergency department (ED) of a tertiary hospital in Oman before the COVID-19 pandemic.

***Methods:*** We retrospectively reviewed the hospital records of all patients aged $\geq 15$ years admitted to ED with hypoglycemia (random blood glucose level (RBS) $\leq$3.9 mmol/L) between January 2010 and January 2017.

***Results:*** A total of N = 242 patients were admitted with hypoglycemia, with incidence increasing from 2011 to 2017 (3.31 to 6.33 per 10,000 individuals) . Non-diabetic patients exhibited significantly higher rates of abnormal heart rates compared to those with diabetes ($p = 0.010$). Non-diabetics were also more likely to have liver disease, liver cirrhosis, malignancies, exposure to drugs/toxins, and infections ($p < 0.050$), while diabetic patients had significantly higher rates of cerebrovascular diseases ($p < 0.050$). To manage hypoglycemia, intravenous dextrose was administered significantly more for patients with diabetes compared to those without diabetes ($p = 0.015$). In the study cohort, glucagon was administered to only one patient.

***Conclusion:*** The incidence of hypoglycemia presentations increased during the study period. Intravenous dextrose was the primary management approach for diabetic patients. Glucagon use was minimal. Further investigation is required to decipher the hypoglycemia trends in the post-pandemic period.

**Keywords:** Diabetes; Type 2 Diabetes; Hypoglycemia; Emergency Department; Glucagon; Oman

## Introduction

Hypoglycemia, mainly associated with diabetes mellitus (DM), is a leading cause for emergency department (ED) visits worldwide.[1] The expected global increase in DM prevalence (from 463 million cases in 2019 to 578 million by 2030) is likely to proportionately elevate the incidence of hypoglycemia as well.[1,2]

The American Diabetes Association (ADA) defines hypoglycemia as an abnormally low random blood sugar (RBS) levels of ≤ 3.9 mmol/L (70 mg/dL).[3] However, this threshold can slightly vary among patients depending on their clinical conditions. For instance, patients with poorly controlled DM, and younger people with newly diagnosed DM, may experience symptoms of hypoglycemia at higher glucose levels than do patients with tightly controlled DM and those with a chronic history of the disease.[4–6]

Hypoglycemia primarily occurs in DM patients who receive insulin or sulfonylurea therapy, often due to incorrect dosing or erratic meal timing.[7] Symptoms of hypoglycemia are categorized into two types: (a) neurogenic, characterized by a rapid drop in blood glucose levels, or (b) neuroglycopenic, where there is insufficient glucose availability in the central nervous system (CNS). The symptoms of neurogenic hypoglycemia are usually sweating, palpitation, tremor, anxiety, and paresthesia. Neuroglycopenic hypoglycemia symptoms manifest as impaired cognition, seizures, and coma.[2]

The severity of hypoglycemic episodes can range from mild nausea to profound neurological impairment. The typical intervention is to attempt to raise the blood glucose level by administering glucose or dextrose.[7] Although glucagon is considered the first line of treatment for patients with severe hypoglycemia,[8] it remains underappreciated and underused.[6] Glucagon is a polypeptide hormone produced by the alpha cells of the pancreas. It binds to glucagon receptors found throughout the body. This activates G-protein-coupled receptors, which in turn activate adenylate cyclase, resulting in an increase in cyclic adenosine monophosphate (cAMP) levels. This process activates glycogenolysis and glucogenesis, causing an increase in blood glucose levels.[2,9,10] The recent availability of novel glucagon formulations—such as intranasal and ready-to-use liquid glucagon—is expected to enhance its accessibility and ease of use in emergencies.[8]

This study aims to identify the incidence of hypoglycemia and its causes in the ED at a tertiary care hospital in Oman during the years prior to Coronavirus disease 2019 (COVID-19) pandemic. The knowledge of the pre-pandemic hypoglycemia trends may serve as a baseline for comparison with the trends at the years during and after the pandemic. We have also investigated hypoglycemia treatment approaches and the use of glucagon as a treatment option during the study period (2010–2017). This may also serve as a baseline for comparison to its present and future use, particularly with the current availability of novel glucagon formulations.

## Methods

Ethical approval was obtained from the Medical & Research Ethics Committee at Sultan Qaboos University, Muscat, Oman (MERC# 1612).

This cross-sectional retrospective study was conducted on all adult patients admitted with hypoglycemia to the ED at Sultan Qaboos University Hospital (SQUH), a tertiary care teaching hospital in Muscat, Oman. Inclusion criteria comprised: age ≥15 years at the time of first presentation at SQUH ED with RBS ≤ 3.9 mmol/L (70 mg/dL) during the period from January 2010 to January 2017. Patient data were retrieved from the Track Care database of SQUH. Patient data extracted included demographic characteristics, presenting symptoms, suspected etiologies of hypoglycemia, treatment provided, and cases of mortality. To assess the overall hypoglycemia, the incidence was expressed as the number of hypoglycemia cases per 10,000 ED visits. The total number of ED visits during the study period was considered as the denominator in the calculation, allowing for a standardized measure of incidence over time.

The extracted data was analyzed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics for continuous and certain categorical variables were presented as mean ± standard deviation (SD). Categorical variables were analyzed using the Chi-square test and presented as numbers and percentages. A $p$-value $\leq 0.05$ was taken to indicate statistical significance.

## Results

We reviewed records of N = 242 patients aged ≥ 15 years admitted to the ER with hypoglycemic episodes from January 2010 to January 2017. This cohort comprised 116 (47.9%) males and 126 (52.1%) females. Their mean RBS at presentation was 2.32 ± 0.69 mmol/L. The majority were DM patients (187; 77.3%), with type-2 diabetes (T2D) being the more prevalent (162; 67%) than type 1 diabetes (T1D) (25; 10.3%). Nondiabetic patients numbered 55 (22.7%). The mean RBS for patients with diabetes was 2.29 ± 0.67 mmol/L and 2.43 ± 0.78 for non-diabetics.

The proportion of non-smokers was significantly higher among diabetic patients than nondiabetic patients (92.5% vs. 81.8%; $p = 0.011$). In addition, 97.3% of diabetics were teetotalers compared to 87.35% of nondiabetics ($p = 0.022$) The other differences were nonsignificant [Table 1 and Figure1].

**Table 1:** Hypoglycemia patients' demography and diabetic status (N = 242).

| **Variables** | **Total (N=242)** | **Diabetes (n=187)** | **Non-diabetes (n=55)** | ***p*-value** |
|---|---|---|---|---|
| | **n (%)** | **n (%)** | **n (%)** | |
| Sex - Male | 116 (47.9) | 85 (45.5) | 31 (56.4) | 0.169 |
| Married | 223 (92.1) | 175 (93.6) | 48 (87.3) | 0.153 |
| Abnormal BMI (≥25 and < 18.5) | 75 (59.1) | 61 (59.2) | 14 (58.3) | 1.000 |
| Nonsmoking | 218 (90.1) | 173 (92.5) | 45 (81.8) | 0.011* |
| Nondrinking | 230 (95.0) | 182 (97.3) | 48 (87.3) | 0.022* |

Note.**Significant; BMI: Body mass index.*

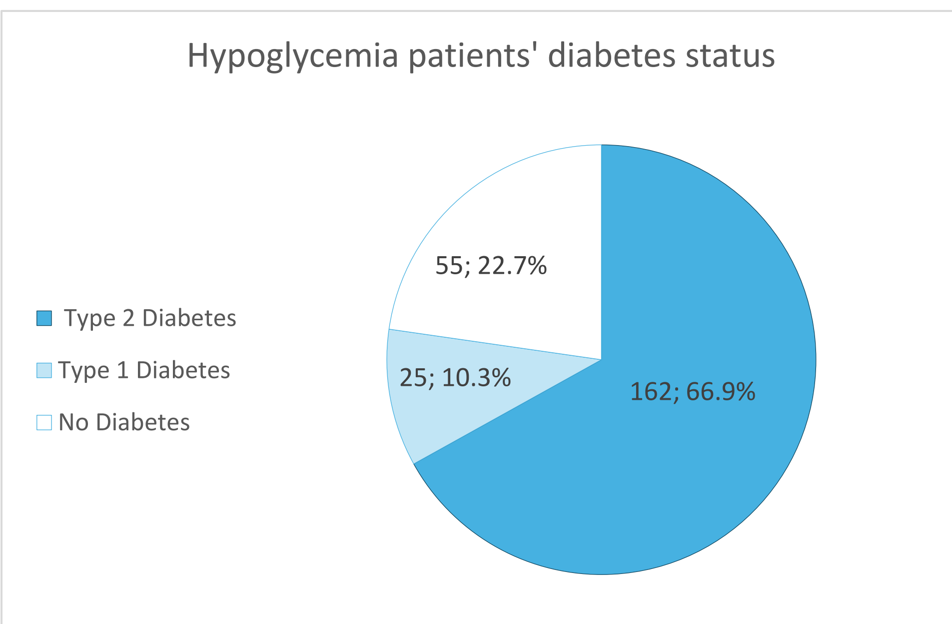


**Figure 1:** The diabetic status of the hypoglycemia patients during 2010–2017 (N = 242).

The yearly incidence of hypoglycemia cases varied considerably during our seven-year study period, with a slight overall increase, as illustrated by Figure 2.

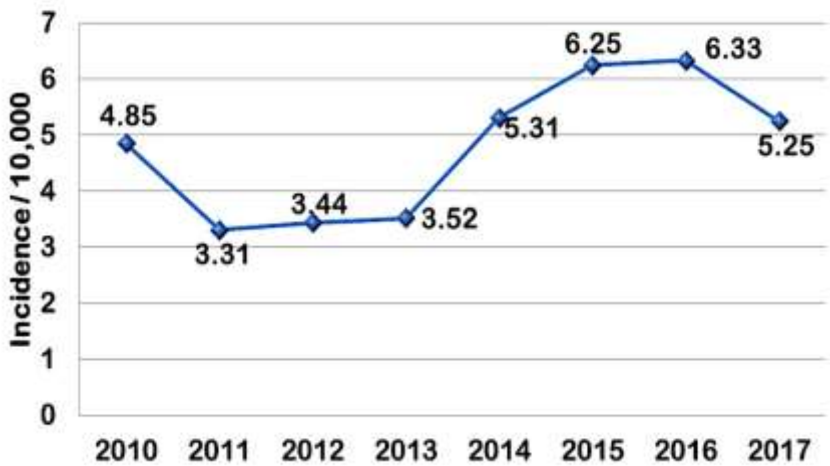


**Figure 2:** Incidence of cases of hypoglycemia per 10,000 total visits at Emergency Department (ED) of Sultan Qaboos University Hospital (SQUH) from 2010 to 2017 (N = 242).

Table 2 presents the study cohort's presenting symptoms, comorbidities, and treatments provided, stratified according to the diabetic status of the patients.

**Table 2:** Association between diabetic status and presenting symptoms, suspected etiology, and emergency interventions given (N = 242).

| **Variables** | **Total (242)** n (%) | **Diabetes (n=187)** n (%) | **Non–diabetes (n=55)** n (%) | ***p*–value** |
|---|---|---|---|---|
| **Presenting symptoms** | | | | |
| Body temperature | 69 (28.5) | 52 (27.8) | 17 (30.9) | 0.734 |
| Heart Rate | 67 (27.7) | 44 (23.5) | 23 (41.8) | 0.010* |
| Systolic blood pressure | 175 (72.3) | 145 (77.5) | 30 (54.5) | 0.002* |
| Diastolic blood pressure | 118 (48.8) | 94 (50.3) | 24 (43.6) | 0.444 |
| Hypoglycemic coma | 2 (0.8) | 2 (1.1) | – | 1.000 |
| Fever | 20 (8.3) | 13 (7.5) | 7 (12.7) | 0.175 |
| Neutropenia | – | – | – | – |
| Electrolyte imbalance | 6 (2.5) | 5 (2.7) | 1 (1.8) | 1.000 |
| Gastrointestinal symptoms | 36 (15.0) | 23 (12.4) | 13 (23.6) | 0.052 |
| Anemia | 2 (0.8) | 1 (0.5) | 1 (1.8) | 0.407 |
| Altered INR / coagulation / bleeding | 2 (0.8) | 2 (1.1) | – | 1.000 |
| Sweating | 23 (9.6) | 19 (10.3) | 4 (7.3) | 0.610 |
| Drowsiness | 43 (17.9) | 30 (16.2) | 13 (23.6) | 0.231 |
| Palpitations | 4 (1.7) | 3 (1.6) | 1 (1.8) | 1.000 |
| Seizures | 3 (1.3) | 1 (0.5) | 2 (3.6) | 0.132 |
| Unconsciousness | 17 (7.1) | 15 (8.1) | 2 (3.6) | 0.476 |
| Motor deficit | 26 (10.9) | 20 (10.9) | 6 (10.9) | 1.000 |
| **Etiology** | | | | |
| Liver disease | 19 (7.9) | 11 (6.0) | 8 (14.5) | 0.049* |

| | | | | |
|---|---|---|---|---|
| Liver cirrhosis | 10 (4.2) | 4 (2.2) | 6 (10.9) | 0.011* |
| Acute renal dysfunction | 7 (2.9) | 7 (3.8) | – | 0.357 |
| Renal dysfunction | 62 (25.9) | 51 (27.7) | 11 (20.0) | 0.295 |
| Malignancies | 12 (5.0) | 6 (3.3) | 6 (10.9) | 0.034* |
| Poor oral intake | 57 (23.8) | 43 (23.4) | 14 (25.5) | 0.723 |
| Drugs / toxins | 5 (2.1) | – | 5 (9.1) | 0.001* |
| Infection / sepsis | 37 (15.4) | 23 (12.4) | 14 (25.5) | 0.031* |
| Cerebrovascular disease | 152 (63.6) | 131 (71.2) | 21 (38.2) | <0.001* |
| Uremia | 3 (1.3) | 3 (1.6) | – | 1.000 |
| Urinary tract infection | 11 (4.6) | 9 (4.9) | 2 (3.6) | 1.000 |
| Pneumonia | 11 (4.6) | 8 (4.3) | 3 (5.5) | 0.719 |
| **Intervention received at ED** | | | | |
| Juice or honey | 58 (24.3) | 46 (25.0) | 12 (21.8) | 0.722 |
| Glucagon | 1 (0.4) | – | 1 (1.8) | 0.230 |
| Glucose gel | 4 (1.7) | 3 (1.6) | 1 (1.8) | 1.000 |
| Bolus glucose | 23 (9.6) | 20 (10.9) | 3 (5.5) | 0.303 |
| Intravenous dextrose | 211 (88.3) | 168 (91.3) | 43 (78.2) | 0.015* |
| **Outcome** | | | | |
| Mortality | 4 (1.7) | 2 (1.1) | 2 (3.6) | 0.226 |

Note.*Significant; ED: Emergency department; INR: International normalized ratio.*

The most prevalent presenting symptom of hypoglycemia was abnormal blood pressure, both systolic (175/242; 72.3%) and diastolic (118; 48.8%). Systolic abnormality was also significantly more prevalent among patients with diabetes (145/187; 77.5%) compared to those without diabetes (n=30/55**,** 54.5%) ($p = 0.002$) [Table. 2]. On the other hand, abnormal heart rate was significantly higher among nondiabetic patients (23/55; 41.8% vs 44/187 44/; 23.5%) ($p = 0.010$) [Table 2].

The etiology of hypoglycemia in the patients admitted to the ER was determined based on their preexisting diseases or comorbidities. The most frequently observed hypoglycemia-linked etiology was cerebrovascular disease (152; 63.6%), whose prevalence was significantly higher among diabetic patients (131/184; 71.2% vs. 21/55; 38.2%, $p <$ 0.001). Other important ones were renal dysfunction (62; 25.9%), poor oral intake (57; 23.8%), and infection/sepsis (37; 15.4%), albeit without significant intergroup differences [Table 2].

A few less-prevalent etiologies deserve mention due to significant differences between the groups. Non-diabetics were significantly more likely to present with liver disease (8/55; 4.5% vs. 11/184; 6.0%; $p = 0.049$), liver cirrhosis (6/55; 10.9% vs. 4/184; 2.2%, $p = 0.011$), malignancies (6/55; 10.9% vs. 6/184; 3.3%), $p = 0.034$), drugs/toxins (5/55; 9.1% vs. 0; 0%); $p = 0.001$), and infection/ sepsis (14/55; 25.5% vs. 23/185; 12.4%; $p = 0.031$), [Table 2]

Regarding the ED interventions for hypoglycemia, the majority received intravenous dextrose (211; 88.3%). Others were orally given fruit juice or honey (58; 24.3%), bolus glucose (23; 9.6%), or glucose gel (4, 1.7%). Glucagon was the least-used intervention, administered to only one patient (0.4%). Additionally, intravenous dextrose was used significantly more for patients with diabetes (168/184, 91.3%) than for patients without diabetes (43/55; 78.2%), $p =$ 0.015 [Table 2].

Although no mortality was attributed to hypoglycemia, four deaths were reported due to pre-existing comorbidities unrelated to the hypoglycemia: metastatic hepatocellular carcinoma, sepsis septic shock, hepatitis C liver cirrhosis, and sepsis and low ejection fraction heart failure.

## Discussion

This study aimed to determine the incidence of hypoglycemia in ED at a single center in Oman and its presenting symptoms, causes, and treatment approaches during the years prior to the COVID-19 pandemic. For patients with T1D, hypoglycemia has been linked to a mortality rate of 2%–6%, and the pandemic era from 2020–2023, their risk of hypoglycemia increased.[11–13] This increase was attributed to several factors such as limited access to health care services and the use of use of certain medications such as hydroxychloroquine (HCQ).[14] Moreover, COVID-19 virus effects on the immune system could trigger episodes of hypoglycemia.[15] Therefore, results from this study of years prior to the pandemic will serve as a baseline for comparison with the hypoglycemia trends in years during and after the pandemic.

Hypoglycemia is associated with various heart rate abnormalities including ventricular tachycardia, atrial fibrillation, ventricular arrhythmias, and bradycardia.[16,17] The low blood pressure during a hypoglycemic event is compensated with the secretion of epinephrine resulting in tachycardia, the body's attempt to supply more glucose to tissues.[17] Moreover, the low blood pressure during a hypoglycemic episode can disrupt the heart's electrical activity resulting in atrial fibrillation or ventricular arrhythmias.[18] In severe cases of hypoglycemia, due to the limited glucose delivery to the vital organs such as the brain, the heart's ability to sustain a normal rate becomes impaired causing bradycardia.[19]

In our study cohort, abnormal heart rate was significantly higher among patients without diabetes, attributable to the significantly higher hypoglycemia-linked etiologies among them—liver disease, cirrhosis, malignancies, drugs /toxins, and infection/sepsis—compared to the diabetic patients. Prevalence of cerebrovascular diseases (CVD) was significantly higher among our patients with diabetes, present independently from the hypoglycemia incidence. In diabetic patients, recurrent episodes of hypoglycemia poses a significant cardiovascular risk as a result of vascular damage.[20,21] This is because each hypoglycemic event triggers a cascade of physiological changes, such as elevation in platelet aggregation and coagulation factors, as well as inducing inflammation, cumulatively impacting the vasculature.[20,21]

Intravenous dextrose was the most used treatment approach (88.3%), especially for diabetic patients. The management of hypoglycemia in ED depends on the severity of the condition. Interventions may also include glucose in the form of juice, honey or glucose gel for mild cases and intravenous dextrose and glucagon for severe cases.[8,22]

Glucagon use was administered to only one (nondiabetic) patient in this cohort. The use of glucagon for hypoglycemia still remains limited despite its demonstrated effectiveness and safety in restoring blood glucose levels and consciousness.[6] Unlike intravenous dextrose, glucagon can be administrated without healthcare workers, also can be administrated subcutaneously or intramuscularly,[6] or through newer formulations. A 2020 study reported a success rate of 90.6% with self-administered nasal glucagon against 7.9% with injectable glucagon.[23] The current availability of novel glucagon formulations such as nasal glucagon and liquid glucagon,[8] as well as providing glucagon kits and educating parents and school nurses on its administration is likely to aid in the future reduction of hypoglycemia incidence in ED.

This study has a few limitations. First, the retrospective nature of the study may have resulted in incomplete data. Second, the study was conducted in a single center, which limits the generalizability of the findings to other institutions in Oman. The study did not compare the effectiveness of different treatment modalities, which warrants further investigation. Finally, as the study period was between 2010 and 2017, our findings do not reflect the hypoglycemia trends during the COVID-19 pandemic period and thereafter. However, the study serves as a baseline for comparison with the latter periods.

## Conclusion

This study presents the hypoglycemia trends at the ED of a tertiary hospital in Oman during the years prior to Coronavirus disease 2019 (COVID-19) pandemic, which may be used as a baseline for comparison with the trends during and after the pandemic in terms of incidence, etiologies, and managements. Our study also revealed the need to promote increased usage of glucagon, especially for severe cases of hypoglycemia.

## Disclosure

The authors declare they have no competing interests. This research did not receive or require any grant or funding.

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