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The Association between Hypoglycemia Requiring Emergency Medical Intervention and Patient Health Outcomes

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ABSTRACT

Objectives: *To examine the association between hypoglycemia requiring presentation at an emergency department and patient health outcomes in terms of duration of hospital stay and mortality rate.* ***Method:*** *A retrospective chart review study of all patients with hypoglycemia as the primary diagnosis admitted to the emergency department and met the inclusion criteria was conducted at King Abdulaziz Medical City in Riyadh (Saudi Arabia) between January 2015 and March 2016. Data were collected from an electronic health records database (Best care) and medical charts and pharmacy records were reviewed.* ***Results:*** *A total of 51 patients were included in the study. Twenty-two patients (42.31%) were admitted because of hypoglycemia. The total mortality rate was 3.92% (2 patients). The total length of hospitalization was higher in deceased patients (4.00 ± 4.24 days) compared to that in surviving patients (1.45 ± 1.21 days). At presentation, 22 patients (44.00%) had no prior interventions; nine were hypoglycemic, while 13 were non-hypoglycemic. In contrast, five patients (10.00%) received hypoglycemic intervention prior to arrival in the ER; one was hypoglycemic, and four were non-hypoglycemic. There was a zero mortality rate among patients who received pre-arrival interventions compared to a rate of 9.09% among patients who did not receive pre-arrival interventions. The chi-square test was used to assess statistical significance.* ***Conclusion:*** *In conclusion, this study shows no correlation between hypoglycemia and mortality or the total duration of hospitalization. In addition, there was no significant relationship between the incidence of hypoglycemic events and different comorbidities.*

Keywords: Hypoglycemia, Health, Blood, Diabetes

INTRODUCTION

Hypoglycemia is an episode characterized by abnormally low blood glucose levels (usually less than 4 mmol/L; 70 mg/dl) associated with the development of autonomic or neuroglycopenic symptoms, including shakiness, sweating, anxiety, chills, confusion, tachycardia, lightheadedness or dizziness, hunger, nausea, blurred vision, tingling in the lips or tongue, headaches, weakness or fatigue, depression, lack of coordination, seizures, and unconsciousness. Hypoglycemic patients may present with one or more of these typical hypoglycemic symptoms. The severity of hypoglycemia is determined based on the blood glucose level and associated symptoms. The Endocrine Society recommends a diagnosis of hypoglycemia based on the combination of a low blood glucose level and evidence of adverse effects [1].

There are several causes of hypoglycemia, which differ between diabetic and non-diabetic patients. In general, drugs are considered to be the most common cause of hypoglycemic episodes among diabetic patients; these include insulin, insulin secretagogues, and other anti-hyperglycemic agents. In contrast, hypoglycemic episodes among non-diabetic patients are associated mainly with critical illnesses such as sepsis, trauma, malnutrition, inanition, post-gastrectomy, hepatic impairment, renal impairment, cardiac failure, and infections. Other causes of hypoglycemia include deficiencies in hormones such as cortisol, glucagon, and epinephrine (in insulin-deficient diabetes mellitus). This condition is rarely caused by non-islet cell tumors and endogenous hyperinsulinism [1-4].

Severe hypoglycemia is a life-threatening event and knowing the predictors can help in limiting such episodes. Several predictive risk factors of severe hypoglycemia have been identified, including age, duration of diabetes, history of hypoglycemic episodes, duration of insulin treatment, assignment to intensive glucose control, lower body mass index (BMI), hypoglycemia-related injury, hypoglycemia-related convulsions, impaired renal function, peripheral neuropathy, lower cognitive function, and use of multi-hypoglycemic agents, as well as the educational level, socioeconomic status, and history of smoking or microvascular disease [3,5-9]. Moreover, severe hypoglycemia is associated not only with cardiovascular events and other adverse clinical complications but can even lead to death. The ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation) study conducted to examine the relationship between severe hypoglycemia in patients with type 2 diabetes mellitus (T2DM) and adverse clinical outcomes revealed that severe hypoglycemia was strongly associated with death ($p<0.001$), with a median time from the onset of severe hypoglycemia to death of 1.05 years [3]. In another study conducted in Japan, investigation of the predictors of mortality within 90 days after severe hypoglycemia revealed significantly higher mortality rates among non-diabetic patients compared with the rates among diabetic patients ($p<0.001$). Based on these findings, it was concluded that the predictors of death in non-diabetic patients with pre-admission severe hypoglycemia include age, advanced liver disease, cancer, sepsis, and blood glucose levels on arrival [10]. Sako et al. analyzed the association between patient characteristics and in-hospital mortality. It was found that the median duration of hospitalization was 7 days, with 3.8% in-hospital mortalities. Furthermore, factors associated with higher in-hospital mortality were older age, male sex, community hospital, lower bed capacity, coma on admission, low BMI, and high Charlson Comorbidity Index (CCI) [11].

Previous studies have assessed the importance of educating hypoglycemic patients who present to emergency departments and the adequacy of written discharge instructions in reducing the risk of recurrent hypoglycemia. It was recommended that emergency departments should develop standard protocols for the management of hypoglycemia with standard discharge instructions and planning to reduce this risk [2,12].

The NICE-SUGAR study was conducted to examine the association between hypoglycemia and death among critically ill patients in intensive care units. It was found that intensive glucose control leads to hypoglycemia, which is associated with a high risk of death. The median time from the first hypoglycemic episode to death was 7 days among moderate hypoglycemic patients and 8 days among severe hypoglycemic patients. Furthermore, the interval from the first hypoglycemic episode to death was shorter among patients who were not being treated with insulin compared with the interval among patients who were receiving insulin when the first hypoglycemic episode occurred ($p=0.004$ for moderate hypoglycemia, $p<0.001$ for severe hypoglycemia) [9]. A similar study to assess the association between hypoglycemia and death in critically ill patients showed that the rate of hospital mortality among hypoglycemic patients was higher than that among non-hypoglycemic patients ($p<0.001$). Furthermore, the rate of death was greater in patients with minimum blood glucose levels lower than 63 mg/dl compared to patients with minimum blood glucose levels between 63 and 81 mg/dl ($p<0.001$), with a median time from the hypoglycemic episode to death of 16 h. The severity of hypoglycemia was independently associated with higher mortality [13].

Despite all the negative consequences of a hypoglycemic attack for both diabetic and non-diabetic patients, most previous studies investigated the predictors of hypoglycemia, its outcomes, and associated mortality, only among diabetic patients [3,5-7,12], or critically ill patients in intensive care units [9,13-16]. The associations between hypoglycemia precipitated by different causes and the length of hospital stay and mortality rate are controversial and remain to be clarified. However, studies investigating the outcomes of hypoglycemia among pediatric and adult diabetic and non-diabetic patients, including those with other comorbidities, have not been reported previously. In this study, we investigated the impact of hypoglycemic events on health outcomes in terms of length of hospitalization and mortality rate among all patients presenting with hypoglycemia to the Emergency Department at King Abdulaziz Medical City, and King Abdullah Specialist Children's Hospital, Riyadh, Kingdom of Saudi Arabia.

The objective of this study was to examine the association between hypoglycemia requiring presentation at an emergency department and patient health outcomes in terms of duration of hospital stay and mortality rate.

MATERIALS AND METHODS

Study Design

The study is a retrospective chart review.

Ethics Approval

The study was approved by the Research Ethics Committee of King Abdullah International Medical Research Center and conducted in accordance with the International Conference on Harmonization Good Clinical Practice Guidelines.

Study Sites

The study was conducted at King Abdulaziz Medical City (KAMC; 1000 beds), a tertiary hospital in Riyadh, Saudi Arabia. All patients included in the study had hypoglycemia as a primary diagnosis on admission to the emergency department between January 2015 and March 2016 and met the inclusion criteria.

Data Collection

Data were collected using the electronic health records database (Best care) at KAMC. Medical charts and pharmacy records were also reviewed.

Collected Data

- Age
- Sex
- Body mass index
- Causes of admission
- Mode of arrival to the emergency department
- Blood glucose level
- Pre-admission interventions (including home and EMS interventions)
- Initial vitals
- Glasgow coma scale score
- Diabetic status
- Hypoglycemic episode (first/recurrent)
- Medication history
- Admission/discharge status
- The total duration of hospitalization

Data Analysis

Data were entered into a Microsoft Excel spreadsheet, coded, and crosschecked for accuracy. Thereafter, data were analyzed using SPSS 21.0 (Release 21.0.0.0, IBM, USA). Data were presented as mean ± SD for all quantitative variables, and as percentages and frequencies for the categorical variables. The chi-square test was used to assess statistical significance. p-values less than 0.05 were considered to indicate statistical significance.

RESULTS

A total of 51 patients were included in the study 32 males (63%) and 19 females (37%). Among these patients, 22 (42%) were admitted because of hypoglycemia, which represented the most common cause of admission. The mean ages of hypoglycemic and non-hypoglycemic patients were 57.71 ± 26.44 years and 58.10 ± 23.11 years, respectively. Out of the 22 hypoglycemic patients, the majority were male [17 (81%) compared to 4 females (19%)]. Additionally, 4 (21%) of patients were on beta-blockers, 6 (32%) were on ACE inhibitors, 8 (42%) were on diuretics, 9 (47%) were on calcium-channel blockers, and 11 (58%) were on aspirin. Other primary causes of admission included digestive system events (10%), neurological events (10%), respiratory system events (8%), cardiovascular events (4%), fever (4%), coma (2%) and other causes (24%). The total mortality rate was 4% (2 patients). The total length of hospitalization was higher in deceased patients (4.00 ± 4.24 days) as compared to the surviving patients (1.45 ± 1.21 days). At the initial presentation, 22 patients (44%) had no prior interventions; nine of these patients were

hypoglycemic at presentation, while 13 were non-hypoglycemic. On the other hand, five of the patients (10%) had received hypoglycemic intervention prior to their arrival in the ER; one of these patients was hypoglycemic, and four were non-hypoglycemic. However, there was no information regarding pre-arrival interventions for 46% of the patients. There was a 0% mortality rate among the patients who received pre-arrival interventions compared to a rate of 9% among those who did not receive pre-arrival interventions (Tables 1-3).

Table 1 Demographics and clinical characteristics

Variable	Statistic*
Age	57.94 ± 24.28
Total duration of hospitalization	1.55 ± 1.42
Sex	
Male	32 (62.75%)
Female	19 (37.25%)
Causes of Admission	
Trauma	
No	50 (100%)
Yes	0 (0%)
Hypoglycemia	
No	30 (57.69%)
Yes	22 (42.31%)
Fever	
No	48 (96%)
Yes	2 (4%)
Coma	
No	49 (98%)
Yes	1 (2%)
Cardiovascular event	
No	48 (96%)
Yes	2 (4%)
Digestive system event	
No	45 (90%)
Yes	5 (10%)
Respiratory system event	
No	46 (92%)
Yes	4 (8%)
Neurological event	
No	45 (90%)
Yes	5 (10%)
Urinary system event	
No	50 (100%)
Yes	0 (0%)
Rash	
No	50 (100%)
Yes	0 (0%)
Urticaria	
No	50 (100%)
Yes	0 (0%)
Other	
No	38 (76%)
Yes	12 (24%)
Mode of Arrival at Emergency Department	
Emergency medical services	15 (29.41%)
Self	31 (60.78%)

Not documented	5 (9.8%)
Pre-admission Interventions	
No	22 (44%)
Yes	5 (10%)
Not documented	23 (46%)
Diabetic Status	
Type I diabetes	21 (41.18%)
Type II diabetes	19 (37.25%)
Not documented	7 (13.73%)
Non-diabetic	4 (7.84%)
Hypoglycemia	
No	30 (57.69%)
Yes	22 (42.31%)
Hypoglycemic episode	
First episode	7 (13.73%)
Recurrent episode	19 (37.25%)
Not documented	24 (47.06%)
None	1 (1.96%)
Medication History	
Beta-blocker	
No	34 (72.34%)
Yes	13 (27.66%)
ACE inhibitor	
No	32 (68.09%)
Yes	15 (31.91%)
Diuretic	
No	29 (61.7%)
Yes	18 (38.3%)
Calcium-channel blocker	
No	31 (65.96%)
Yes	16 (34.04%)
Aspirin	
No	22 (46.81%)
Yes	25 (53.19%)
Quinolone	
No	47 (100%)
Yes	0 (0%)
Indomethacin	
No	47 (100%)
Yes	0 (0%)
Other	
No	11 (23.4%)
Yes	36 (76.6%)
Admission	
Discharged	42 (82.35%)
Admitted	9 (17.65%)
Mortality	
Died	2 (3.92%)
Survived	49 (96.08%)
*Reported statistics represent the mean ± standard deviation or (n)%	

Table 2 Association of variables with Hypoglycemia

Variable	Non-hypoglycemic	Hypoglycemic	p-value
Age	58.10 ± 23.11	57.71 ± 26.44	0.6962
Total duration of hospitalization	1.70 ± 1.74	1.33 ± 0.73	0.869
Sex			
Male	15 (50.00%)	17 (80.95%)	0.0389*
Female	15 (50.00%)	4 (19.05%)	
Causes of Admission			
Trauma			
No	29 (100.00%)	21 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Fever			
No	27 (93.10%)	21 (100.00%)	0.5029
Yes	2 (6.90%)	0 (0.00%)	
Coma			
No	28 (96.55%)	21 (100.00%)	1.0000
Yes	1 (3.45%)	0 (0.00%)	
Cardiovascular event			
No	28 (96.55%)	20 (95.24%)	1.0000
Yes	1 (3.45%)	1 (4.76%)	
Digestive system event			
No	26 (89.66%)	19 (90.48%)	1.0000
Yes	3 (10.34%)	2 (9.52%)	
Respiratory system event			
No	26 (89.66%)	20 (95.24%)	0.6298
Yes	3 (10.34%)	1 (4.76%)	
Neurological event			
No	26 (89.66%)	19 (90.48%)	1.0000
Yes	3 (10.34%)	2 (9.52%)	
Urinary system event			
No	29 (100.00%)	21 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Rash			
No	29 (100.00%)	21 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Urticaria			
No	29 (100.00%)	21 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Other			
No	22 (75.86%)	16 (76.19%)	1.0000
Yes	7 (24.14%)	5 (23.81%)	
Mode of Arrival at Emergency Department			
Emergency medical services	10 (33.33%)	5 (23.81%)	0.8305
Self	17 (56.67%)	14 (66.67%)	
Not documented	3 (10.00%)	2 (9.52%)	
Pre-admission Interventions			
No	13 (43.33%)	9 (45.00%)	0.7689
Yes	4 (13.33%)	1 (5.00%)	
Not documented	13 (43.33%)	10 (50.00%)	
Diabetic Status			
Type I diabetes	13 (43.33%)	8 (38.10%)	0.7488
Type II diabetes	12 (40.00%)	7 (33.33%)	
Not documented	3 (10.00%)	4 (19.05%)	
Non-diabetic	2 (6.67%)	2 (9.52%)	

Hypoglycemic Episode			
First episode	4 (13.33%)	3 (14.29%)	0.9547
Recurrent episode	12 (40.00%)	7 (33.33%)	
Not documented	13 (43.33%)	11 (52.38%)	
None	1 (3.33%)	0 (0.00%)	
Medication History			
Beta-blocker			
No	19 (67.86%)	15 (78.95%)	0.5147
Yes	9 (32.14%)	4 (21.05%)	
ACE inhibitor			
No	19 (67.86%)	13 (68.42%)	1.0000
Yes	9 (32.14%)	6 (31.58%)	
Diuretic			
No	18 (64.29%)	11 (57.89%)	0.7632
Yes	10 (35.71%)	8 (42.11%)	
Calcium-channel blocker			
No	21 (75.00%)	10 (52.63%)	0.1308
Yes	7 (25.00%)	9 (47.37%)	
Aspirin			
No	14 (50.00%)	8 (42.11%)	0.7668
Yes	14 (50.00%)	11 (57.89%)	
Quinolone			
No	28 (100.00%)	19 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Indomethacin			
No	28 (100.00%)	19 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Other			
No	8 (28.57%)	3 (15.79%)	0.485
Yes	20 (71.43%)	16 (84.21%)	
Admission			
Discharged	26 (86.67%)	16 (76.19%)	0.4601
Admitted	4 (13.33%)	5 (23.81%)	
Mortality			
Died	2 (6.67%)	0 (0.00%)	0.5059
Survived	28 (93.33%)	21 (100.00%)	
*Wilcoxon two-sample test for continuous variables and Fisher's exact test for categorized variables			

Table 3 Association of variables with mortality

Variable	Died	Survived	p-value
Age	53.00 ± 19.80	58.14 ± 24.59	0.6123
Total duration of hospitalization	4.00 ± 4.24	1.45 ± 1.21	0.1892
Sex			
Male	1 (50.00%)	31 (63.27%)	1.0000
Female	1 (50.00%)	18 (36.73%)	
Causes of Admission			
Trauma			
No	2 (100.00%)	(48) (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Hypoglycemia			
No	2 (100.00%)	28 (57.14%)	0.5059
Yes	0 (0.00%)	21 (42.86%)	

Fever			
No	2 (100.00%)	46 (95.83%)	1.0000
Yes	0 (0.00%)	2 (4.17%)	
Coma			
No	2 (100.00%)	47 (97.92%)	1.0000
Yes	0 (0.00%)	1 (2.08%)	
Cardiovascular event			
No	2 (100.00%)	(46) (95.83%)	1.0000
Yes	0 (0.00%)	2 (4.17%)	
Digestive System event			
No	2 (100.00%)	43 (89.58%)	1.0000
Yes	0 (0.00%)	5 (10.42%)	
Respiratory System event			
No	2 (100.00%)	44 (91.67%)	1.0000
Yes	0 (0.00%)	4 (8.33%)	
Neurological event			
No	2 (100.00%)	43 (89.58%)	1.0000
Yes	0 (0.00%)	5 (10.42%)	
Urinary system event			
No	2 (100.00%)	48 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Rash			
No	2 (100.00%)	48 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Urticaria			
No	2 (100.00%)	48 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Other			
No	2 (100.00%)	36 (75.00%)	1.0000
Yes	0 (0.00%)	12 (25.00%)	
Mode of Arrival at Emergency Department			
Emergency medical services	1 (50.00%)	14 (28.57%)	1.0000
Self	1 (50.00%)	30 (61.22%)	
Not documented	0 (0.00%)	5 (10.20%)	
Pre-admission Interventions			
No	2 (100.00%)	20 (41.67%)	0.3804
Yes	0 (0.00%)	5 (10.42%)	
Not documented	0 (0.00%)	23 (47.92%)	
Diabetic Status			
Type I diabetes	0 (0.00%)	21 (42.86%)	0.0212
Type II diabetes	0 (0.00%)	19 (38.78%)	
Not documented	2 (100.00%)	5 (10.20%)	
Non-diabetic	0 (0.00%)	4 (8.16%)	
Hypoglycemic episode			
First episode	0 (0.00%)	7 (14.29%)	1.0000
Recurrent episode	1 (50.00%)	18 (36.73%)	
Not documented	1 (50.00%)	23 (46.94%)	
None	0 (0.00%)	1 (2.04%)	
Medication History			
Beta-blocker			

No	1 (100.00%)	33 (71.74%)	
Yes	0 (0.00%)	13 (28.26%)	1.0000
ACE inhibitor			
No	1 (100.00%)	31 (67.39%)	
Yes	0 (0.00%)	15 (32.61%)	1.0000
Diuretic			
No	1 (100.00%)	28 (60.87%)	
Yes	0 (0.00%)	18 (39.13%)	1.0000
Calcium-channel blocker			
No	1 (100.00%)	30 (65.22%)	1.0000
Yes	0 (0.00%)	16 (34.78%)	
Aspirin			
No	1 (100.00%)	21 (45.65%)	0.4681
Yes	0 (0.00%)	25 (54.35%)	
Quinolone			
No	1 (100.00%)	46 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Indomethacin			
No	1 (100.00%)	46 (100.00%)	
Yes	0 (0.00%)	0 (0.00%)	
Other			
No	1 (100.00%)	10 (21.74%)	0.234
Yes	0 (0.00%)	36 (78.26%)	
Admission			
Discharged	2 (100.00%)	40 (81.63%)	1.0000
Admitted	0 (0.00%)	9 (18.37%)	
*Wilcoxon two sample test for continuous variables and Fisher's exact test for categorized variables			

DISCUSSION

In this study, we found that the mortality rate associated with hypoglycemia was 0.00%. Hypoglycemia in diabetic patients is usually due to poor dietary intake or an excessive dose of anti-diabetic medication. However, in non-diabetic patients, it is usually caused by digestive or neurologic system events or is induced by drugs or other comorbidities such as fever or coma. The incidence of hypoglycemia among patients who received pre-arrival hypoglycemic interventions was less than that among patients who did not. In cases where the hypoglycemic episode is not controlled by the hypoglycemic intervention alone, the patient should be advised to go to the emergency room despite receiving prior hypoglycemic intervention. The problem with hypoglycemia is not with the management of hypoglycemia alone, but with the associated complications, such as acute cerebrovascular disease, myocardial infarction, neurocognitive dysfunction, retinal cell death, and loss of vision, which may lead to a higher incidence of infections, higher costs, low quality of life (QoL), fewer available beds, and higher staff workload if hospitalization is required. These disadvantages can be prevented by effective education of patients. The timing of the hypoglycemic intervention is also crucial. As suggested by our results, patients who were taken to the emergency room by emergency medical services received hypoglycemic intervention earlier than those who arrived independently. This indicates that receiving hypoglycemic interventions like oral carbohydrates, dextrose (50% intravenous bolus), or glucagon (subcutaneously or intramuscularly) earlier may reduce hypoglycemic complications.

CONCLUSION

This study showed no correlation between hypoglycemia and mortality or the total length of hospitalization. Furthermore, there was no significant relationship between the incidence of hypoglycemic events and different comorbidities.

DECLARATIONS

Acknowledgment

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Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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