Research Article

Concurrent Risk Factors to Mortality in Hypoglycemia

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Abstract

Background & Objectives: In this study we aim to identify the demographic and clinical characteristics of hypoglycemic patients in emergency department that associated with mortality. This is a retrospective cross-sectional descriptive study.

Methods: Adult patients with hypoglycemia received in an emergency department over a 27 month period were included. Hypoglycemia is defined as an initial fast glucose or serum glucose of less than 60 mg/dL. The associations of demographic and clinical characteristics with the patient mortality were evaluated using Student's t-test for continuous parameter and χ (2) test for discontinuous parameters. There were 186 hypoglycemic patients included in this study.

Results: Of the patients included in this study, the mean age was 70.5±15.3years and 90 (48%) were females. The mean glucose level was 34.9±12.4 mg/dL. There were 21 (11.3%) non-survivors. Characteristics significantly associated with mortality were elevated heart rate (HR 85.3 ±15.9 / min vs 95.7± 29.5 /min $p<0.05$), lower blood pressure (SBP 141.7 ±27.3 mmHg vs 120.0 ±41.2 mmHg $p<0.05$, DBP 74.6±16.9 mmHg vs 63.7±23.8 mmHg $p<0.05$) , elevated liver function test (GOT 82±312 IU/L vs 324±460.8 IU/L $p<0.05$), elevated potassium (4 ±1 vs 4.7±1.2 $p<0.05$), liver cirrhosis (7.3% vs 33.3% $p<0.01$) , acute renal failure (23.6% vs 47.6% $p<0.05$) , biliary tract infection (BTI 1.8% vs 9.5% $p<0.05$) and/or cancer (7.3% vs 42.9% $p<0.05$).

Conclusion: Several clinical characteristics were identified that associated with the mortality of hypoglycemic patients in emergency department. Mortality rates of hypoglycemic patients who present to the emergency department are significantly higher in those with signs of cardiovascular compromise, hepatic problem (liver cirrhosis, biliary tract infection), acute renal failure and concomitant malignancy. Elderly is not an aggravating factor in hypoglycemic mortality.

Keywords: Acute renal failure; Hypoglycemia; Infection; Liver cirrhosis; Mortality rate

Introduction

Hypoglycemia is a commonly seen medical emergency in Emergency Department (ED). It may lead to variable degrees of brain dysfunction such as blurred vision, lethargy, confusion, drowsiness, delirium, convulsion and coma. Although treatment of hypoglycemic patients is very effective and rapid after administration of intravenous dextrose water, it may probably result in some comorbidity even debilitated complications. There are some predisposing factors such as polypharmacy, liver impairment, chronic renal insufficiency or acute renal failure, stroke, malignancy easily causing hypoglycemia [1,2]. Microbial infection and missed meal / inadequate intake are also common causes resulting in hypoglycemic episode [3]. Diabetic patients who presented micro- or macro-vascular complications easily increased relative rate of hypoglycemic episodes [4]. The objective of this study was to explore the possible association between mortality and demographic or clinical characteristics of hypoglycemic patients in ED.

Materials and Methods

This is a retrospective cross-sectional descriptive study that reviewed medical records from patients with hypoglycemia in the ED of an urban teaching medical center at northern Taiwan. Medical records with incomplete data analyzed in this study were excluded. Medical records from neonatal / pediatric and traumatic patients were also excluded. Although the definition of hypoglycemia is variable and individualized by symptoms presented by the patients, in this study, hypoglycemia is defined as initial fast glucose test or blood glucose level below 60 mg/dL [5]. Overall, 186 hypoglycemic cases admitted between 2009 December and 2012 February were included consistently. We recorded multiple parameters including age, Body Temperature (BT) at triage, heart rate, Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), White Blood Cell Count (WBC), blood glucose level, C - reactive protein (CRP), Glutamic Oxaloacetic Transaminase (GOT), creatinine, sodium, potassium. We also traced the past history and present illness including liver cirrhosis, uremia, malignancy, acute renal failure (ARF), stroke, concomitant infection like Urinary Tract Infection (UTI), pneumonia, or Biliary Tract Infection (BTI). Hospital stay and mortality were also recorded to make comparisons between survival and lethal hypoglycemic patients.

Table 1: Demographic data of 186 hypoglycemic patients.

Gender	96 Male		90 Female	
	Minimum	Maximum	Mean	Standard Deviation
Age (years old)	26	98	70;5	15;3
BT (°C)	31;8	39;1	36;4	1;2
HR (/min)	0	139	86;5	18;1
SBP (mmHg)	0	207	139;3	86;5
DBP (mmHg)	0	133	73;3	18;1
WBC (/μL)	72	55000	11223	7198
BS (mg/dL)	5	59	34;9	12;4
CRP (mg/dL)	0;04	42;35	5;1	6;5
GOT (IU/L)	12	3409	110	340
Cr (mg/dL)	0;2	13;9	2;8	2;6
Na (meq/L)	130	161	134;5	11;1
K (meq/L)	2	7;6	4;1	1;0
HS (days)	1	161	15;2	18;9

	n/186	(%)
Non-Diabetic	28/186	15%
Type 1 Diabetes	3/186	1;6%
Type 2 Diabetes	155/186	83;3%
OHA control	154/186	82;8%
Liver cirrhosis	19/186	10;2%
Uremia	13/186	7%
Acute Renal Failure	49/186	26;3%
With infection	103/186	55;4%
Urinary tract infection	62/186	33;3%
Pneumonia	43/186	23;1%
Biliary tract infection	5/186	2;7%
With stroke	4/186	2;2%
With Cancer	22/186	11;8%
Mortality	21/186	11;3%

BT: Body Temperature; HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; WBC: White Blood Cell Count; BS: Blood Sugar; CRP: C - reactive protein; GOT: Glutamic Oxaloacetic Transaminase; Cr: Creatinine; HS: Hospital Stay; OHA: Oral Hypoglycemic Agent; UTI: Urinary Tract Infection; BTI: Biliary Tract Infection.

Uremic patient are cases who have ever received hemodialysis at the time of ED arrival and ARF was defined as a doubling of creatinine level within one month.

We divided cases into survival and mortality groups to make comparisons. We analyzed the data using commercial statistical software (SPSS for Windows, version 11.0, SPSS Ltd., Chicago, IL). We used the Student's t-test and χ (2) test for statistical analyses, and significance was set at a p value less than 0.05.

Results

There are 96 male and 90 female hypoglycemic patients enrolled into our study with an age of mean ± standard deviation (SD): 70 ± 15.3 years old. The demographic data, vital signs, laboratory data, and co-morbid conditions are listed in Table 1.

Table 2: Factors associated with mortality in hypoglycemia patients.

|	Survival	Mortality	p-value (t-test; 2-tailed)
Age (years old)	70.5 ±15.1	70.3 ±17.2	0.95
BT (°C)	36.4 ±1.1	36.3± 1.4	0.76
HR (/min)	85.3 ±15.9	95.7± 29.5	0.014 <0.05
SBP (mmHg)	141.7 ±27.3	120.0 ±41.2	0.001 <0.01
DBP (mmHg)	74.6±16.9	63.7±23.8	0.009 <0.01
WBC (/μL)	10969±6437.4	13219 ±11607.6	0.18
BS (mg/dL)	35.1 ±11.9	33.1±15.6	0.49
CRP (mg/dL)	4.7±5.4	9.1±13.1	0.05
GOT (IU/L)	82±312	324±460.8	0.002 <0.01
Cr (mg/dL)	2.8±2.6	2.9±2.9	0.82
Sodium (meq/L)	135 ±11.1	131.8±11.2	0.24
Potassium (meq/L)	4 ±1	4.7±1.2	0.005 <0.01
HS (days)	14.6±16	20.2±34.3	0.20
	Survival	Mortality	p-value (Chi Square-test; 2-tailed)
Gender (M/F)	82/83	14/7	0.15
OHA control	88.5%	38.1%	0.000<0.01
Liver Cirrhosis	7.3%	33.3%	0.000 <0.01
Uremia	6.7%	9.5%	0.63
Acute Renal Failure	23.6%	47.6%	0.019 <0.05
With infection	53.9%	66.7%	0.27
UTI	32.7%	38.1%	0.62
Pneumonia	21.8%	33.3%	0.24
BTI	1.8%	9.5%	0.041 <0.05
With Stroke	1.8%	4.8%	0.38
With Cancer	7.3%	42.9%	0.001 <0.05

BT: Body Temperature; HR: Heart Rate; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; WBC: White Blood Cell Count; BS: Blood Sugar; CRP: C - reactive protein; GOT: Glutamic Oxaloacetic Transaminase; Cr: Creatinine; HS: Hospital Stay; OHA: Oral Hypoglycemic Agent; UTI: Urinary Tract Infection; BTI: Biliary Tract Infection.

Compared to survival group, hypoglycemic patients in mortality group are significantly tachycardia (HR 85.3 ±15.9 /min vs 95.7± 29.5 /min p<0.05) and hypotensive (SBP 141.7 ±27.3 mmHg vs 120.0 ±41.2 mmHg p<0.05, DBP 74.6±16.9 mmHg vs 63.7±23.8 mmHg p<0.05) Also they have higher liver dysfunction level (GOT 82±312 IU/L vs 324±460.8 IU/L p<0.05) and potassium level (4 ±1 vs 4.7±1.2 p<0.05). In co-morbidity, mortality patients have higher rate in having malignancy (7.3% vs 42.9% p<0.05), BTI (1.8% vs 9.5% p<0.05), liver cirrhosis (7.3% vs 33.3% p<0.01) and concomitant ARF (23.6% vs 47.6% p<0.05) (Table 2).

There are no significant differences in age, body temperature, WBC count, blood glucose level, CRP, creatinine, sodium, gender, uremia, with infection, UTI, pneumonia, with stroke and hospital stay between survival and mortality group. Risk factors of mortality in hypoglycemic patients are shown in Figure 1.

Discussion

Hypoglycemia is a true medical emergency in Emergency
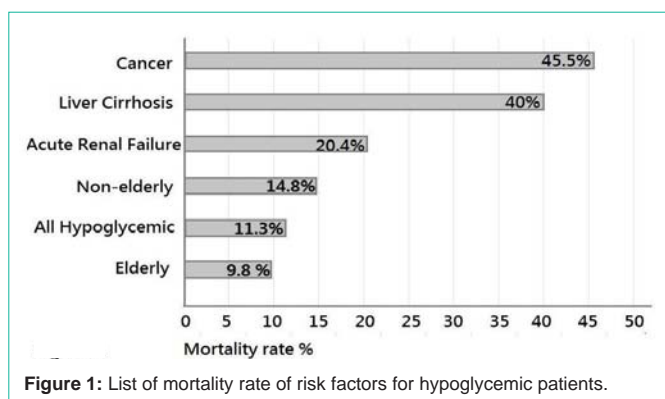
Figure 1: List of mortality rate of risk factors for hypoglycemic patients.

Department (ED) leading to variable degrees of brain dysfunction. The common presentations include cold sweats, complaints of blurred vision, feeling cold and lethargy, confusion, drowsiness, delirium, convulsion and coma. It can result in some accidents such as collapse, accident, cardiovascular adverse events, and internal medicine emergencies [6,7]. It leads to longer hospital stay in medical emergencies related hospitalization and higher mortality rate especially sepsis [8]. It is also a prognostic factor for in-hospital mortality in the elderly [9]. In our study, the mean age of hypoglycemic patients is 70.5 years old younger than a study from Japan national inpatient database (73.4 years old) [10]. The common causes of hypoglycemia include elderly, comorbidity, sepsis, malignancy, poor nutrition, and other in-hospital testing need nothing-by mouth [11].

In this study, by comparing the demographic information, co-morbidities, vital signs, lab results of hypoglycemic patients, we have identified several factors that are associated with mortality of this group of patients. Among them, irregularities in cardiac functions like HR and BP, liver function like GOT and cirrhosis, malignancy and renal failure are significantly associated with the death of hypoglycemic patients. In age, it is close in mean between the survival and death group of hypoglycemic patients.

In the novel finding, there are higher rate of hypoglycemic patients with liver cirrhosis in mortality group than survival group (33.3% vs. 7.3%, p<0.01).

Actually, etiologies of hypoglycemia are mixed and mosaic. Patients who are infected or having malignancy easily have low appetite with inadequate intake. Patients who suffered from stroke leading to altered mental status or having difficulty in daily activity also easily miss meal. In our study, there are 55.4% hypoglycemic episodes related to infected status. Of them, Urinary Tract Infection (UTI) is commonly seen than pneumonia and biliary tract infection (33.3% vs. 23.1% and 2.7%). In hypoglycemia with UTI and pneumonia, they do not increase risk to mortality.

Missed meal or inadequate intake accounted for 44.6% of causes in hypoglycemia, higher than 30.8% from a Greece data in year of 2005 [12]. Pancreatic parenchymal insulinoma is also a rare disease resulting in hypoglycemia [13]. Some factors are predisposing patients to hypoglycemic episode, such as elderly, micro-or macro-vascular complications, previous emergency department visits, renal impairment, multiple medications, recent hospitalization, and inadequate intake [1,2,4,14]. Patients who took medications including sulfonylurea, ACE inhibitors and nonselective beta-adrenoceptor

antagonists can also predispose patients to hypoglycemia [2]. In year 2007, Dr. Cox described fluctuation of self-monitored glucose level at home is also an omen of hypoglycemic episode [15].

About twenty-six percent of hypoglycemic patients have Acute Renal Failure (ARF) due to hypoglycemia related debilitated status (altered mental status, difficult to walk, decreased intake and possible febrile / infection). In mortality group, hypoglycemic patients have higher rate of ARF than survival group (47.6% vs. 23.6%, p<0.05).

Sometimes hypoglycemia is not the cause directly leading to fatal outcome, but the warning sign for severe illness [16]. Dr. Kinsley's finding suggests the mortality rate of severe hypoglycemia (glucose level less than 40 mg/dl) reaches 55.9% [17]. But in our study, severe hypoglycemic patients had lower mortality rate than overall ones (9.9% vs. 11.8%). The relative lower incidence of hepatic problem (liver cirrhosis and biliary tract infection) in severe hypoglycemic patients (9.9% vs. 10.2% and 2.5% vs. 2.7%) resulted in lower mortality rate than overall ones. In critical ill patients with hypoglycemia, mortality rate is high up to 36.6%, and overall mortality rate of hypoglycemia is 11.8% in our study [18]. Owing to our data is from a medical center in northern Taiwan, the mortality rate is higher than a report of national inpatient database from Japan (3.8%) in the year of 2015 [10].

Conclusion

Age, gender and serum glucose, CRP level, WBC count are not ominous factors in hypoglycemic prognosis. Hypoglycemic patients who are hypotensive, tachycardia, and high serum potassium and GOT, having malignancy, liver cirrhosis, biliary tract infection, and acute renal failure are associated with mortality rather than elderly. That is, elderly is one of the cause of hypoglycemia especially concomitant with infection, but it did not worsen the outcome in hypoglycemia. The outcome in hypoglycemia depends on comorbidity such as malignancy, liver cirrhosis, biliary tract infection, and acute renal failure.

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