

Admission Hyperglycemia is a Poor Prognostic Sign in Both Diabetics and Non-Diabetics

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ABSTRACT. To study the prognostic effect of admission hyperglycemia in known and unknown diabetics who were admitted to the general medical ward. A random sample of patients admitted to the medical ward over one year who had blood glucose measurement on admission was selected. In addition to demographic data, the following data were recorded; blood glucose measurement on admission, duration of hospital stay, admission to intensive care unit, presence of coronary heart disease, renal failure, and infection. A total of 480 patients were studied. Admission hyperglycemia were present in 170 (36%), 139 (29%) were known diabetics, and 31 (7%) were new hyperglycemia. New hyperglycemic had a longer hospital stay compared to both diabetics and non-diabetics; 20 days versus 15 days in diabetics, $p < 0.01$ and 11 days in non-diabetics $p < 0.001$. In addition new hyperglycemia had a higher in hospital mortality compared to diabetics and non-diabetics; 19% versus 12% in diabetics $p < 0.04$ and versus 9% in non-diabetics $p < 0.001$. Higher intensive care admission were also reported in new hyperglycemic compared to diabetics and non-diabetics; 36% versus 22% in diabetics $p < 0.01$ and versus 13% in non-diabetics $p < 0.001$. Admission hyperglycemia is a common finding. New hyperglycemia is significantly associated with higher in-hospital mortality, intensive care unit admission, and longer hospital stay.

Keywords: Hyperglycemia, Diabetics, Intensive care unit admission.

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Introduction

It is well known that *diabetes mellitus* increases the risk of morbidity and mortality^[1-3]. Studies had shown that the degree of admission hyperglycemia is an important predictor of morbidity and mortality among diabetic patients with myocardial infraction, stroke, and in those undergoing surgical procedure^[4-8]. The aim of our work is to study the prognostic effect of admission hyperglycemia in known and unknown diabetics who were admitted to the general medical ward.

Material and Methods

In order to meet our objectives, this study was carried out at King Abdulaziz University Hospital (KAUH), a teaching hospital which provides also medical services to the community of Jeddah. Out of the total 876 adult patients who were admitted to the medical wards during the period between January, 2002 till February, 2003, a random sample of 480 medical records, who had blood glucose measurement done on admission, were reviewed regarding the followings: blood glucose levels on admission, days of stay in the hospital, types of treatments given for hyperglycemia whether diet, oral hypoglycemic agents, or insulin. Patients were classified as known diabetics, new hyperglycemic and on-diabetics according to their part history of diabetes and blood glucose levels on admission. Patients with previous history of diabetes were recorded as diabetic patients, secondly, patients with no previous history of diabetes but had high level of glucose level on admission were recorded as newly hyperglycemic, the non diabetic had normal blood glucose on admission. Hyperglycemia was defined as in hospital fasting glucose level more than 7 mmol/l or random glucose level than 11.1 mmol/l. Fasting blood glucose were those samples drawn from patients while fasting or sample drawn between 0400 - 0600 h. In addition, more information were recorded such as demographic characteristics, admission blood pressure (systolic and diastolic), smoking status, body mass index (BMI), admission to intensive care unit (ICU), presence of coronary heart disease, renal failure and infection. The primary end point of the study was the in-hospital mortality and the causes of the death. The secondary end points were blood glucose level, the treatment of hyperglycemia, length of stay in the hospital and prognostic variables age, gender, BMI, admission blood pressure, smoking status, presence of coronary heart disease or renal failure, presence of infection, the need of intensive care unit admission.

Statistical Analysis

The data collected from medical records regarding all the variables mentioned was analyzed by an SPSS program, version 10. Different statistical anal-

ysis was used when appropriate, the *t* test for the continuous variable and the Chi-squares for the categorical variables. Logistic regression was done to determine the influence of demographic and clinical characteristics on mortality rates. *P* value < 0.05 were considered significant.

Results

Out of the randomly 480 selected patients admitted to the medical wards, 310 (64%) were non-diabetic, the known diabetes group was 139 (29.0%) and the newly diagnosed hyperglycemia consisted of 31 (6.5%) patients. The clinical characteristics of these three groups were shown in Table 1; there were statistical significant differences in the mean age among the known diabetics, the new hyperglycemic and the non diabetics (56.9, 51.48, and 45.26, respectively; *P* < 0.001) and more male than female among only known diabetic and non-diabetic groups. There were no significant difference in BMI and smoking status between the three groups of patients. In addition, as expected the results of the mean blood glucose levels on admission were significantly higher among known diabetics compared to the non-diabetics (16.96 mmol/l, 6.71 mmol/l, respectively, *P* < 0.005) and similarly between new hyperglycemic and the non diabetics (14 mmol/l, 6.71 mmol/l, respectively, *P* < 0.005). There were no significant level differences between the known diabetics and the new hyperglycemic in the mean blood glucose on admission. Patients with new hyperglycemia were more likely to stay longer in hospital compared to known diabetics and non-diabetics (20 days versus 15 days in diabetics, *P* = 0.02, and 11 days in non-diabetics, *P* = 0.001). Table 2 shows total and ICU admission and mortality.

TABLE 1. Patients' characteristics on admission.

Variables	Known Diabetics N=139	New Hyperglycemic N=31	Non-Diabetics N=310
Mean Age (yr)	56.9 ± 8.5 ^a	51.5 ± 4.3 ^{a,b}	45.3 ± 2.1
Gender (M:F)	2 : 1	1 : 1.8	1.4 : 1
Mean BMI (kg/m ²)	28.3 ± 1.6	27.2 ± 1.3	26.6 ± 1.1
Mean BP (systolic in mmHg)	136.4 ± 3.2 ^a	131.8 ± 3.2	126.1 ± 6.6
Mean BP (diastolic in mmHg)	75.0 ± 1.9	71.7 ± 2.2	72.9 ± 1.5
Nationality (S:NS)	1 : 1.5	1 : 2.1	1 : 1.7
Smoking	32 (30)	4 (17)	74 (32)
Mean BG (mmol/l)	16.9 ± 1.2 ^a	14.1 ± 1.0 ^{a,b}	6.7 ± 1.0
Mean Hospital Stay (days)	15.15 ± 2.3 ^a	20.29 ± 2.0 ^{a,b}	11.37 ± 3.0

BMI = body mass index; BP = blood pressure; S = Saudi; NS = Non-Saudi; BG = blood glucose

Results are in mean ± SD

^a = *P* < 0.05 vs. non-diabetics

^b = *P* < 0.05 vs. known diabetics

TABLE 2. Total and intensive care unit mortality and admission.

Variables	Known Diabetics N=139	New Hyperglycemic N=31	Non-Diabetics N=310
Total Mortality	17 (12) ^a	6 (19) ^{a,b}	28 (9)
ICU Mortality	8 (6)	3 (10) ^a	10 (3)
Non-ICU Mortality	9 (6)	3 (10)	18 (6)
Total ICU Admission	30 (22) ^a	11 (36) ^{a,b}	40 (13)
Non-ICU Admission	109 (78)	20 (64)	270 (87)

ICU = intensive care unit

^a = $p < 0.05$ vs. non-diabetics^b = $p < 0.05$ vs. diabetics

The total ICU admission were significantly higher among the new hyperglycemic compared to known diabetics and non-diabetics, ($P = 0.001$) and similarly total mortality were higher among the first two groups compared to non-diabetics (19% in new hyperglycemic versus 9% in non-diabetics, $P = 0.001$ and 12 % in diabetics, $P = 0.04$). The total ICU percent mortality of new hyperglycemic were significantly higher than non-diabetics 10%, versus 3% ($P = 0.02$). In the deceased patients, the mean age of the new hyperglycemic was younger than diabetics and non-diabetics (54, 65, and 56, respectively). The mean blood glucose on admission were found to be higher among new hyperglycemic compared to non-diabetics (14 mmol/l versus 6.8 mmol/l, $P = 0.001$) and lower compared to diabetics (14 mmol/l versus 16 mmol/l, $P = 0.6$). No significant differences were found in the length of hospital stay between the three groups. Cardiovascular causes were the most common cause of death in the three groups (Table 3).

TABLE 3. Clinical characteristics of deceased patients.

Variables	Known Diabetics N=139	New Hyperglycemic N=31	Non-Diabetics N=310
Mean Age (yr)	65.1 ± 4.8 ^a	54.0 ± 6.0 ^b	55.9 ± 2.0
Gender (M:F)	2.6 : 1 ^a	1 : 5	1 : 1
Nationality (S:NS)	1.2 : 1	1 : 2	1 : 1.5
BP (systolic in mmHg)	124.1 ± 3.5	113.6 ± 3.7	119.0 ± 3.2
BP (diastolic in mmHg)	73.5 ± 1.6	60.6 ± 2.1	67.4 ± 1.6
Mean BG (mmol/l)	16.1 ± 1.6 ^a	14.3 ± 2.0 ^{a,b}	6.8 ± 0.1
Mean Hospital Stay (days)	12.1 ± 2.0	14.2 ± 1.3	11.3 ± 1.7
Cause of death			
Infection	5 (27)	1 (17)	6 (21)

TABLE 3. Contd.

Variables	Known Diabetics N=139	New Hyperglycemic N=31	Non-Diabetics N=310
Cardiovascular	10 (55)	2 (33)	11 (39)
Neurologic Events	2 (11)	1 (17)	2 (7)
Malignancy	1 (5)	—	1 (4)
Others	5 (28)	2 (33)	8 (28)

BP = blood pressure, BG = blood glucose

^a = $p < 0.05$ vs. non-diabetics

^b = $p < 0.05$ vs. diabetics

However, in logistic regression model, odds ratio were adjusted for age, gender, BMI, hypertension, coronary heart disease, presence of infection, renal failure, and intensive care admission, the new hyperglycemia group had 2.5 fold increase mortality rate compared to 1.4 fold increase in known diabetics.

During hospital course 16.6% new hyperglycemic were prescribed diet, 4% were given oral hypoglycemic agents, non-were given insulin, 20% were given sliding insulin scale. Their treatment modalities were lower than those given to known diabetics were it was 42%, 71%, 55%, and 85%, respectively.

Discussion

Our study showed that 36% of the patients admitted to the medical ward had hyperglycemia on admission and almost 185 of them were not know diabetics. These patients (new hyperglycemic) had a higher in-hospital mortality rate, were more likely to require intensive care unit admission and had an increased length of hospital stay compared to known diabetics and non-diabetics which is in agreement with what had been reported by Umpierrez *et al.*^[9]. There is a lot of controversy about whether admission hyperglycemia is independently associated with a poor prognosis^[10,11] or it indicates a more severe illness with an increased response to stress^[12-14]. Stress hyperglycemia which is a transient increase in blood glucose during acute physiological illness can occur either in patients with undiagnosed diabetes or as a result of severe stress and increased counter regulatory hormones. The exact mechanism of stress hyperglycemia is not yet clear. Several hypotheses had been proposed which include increase insulin-like growth factor (IGF)-1 and growth hormone dependent IGF-binding proteins^[15], increase gluconeogenesis, decrease glycogenolysis, due to increased counter regulatory hormones and peripheral insulin resistance^[16-18].

Studies showed that hyperglycemia by itself creates a toxic cellular milieu causing intracellular and extracellular dehydration inducing electrolyte ab-

normalities and depression of immune function, which contribute to high morbidity^[19-22].

In a recent study on 108 patients with acute myocardial infarction, new hyperglycemic, compared to diabetics and non-diabetics, had a higher plasma IL-18 C-reactive protein, CD16+/CD56+ cells and CD4/CD8 ratio indicating that increased inflammatory immune process seems likely mechanism linking acute hyperglycemia to poor cardiac outcome in myocardial infarction patients^[23]. It is well known from several studies that admission hyperglycemia is associated with high morbidity and mortality in patients with acute myocardial infarction and stroke. In patients with myocardial infarction it is associated with increased risk of mortality, heart failure, cardiogenic shock and recurrent myocardial infarction in patients with and without diabetes^[4,6,11,24,25]. In acute phase of stroke, hyperglycemia is a poor prognostic index, associated with mortality and residual disability^[7,12,26-29].

Treatment of admission hyperglycemia in patients with and without history of diabetes had been shown to reduce morbidity and mortality. In a large prospective study by Scheen^[30] on 1,548 critically ill patients hospitalized to the intensive care unit, patients who received intensive insulin treatment to maintain their blood glucose between 80-110 mg/dl had a 40% lower mortality and morbidity compared to those who received insulin only if blood glucose exceeded 215 mg/dl and maintain blood glucose at 18-200 mg/dl. Another study by van den Berghe *et al.*^[31] reported that among mechanically ventilated adults admitted to intensive care unit, strict normalization of blood glucose levels (4.5-6.1 mmol/l with continuous insulin infusion compared to restrictive insulin regimen to maintain blood glucose between 10-12 mmol/l resulted in reduced hospital morbidity and mortality. It reduces intensive care mortality by 43% hospital mortality by 34%, mean intensive care unit stay by 22% and incidence of bacteremia and hemodialysis by 50%.

In agreement with previous reports^[9,32], we found that 18% of all hyperglycemic had not history of diabetes. As there is an average delay of a decade between the onset and diagnosis of diabetes^[32,33], patients with admission hyperglycemia and not history of diabetes should have their glycoselated hemoglobin measured for early diagnosis and treatment of diabetics to prevent chronic complications.

It is clearly shown in our study that admission hyperglycemia is frequently left untreated, especially in non-diabetics. As it is a common problem that is associated with poor prognosis, particularly in patients without a history of diabetes, it should be recommended that blood glucose should be checked on admission and intensively controlled whether the patient is a known or unknown diabetic.

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زيادة السكر في الدم عند التنويم إنذار خطير لدى مرضى السكري وغير المصابين بالسكري

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المستخلص. الهدف من البحث هو دراسة تأثير ارتفاع نسبة السكر في الدم عند التنويم لمرضى السكري وغير المصابين بالسكري. وعليه فقد تمت دراسة مرضى تم تنويمهم في عنبر الباطنة وتم قياس مستوى السكر في الدم عند التنويم على مدار سنة كاملة، ومن ثم تسجيل مستوى السكر في الدم عند التنويم، وفترة التنويم في المستشفى، ومدة التنويم في العناية المركزة، وجود قصور في شرايين القلب، فشل كلوي والتهابات جرثومية. تمت دراسة ٤٨٠ مريض، وجد ارتفاع مستوى السكر عند التنويم في ١٧٠ (٣٦٪) منهم، ١٣٩ (٢٩٪) مصابون بالسكري، و ٣١ (٧٪) غير مصابين بالسكري. ارتفاع مستوى السكر في الدم عند التنويم المكتشف حديثاً أدى إلى زيادة مدة التنويم، مقارنة بالمرضى المصابين بالسكري وغير المصابين بالسكري، ٢٠ يوماً، مقارنة ١٥ يوم عند مرضى السكري، ١١ يوماً عند المرضى غير المصابين بالسكري، هذا بالإضافة إلى زيادة نسبة الوفاة والتنويم في العناية المركزة. وُجد أن ارتفاع نسبة السكر في الدم عند التنويم المكتشف حديثاً له علاقة وثيقة بزيادة نسبة الوفاة، والتنويم في العناية المركزة وفترة التنويم في المستشفى.