

Impact of Admission Blood Sugar and HbA1c on Mortality in Intensively ill patients in Critical Care Unit

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Abstract

Original Research Article

Background: Hyperglycemia is a poor prognostic factor in various subsets of intensively ill patients. Hyperglycemia is a common reason for increased mortality in critical care unit during critical illness. Thus the present study was designed and conducted with an aim to evaluate the impact of admission blood sugar and HbA1C on mortality in intensively ill patients in critical care unit. **Methods:** This was a retrospective study where medical records between January 2018 and December 2018 of all diabetic patients admitted in CCU were enrolled after obtaining the approval from the institutional ethical committee. 325 diabetic patients admitted to CCUs were enrolled. HbA1c concentrations on CCU admissions were taken from the patients reports. Age, sex, history of DM, co-morbidities, APACHE II score, SOFA score, low blood sugar episodes, medication history, death rate, liver and kidney failure were recorded. **Results:** Non survivors had significantly higher mean blood sugar values compared to survivors (184.67 mg/dl vs. 135.54 mg/dl respectively). Non survivors showed significantly high values of HbA1c than survivors, without considering the history of diabetes (9.5% vs. 7.5%, respectively). At admission, critical care unit blood glucose has shown a significant relationship with increased mortality rate. Mortality rate was higher when the blood glucose level was more than 200 mg / dl and lower when blood glucose level was below 150 mg /dl. **Conclusions:** High blood sugar is related significantly with high mortality rate in intensively ill patients. Stress induced hyperglycemia also significantly increases mortality rate in intensively ill patients; this association is affected by chronic hyperglycemia.

Keywords: Blood sugar, critically ill patients, Hyperglycemia, Mortality.

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INTRODUCTION

During intensive illness, hyperglycemia is a very common reason associated with increased death rate [1]. High blood sugar levels induced by stress have been found to be poor prognostic factor in various subsets of critically ill patients including trauma patients. Therefore, it seems that the relation of high blood sugar on outcome depends on previous glycemic control [2]. Previous research has shown that hyperglycemia is related with high mortality and morbidity in critical care unit admitted patients and supported by the results showing correction of high blood sugar can improve mortality rates [3,4].

Recent studies showed that the association between high blood sugar and mortality rate could be influenced by the presence of chronic hyperglycemia [5,6]. Glycosylated hemoglobin (HbA1c) shows persons average blood sugar level in the past three

months and is a conventional biomarker for monitoring sugar control in diabetic patients. American Diabetes Association has suggested HbA1c of 6.5% for diagnosis of diabetes [7, 8]. Hence HbA1c status gives an insight into the association between chronic sugar control and patient mortality rate. Hyperglycemia predicts not only diabetes but also cardiovascular morbidity and mortality among people with diabetes. It has been estimated that each 1% augmentation in HbA1c concentrations is associated with 15–20% greater cardiovascular risks [9]. Thus, it seems that HbA1c level on admission might be a more proper reflector of chronic hyperglycemia, which would detect occult diabetes as well. HbA1c can also be used to indicate the correlation between its higher levels and increased death rate in intensively ill patients [10, 11]. Most of these previous studies have showed an increased risk of mortality from diabetic high HbA1c levels [12]. But few studies showed a linear relationship between HbA1c and death

rate [13], others have shown a J-shaped association [12].

No studies have directly compared the risk of mortality rate to high blood sugar among many reasons responsible for admission in critical care unit and death. Recent studies have linked higher HbA1C levels to increased mortality. Hence a study of this facet of diabetes mellitus is important to evolve the need of early sugar management. So the objective of our study was to evaluate the impact of admission blood sugar and HbA1C on mortality in intensively ill patients in critical care unit.

METHODOLOGY

Three hundred and twenty five diagnosed diabetic patients admitted in critical care unit were enrolled in the study. The institutional ethical clearance was obtained and data was collected from all diabetic patients admitted to CCU from Jan 2018 to Dec 2018. CCU admission blood sugar and HbA1c were measured for all patients. Age, sex, duration of DM, comorbidities, APACHE II score, SOFA score, low blood sugar episodes, medication history (aspirin,

corticosteroids, beta blockers, metformin, and glibenclamide), death rate, liver and kidney failure were recorded for all patients.

STATISTICAL ANALYSIS

Analysis was performed with SPSS version 16. Microsoft word and excel has been used to generate tables and graphs. Statistical methods used were student t-test to compare mean changes between two parameters, ANOVA for comparison of changes between groups in quantitative variables. We analyzed the effects of CCU admission blood glucose, Hb1Ac, and hypoglycemic episode as independent variables on mortality.

RESULTS

Three hundred and twenty five diabetic patients admitted in critical care unit were enrolled in the study. Age, sex, history of DM, co-morbidities, APACHE score, SOFA score, low blood sugar episodes, mortality rates and the demographic characteristics of the patients have been presented in Table 1.

Table-1: Demographic Characteristics of study population

Characteristics	N (%)	Survivors	Non Survivors
Number of Patients	325	215	110
Males	210 (64.6 %)	135	75
Females	115 (35.4 %)	75	35
Mean Age	64 (60-69)	65 (58-68)	65 (62-70)
APACHE II score	18.8	18.2	28.2
SOFA score	8.2	8.8	15.2
Mean Blood Sugar (mg/dl)	162.43	135.54	184.67
HbA1C	8 % -9 %	6.5 % -7.5%	9.5%- 10.5%

The patient population was predominantly males (64.6%), older than 60 years (57%) and overweight or Obese. In 68.2 % of patients, a history of oral glucose control agents was noted. The most common reasons for CCU admission were cardiac causes, stroke, CKD, sepsis, and COPD (Table 1). Most admissions in ICU were of Cardiac cause (45.2%) and Stroke (30.3%). The data sets for APACHE II score and SOFA score were 98.72% and 99.52 % respectively. APACHE II score for survivor and nonsurvivor was 18.2 and 28.2 respectively. SOFA score for survivor and nonsurvivor was 8.2 and 8.8 respectively. ICU mortality was 33.8%.

Non survivors had significantly higher mean blood sugar values compared to survivors (184.67 mg/dl vs. 135.54 mg/dl respectively). Non survivors showed high values of HbA1c significantly than

survivors, without considering the history of diabetes (9.5% vs. 7.5%, respectively). At admission critical care unit blood glucose has shown a significant relationship with increased mortality rate. Mortality rate was higher when the blood glucose level was more than 200 mg / dl and lower when blood glucose level was below 150 mg / dl as shown in fig 1 and 2.

Mortality rate for mean glucose 140 –199 , 200–300 , > 300 mg/dl was , 55.05%, 84.2% , 28.6%) respectively. Results from the study showed mortality rate was highest in deaths due to cardiac cause (31.0%) when blood sugar level was more than 200 mg/ dl (19.8%). Mortality rates were high in deaths due to Stroke (10.5 %), CKD (17.7 %), DKA (17.5%), Sepsis (20.8%), COPD (18.7 %), when blood sugar level was more than 200 mg/ dl shown in table 2.

Table-2: Association of Mean Blood Sugar (mg/dl) with increased Mortality Rate (%)

Number of patients	N	RBS Mean glucose (mg/dl)					
		140-199		200-300		>300	
		S	NS	S	NS	S	NS
Patients due to Cardiac cause	101 (31.0%)	35.6	9.9	23.7	19.8	5.9	4.9
Patients due to stroke	19 (5.8%)	36.8	10.5	21.0	10.5	15.7	5.2
Patients due to CKD	45 (13.8%)	31.1	11.1	22.2	17.7	13.3	4.4
Patients due to Diabetic Ketoacidosis	80 (24.6%)	37.5	10.0	18.7	17.5	6.25	10.0
Patients due to Sepsis	48 (14.7%)	41.6	6.25	10.4	20.8	6.25	4.1
Patients due to COPD	32 (9.8%)	37.5	9.3	25.0	18.7	6.2	3.1

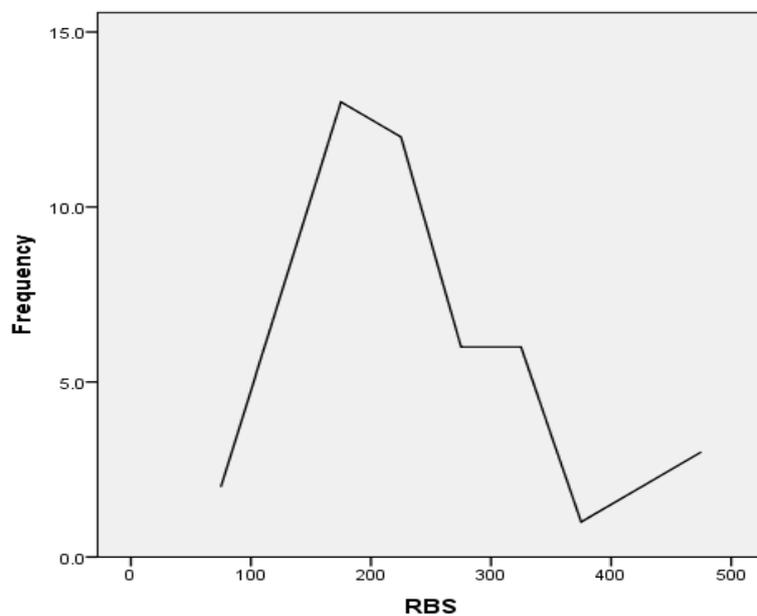


Fig-1: Mortality risk from hyperglycemia in Survivors

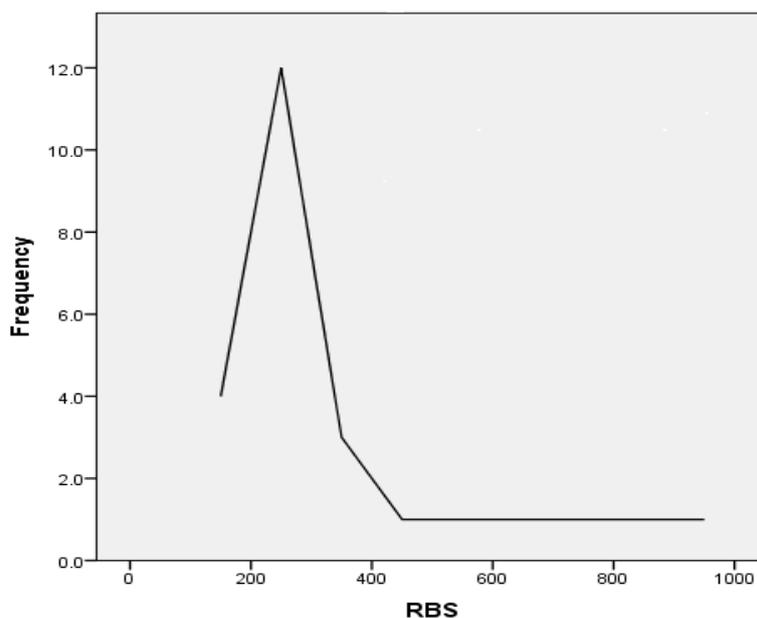


Fig-2: Mortality risk from hyperglycemia in Non Survivors

DISCUSSION

Diabetes Mellitus has been shown to result in increased mortality rates during critical illness [14]. Perioperative blood glucose control also decreases death rate in intensively ill patients [15, 16]. Impact of acute hyperglycemia on outcome depends on pre-morbid glycemia control. Studies have shown that the association between high blood sugar and outcome could be influenced by the presence of chronic hyperglycemia, and they have suggested that ideal blood sugar level may be high in these patients [17, 18]. Studies have reported that hyperglycemia is associated with increased death rate in hospitalized patients [19]. Our study showed that CCU admission blood glucose levels and HbA1c were correlated with patient's mortality. These findings showed that acute hyperglycemia has a correlation with mortality, which might be influenced by previous hyperglycemia. There are numerous studies suggesting strong associations between hyperglycemia and death rate in intensively ill patients [20]. One study in intensively ill patients showed that acute hyperglycemia is strongly related with high mortality in patients with previously uncontrolled hyperglycemia.²¹ Another study showed that high admission sugar level is a strong anticipator of severe adverse outcome in patients with unstable angina [22].

Another study showed J-shaped relationship of HbA1c with the risk of death rate in non-insulin dependent diabetes mellitus. In men with HbA1c $\geq 11.0\%$, and in women with HbA1c $\geq 10.0\%$, mortality was significantly high as compared in patients with HbA1c level of 6.5 - 6.9% [23]. Positive association is seen in many studies between HbA1c and mortality [24], but other studies have shown that low normal HbA1c and high HbA1c levels were related with increased risk of mortality [25]. Another review suggested that 1% increase in HbA1c among hyperglycemic patients may have a 1.15 fold increase in mortality risk [26]. The mechanism is explained well to show the association between hyperglycemia and increased death rate. The main causes of mortality are diabetes complication because of toxicity caused by advanced glycosylated end products, oxidants, hyperosmolarity on tissues and changes in cell signaling pathways like alteration in kinases and phospholipids [27]. Egi *et al.* showed that the higher mean glucose levels (>180 mg/dl) during CCU stay is related to lower hospital death rate in patients with high HbA1c ($>7\%$) compared to low HbA1c ($<7\%$) [20]. On the other hand, in a similar study hyperglycemia at the time of admission were introduced as a predictor of death rate, while no relation between HbA1c and cortisol levels on admission was found [28]. A risk adjusted analysis of 120 traumatic patients showed that patients with HbA1c of more than 6% were 4.5 times more likely to have poor outcomes compared with those with HbA1c of $<6\%$ [29].

The possible mechanisms explaining the effects of HbA1c are low socio-economic status due to improper management of diabetes, high insulin resistance [30], and homeostatic imbalance are through intracellular sorbitol accumulation [31]. Many studies have shown that high HbA1c levels have negative impact on DM patients admitted in critical care unit. The effect of preexisting hyperglycemia in addition to acute hyperglycemia on mortality of critical ill patients is because of high cytokine concentration which leads to inflammation.

CONCLUSION

High blood sugar is related significantly with high mortality rate in intensively ill patients. Stress induced hyperglycemia also significantly increases mortality rate in the intensively ill patients, this association is affected by chronic hyperglycemia. Our study results showed high blood sugar as a potentially fatal and correctable abnormality in intensively ill patients and management of high blood sugar as a therapeutic target to improve outcomes in hospital admitted patients.

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