ORIGINAL ARTICLE

A STUDY TO ESTABLISH ASSOCIATION OF HYPERGLYCEMIA AND INPATIENT MORTALITY IN PATIENTS WITH UNDIAGNOSED DIABETES MELLITUS

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ABSTRACT: The aim of this study was to establish the prevalence, survival, and outcome of patients presented with in-hospital hyperglycemia in which there is prior history of diabetes and without a history of diabetes. We reviewed the medical records of 2000 consecutive adult patients admitted to MNR Medical College, a teaching hospital in Telangana; from Jan 2014 to Nov 2014 and 1886 patients were studied 144 were excluded as glycemic records were not available. New hyperglycemia was defined as fasting glucose level of 126 mg/dl on admission or in-hospital or random blood glucose of more than 200 mg/dl or more on 2 or more determinations. Hyperglycemia was present in 38% of patients admitted to the hospital, of whom 26% had a known history of diabetes, and 11.96% had no history of diabetes before the admission. It was observed that there was higher in-hospital mortality rate (16.21%) in newly diagnosed hyperglycemia when compared to known diabetic patients (3.31%) and subjects with normoglycemia (1.56%; both P< 0.01). In addition, new hyperglycemic patients had a prolonged hospital stay, a higher admission rate to an intensive care unit, and were less likely to be discharged to home, frequently requiring transfer to a transitional care unit or nursing home facility. Our results indicate that in-hospital hyperglycemia is a common finding and represents an important marker of poor clinical outcome and mortality in patients with and without a history of diabetes. Patients with newly diagnosed hyperglycemia had a significantly higher mortality rate and a lower functional outcome than patients with a known history of diabetes or normoglycemia.
KEYWORDS: Diabetes mellitus, New hyperglycemia, Mortality, Insulin therapy, Icu hyper-glycemia.

INTRODUCTION: In-hospital mortality and hyperglycemia, at the onset of presentation in patients with acute myocardial infarction[1-5] and acute stroke has been established.[6-7] During acute phase and long-term follow-up in diabetic patients with myocardial infarction there was an increased risk of congestive heart failure and increased mortality rate.[8] Similarly, several studies have indicated that patients with diabetes are more likely to die or to have substantial neurological disability after acute stroke than non-diabetic subjects.

There is dispute, however, about whether a raised blood glucose concentration is independently associated with a poor prognosis or may indicate a more severe illness with an increased response to stress.

Furthermore, it is not known whether hyperglycemia in patients without critical illness admitted to general hospital wards is associated with poor outcome. If stress hyperglycemia is

proven to be an independent predictor of poor outcome, a policy for early detection and glucose control may be warranted.

The aim of this study was to determine the prevalence of diabetes and hyperglycemia in hospitalized patients at a community hospital and to determine the effects of newly diagnosed hyperglycemia on survival and functional outcome after adjusting for known prognostic factors.

MATERIAL AND METHOD: We reviewed the medical records of 2000 consecutive adult patients admitted to MNR Medical college, a teaching hospital in Telangana, from Jan 20012 to Nov 2012.

Of the 2000 admitted patients, 144 patients (7%) were excluded because no blood glucose measurement was recorded during the hospital stay. The remaining patients who had 1 or more glucose measurements made were divided into 3 study groups.

A normoglycemic group included those patients with normal plasma glucose and no previous history of diabetes.

Patients with hyperglycemia were subdivided between those with a previous history of diabetes (known diabetics) and those without a previous history of diabetes (new hyperglycemia). Hyperglycemia was defined as fasting blood glucose level of 126 mg/dl or more or a random blood glucose level of 200 mg/dl or more on 2 or more determinations.

Fasting blood glucose were those samples drawn from patients kept NPO or samples drawn between 6am–7am. Information regarding types of IV fluid was not recorded in this study; thus, it is possible that some patients may have received dextrose solutions at the time of hyperglycemia. Patient information were collected like age, sex, height, weight, previous diabetic history, drugs used for diabetes, family history of diabetes, any cardiovascular or renal involvement, present medical treatment, hospital stay, treatment during hospitalization, outcome, mortality or discharged.

The primary end point of the study was in-hospital mortality. Secondary end points included treatment of hyperglycemia, length of hospital stay, and patient disposition at discharge (discharge to personal home, transitional care or rehabilitation unit, and nursing home facility). In addition to blood glucose levels, prognostic variables considered were age, gender, body mass index, admission blood pressure, smoking status, coronary heart disease or renal failure, presence of infection, and the need for intensive care unit (ICU) admission.

RESULT: Of the 1886 study patients, 1168(62%) had blood glucose levels within normal limits. The diabetes group consists of 495 patients (26%) with pre-existing history of diabetes mellitus before admission. The newly diagnosed hyperglycemia group consisted of 222(11.96%) patients with no prior history of diabetes who were found to have an admission or in-hospital fasting glucose level greater than 126 mg/dl or a random blood glucose level greater than 200 mg/dl on 2 or more determinations.

The clinical characteristics of the three study groups are shown in Table 1. There were slight differences in the admission blood pressure, mean age, gender distribution, among the three groups. Higher age and increased body mass index was noted in known diabetic patients. As expected, patients with known diabetes had significantly higher fasting and random blood glucose levels compared with the normoglycemia group ($P<0.01$). The admission blood glucose

level in patients with known diabetes (254±36mg/dl or 13±2 mmol/liter) was higher than that in the new hyperglycemia group (220±18mg/dl or 12±1mmol/liter), but results were not statistically significant. We observed no differences among the three groups in the proportion of patients who were admitted to a medicine service vs. a surgical service.

Patients with new hyperglycemia were more likely to be admitted to the ICU (29%) and had a longer length of hospital stay (9.8±0.3 d) compared with patients with a prior diagnosis of diabetes (14.4% and 5.1±0.3 d; both P<0.01) and normoglycemic subjects (9.1% and 4.0±0.1 d; both, P<0.01).

In addition, new hyperglycemic patients were less likely to be discharged home and were more likely to be discharged to a transitional or extended care facility compared with known diabetic and normoglycemic patients.

Patients with new hyperglycemia had a higher in-hospital mortality (16.21%) compared with patients with a known history of diabetes (3.31%) and normoglycemia (1.56%; both P<0.01). The increased mortality was observed both in patients admitted to the ICU and in patients admitted to a general medicine or surgery wards (Table 2). The mortality rate in non-ICU patients was 0.8% in patients with normoglycemia, 1.7% in those with previous history of diabetes, and 10% in patients with new hyperglycemia (both P<0.01).

Among patients admitted to the ICU, patients with newly diagnosed hyperglycemia had a 3-fold higher mortality rate (31%) than patients with a known history of diabetes or with normoglycemia who had ICU mortalities of 10% and 11.3%, respectively (P<0.01). Although the mortality rate in known diabetics was higher than that in the normoglycemic group, the differences did not reach statistical significance.

The clinical characteristics of deceased patients are shown in Table 3. The mean age of patients with newly discovered hyperglycemia who died was 59±4 yr. These patients were significantly younger than known diabetics (66±6 yr) or normoglycemic patients (74±3 yrs).

Among the deceased patients, we observed no significant differences in gender, length of hospital stay, or percentage of patients admitted to the ICU among the three study groups. The mean admission and random blood glucose levels in new hyperglycemic patients who subsequently died were lower than those in patients who died in the diabetic group; however, there were no statistically significant differences in admission, fasting, or random mean blood glucose levels between the two hyperglycemic groups. New hyperglycemia patients had a higher mortality rate due to infectious disorders and acute neurological events than the other two groups, and were less likely to die of cardiovascular causes compared with normoglycemic patients and known diabetic subjects. As some patients had one or more ongoing medical problems, the total cause of death percentages in Table 2 may add up to more than 100%.

Newly diagnosed hyperglycemia was frequently left untreated. During the hospital course, only 15% had orders for a diabetic diet, 3% were prescribed oral hypoglycemic agents, 7% received scheduled dose insulin, and 39% received sliding scale insulin. These treatment modalities were significantly lower than those in patients with a history of diabetes, in whom 54% had orders for a diabetic diet, 30% were prescribed oral hypoglycemic agents, 36% received scheduled dose insulin, and 78% received insulin therapy.

DISCUSSION: In 38% of patients admitted to the hospital it was found that hyperglycemia was present, out of which one third of patients never had any history of diabetes before the admission. In-hospital mortality rate was higher in patient with new onset of hyperglycemia and outcome was also worse compared to patients with a known history of diabetes and subjects with normoglycemia. It was also observed that patients had prolonged length of hospital stay in new onset hyperglycemia, and were more likely to require transfer to a transitional care unit or nursing home facility at discharge.

Capes SE. et.al (2000), Yudkin JS et.al 1987 have proved that hyperglycemia during admission has been associated with increased morbidity and mortality in patients with acute critical illnesses, such as myocardial infarction and stroke.[4]

Fava S. et.al(1996), Norhammar AM et.al (1999), have shown that in patients with acute myocardial infarction there was increased risk of mortality, congestive heart failure incidences due to hyperglycemia than compared to nondiabetic patients.[9]

Weir CJ. et al(1997), Candelise L et.al (1985), Murros K et.al (1992) suggested that hyperglycemia in the acute phase of stroke is a predictor of worse prognosis, in terms of both mortality and residual disability. This study confirms these observations, but in addition it indicates that hyperglycemia is an important marker of poor clinical outcome and mortality not only in critical patients admitted to the ICU, but also in patients admitted to general medicine and surgery wards.[10-11]

Newly diagnosed hyperglycemia patients were more likely to be admitted to the ICU and had a longer length of hospital stay. More strikingly, 16% died compared with 3% of patients with a known history of diabetes and 1.7% of the normoglycemic group.

Wass CI et.al (1996), Smith ML et.al (1986), Melamed E et.al (1976) suggested that the higher morbidity and mortality related to the associated illness precipitating the stress, hyperglycemia itself may contribute to morbidity by creating a toxic cellular milieu, causing intracellular and extracellular dehydration, inducing electrolyte abnormalities, and depressing immune function.[12-14]

Our study did not address the question of whether treatment of hyperglycemia may reduce the high morbidity and mortality associated with hyperglycemia in patients with and without a history of diabetes.

Van den Berghe et al. reported that patients in ICU who were on mechanical ventilator, were maintained on strict normalization of blood glucose levels (4.5–6.1 mmol/liter) with continuous infusion of insulin compared with a restrictive insulin regimen to maintain blood glucose levels between 10–12 mmol/liter resulted in reduced hospital morbidity and mortality. The intensive insulin schedule significantly reduced ICU mortality by 43%, hospital mortality by 34%, mean ICU stay by 22%, and incidence of bacteremia and hemodialysis by 50%. These results suggest that strict glucose control in hospitalized patients with hyperglycemia is warranted.[15]

In agreement with a previous report Levetan CS et. al(1998),[16] we found that 12% or one third of all hyperglycemic patients on both medical and surgical services had no prior history of diabetes. We believe that newly diagnosed hyperglycemia is usually considered a transient finding in response to the acute illness not requiring medical intervention, as indicated by the fact

that more than two thirds of these patients did not receive diabetic diet or antidiabetic drug therapy. However, given the average delay of a decade between the onset and the diagnosis of diabetes, further evaluation of new hyperglycemic patients with in-patient determination of hemoglobin A_{1C} may allow earlier diagnosis and treatment, which may prevent the development of chronic complications of diabetes.

CONCLUSION: In conclusion, we have shown that in-hospital hyperglycemia is a common finding and should be considered an important marker of poor clinical outcome and increased mortality, in particular in patients without a history of diabetes. Patients with new hyperglycemia admitted to critical care areas or to general medical and surgical wards had a significantly higher mortality rate and lower functional outcome than patients with a known history of diabetes or normoglycemia. Our observations indicate that all hospitalized patients should be screened for hyperglycemia.

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	New hyperglycemia	**Known diabetes**	**Normoglycemia**
No. of patients (%)	222(11.96%)	495 (26)	1168 (62)
Mean age (yr)	59±1	63±1	54±1
Body mass index (kg/m^2)	26.2±0.5	29.1±0.7	27.2±0.4
Mean BP (mm Hg)	98±2	103±1	98±1
Blood glucose	207±18(mg/dl) 11.5±1(mmol/lit)	230.4±16.2(mg/dl) 12.8±0.9(mmol/lit)	6±0.06
Admission service			
Medicine (%)	54	66	52
Surgery (%)	36	25	33
ICU admissions (%)	29	14	9

Table 1: Patient characteristics on admission

	New hyperglycemia	**Known diabetes**	**Normo-glycemia**
Total no. of patients (%)	222(11.96%)	483(26.02%)	1151(62.01%)
Total mortality (%)	36(16.21%)	16(3.31%)	18(1.56%)
Total non-ICU admissions (%)	159(10)	421(26)	1063(64)
Non-ICU mortality (%)	16(10)	7(1.7)	9(0.8)
Total ICU admission (%)	65(27)	71(29)	107(44)
ICU mortality (%)	20(31)	8(11)	11(10)

Table 2: ICU and non-ICU mortality

	New Hyperglycemia	Known Diabetes	Normo-glycemia
No. of patients	36	16	18
Mean age (yr)	59±4	66±6	74±3
Gender (M/F)	17/19	7/9	10/8
ICU admission (%)	20(56)	8(54)	11(55)
Admission BG	220±18 (mg/dl) 12.2±1(mmol/lit)	254±36(mg/dl) 13±2 (mmol/lit)	97±9(mg/dl) 6.6±0.5(mmol/lit)
Mean FBG	174±7.2 (mg/dl) 9.7±0.4 (mmol/lit)	187±25.2 (mg/dl) 10.4±1.4(mmol/lit)	93±7.2 (mg/dl) 5.2±0.4(mmol/lit)
Mean RBG	190±9(mg/dl) 10.8±0.5(mmol/lit)	252±30.6 (mg/dl) 14±1.7(mmol/lit)	104±3.6 (mg/dl) 5.8±0.2(mmol/lit)
Cause of death			
Infection (%)	12 (33)	4 (27)	4 (20)
Cardiovascular (%)	10 (28)	8 (53)	10 (50)
Neurologic events (%)	7 (19)	2 (13)	2 (10)
Malignancy (%)	3 (8)	1 (7)	1 (5)
Other (%)	6 (17)	3 (20)	3 (15)

Table 3:Clinical characteristics of deceased patients

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