

Admission Hyperglycemia in COVID-19 patients as Outcome Predictor: a Single Centre Study

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Abstract

Background: Hyperglycemia on admission among COVID-19 may affect the patient outcome.

Objective: To determine the effect of admission hyperglycemia on outcome among COVID-19 patients.

Methodology: It was a cross-sectional analytical study in which 421 COVID-19 patients were admitted with high blood sugar levels (BSR>180mg/dl) to the High Dependency Unit, Sir Sadiq Abbasi Hospital, Bahawalpur, from April to May 2021 were included. Preexisting diabetes status was confirmed on the basis of history taken from the patients. Patients were divided into two groups on basis of BSR, moderate hyperglycemia (180-299mg/dl) and severe hyperglycemia (300-450mg/dl). The primary outcome was taken as an increase in oxygen demand leading to shifting of the patient to ICU for Non-Invasive Ventilator (NIV) support or a decrease in oxygen demand leading to discharge home.

Results: Among 421 COVID-19 patients; 349 (83%) patients had moderate hyperglycemia and among them, 172 (49.4%) were shifted to NIV, and 177 (50.6%) patients were discharged after improving. Seventy-two patients came out to have severe hyperglycemia out of which 61 (84.3%) were shifted to NIV and 11 (15.3%) patients were discharged home (p-value = 0.01). Among 83 patients who were shifted to NIV, 22 (26.5%) were diabetic and 61 (73.5%) were non-diabetic and had risk factors other than diabetes.

Conclusion: Hyperglycemia on admission is a strong predictor of poor outcomes regardless of the previous history of diabetes and other confounders.

Keywords: Admission hyperglycemia, COVID-19, Predictor, Outcome

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Introduction

As COVID 19 pandemic has hit the world since December 2019, Pakistan has received its fair share. COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ SARS-CoV-2 is an enveloped virus with a positive sense, single-stranded RNA.¹ COVID-19 is characterized by cytokine storm and pneumonia. On the basis of severity, the disease is categorized into mild, moderate, severe, and critical illnesses.² Patients who cannot maintain their oxygen saturation >94% at room air and have increased respiratory rate >30/min in order to do it are kept in the severe illness category, whereas, those who require non-invasive or invasive ventilator support have a critical illness. Patients with mild illness and moderate disease do not require hospital admission or oxygen support.³ Patients with severe illness require high dependence unit for oxygen support and those

with critical illness require Intensive Care Unit Admission for Non-Invasive or Invasive Ventilator support.⁴

According to a systematic review, different studies have shown different rates of hospitalization, ICU admissions (3%-100%), and mortality (as high as 86% in hospitalized patients).⁴ Among SARS-CoV-2 infected patients who needed intensive care, mortality was higher.⁴ These numbers reflect the challenge that the health care system had to face worldwide. In developing countries like Pakistan, it is imperative to stratify patients according to their prognosis in order to allocate our resources judiciously. Research has been ongoing to find parameters that can provide an estimate of outcomes among patients infected by SARS-CoV-2. Lymphopenia, serum Ferritin, IL-6, LDH, and D-dimers are known predictors of cytokine storm and of poor prognosis.⁵ Blood glucose level is one such parameter that has been proposed to predict

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outcomes independent of other factors.⁶ Persistent hyperglycemia causes up-regulation of ACE receptors in the lungs causing increased binding of SARS-COV-2 to receptors via spike proteins, leading to increased inflammatory response.⁷

There are many risk factors identified for cytokine storms and severe and critical illness. Type 2 Diabetes Mellitus is one of the most important risk factors identified so far.⁸ Irrespective of the presence or absence of diabetes, elevated blood glucose levels (>6.1 mmol/L) at admission and during hospitalization were associated with higher rates of ICU admission.⁹ Among patients receiving critical care, hyperglycemia was associated with higher mortality.^{10,11} Another study conducted in Wuhan Huoshenshan Hospital, showed that higher blood sugar level is associated with increased progression of COVID-19 and fatality. In this study, mortality at day 21 was four times higher in patients with blood glucose > 6.1 mmol/L than blood glucose in the range of 3.9-6.1 mmol/L.¹²

Blood glucose level is an affordable and accessible investigation. If blood glucose levels at admission are associated with the severity of COVID-19, we are going to have a useful tool for earlier identification of patients at risk. It can help us stratify patients according to the risk of worsening the disease and use our limited resources much more effectively. So, we have designed an observational study at a COVID dedicated center to see whether admission hyperglycemia is found in patients with severe or critical illness or not and whether those who had hyperglycemia at admission developed a critical illness or just improved and were discharged home.

Methodology

After approval from the ethical committee, this analytical cross-sectional study was conducted at Sir Sadiq Abbasi Hospital, Bahawalpur, a COVID-19 dedicated hospital, in collaboration with Pathology Department, from April 15 to July 15, 2021. All 421 patients admitted to the High Dependency Unit and isolation rooms, having BSR > 180 mg/dl, were included in the study by convenience sampling after taking informed consent. Blood samples of 5ml were taken from patients included and the levels were measured using a fully automated chemistry analyzer

AU460. Patients having BSR 180-299 mg/dl and 300-450mg/dl were categorized to have moderate hyperglycemia and severe hyperglycemia respectively. The primary outcome was taken as an increase in oxygen demand leading to shifting of the patient to ICU for Non-Invasive Ventilator (NIV) support or a decrease in oxygen demand leading to discharge home.

All patients were above 19 years of age. Patients diagnosed as having moderate to severe COVID-19 based on HRCT, respiratory rate, and oxygen requirement was included in the study. Patients having diabetic ketoacidosis, hyperosmolar non-ketotic coma, active malignancy, end-stage renal disease, liver cirrhosis, or patients using immunosuppressive treatment were excluded. Data were analyzed according to the categorization of moderate hyperglycemia and severe hyperglycemia respectively. Patients were followed up for the outcome of increasing oxygen demand i.e. needing NIV and decreasing oxygen demand leading to discharge home. Biodata and the rest of the parameters including blood sugar levels were recorded on proforma. Data were analyzed using SPSS version 20. Mean and standard deviation was calculated for numerical data. For descriptive variables, frequency and percentages were calculated. A Chi-square test was applied to see the association of blood sugar levels with the outcome of the patients. P-value <0.05 was considered significant.

Results

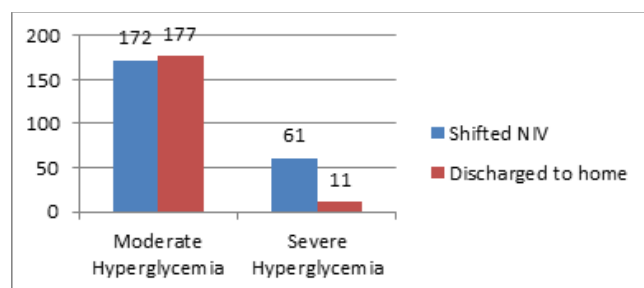
A total of four hundred and twenty-one patients, who had admission hyperglycemia were included in the study. Patients in the age group from 20 to 75 years of age were included in the study, with a mean age of 59 ± 9.27 years. Two hundred and fifty-one patients (59.6%) were male and one hundred and seventy patients (40.3%) were females. Frequencies and percentages of descriptive variables are given in table-I. Of the 421 patients, 135 (32%) did not have any comorbid condition while known comorbid conditions were, hypertension, ischemic heart disease, diabetes mellitus, and obesity in 92 (21.85%), 73 (17.33%), 106 (25.17%) and 15 (3.5%) patients, respectively.

Table-I: Descriptive statistics of study subjects

Variables	Groups	Frequency n (%)
Age Groups (years)	20-39	4(0.9%)
	40-49	226(53.68%)
	60-75	191(45.36%)
Gender	Male	251(63.4%)
	Female	170(34.6%)

Among known diabetic patients 106 (25.17%); 69 (65%), were shifted to ICU and 37 (35%) were discharged home. Diabetic patients with hyperglycemia had chances of developing poor outcomes as compared to non-diabetic patients and the calculated RR was 1.12. Among 421 patients; 349 (83%) patients had moderate hyperglycemia and 72 (17%) had severe hyperglycemia. (Figure-I)

Figure-I: Outcome (NIV admission & Discharged to home) among COVID-19 patients according to Hyperglycemia status



A chi-square test of independence was performed to examine the relationship between blood sugar levels and outcome. The relation between the two variables was found to be significant with a p-value of 0.01. Higher blood sugar levels at admission were associated with worsening of the disease and the need for non-invasive ventilation in patients admitted to the hospital with a diagnosis of moderate and severe COVID. One hundred and nineteen patients were admitted with severe disease, among them 69 (58%) and 50 (42%) had moderate and severe hyperglycemia respectively. Among 13 patients who had the moderate disease at admission, 12 (92.3%) and one (7.7%) had moderate and severe hyperglycemia respectively. (p=0.01)

Discussion

In our study, our hypothesis has been confirmed that the higher the blood sugar levels at admission, the higher will be the chances that the patient is going to worsen during the hospital stay. Patients with higher blood sugar levels at admission are

going to have increased oxygen demand and may require Non-Invasive Ventilator support. Moreover, patients with severe hyperglycemia have more chances to worsen as compared to those with moderate hyperglycemia. Patients who improved and were discharged had moderate hyperglycemia (83%) and 17% had severe hyperglycemia. Those who were diabetic and had severe hyperglycemia had more chances to develop severe disease and further worsening clinical conditions. Patients who were admitted with severe disease were found to have severe hyperglycemia as compared to those with moderate disease.

Diabetes is a known risk factor for poor prognosis in COVID.⁸ However, we found higher blood sugar levels in non-diabetics with COVID-19. Hyperglycaemia in COVID-19 can be just a short-term complication of the disease itself.¹³ In our study, the population only 25.2 % had diabetes but at admission, all of them had blood sugar levels of more than 180 mg/dl (10 mmol/L). Before generalizing findings of hyperglycemia as a complication of disease in this study, we need larger-scale studies which have a higher number of participants and have a longer follow-up period to confirm the diabetogenic effect of COVID-19.

In comparison to a study that showed that tight glycaemic control in moderate COVID pneumonia is associated with a better outcome as compared to those with uncontrolled blood sugar levels.¹⁴ In this study, Sardu et al, used high-dose insulin to achieve tight glycaemic control.¹⁴ We did not observe the effect of any oral hypoglycaemic agent or insulin therapy on blood sugar levels in comparison to the above mentioned study. We need another study to see the effect of tight glycaemic control by adding insulin to diabetic or non-diabetic patients and the effect of tight glycaemic control on the outcome. Intravenous steroids are also found to cause in patients hyperglycemia,¹⁵ we have taken admission blood sugar levels as a predictor of outcome to omit the confounding factor of steroid-induced hyperglycemia. Another study mentions that bed rest in isolation or quarantine and airway inflammation causes increased blood sugar levels and insulin resistance which inversely causes increased oxidative stress as a result of up-regulation of ACE receptors in the lungs and further lung damage leading to acute respiratory distress syndrome.¹⁰ So, hyperglycemia itself can cause poor outcomes in COVID-19 as shown in this study.

Conclusion

It has been concluded that admission hyperglycemia is a predictor of poor outcomes in COVID-19 regardless of confounding factors. The higher the blood sugar level at admission is, the higher will be chances of having a critical illness and admission to the Intensive Care Unit for Invasive or Non Invasive Ventilator Support. Moreover, patients who are already known diabetic have a poorer outcome with admission hyperglycemia as compared to those who are non-diabetic.

Authors Contribution: **SW:** Acquisition and analysis of data and Drafting. **AM:** Design of work and revising. **OF:** Conception of work and drafting. **NW:** Interpretation of data and revising. **AM:** Acquisition and analysis of data and revising. **MU:** Design of work and drafting. All authors critically revised and approve its final version.

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