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HYPERGLYCEMIA AS A PROGNOSTIC MARKER IN COVID-19 INFECTED PATIENTS ADMITTED IN HSK HOSPITAL, BAGALKOT

Dr.Harshitha S* — 3rd year post graduate student, S.N.Medical College, Bagalkot. *Corresponding Author

Dr.Kadappa Jaligidad — Assistant Professor, Department of General Medicine, S.N.Medical College, Bagalkot.

ABSTRACT The rapidly spreading coronavirus disease 2019 (COVID-19) pandemic has placed significant burdens on healthcare systems worldwide, with millions of cases and hundred-thousands of deaths. This is further aggravated by the fact that COVID-19 patients are at risk of rapid health deteriorations leading to multiorgan failure and death indicating that early and reliable indicators to enable risk stratifications are urgently needed to help clinicians anticipate and promptly treat these patients. Admission hyperglycemia is associated with poor prognosis and mortality in patients admitted in view of COVID-19 and can be used as a prognostic marker to stratify based on risk of severe disease and death, thus enabling early intervention resulting in improved patient outcomes.

KEYWORDS : Hyperglycemia, Covid-19 infection, Prognosis

INTRODUCTION

The first case of novel coronavirus, also known as SARS-CoV-2 (severe acute respiratory distress syndrome coronavirus-2), emerged in December 2019 in Wuhan, China, has a high transmission rate. [1]SARS-CoV-2 interacts with the body's glucose metabolism via a variety of pathways, the commonest being ACE-2 expression in the pancreas. [2,3] Since an acute rise in blood glucose is associated with increased inflammatory mediators, [4] it can potentiate the harmful effects of cytokine storm in patients with COVID-19 pneumonia. This study aims to study the correlation between hyperglycemia and COVID-19-related clinical outcomes.

SUBJECTS AND METHODS:

STUDY DESIGN :

Retrospective study.

INCLUSION CRITERIA :

Confirmed Covid-19 cases willing to participate in the study will be included in the study group.

EXCLUSION CRITERIA :

RTPCR negative for COVID-19, admitted as Severe Acute Respiratory Illness(SARI) and patients not willing for participation in the study.

Data Collection :

We collected data from 125 patients with laboratory-confirmed COVID-19 infection who were admitted in S.Nijalingappa Medical College and Hsk hospital between July 2020 to October 2020.A confirmed case of COVID-19 was defined by a positive result on a reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of a specimen collected on a nasopharyngeal swab. Clinical specimens for COVID-19 were obtained in accordance with Centers for Disease Control and Prevention (CDC) guidelines. [5] We included only laboratory-confirmed cases.For all patients, we recorded the following information: demographics (age, sex), concomitant cardiovascular risk factors (smoke, hypertension, dyslipidemia), comorbidities (chronic obstructive pulmonary disease and history of cancer), complications (cardiovascular disease and microangiopathy), presence or absence of COVID-19 related pneumonia or interstitial lung disease (ILD), ongoing therapies before hospitalization. We collected information on symptoms of COVID-19 upon admission (time from onset of symptoms to hospitalization; presence of fever, cough, dyspnea, and gastrointestinal symptoms). Hyperglycemia was defined as blood glucose level ≥140 mg/dl after admission. [6,7]

Clinical severity were graded as ,MILD (asymptomatic), MODERATE (SARI : sat 90-94%), Severe (SARI: sat <90%/NIV/02 support) and death. Duration of the hospital stay of each patient is noted.

Investigations :

Blood glucose levels by the Glucose Oxidase method, at the time of admission.

Admission blood glucose level was measured from the first blood sample after admission. The initial blood glucose level of critical diagnosis was defined as the first blood glucose level after being diagnosed as critical case.

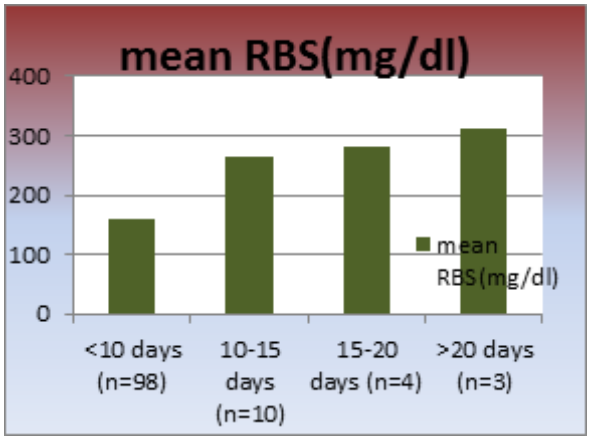
STATISTICAL ANALYSIS :

Sample size estimation was done using open epi software version 2.3.1. According to the study conducted by Sufei Wang et al,Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study,

Sample size $n = [DEFF*Np(1-p)]/[(d^2/Z^2_{1-/2}*(N-1)+p*(1-p)]$

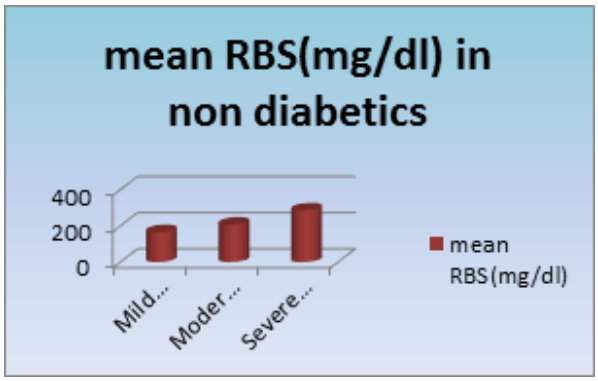
RESULTS:

Graph 1 : Association of mean RBS and duration of hospital stay in covid-19.



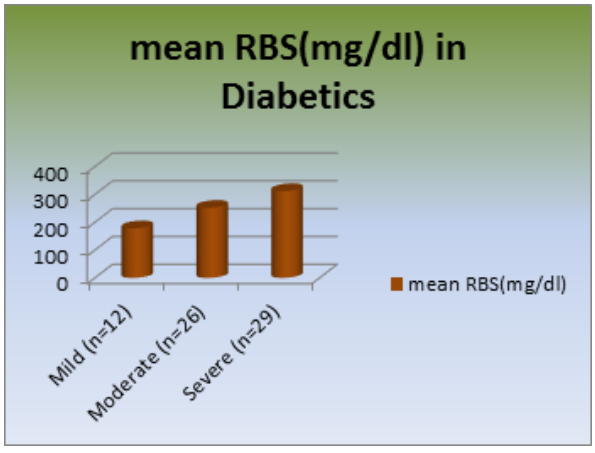
This graph shows that, mean RBS was 158mg/dl in patients with duration of hospital stay <10 days, 265mg/dl in patients with duration of hospital stay 10-15 days, 280mg/dl in patients with duration of stay 15-20 days and 310mg/dl in patients with duration of hospital stay >20 days.

Graph 2 : Association of mean RBS in non diabetics and severity of covid-19.



In the above graph,mean RBS was 166±90.58mg/dl, observed in 10 mild cases of covid-19, 208±89.21mg/dl observed in 16 moderate cases of covid 19, 286±67.75mg/dl observed in 22 severe cases of covid-19 who had no prior history of Diabetes.

Graph 3 : Association of mean RBS in diabetics and severity of covid-19.



In the above graph, mean RBS was 178±68.68mg/dl observed in 12 mild cases of covid-19, 252±95.85mg/dl observed in 26 moderate cases of covid 19, 312±74.75mg/dl observed in 29 severe cases of covid-19 who had a prior history of Diabetes.

Of 115 total covid-19 cases, 26 cases died, in whom mean RBS was 297±88.69.

Thus admission hyperglycemia is associated with poor prognosis in covid-19 cases.

DISCUSSION:

This retrospective study showed that high admission blood glucose level was associated with poor prognosis in COVID-19 patients.According to our study, at-admission hyperglycemia was associated with poorer outcomes regardless of prior diabetes status, suggesting the existence of a more direct link between glycemic status and poor COVID-19 outcomes.The relationship between COVID-19 severity and hyperglycemia is possibly bidirectional, wherein infection might bring about state of stress and trigger an enhanced release of proinflammatory cytokines which may lead to insulin resistance. [8]

Stress may also induce the release of stress hormones which trigger liver glycogenolysis, aggravating the effects. [9]Furthermore, SARS-CoV-2 is known to bind to angiotensin-converting enzyme 2 (ACE2) receptors, which are found to be expressed in pancreatic beta-cells, thus rendering it a target for the viral attack. Such binding provides a route for the virus to enter and damage the pancreatic islets, resulting in a defect of insulin production, as indicated in previous study with its SARS virus counterpart. [10] Together, these factors may contribute to the development of acute hyperglycemia in COVID-19 patients.

The mechanism by which acute hyperglycemia drives the progression of COVID-19 remains largely unexplored. A study by Fadini et al. found that a decline in respiratory parameters was most responsible for mediating the effects of hyperglycemia on the outcome. [11]

Diabetes and hyperglycemia were previously known to induce structural changes in the lungs, giving rise to pulmonary remodelling and the subsequent restrictive respiratory pattern. [12]Moreover, hyperglycemia is also known to generate reactive oxygen species and induces oxidative stress, leading to endothelial dysfunction which may cause further hyperglycemic pulmonary microangiopathy. [13]

This is in line with the findings of a study by Lampasona et al. which demonstrated that inflammation and coagulopathy, rather than impaired antibody response as such present in individuals with diabetes, were more responsible in aggravating the outcomes. [14]

In the CORONADO study, an association was noted between plasma glucose concentration at admission and the primary outcome. In a retrospective study, [15] of 85 patients with COVID-19, hyperglycaemia at hospital admission was the best predictor of worst chest radiographic imaging results.

Another study, [16] found a higher risk of a composite outcome (ICU admission, mechanical ventilation, and death) in patients with hyperglycaemia at admission (fasting blood glucose >7 mmol/L) and without history of diabetes compared with patients without diabetes and normoglycaemia (OR 5·47, 95% CI 1·56–19·82).

Bode et al, [17] reported a significantly higher percentage of death (41.7 vs. 14.8%, $p < 0.001$) in patients with COVID-19 ($n = 184$) who had uncontrolled hyperglycemia (defined as ≥ 2 blood glucose value, >180 mg/dl within any 24-hour period) but were not diagnosed as diabetes (HbA1c < 6.5%), compared to the patients with diabetes (HbA1c ≥ 6.5%).

CONCLUSION :

Hyperglycemia is a significant blood finding in patients admitted in view of COVID-19 and can be used as a prognostic marker to stratify based on risk of severe disease and death, thus enabling early intervention resulting in improved patient outcomes. The need for timely recognition and management of blood glucose levels should be emphasized in COVID-19 disease. Large-scale patient studies are warranted in order to establish appropriate treatment guidelines for hyperglycemia in COVID-19 patients, so as to minimize worse outcomes for these patients.

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