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Original Research Article

Hyperglycaemia in COVID-19 Patients at Admission, a Study during the Beginning of the Pandemic in Sidi-Bel-Abbes, Algeria

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Abstract

Reportedly, SARS-CoV-2 infection impairs glucose homeostasis and metabolism. Moreover, hyperglycaemia has emerged as an important risk factor for COVID-19 mortality. A cross-sectional study involving hospitalized patients in Sidi-Bel-Abbes with COVID-19 critical infection regardless of diabetes status was conducted. Data was collected from COVID-19 Registry, including age, sex, and blood sugar level at admission. Out of 800 patients admitted for SARS-CoV-2, 332 patients (206 males, 126 females) exhibited hyperglycaemia, which equates to a prevalence of 41,5%. Patients had a median age of 64 years and a median blood sugar of 1,59. Admission hyperglycaemia was not statically associated with age and sex. Blood glucose status is paramount for ensuring safe and effective treatment of inpatients COVID-19. Additional studies are forthcoming to address the study's limitations and to better understand the impact of hyperglycaemia on COVID-19 patients.

Keywords: SARS-CoV-2 infection, hyperglycaemia, COVID-19 mortality, Blood glucose.

INTRODUCTION

COVID-19 was declared a Public Health Emergency of International Concern by the World Health Organization (WHO) on January 30, 2020, and quickly changed its name to a pandemic on March 11, 2020. SARS-CoV-2 infection impairs glucose regulation and metabolism in DM (diabetes mellitus) and non-DM patients, due to developpement of cytokine storm (CS), downregulation of ACE2 and direct damage to pancreatic beta cells. Hyperglycemia at admission has been considered as a mortality predictor factor in COVID19 patients, and is associated with adverse outcomes of the disease [1], and Data shows that high blood sugar is an important mortality risk factor from COVID-19 in both diabetic and non-diabetic individuals [2-5].

On the contrary, some authors argue that the increased incidence and severity of DM is due to altered patient's status during the pandemic rather than the direct impact of COVID-19 [6, 7]. Some investigators have suggested that COVID-19 patients may be at increased risk of more severe hyperglycemia due to virus-mediated effects on beta-cell function and/or insulin sensitivity [8, 9, 4].

Elevation of blood glucose level predicts worse outcomes in hospitalized patients with COVID-19 [4].

Hyperglycemia at the time of healthcare admission is more relevant as risk factor than the previous glycemic control evaluated by HbA1c [2].

The aim of our study is to estimate the prevalence of high glucose blood level in critical COVID-19 patients at admission.

MATERIAL AND METHODS

All patient enrolled in this study were diagnosed with 2019 novel Corona virus infection with pneumonia, the diagnosis was confirmed by PCR. The initial blood glucose level was noticed on the 1st day after admission, The collected data included sex, and age of each patient, extracted from the hospitalisation register comprising initial patients' data. We collected a total of 800 glycaemia of confirmed cases of critical COVID-19 admitted in COVID-19 inpatient of Sidi-Bel-Abbes, Algeria.

For each patient blood glucose was mesured upon admission for COVID-19 management (presumed to be a fasting measurement, as the patients had not eaten for at least 6–8 h before this event).

Hyperglycemia was defined as blood glucose greater than 125 mg/dL based on the first glucose measurement upon admission.

Analyse statistique

The Kolmogorov-Smirnov normality test was used to examine the distribution of the values. Continuous variables are expressed as the mean and standard deviation (SD), or median and range in the case of non-normally distributed data. The t-test or the Mann-Whitney U-test was used to compare groups. Moreover, qualitative variables were reported as numbers or percentages. The chi square test was used to check frequency difference. We performed statistical analysis using the Statistical Package for Social Sciences (SPSS) version 25 (IBM Corp., Armonk, NY, USA). For all statistical tests, the level of significance was set at a p-value of 0.

RESULTS

Out of 800 COVID-19, 332 patients exhibited hyperglycaemia corresponding to a prevalence of 41,5%.

The Table 1, provides the characteristics data of our COVID-19 population. The glycemic status at admission is showed in the dispersion Figure 1.

Hyperglycaemia have been found in 206 males and 125 females, no statistical relations were between hyperglycaemia and the variables age, and sex (Table 2).

Table 1: Statistical description of the COVID-19 patients sample

Variable	All	Male	Female	P value
N of subjects	800	494	306	
Age (years)	64 (6-98)	66 (6-98)	61(10-97)	NS
Glycaemia	1,5 (0,10-7,87)	1,61(0,10-7,87)	0(0,3-5,64)	NS

Table 2: Factors related to hyperglycaemia in patients covid positif

Variable	Hyperglycemia	Absence Hyperglycemia	P value
Age (years)	65 (6-98)	62 (16-97)	NS
Sex male/female	206/126	288/108	NS

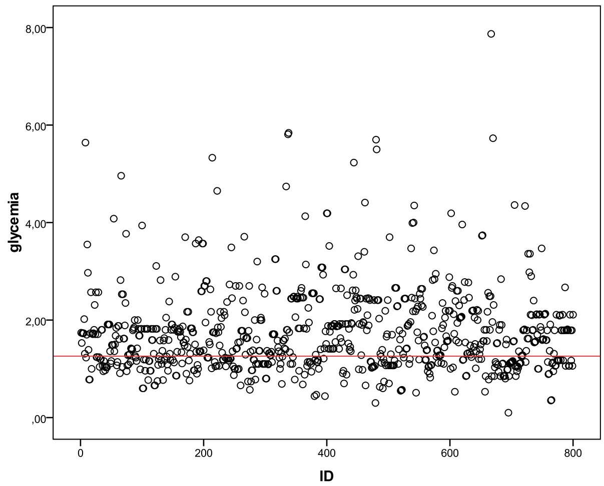

Figure 1: Admission glycaemia dispersion of COVID-19 critical inpatients

DISCUSSION

During previous SARS epidemics, diabetes and hyperglycemia have been risk factors for poor prognosis of the disease [10]. Acute hyperglycemia in healthy patients without prior known diabetes (as well as in patients with known diabetes) has been identified as a complication of SARS disease and a risk factor for respiratory failure and death [10]. Moreover, It has been reported that DM and reactive hyperglycemia are regarded as predictors of severity in SARS-CoV and MERS-CoV infected patients [11, 6, 8]. Diabetes is one of the comorbidities most associated with worsening COVID-19 outcomes [12,13].

Apparently, hyperglycaemia on admission appears to have greater impact on COVID-19 outcomes in non-diabetic patients than in diabetic patients [2]. Through the Spanish study carried out on 11,312 COVID-19 patients, hyperglycemia even without DM was associated with a significant risk of death, the parameter is even considered as a predictive value for mortality [14]. Furthermore, it has been reported that acute hyperglycemia occurs in about 50% of patients hospitalised for COVID-19, while the prevalence of diabetes in the same population was about 7% [15, 12, 13], this finding is in line with our results, our prevalence of hyperglycemia was 41,5%, and the reported prevalence of DM in Algeria is 14,4% [15]. The burden of diabetes mellitus has been increasing steadily around the world during the past decade [16], DM is prevalent in patients with coronavirus disease 2019 (COVID-19) and is associated with an increased risk of severe COVID-19 illness and death [7].

However, even in the absence of diabetes, critically ill and non-critically ill individuals with SARS-CoV-2 infection (Covid-19) may have higher-than-expected glycemia [18,11,13,4,14]. Increased risk of unfavorable outcomes were observed with glucose levels >160 mg/dL and <70 mg/dL among COVID-19 patients [1], patients with uncontrolled hyperglycemia (defined as being present when two or more BGs > 180mg/dL). Furthermore, Stress hyperglycemia is specifically characterized as a transitory elevation in blood glucose in the setting of acute illness or after surgery in a patient. In-hospital mortality appears to be lower in patients with good glycemic control than in patients with poor glycemic control [5]. In our study high blood sugar levels were noticed especially among male gender, in accordance the study of Carrasco-Sanchez *et al*., [14].

Acute hyperglycemia induces endothelial dysfunction, thrombosis and inflammation by generating oxidative stress [13]. Reportedly, acute hyperglycemia in the ICU is more dangerous for people without diabetes than for people with diabetes [19]. In diabetes, chronic hyperglycemia caused by oxidative stress leads to an increase in antioxidant defenses in cells, so tissues are protected to some extent during acute hyperglycemia [12], but in patients without diabetes, this would not be the case, causing more tissue damage. In vitro experiments demonstrate the critical role of miRNAs in this phenomenon. One possible hypothesis is that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may affect the beta cells of the pancreas, resulting in decreased insulin secretion [12, 13]. COVID-19 Infection is also accompanied by the production of a large number of cytokines that can induce insulin resistance [12], these inflammatory cytokines, such as transforming growth factor-beta and IGF-I-binding protein-3, may be increased by blood sugar fluctuations rather than persistent hyperglycemia [20, 21]. Furthermore, a study suggests that blood glucose fluctuations, especially postprandial fluctuations, are a stronger trigger for oxidative stress than persistent hyperglycemia [22].

However, many complex, interconnected processes may be involved, including stress hyperglycemia, previously undiagnosed diabetes mellitus, steroid-induced hyperglycemia, and direct infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and its influence on beta cells [7-9, 4]. In a recent mechanistic study, Viral adipocyte infection has been reported to cause COVID-19-associated hyperglycemia, resulting in decreased release of adiponectin, a blood glucose-regulating hormone, and secondary insulin resistance [8, 23]. in addition, multiple immune system abnormalities are thought to explain the relationship between hyperglycemia and immune dysfunction, including impaired chemotaxis and phagocytosis of polymorphonuclear and mononuclear leukocytes, complement function, and dysregulation of cytokines [24, 25, 26].

Recent U.S. study of 5,029 patients (average age 47 years) from 175 hospitals found that patients with COVID-19 had higher BMI, higher insulin requirements, higher DKA compared with patients without COVID-19 Longer resolution and higher mortality [27].

However, little is known about the association between SARS-CoV-2 and DM; nevertheless, different recent studies observed the link between hyperglycemia and SARS-CoV-2 even in non-DM patients [18, 15, 20, 24]. An Italian study of 271 COVID-19 patients, 20.7% of whom had diabetes, found that high blood sugar was independently associated with mortality [27]. The study also showed that people with diabetes and hyperglycemia had worse inflammatory profiles [27]. In a Chinese study, 42 patients had COVID-19 and ketoacidosis, and 27 patients had no previous diabetes diagnosis [28].

Severe hyperglycemia is common in critically ill patients and is often considered a marker of disease severity [7], but there is an inherent risk of residual confounding in observational studies, meaning that ideal glycemic targets can only come from randomized controlled trials with adequate power.

Two important questions raised by these data are whether the probable severe outcome of COVID-19 infection is primarily due to metabolic disturbances and their associated sequelae [29], and whether relief of acute hyperglycemia through effective glycemic management plays a role. Our data set does not include recognized co-morbidities of COVID-19 death, such as hypertension or cardiovascular disease, this single-center study with Algerian patients may limit the generalizability of our findings. Furthermore, the absence of patients informations likely led to misclassification bias toward uncontrolled hyperglycemia in patients with possible underlying diabetes. Thus, these findings may be insufficient for establishing a causal relationship between the goal of glycemic control and the outcome of COVID19 patients with or without diabetes.

CONCLUSION

Prevention and treatment of COVID19 and its associated complications is a major challenge in Algeria due to multiple issues and barriers, including a lack of a multisectoral approach, surveillance data, and diabetes awareness.

Because long-term follow-up of these patients is limited, prospective studies of the metabolism of COVID-19 patients are needed to understand etiology, prognosis, and treatment options.

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