

## Risk of Mortality due to Sudden Hyperglycemia in COVID-19 Patients

### ARTICLE INFO

#### Article Type

Short Communication

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#### How to cite this article

Awad W, Kadhim H, Hassan D.M, Al-Yassiry K.A.R. Risk of Mortality due to Sudden Hyperglycemia in COVID-19 Patients. *Iranian Journal of War & Public Health*. 2021;13(3):199-202.

### ABSTRACT

**Aims** One of the most dangerous complications of COVID-19 is sudden hyperglycemia that may carry a high incidence of the death rate. This study aimed to evaluate the relationship between death rate and hyperglycemia caused by COVID-19 infection in non-diabetic patients.

**Materials & Methods** In this study, 296 patients were selected randomly, 57 patients complaining of sudden hyperglycemia (>400 mg/dl) one week after the high fever subsided; the others did not show such complain. Statistical analysis was done to evaluate the relative risk of hyperglycemia upon the incidence of mortality rate between two groups.

**Findings** The X2 value was 20.5959 for all, and the p-value was not significant except for COVID-19 with hyperglycemia that showed a highly significant mortality rate (X2=15.9, p<0.001).

**Conclusion** Hyperglycemia should be monitored even after regression of COVID-19 symptoms, and insulin therapy must be considered to minimize the risk of death.

**Keywords** COVID-19; Hyperglycemia; Mortality Rate

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#### Article History

Received: August 16, 2021

Accepted: August 25, 2021

ePublished: November 11, 2021

### CITATION LINKS

[1] The management of coronavirus disease 2019 ... [2] Corona virus: a review of COVID ... [3] The corona virus disease 2019 ... [4] Epidemiological and clinical predictors of ... [5] The impact of coronavirus disease 2019 ... [6] Coronavirus disease 2019 and gender ... [7] Bibliometric analysis of global scientific ... [8] Clinical characteristics of 161 cases of ... [9] The origin, transmission and clinical therapies on ... [10] Online learning to prevent the spread of pandemic ... [11] Obesity and its implications for COVID-19 ... [12] Clinical characteristics of refractory COVID-19 ... [13] A comprehensive literature review on the clinical presentation ... [14] Hyperglycemia at hospital admission is associated with severity of the prognosis ... [15] Hyperglycemia and the worse prognosis ... [16] Importance of hyperglycemia in COVID-19 intensive ... [17] Inpatient hyperglycemia management ... [18] Letter to the Editor: "Our Response to COVID-19 as Endocrinologists ... [19] COVID-19 coronavirus vaccine T cell epitope prediction ... [20] Probable Interaction Between Warfarin and the Combination ... [21] Managing hyperglycemia in the COVID-19 ... [22] Hyperglycemia without diabetes and new-onset ... [23] Hyperglycemia, hydroxychloroquine, and the COVID-19 ... [24] Onset of ketosis-prone diabetes in the setting ... [25] Use of dexamethasone, remdesivir, convalescent ... [26] Analysis of Toll like Receptor2 & 4 (TLR2 & TLR4) ...

## Introduction

General health care centers have focused on the ongoing master problem, i.e. COVID-19 infection, which spends much time and economical resources for both research and preparation of effective therapy against this disaster [1]. COVID-19 infection is a peculiar viral infection caused by a certain strain of the coronavirus family [2], and it tends to affect the respiratory system [3], causing variable symptoms that vary from mild to severe life-threatening conditions [4]. Worldwide speaking, it was found that no specific race is more targeted by this disease, although the younger age group is the least risky persons [5]. One predictive factor for the risk of complications and death rate associated with COVID-19 infection is the gender of patients, i.e., males have a higher risk for both morbidity and mortality [6]. The most remarkable phenomenon of recent pandemic infection with COVID-19 is the rapid generation of multiple strains with different clinical and epidemiological presentations [7]. It was found that the mortality rate is directly related to disease complications like cerebrovascular insults [8], cardiovascular sequel [9], and respiratory failure [10]. The importance of this comes from its liability to cause a high mortality rate among suffering humans [11]. COVID-19 infection is regarded as a complex health challenge because of its wide spectrum of presentation, fast spread among humans, and potential induction of death among affected persons [12]. The causes of death varied from respiratory compromise, renal involvement, coagulopathic complications, and endocrine insults [13]. One of the noticeable presentations of COVID-19 infection is hyperglycemia that may occur even after the subsidence of main respiratory symptoms of the disease [14]. In many studies, it was found that hyperglycemia may reach up to >400mg/dl, which carries a high risk of morbidity and an even higher mortality rate [15]. The reason(s) for the state of elevated blood glucose level in patients with COVID-19 infection is multifactorial, i.e., it comes from either direct pancreatic damage by viremia [16], increased glucose resistance [17], or due to increased metabolic demands of the body associated with increased the secretion and activity on natural body compensatory mechanisms that antagonize insulin function like thyroxin and adrenalin [18].

Although many brand companies for drugs and vaccine manufacturing have made a great effort to provide humanity with effective protection, still up to now, effective eradication for this pandemic infection is highly difficult [19]. Using Remdesivir as selective antiviral agent against COVID-19 infection helps reduce the severity of insults in many patients, although highly percentage of effectiveness is not well proved [20].

This study aimed to evaluate the relationship between death rate and hyperglycemia caused by COVID-19 infection in non-diabetic patients.

## Materials and Methods

This retrospective study was conducted from June to August 2020 depending on data obtained from a special COVID-19 care center in Al-Hussien General Hospital in Kerbala, Iraq. A total of 296 patients aged between 35-45 years old males whose COVID-19 infection was proved by polymerase chain reaction (PCR) test, with no history of previous hyperglycemia, hypertension, cardiovascular diseases, or other endocrine disorders were randomly selected. The blood samples (10 ml) were taken from the patients and stored in EDTA tubes, then centrifuged at 5000 RPM for 5 minutes to separate the serum, then PCR augmentation to augment the amount of IgM immunoglobulin to demonstrate the presence of targeted antibody against coronavirus. Random blood sugar was done routinely for every patient with a positive COVID-19 test every day while receiving medications using digital Reflomite. The death rate was assessed in both hyperglycemia and non-hyperglycemia patients.

Statistical analysis was done using the Chi-square test to detect any significant difference in death rate by SPSS 19.

## Findings

Of the 296 selected COVID-19 patients, 57 were diagnosed with more than 400mg/dl hyperglycemia. There was a significant relationship between death rate and COVID-19 patients with hyperglycemia (Table 1).

**Table 1)** The death rate difference between COVID-19 patients with- and without hyperglycemia (n=296)

Parameters	Number	$\chi^2$	p Value
<b>With hyperglycemia</b>			
Death	13	15.9	<0.001
Alive	44	1.37	
<b>Without hyperglycemia</b>			
Death	15	3.06	0.524
Alive	224	0.26	

## Discussion

This result suggests that the occurrence of hyperglycemia is highly associated with death chances for a patient with COVID-19 infection. The ethical permissions were taken from the COVID-19 specific care center employers who communicate with the lived patients to get acceptance to achieve the statistical analysis based on their results. Despite obtaining important data from this study, our team faced some limitations, especially regarding time for study conduction and sample size. The complication of hyperglycemia can be the direct cause of death, such as diabetic ketoacidosis [21] or disturbed coagulation process that may induce thromboembolic phenomenon [22]. Many studies postulated that inflammatory storms caused by a sudden COVID-19 viremia could potentiate an

abrupt and unpredicted pancreatic dysfunction with a sudden reduction in insulin secretion levels that result in sudden hyperglycemia, in turn increasing mortality rate [23]. Conclusion: Hyperglycemia should be monitored even after regression of COVID-19 symptoms and insulin therapy to minimize the risk of death.

In a similar study done in 2020, a higher mortality rate was observed in patients with diabetes mellitus during the first ten days of the disease due to diabetic ketoacidosis because of the increased metabolic rate at a rate that exceeds the capacity of insulin function [24]. Another study revealed that sudden hyperglycemia could have resulted from direct drug toxicity, mostly Remdesivir and corticosteroids, with subsequent increased risk of mortality [25]. One of the interesting findings regarding the pathogenesis of hyperglycemia in the patient suffering from COVID-19 infection is the disturbance of normal expression of toll-like receptors type II and IV in peripheral blood monocytes and granulocytes with the subsequent dramatic increase in peripheral insulin resistance [26]. However, more studies are required to evaluate the signaling pathway that may be affected by COVID-19 infection, which plays a crucial role in the pathogenesis of abruptly increased blood sugar, to find more methods to minimize the mortality risk associated with this complication.

## Conclusion

Even after regression of COVID-19 symptoms, hyperglycemia should be monitored, and insulin therapy must be considered to minimize the risk of death.

**Acknowledgments:** None declared by the authors.

**Ethical Permissions:** None declared by the authors.

**Conflicts of Interests:** None declared by the authors.

**Authors' Contribution:** Awad W (First Author), Introduction Writer/Main Researcher (25%); Kadhim HM (Second Author), Methodologist/Assistant Researcher/Statistical Analyst (25%); Hassan DM (Third Author), Assistant Researcher/Discussion Writer (25%); Al-Yassiry KAR (Forth Author), Assistant Researcher (25%)

**Funding/Support:** None declared by the authors.

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