

Original Research

# Hyperglycemia Induced by COVID-19 with and without Present Diabetes: A Systematic Review

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**Abstract**—COVID-19 is a major emerging disease that affects any certain condition. However, a recent report suggests the occurrence of hyperglycemia without any present diabetes in COVID-19 patients. This study aimed to systematically review recent evidence on hyperglycemia in COVID-19 patients. Literature research was done using four search engines, consist of Google Scholar, PubMed, ScienceDirect, and ProQuest, and limited to English manuscript only and published from February 2020 to September 2020. SARS-CoV-2 could damage the pancreas by causing the destruction of the  $\beta$ -cell structure that leads to impairment of glucose metabolism and worsen pre-existing diabetes or determine the appearance of hyperglycemia in non-diabetes. Inflammation also plays a major important role in hyperglycemia related to COVID-19. Hyperglycemia increased the vulnerability of the lung, by promoting and facilitating the entry of the SARS-CoV-2 into the host cells, and decreasing lung function. Moreover, the mortality and morbidity rate conceivable increased due to hyperglycemia. The presence of high glucose levels is linked with the progression of COVID-19 severity. Thus, the glucose level should be concerned, either in a patient with present diabetes or without any presence of diabetes. Examination and monitoring of glucose levels might be a useful tool to prevent the seriousness of COVID-19.

**Keywords:** diabetes mellitus, SARS-CoV-2, high glucose level, pulmonary infection

**Abstrak**—COVID-19 adalah penyakit yang muncul yang mempengaruhi kondisi tertentu. Namun, sebuah laporan baru-baru ini menunjukkan terjadinya hiperglikemia tanpa adanya diabetes pada pasien COVID-19. Penelitian ini bertujuan untuk meninjau secara sistematis bukti terbaru tentang hiperglikemia pada pasien COVID-19. Penelitian literatur dilakukan dengan menggunakan empat mesin pencari, yaitu Google Scholar, PubMed, ScienceDirect, dan ProQuest, dan terbatas hanya pada manuskrip berbahasa Inggris dan diterbitkan dari Februari 2020 hingga September 2020. SARS-CoV-2 dapat merusak pankreas dengan menyebabkan kerusakan pada pankreas. struktur sel  $\beta$  yang menyebabkan gangguan metabolisme glukosa dan memperburuk diabetes yang sudah ada sebelumnya atau menentukan munculnya hiperglikemia pada kelompok non-diabetes. Peradangan juga memainkan peran penting utama dalam hiperglikemia terkait COVID-19. Hiperglikemia meningkatkan kerentanan paru-paru, dengan mendorong dan memfasilitasi masuknya SARS-CoV-2 ke dalam sel inang, dan menurunkan fungsi paru-paru. Selain itu, angka mortalitas dan morbiditas yang diperkirakan meningkat karena hiperglikemia. Adanya kadar glukosa yang tinggi dikaitkan dengan perkembangan keparahan COVID-19. Dengan demikian, kadar glukosa harus diperhatikan, baik pada pasien dengan diabetes saat ini atau tanpa adanya diabetes. Pemeriksaan dan pemantauan kadar glukosa mungkin menjadi alat yang berguna untuk mencegah derajat keparahan COVID-19.

**Kata kunci:** diabetes mellitus, SARS-CoV-2, peningkatan kadar glukosa, infeksi paru

## INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) pandemic is not over and the solution has yet to be found. It is more than a health crisis, COVID-19 affected many aspects in life. To date, more than 1.000.000 deaths is caused by COVID-19 [1]. Compared to other countries in South East Asia, Indonesia has higher mortality [2]. Several factors contribute to the severity and mortality of COVID-19. Comorbidities has been known to increase the severity of COVID-19 and diabetes is included [3]. It is also known that diabetic patients tend to have high blood glucose level or hyperglycemia [4]. However, a recent report suggests the occurrence of hyperglycemia without any present diabetes in COVID-19 patients [5–8]. Some studies suggest hyperglycemic condition could be a predictor of mortality in COVID-19 patients [4,9–14]. The systematic review was conducted to analyze the occurrence of hyperglycemia in COVID-19 patients with diabetes and without present diabetes.

## METHODS

Comprehensive literature searches were conducted using four electronic databases, PubMed, ProQuest, Science Direct, and Google Scholar. A limitation is set on literature searches using only published journals from February 2020 to September 2020 and English-

language manuscripts. Boolean logic was used to combine search terms as seen in the following Table 1. Literature searches in each database were conducted to find journals that contain information about hyperglycemia-associated COVID-19. Full text articles with cohort studies containing hyperglycemia-associated COVID-19 were obtained.

Afterwards, screening on journals abstract and title were done using inclusion criteria according to the following PICO, P: confirmed COVID-19 patients, I: diabetes and non-diabetes, C: not available, O: hyperglycemia. While the exclusion criteria were those journals contained a restricted discussion about diabetes as a comorbidity in COVID-19 patients without any further data about non-diabetes and those only discussed COVID-19 with or without diabetes, yet not associating hyperglycemia. Critical appraisals were conducted using Oxford's Centre for Evidence-Based Medicine worksheets [15].

**Table 1**

*Literature Search Strategy Using Boolean Logic*

Database	Keywords	Results
PubMed	"covid-19" or "sars-cov-2" and "hyperglycemia" and "diabetes"	101
ProQuest	"covid-19" and "hyperglycemia" and "diabetes" and "without diabetes" or "non diabetes"	365
Science Direct	covid-19 or sars-cov-2 and diabetes and without diabetes and hyperglycemia	172
Google Scholar	"covid-19" and "hyperglycemia" and "diabetes" and "without diabetes" or "non diabetes"	66

## RESULTS

A total of 704 published papers about hyperglycemia in COVID-19 patients with diabetes or without present diabetes from four electronic databases were identified and 692 were excluded. Eight articles were analyzed and discussed, the critical appraisals can be seen in Table 2 below. Each study compared high blood sugar levels or hyperglycemia in diabetic patients group and non-diabetic patients group. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart can be seen in Figure 1.

**Table 2**  
*Critical Appraisal Of The Studies Included In The Systematic Review*

First author and year	Study size and settings	Study design	Study period	Outcomes
Mamtani, 2020 <sup>5</sup>	403 patients admitted to John H Stroger Chicago	Observational cohort	March 15, 2020 to May 15, 2020	<p><b>Mortality</b> DM(-)HG(+) 20.5% DM(-)HG(-) 1.8%</p> <p><b>Admission to ICU</b> DM(+)HG(+) 32.4% DM(+) HG(-) 20.0% DM(-)HG(+) 43.4% DM(-)HG(-) 7.2%</p> <p><b>Mechanical ventilation</b> DM(+)HG(+) 18.6% DM(+) HG(-) 10.0% DM(-)HG(+) 32.5% DM(-)HG(-) 0.6% DM = history of diabetes HG = blood glucose <math>\geq 7.78</math> mmol/L</p>
Wu, 2020 <sup>10</sup>	2,041 patients from two medical centers in Wuhan	Retrospective cohort	December 26, 2019 to March 15, 2020	<p><b>Critical condition</b> Normal initial glucose 33.7% Hyperglycemia initial glucose 66.3%</p>
Zhu, 2020 <sup>11</sup>	293 patients from five hospitals in Wenzhou, China	Retrospective cohort	January 17 to February 22, 2020	<p><b>Severe or critical case</b> FPG &lt;7.05 mmol/L 32.8% FPG <math>\geq 7.05</math> mmol/L 67.2%</p>
Yan Zhang, 2020 <sup>15</sup>	166 patients at Tongji Hospital, Wuhan	Retrospective cohort	February 8 to March 21, 2020	<p><b>Mortality</b> 9.5% in No diabetes &amp; FPG &lt; 7.0 mmol/L 14.3% in No diabetes &amp; FPG <math>\geq 7.0</math> mmol/L 21.3% in Diabetes &amp; FPG <math>\geq 7.0</math> mmol/L</p> <p><b>Composite outcomes</b> 10.7% in No diabetes &amp; FPG &lt; 7.0 mmol/L 38.1% in No diabetes &amp; FPG <math>\geq 7.0</math> mmol/L 27.9% in Diabetes &amp; FPG <math>\geq 7.0</math> mmol/L</p>
Yang Zhang, 2020 <sup>12</sup>	263 patients at Tongji Hospital Wuhan	Retrospective cohort	February 4 to March 10, 2020	<p><b>Hyperglycemia</b> 61.7% in diabetes 38.3% in non-diabetes</p> <p><b>28-day mortality:</b> 54.8% in diabetes 36.8% in non-diabetes</p>
Liu, 2020 <sup>4</sup>	255 patients admitted to Tongji Hospital, China	Retrospective cohort	February 1 to February 24, 2020	<p><b>Required ICU</b> FPG &gt;7.0 mmol/L 85.4% FPG <math>\leq 7.0</math> mmol/L 14.6%</p>
Carrasco, 2020 <sup>13</sup>	11,312 patients in 109 hospitals in Spain	Retrospective cohort	March 1 to May 31, 2020	<p><b>Mortality</b> 15.7% in Admission BG &lt;140 mg/dl</p>

				33.0% in Admission BG 140 - 180 mg/dl
				41.1% in Admission BG >180 mg/dl
				<b>Mechanical ventilation</b>
				9.0% in Admission BG <140 mg/dl
				14.3% in Admission BG 140 - 180 mg/dl
				16.1% in Admission BG >180 mg/dl
				<b>ICU admission</b>
				7.5% in Admission BG <140 mg/dl
				10.6% in Admission BG 140 - 180 mg/dl
				11.4% in Admission BG >180 mg/dl
				<b>Composited endpoint</b>
				21.7% in Admission BG <140 mg/dl
				40% in Admission BG 140 - 180 mg/dl
				48.6% in Admission BG >180 mg/dl
Coppelli, 2020 <sup>14</sup>	271 patients admitted to the University Hospital, Italy	Retrospective cohort	March 20 to April 30, 2020	<b>In-hospital mortality</b> 16.8% in Normoglycemia 39.4% in Hyperglycemia 28.6% in Known diabetes <b>Need for mechanical ventilation</b> 11.4% in Normoglycemia 33.3% in Hyperglycemia 12.5% in Known diabetes <b>Admission to ICU</b> 24.2% in Normoglycemia 45.4% in Hyperglycemia 25.0% in Known diabetes <b>Acute respiratory distress syndrome</b> 32.9% in Normoglycemia 59.1% in Hyperglycemia 64.3% in Known diabetes

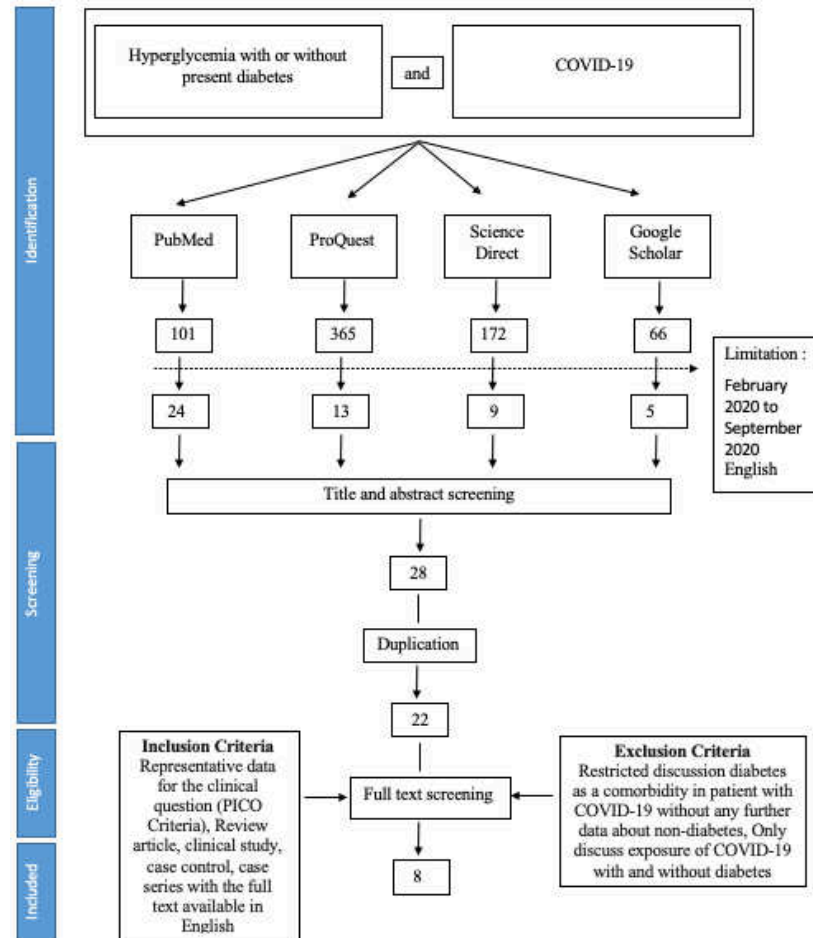


Figure 1. PRISMA flowchart for studies of hyperglycemia induced by COVID-19 with and without present diabetes.

## DISCUSSION

### Hyperglycemia in COVID-19

Hyperglycemia is a condition of blood glucose greater than 100 mg/dl while fasting (8-12 hours) or 200 mg/dl randomly. This condition occur when body when body has a little insulin or can't regulate insulin properly. It has been known that hyperglycemia is associated with Diabetes. Nevertheless, hyperglycemia can also be found in several condition such as stress from illness, such as infection. COVID-19 is a highly contagious disease and has still become a major health problem. The mechanism of infection, therapies, and complications caused by COVID-19 is still being studied. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infected cell host through S-Glycoprotein structure that binds Angiotensin Converting Enzyme 2 (ACE-2) receptor [6,7].

Hyperglycemia in COVID-19 has several mechanisms. The major action can be divided into two subdivided. First, there was a direct mechanism via  $\beta$  cells impairment from the virus itself. Secondly, an indirect mechanism was found via the impact of pro-inflammatory cytokines, acute stress factors, or a history of glucocorticoid therapy usage.<sup>5</sup> SARS-CoV-2 could damage pancreatic  $\beta$  cells by binding to ACE-2 receptor, hence insulin secretion is impaired. As a consequence, blood sugar level will increase and worsen the diabetes condition or induce hyperglycemia in patients without prior diabetes. This condition causes glycation of immunoglobulin, thus impair the antibodies function, weaken the immune systems, and elevation of HbA1c level. Furthermore, pancreatic beta cells impairment may worsen and insulin resistance occurs [6]. ACE-2 may also be glycosylated aberrantly, enhancing cellular intrusion of SARS-CoV2 and increase the severity of the disease [6,8,10,15,16].

SARS-CoV-2 may affect the innate immune system by downregulating and shedding virus-induced ACE-2, thus stimulate abundant proinflammatory cytokines release in hosts cell resulting in cytokine storm [5,8]. Structural and functional damage in endothelial cell occurs in this condition leading to impairment in insulin secretion and pancreatic beta cell causing hyperglycemia. Meta-analyses studies by Lee et al<sup>9</sup> and Sachdeva et al [8] showed that host immune response dysregulation which cause cytokine production impairment (e.g. IL-6) will induce or worsen insulin resistance and disrupt the insulin secretion. Zhou et al [6] and Mamtani et al [5] in their studies showed that elevation of proinflammatory cytokines in circulation, such as CRP, IL-6, Interferon Gamma, and Tumor Necrosis Factor Alpha occurred in hyperglycemic patients either with diabetes or without diabetes. Sachdeva et al [8] found that IL-6 level decreased after the hyperglycemia was treated. Another finding in a study conducted by Zhou et al [6] shows a low level of CD3+ and CD4+/CD8+ ratio in hyperglycemic patients with and without prior diabetes indicated immune system impairment process. This led to surge mechanism of activated-NK cells, proinflammatory cytokine production, reducing T-helper associated chemokine receptors, and disrupting T cell proliferation in initial stage of infection, thus worsen patient condition. Lee et al also stated that hyperglycemia in COVID-19 patients with diabetes was caused by inflammation and counterregulatory hormones [9]. A study by Wu et al shows that the infection process caused an inflammatory storm. Furthermore, insulin resistance can occur. Thus, infection also inducing stress mechanism and sympathetic stimulation [10]. These support the hypothesis of inflammatory factor overexpression induces hyperglycemia.

Another mechanism of high blood sugar level was related to stress-induced. Zhou et al [6] and Yan Zhang et al [15] in their studies showed that high cortisol level induced by stress resulting in hyperglycemia by activating enzymes that involved in the gluconeogenesis process in the liver and inhibiting glucose uptake in peripheral tissues, such as the skeletal muscle. Glucocorticoid therapy in severe or critical COVID-19 patients may induce hyperglycemia by similar mechanism as stress-induced. However, glucocorticoid therapy is still used in many health facilities to manage the inflammation in COVID-19 patients.

### ***Mortality and Morbidity in Hyperglycemia induced by COVID-19***

Hyperglycemia was an independent risk factor to critical condition and death in many infectious diseases, such as SARS and COVID-19 [17]. Dysregulation of immune system associated with hyperglycemia may contribute to high infection susceptibility and disease severity [18]. CT scans of patient with high fasting blood glucose showed more abnormalities rather than normoglycemic patients [8] Length of stay (LOS) was found to be slightly longer in patients with blood sugar level > 180 mg/dl than in patients with blood sugar level 140 – 180 mg/dl and < 140 mg/dl, *i.e.* 12 days, 11.5 days, and 11.1 days, respectively ( $p < 0.011$ ) [13].

Mortality rate of COVID-19 patients with hyperglycemia was found to be high. A study by Carrasco et al [13] showed higher mortality rate in patient with blood sugar level on admission >180 mg/dl (41.1%) than in patient with blood sugar level on admission 140 – 180 mg/dl (33.0%) and <140 mg/dl (15.71%). Yang et al reported that death within 28 days in COVID-19 patients was associated with high level of fasting blood sugar. There were 27.4% subjects with fasting blood sugar level around 7.0 – 11.1 mmol/L and 21.3% subjects  $\geq 11,1$  mmol/L [16]. Moreover, the blood sugar level is also an independent factor of any inpatient death cause. This showed that there were correlation between uncontrolled hyperglycemia with high mortality rate [19].

Hyperglycemia could disrupt the defensive capacity of airway epithelial, furthermore it will induce oxidative stress production. High level of oxidative stress and the reduction of heparan sulfate induced by hyperglycemia may result in thrombosis [9,12]. Elevation of glucose concentration in respiratory tract may results in local inflammation and worsen patient condition. Hyperglycemia in diabetic patient may impair the pulmonary function by decreasing



vital capacity and forced expiratory volume in one second (FEV1) due to microangiopathy development [8,12]. The immune system may also be harmed mainly innate immunity, hence the risk of being infected is increased in line hyperglycemia condition. Matrix metalloproteinases gene expression can be escalated in hyperglycemia condition resulting in more extensive spreading of the inflammation. In hypoxemic and hyperglycemic condition, in order to obtain adenosine triphosphate (ATP), anaerobic glycolysis must occur. As a consequence, lactate and LDH level will increase. High lactate and LDH level were associated with high mortality in COVID-19 patients [8].

A study by Zhang et al [12] showed that liver function impairment, elevation of LDH and IL-8 ratio were found more in COVID-19 patients with hyperglycemia without prior diabetes. Moreover, hyperglycemic condition in non-diabetic patients may aggravate the symptom of COVID-19 by increasing proinflammatory cytokines, such as interferon alpha (IFN- $\alpha$ ), interleukin 1 beta (IL-1 $\beta$ ), interleukin 6 (IL-6), monocyte chemoattractant protein 1 (MCP1), interferon- $\gamma$ -inducible protein 10 (IP-10), oxidative stresses, as well as disrupting inflammatory and anti-inflammatory cytokines balance [16]. As many as 20.6% subjects with COVID-19, hyperglycemic conditions, and no diabetes history were having severe symptoms and high mortality rate as showed in a study by Mamtani et al [5], while study by Coppelli et al [14] was 24% and Zhou et al [6] was 27.5%.

Diabetes is a common comorbid disease in COVID-19 patients and linked to severity of the symptom. Chronic inflammation and dysfunction of immune system may happen progressively in diabetic patients showed by the presence of abnormal T cell, hence cytokine storm occurs faster [12]. Immune paralysis, or the inability of the immune response to recover despite clearance of pathogens by antimicrobials taking a major part in COVID-19 patients with diabetes and associated with high mortality rate [15]. Another study showed that deaths in hospital caused by COVID-19 were found to be higher in patient with diabetes than in patient without any comorbidities [20]. Mortality rate in COVID-19 patients with diabetes caused by hyperglycemic condition was 21.3%, higher than control group which was only 9.5% [12]. Hyperglycemia in diabetes also linked to higher chance for patients to acquire acute respiratory distress syndrome (ARDS) (58%), acute cardiac injury events (38.7%), shock (40.3%), secondary infection (43.5%) and acute kidney injury (AKI) (16.1%) than patients without diabetes ( $p < 0.05$ ) [19].

Patient with new-onset hyperglycemia, such as stress hyperglycemia and undiagnosed diabetes, had higher mortality rate in hospital than patient with history of diabetes or normoglycemia as shown in a study by Cakir et al [21]. This condition is linked to more gluconeogenesis and less glycogenolysis caused by the increase of counterregulatory hormone secretion. An autopsy of COVID-19 patient found Langerhans cell degeneration supports the statement [19]. Acute hyperglycemia occurred in 22% of confirmed COVID-19 patients in hospital and 18.9% of them have been diagnosed with diabetes.<sup>19</sup> Another study showed 50% confirmed COVID-19 patients had hyperglycemia and only 7% of them had diabetes history [22].

Hyperglycemia may worsen the severity of COVID-19 and cause critical condition in patients [23]. Study by Zhang et al [15] showed significant increment of patient risk having worse condition, for example mechanical ventilation usage, intensive care unit (ICU) admission, and death in group of patients with COVID-19 and hyperglycemia without history of diabetes (fasting blood sugar level  $\geq 7.0$  mmol/L, yet HbA1c level  $< 6.5\%$ ) than in group of normoglycemic patients (OR 5.47; confidence interval 95% (CI), 1.51 – 19.82;  $p = 0.010$ ). Hyperglycemia increase the mortality risk in COVID-19 patients three times greater than normoglycemic patient (OR 2.822, 95% CI=1.587–5.019,  $p < 0.001$ ) [16]. Sardu et al [24] also showed 71% relative increase of mortality in group of patient with severe COVID-19 and hyperglycemia on admission (new-onset hyperglycemia without history of diabetes; plasma blood sugar level  $> 7.77$  mmol/L or 140 mg/dl) than in group of normoglycemic or non-diabetes

patient, within 18 days. Thus, insulin therapy in hyperglycemic patient has been proved to decrease the severity of COVID-19 than no insulin therapy.

Yang et al [16] reported significant raise of emerging complication during 28 days of hospital stays (OR 2.61; 95% CI=1.64 – 4.41) in group of patients with COVID-19 and hyperglycemia without diabetes (blood sugar level 6.1 – 6.9 mmol/L) compared to normoglycemic patients. Meanwhile, Li et al [22] showed increment of death caused by COVID-19 in a group of hyperglycemic patients without diabetes (fasting blood sugar level 5.6 – 6.9 mmol/L or HbA1c level 5.7 – 6.4%) compared to normoglycemic patients (fasting blood sugar level <5.6 mmol/L and HbA1c <5.7%) (HR 3.29; 95% CI=0.65-16.6). Coppelli et al [14] stated that mortality was found to be significantly higher in a group of COVID-19 patients with hyperglycemia and no diabetes history (defined as no history of diabetes and blood sugar level  $\geq 7.78$  mmol/L on admission) compared to group of normoglycemic patients (blood glucose level <7.78 mmol/L on admission) (39.4% vs 16.8%, respectively; HR 2.20; 95% CI=1.27 – 3.81;  $p=0.005$ ) on 17 days observation.

The number of diabetic COVID-19 patients having high fasting blood sugar was found to be greater than non-diabetic patient, 82.3% versus 38.3%. This study also showed that diabetes patients had blood sugar levels in the range of 8.49 – 19.09 mmol/L, while patients without diabetes in the range of 5.67 – 7.95 mmol/L. Another parameter was used to compare COVID-19 patient with diabetes and without diabetes, for example differential white blood cell count, D-dimer level, albumin level, inflammatory markers (hsCRP, procalcitonin, ferritin, IL-2R, IL-6, and TNF- $\alpha$ ). In patients with diabetes, absolute neutrophil count was higher compared to lymphocyte count, D-dimer and inflammatory markers level increased, and albumin level was lower than patients without diabetes [22].

Hyperglycemia also can be found in COVID-19 patients during the hospital stay, even in patients without history of diabetes [10]. Hyperglycemia in non-diabetic patients may worsen the prognosis of COVID-19. The median of blood sugar level was observed to be high in patients whose condition was critical. (OR 2.39; 95% CI=1.41-4.07,  $p=0.001$ ) [13]. Compared to hyperglycemic patients with diabetes, hyperglycemic patients without diabetes history had significantly higher mortality rate. In a study by Bode et al [23] showed that mortality rate was found to be very high in non-diabetic patients with uncontrolled hyperglycemia (41.7%) compared to diabetic patients (14.8%) ( $p<0.001$ ). This finding is supported by study from Carrasco et al that showed mortality rate in non-diabetic COVID-19 patients with blood sugar level >180 mg/dl on admission was 43.3% [13].

A study by Zhang et al [12] evaluated the association between hyperglycemia in confirmed COVID-19 patients with diabetes and without diabetes. The study divided subjects to three group: control group or first group (patients had no diabetes history and the fasting blood glucose level was <126 mg/dl), secondary hyperglycemia or second group (patients had no diabetes history and the HbA1c level <6.5%, but the fasting blood glucose level was  $\geq 126$  mg/dl), and diabetes group or third group (patients had diabetes history, the HbA1c level  $\geq 6.5\%$ , and the fasting blood sugar level was  $\geq 126$  mg/dl). Mortality rate of second and third group were significantly higher than the first group (21.3%, 14.3%, dan 9.5%, respectively;  $p<0.05$ ). After the confounding factors were controlled, the odd ratio between the second group and third group versus first group were 5.47 (95% CI=1.56-19.82) and 2.61 (CI 95%=0.86-7.88), respectively. This data showed that hyperglycemia is associated with bad prognosis and high mortality rate in COVID-19 patients.

It has been mentioned that hyperglycemia in COVID-19 leads to a more severe prognosis (intensive care unit care necessity, mechanical ventilation usage, and hemodynamic instability) and higher mortality rate either patients have diabetes or not. In other words, blood glucose level can be used as a predictor for COVID-19 patients outcome [12,13]. Hyperglycemia also has been used as independent factor to predict the severity in viral infection, such as influenza A (H1N1) in 2009, MERS-CoV, and SARS-CoV [17,25,26]. Based on Mamtani et al [5] study, random blood glucose level  $\geq 10$  mmol/L in more than two tests or



fasting blood glucose level  $\geq 7$  mmol/L in COVID-19 patients lead to worse prognosis. While another study by Liu et al [4] showed more severe COVID-19 condition were found in patients with fasting blood glucose level  $\geq 6.50$  mmol / L. For every 2 mmol/L or 36 mg/dL the fasting blood glucose rises, the outcome will be more severe [27].

Blood sugar levels may fluctuate at different time. A study by Yang et al [16] showed that sample collection time affect the level of blood sugar. Blood glucose level test on admission could predict the mortality rate in COVID-19 patient, higher blood glucose level resulting in higher mortality risks. The controlled blood glucose levels in hyperglycemic COVID-19 patients either with or without a history of diabetes showed a decrease in mortality and severity. We recommend every healthcare facilities to test blood glucose level periodically for COVID-19 patients on admission and daily during the hospital stay. The earlier it is detected, the earlier patients are treated. As a consequence, a better outcome in COVID-19 patients.

## CONCLUSION

Hyperglycemia is associated with COVID-19 either in diabetic or non-diabetic patients and it increases the severity in both conditions. High mortality and morbidity were found in hyperglycemic COVID-19 patients. Therefore, blood sugar level could predict the outcome of COVID-19 patient. Blood sugar level test, especially fasting blood sugar level and random blood sugar level can be used to detect hyperglycemia as an indicator for COVID-19 severity. Monitoring on blood sugar level should be done periodically on COVID-19 patients despite the symptoms are absent or not severe. Early detection of hyperglycemia leads clinicians to the early and right management for the patients. As a result, mortality rate due to COVID-19 decreases. We suggest periodic blood sugar test as screening for hyperglycemia in hospitalized COVID-19 patients since COVID-19 can induce hyperglycemia in both diabetic patients and non-diabetic patients.

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