

Original article

## Blood Sugar Measurements in non-diabetic Patients Presented with COVID-19

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### Abstract:

- **Background:** The COVID-19 pandemic has led to widespread illness and death globally. Hyperglycemia, even in individuals without diabetes, is commonly observed in COVID-19 patients. This study aimed to assess the prevalence of hyperglycemia among non-diabetic COVID-19 patients and explore its association with disease severity.
- **Methods:** A descriptive cross-sectional study was conducted over six months (January to June 2021) at Al-Shifaa 14 Hospital in Kirkuk, Iraq. A total of 250 non-diabetic COVID-19 patients were included using a convenient sampling method. Diagnosis was confirmed through clinical assessment, RT-PCR, and CT imaging. Disease severity was categorized according to Iraqi Ministry of Health guidelines.
- **Result:** Hyperglycemia was observed in 8% of patients. Disease severity was distributed as mild (27.2%), moderate (13.6%), and severe (59.2%). Patients with severe COVID-19 had significantly higher levels of random blood glucose and HbA1c ( $p < 0.001$ ). Factors significantly associated with severe disease included older age, unemployment, marital status, existing co-morbidities, and pregnancy.
- **Conclusions:** Hyperglycemia is present in a subset of non-diabetic COVID-19 patients and is significantly associated with increased disease severity. Monitoring blood glucose may aid in early identification of patients at risk for severe outcomes.
- **Keywords:** COVID-19, Non-diabetic, Hyperglycemia.



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## INTRODUCTION

The novel coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as one of the most significant pandemics of the century, posing a serious threat to global public health. As of July 19, 2020, more than 130 million individuals had been infected, resulting in over 2.8 million deaths worldwide (1,2). The burden of COVID-19 has been disproportionately higher among certain population groups, particularly males, the elderly, and individuals with underlying health conditions. One of the most frequently reported comorbidities in patients with COVID-19 is type 2 diabetes mellitus (T2DM), which significantly increases the risk of adverse outcomes, including morbidity and mortality (3).

Interestingly, recent studies have also highlighted the emergence of new-onset hyperglycemia in hospitalized COVID-19 patients with no prior history of diabetes. Admission hyperglycemia, even in the absence of known diabetes, has been associated with a poor prognosis in COVID-19 patients (4,5). Reports from countries including the United States, Italy, Spain, and China have consistently shown that patients presenting with hyperglycemia at hospital admission—regardless of previous diabetes diagnosis—have an increased risk of requiring intensive care, mechanical ventilation, and face a higher risk of mortality (6,7).

Hyperglycemia, whether due to undiagnosed diabetes, impaired glucose tolerance, or acute stress-related metabolic changes ('stress hyperglycemia'), has been independently associated with worse clinical outcomes in hospitalized patients (8). Stress hyperglycemia can occur either due to unrecognized pre-existing glyceic abnormalities or as a direct response to the metabolic stress imposed by severe illness, including elevated counterregulatory hormones such as cortisol and catecholamines (9). Both diabetes and hyperglycemia have been shown to predict greater severity and increased mortality in COVID-19 (10). Furthermore, admission hyperglycemia has been linked with greater radiographic involvement in SARS-CoV-2 infection, regardless of diabetes status (11).

Globally, diabetes is a major contributor to morbidity and mortality. In 2019, approximately 463 million people were living with diabetes, and this number is expected to rise to 578 million by 2030 and 700 million by 2045. Among the top ten countries with the highest prevalence of diabetes, Mexico ranks sixth with around 12.8 million individuals affected (12). These figures highlight the growing burden of diabetes and the potential for its interaction with COVID-19 to further complicate disease outcomes.

Patients with COVID-19 who also have T2DM or cardiovascular disease (CVD) are more frequently admitted to intensive care units compared to those without these conditions (13). While both older age and T2DM are established risk factors for COVID-19 severity, the high prevalence of T2DM among elderly individuals complicates the understanding of their individual contributions to adverse outcomes (14). Poor glycemic control further worsens infection severity and increases mortality risk (15). Early studies indicated that diabetes was 2.26 times more common in patients with severe COVID-19 compared to those with milder disease, and the presence of diabetes carried an odds ratio of 2.85 for in-hospital mortality. In Italy, about one-third of COVID-19 fatalities occurred in patients with diabetes, predominantly elderly males. Compared to the baseline prevalence of diabetes in that age group, the relative risk of COVID-19 mortality associated with diabetes was estimated at 1.75 (16).

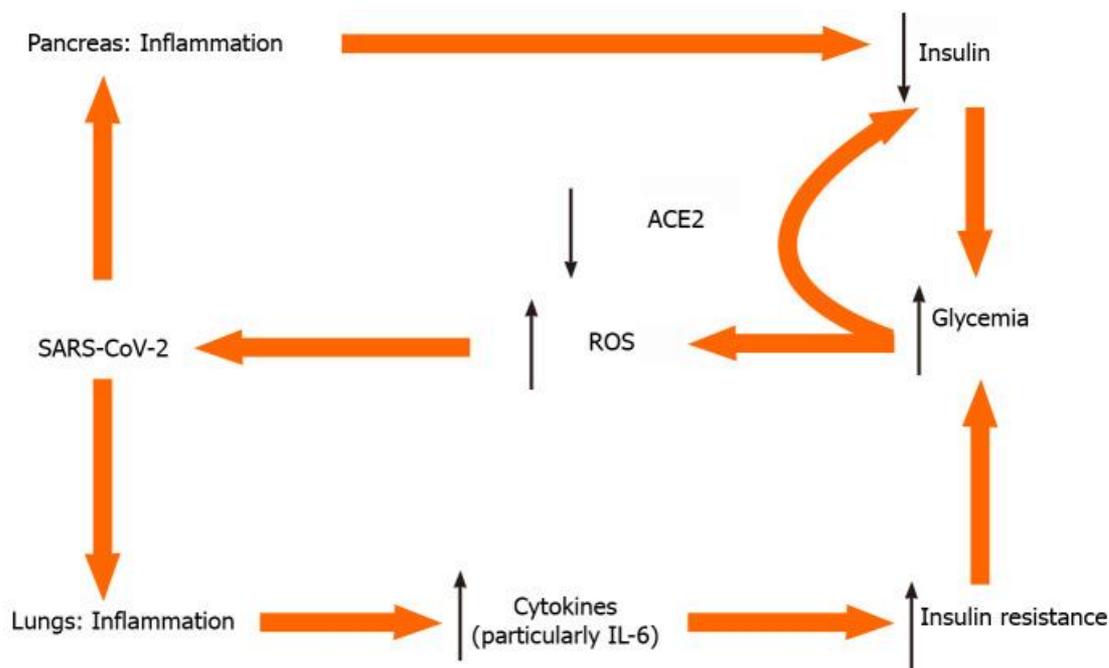
The pathophysiology of COVID-19 involves an exaggerated immune response in some patients, known as a "cytokine storm," characterized by excessive production of inflammatory mediators such as interleukins (ILs), interferons (IFNs), chemokines, and tumor necrosis factor-alpha (TNF- $\alpha$ ) (17). Inflammatory cell infiltration and damage to multiple organs including the lungs, heart, liver, and pancreas have been observed (18). Notably, a deficiency in type I interferon responses contributes to the severity of this immune dysregulation (19), and this cytokine storm is recognized as a life-threatening complication in severe cases (20).

Elevated inflammatory markers such as IL-6, CRP, D-dimer, and ferritin are frequently observed in COVID-19 and are associated with disease progression (21,22).

Diabetes, particularly T2DM, shares many of the same inflammatory and metabolic pathways as COVID-19. Although type 1 diabetes mellitus (T1DM) is not generally associated with obesity, most individuals with T2DM are overweight or obese. Chronic hyperglycemia impairs immune function and leads to increased oxidative stress, promoting insulin resistance and worsening metabolic control (18). Inflammation within the pancreatic  $\beta$ -cells (insulinitis) and activation of IL-1 $\beta$  pathways by macrophages are key mechanisms underlying diabetes-related immune dysfunction (23). Lipotoxicity and the presence of free fatty acids further exacerbate pancreatic injury. Additionally, cytokines like TNF- $\alpha$  and IL-6 contribute to insulin resistance, islet cell apoptosis, and overall deterioration of glycemic control. The inflammatory milieu in obesity and diabetes favors a shift toward pro-inflammatory macrophage populations, intensifying systemic inflammation. Furthermore, natural killer (NK) cell activity is reduced in patients with poorly controlled diabetes, and higher HbA1c levels are inversely related to NK cell function (24).

Obesity, which is often comorbid with T2DM, is another significant risk factor for poor COVID-19 outcomes. The inflammatory state associated with obesity mimics the cytokine storm seen in COVID-19, involving elevated levels of TNF- $\alpha$ , IL-1, IL-6, and adipokines such as leptin and resistin. Hypoxia and endothelial dysfunction within adipose tissue exacerbate oxidative stress, leading to widespread tissue damage. These processes further compromise vascular integrity and amplify COVID-19-related complications (20).

The impact of COVID-19 on glucose metabolism resembles that of earlier coronavirus infections such as SARS in 2003, which was linked to transient islet cell dysfunction. Like MERS-CoV, SARS-CoV-2 uses dipeptidyl peptidase-4 (DPP-4) and ACE2 receptors for cell entry, potentially impairing insulin regulation (25). Hyperglycemia has been shown to enhance SARS-CoV-2 replication via increased glycolysis and reactive oxygen species (ROS) production (26), while COVID-19 in turn worsens glycemic control in both T1DM and T2DM patients (27). Critically ill patients often require high doses of insulin to maintain euglycemia (26).



**Figure 1: Selected tentative pathways for hyperglycemia in severe acute respiratory syndrome coronavirus 2 infection. ACE2: Angiotensin converting enzyme 2; IL-6: Interleukin 6; ROS: Radical oxygen species; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2 <sup>28</sup>.**

In some cases, COVID-19 triggers diabetic ketoacidosis (DKA) in patients without prior diabetes. This may result from direct viral injury to pancreatic  $\beta$ -cells via ACE2 receptors, leading to new-onset diabetes or hyperglycemia (30,31). According to ADA definitions, new-onset hyperglycemia is characterized by fasting glucose of 100–125 mg/dL or HbA1c of 5.7–6.4% without a previous diagnosis. In contrast, new-onset diabetes is defined by fasting glucose >126 mg/dL or HbA1c >6.5% (30).

Case reports have documented new-onset diabetes and DKA precipitated by COVID-19 in previously healthy individuals, reinforcing the hypothesis of viral-mediated  $\beta$ -cell dysfunction (33,34). In one study, 6.4% of 658 COVID-19 patients presented with ketosis at admission, which was associated with increased hospitalization duration and mortality (35). Whether these cases represent permanent diabetes or transient stress-induced hyperglycemia remains to be determined, and initiatives like the COVIDIAB registry have been established to track these patients (36).

New-onset hyperglycemia without diabetes is associated with worse outcomes than normoglycemia in COVID-19 patients. These patients are more likely to require ICU admission, mechanical ventilation, and experience higher mortality rates (37,5,38,39). Some studies report even greater mortality risk in patients with new-onset hyperglycemia than those with pre-existing diabetes, though ICU admission rates may not differ significantly (40-42).

New-onset diabetes during COVID-19 has been reported in up to 21% of patients (33,43), with associated increases in complications, ICU admissions, and intubation. Mortality risk in patients with new-onset diabetes is nearly double that of those with pre-existing diabetes (44).

Hyperglycemia may also be exacerbated by treatments such as corticosteroids and previously used agents like hydroxychloroquine, which have glyceic effects (45-49).

Given this background, the present study aims to identify the prevalence of hyperglycemia among COVID-19 patients and evaluate its relationship with disease severity.

## **PATIENT and METHOD**

A descriptive cross-sectional study was conducted at AL-Shifaa 14 Hospital in Kirkuk city, Iraq, over a six-month period from January 1 to June 30, 2021. The study targeted hospitalized patients who tested positive for COVID-19 through reverse transcription polymerase chain reaction (RT-PCR) and did not have a prior history of diabetes mellitus. Only adult patients aged 20 years and above were included in the study. Patients were excluded if they had a known diagnosis of diabetes or were under 20 years of age.

From the eligible population, a convenient sample of 250 non-diabetic patients with confirmed COVID-19 was selected. The diagnosis of COVID-19 in these patients was confirmed by the attending supervisor based on a combination of clinical signs and symptoms, RT-PCR results, and chest computed tomography (CT) scan findings.

Data were collected directly by the researcher using a structured questionnaire that had been jointly developed with the study supervisor. For each patient, the questionnaire recorded demographic details (age and gender), social characteristics (residence, occupation, marital status), and presenting clinical complaints (including fever, cough, anosmia, ageusia, dyspnea, and chest pain). Additional information gathered included past medical and surgical history, drug usage, family history, smoking and alcohol history, pregnancy status, endocrine symptoms, physical examination findings, and vital signs. Laboratory parameters included random blood sugar (RBS), glycated hemoglobin (HbA1c), D-dimer, and C-reactive protein (CRP). RT-PCR results and chest CT-scan findings were also documented.

Each participant underwent a full clinical evaluation by the researcher, including the collection of a 5 mL venous blood sample for laboratory investigations. Chest CT scans were performed either at Kirkuk General Hospital, Azadi Teaching Hospital, or private diagnostic centers when referred from AL-Shifaa 14 Hospital. The Siemens 64-slice CT scanner (Germany) was used for imaging. The severity of lung involvement was scored using a semi-quantitative method based on the extent of lesions in each of the five lung lobes: a score of 0 indicated no involvement; 1 indicated less than 5% involvement; 2 represented 5–25%; 3 represented 26–50%; 4 represented 51–75%; and 5 represented more than 75% involvement. The total chest CT score ranged from 0 to 25.

The severity of COVID-19 disease was categorized based on clinical criteria established by the Iraqi Ministry of Health (Appendix 1). Hyperglycemia was defined as a random blood sugar level exceeding 180 mg/dL. All laboratory analyses were conducted at the AL-Shifaa 14 Hospital laboratory.

Ethical approval for the study was obtained from the Iraqi Board of Medical Specializations. Additionally, institutional permission was secured from hospital authorities, and verbal informed consent was obtained from all participating patients before data collection commenced.

The collected data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS) software, version 22. Descriptive statistics were presented as means and standard deviations for continuous variables, and frequencies and percentages for categorical variables. Relationships between variables were assessed using multiple contingency tables. The Chi-square test was employed for categorical comparisons, and Fisher's exact test was used when expected counts were below 20% of the total. One-way analysis of variance (ANOVA) was applied for comparing more than two group means. A p-value of  $\leq 0.05$  was considered statistically significant. The results were summarized and displayed in tables and graphs where appropriate.

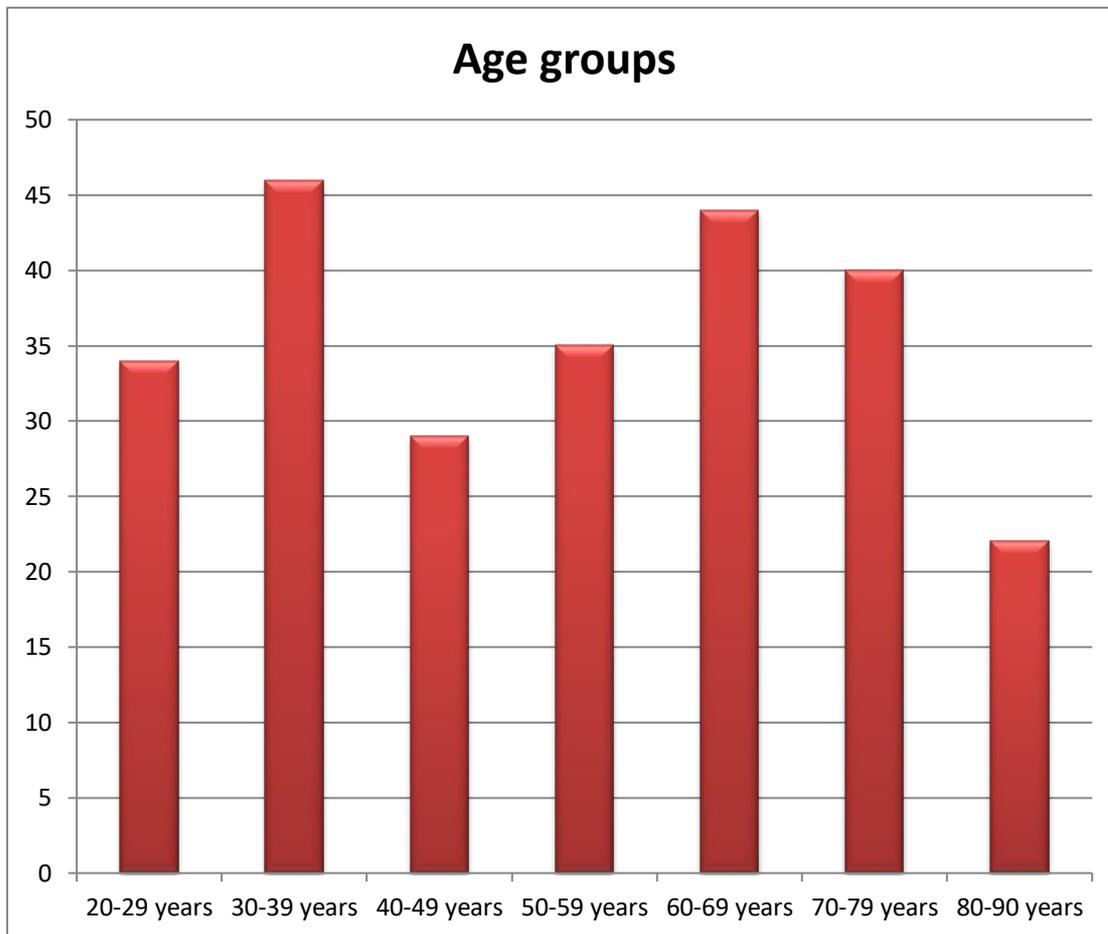
## RESULTS

This study included 250 COVID-19 patients admitted with mean age of  $52 \pm 19.2$  years and range of (20-90 years); 13.6% of patients were in age group 20-29 years, 18.4% of patients were in age group 30-39 years, 11.6% of them were in age group 40-49 years, 14% of them were in age group 50-59 years, 17.6% of them were in age group 60-69 years and 16% of them were in age group 70-79 years and 8.8% of COVID-19 patients were in age of 80-90 years. Male COVID-19 patients were more than females with male to female ratio as 2:1.

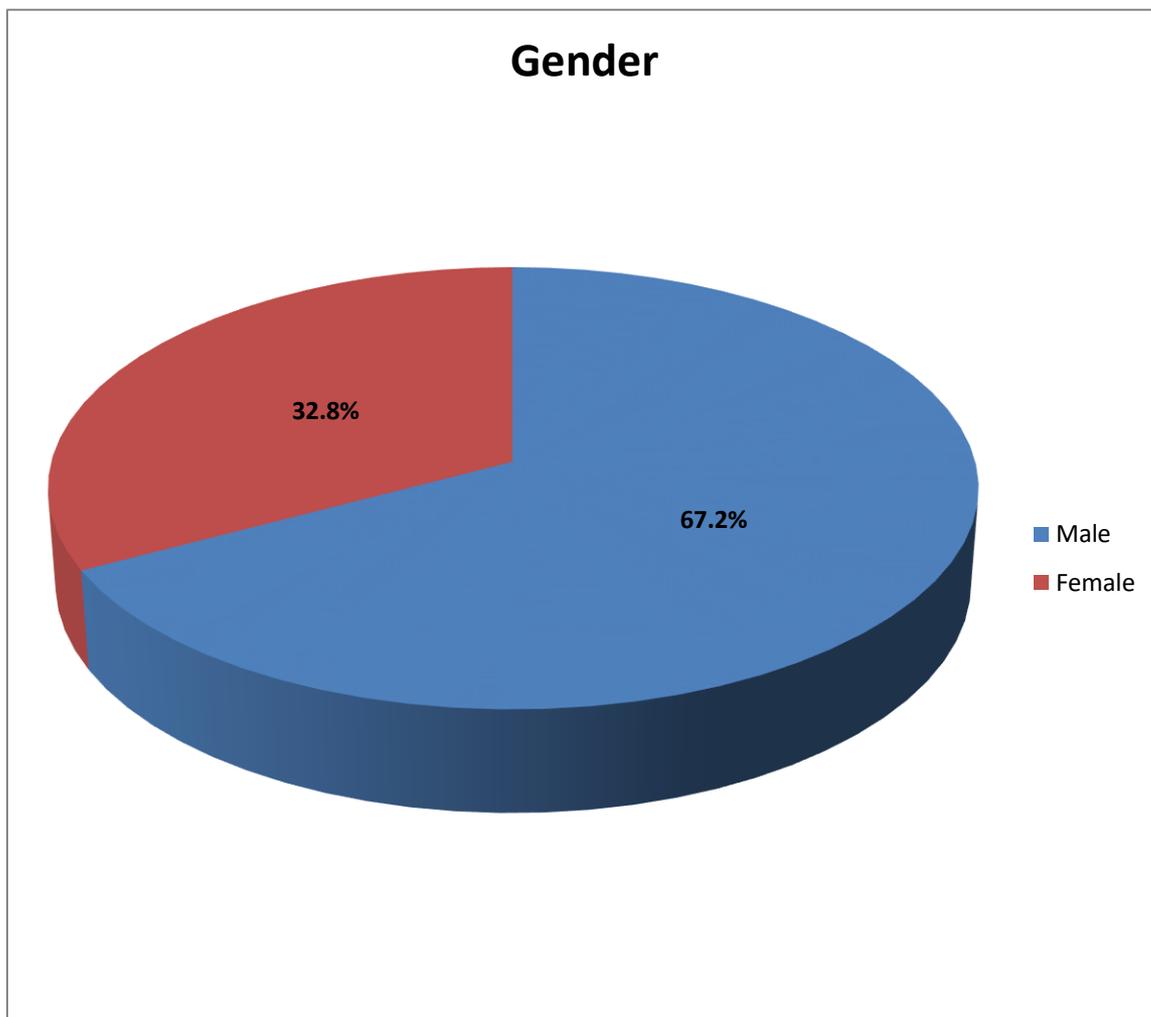
*(Table 1 and Figures 2, 3)*

**Table 1. Demographic characteristics of COVID-19 patients.**

<b>Variable</b>	<b>No.</b>	<b>%</b>
<b>Age</b>	Mean±SD (52±19.2 years)	
20-29 years	34	13.6
30-39 years	46	18.4
40-49 years	29	11.6
50-59 years	35	14.0
60-69 years	44	17.6
70-79 years	40	16.0
80-90 years	22	8.8
Total	250	100.0
<b>Gender</b>		
Male	168	67.2
Female	82	32.8
Total	250	100.0



**Figure 2: Age distribution of COVID-19 patients.**



**Figure 3: Gender distribution of COVID-19 patients.**

Most of studied COVID-19 patients were urban residents and 4.8% of them were rural residents. The occupation of COVID-19 patients was distributed as followings; public servants (34.4%), students (4.8%), self-employed (15.2%), retired (14.4%) and housewife (31.2%). Married COVID-19 patients represented 88% of them, while single patients represented 12% of them. (*Table 2*)

**Table 2. Social characteristics of COVID-19 patients.**

Variable	No.	%
<b>Residence</b>		
Urban	238	95.2
Rural	12	4.8
Total	250	100.0
<b>Occupation</b>		
Public servant	86	34.4
Student	12	4.8
Self employed	38	15.2
Retired	36	14.4
Housewife	78	31.2
<b>Marital status</b>		
Married	220	88.0
Single	30	12.0
Total	250	100.0

The common clinical complaints of patients with COVID-19 disease were cough (91.2%), fever (83.2%), dyspnea (74.4%), chest pain (66.4%), loss of smell (31.2%) and loss of taste (27.2%). (*Table 3*)

**Table 3: Clinical complaints of COVID-19 disease.**

<b>Variable</b>	<b>No.</b>	<b>%</b>
<b>Fever</b>		
Yes	208	83.2
No	42	16.8
Total	250	100.0
<b>Cough</b>		
Yes	228	91.2
No	22	8.8
Total	250	100.0
<b>Loss of smell</b>		
Yes	78	31.2
No	172	68.8
Total	250	100.0
<b>Loss of taste</b>		
Yes	68	27.2
No	182	72.8
Total	250	100.0
<b>Dyspnea</b>		
Yes	186	74.4
No	64	25.6
Total	250	100.0
<b>Chest pain</b>		
Yes	166	66.4
No	84	33.6
Total	250	100.0

The endocrine symptom of COVID-19 patients was commonly thirst (32.8%), followed by; thirst and sweating (26.4%), thirst, polyurea and sweating (3.2%), etc. (**Table 4**)

Table 4: Endocrine symptoms of COVID-19 patients.

<b>Variable</b>	<b>No.</b>	<b>%</b>
<b>Endocrine symptoms</b>		
<b>No</b>	86	34.4
<b>Thirst</b>	82	32.8
<b>Sweating</b>	4	1.6
<b>Thirst and polyurea</b>	4	1.6
<b>Thirst, polyurea and sweating</b>	8	3.2
<b>Thirst and sweating</b>	66	26.4
<b>Total</b>	250	100.0

The past medical history was hypertension in 25.6% of COVID-19 patients and hypertension and thyroid in two patients. The drug history was positive for steroids and others in four patients and positive for 25.6% of patients. The family history for DM was recorded among 5.6% of COVID-19 patients and family history of others among four patients. Smoking history was present among 28.8% of COVID-19 patients, while alcohol history was recorded for four patients and pregnancy was detected in two patients only. (*Table 5*)

**Table 5: Clinical history of COVID-19 patients.**

<b>Variable</b>	<b>No.</b>	<b>%</b>
<b>Past medical history</b>		
No	184	73.6
Hypertension	64	25.6
Hypertension and thyroid disease	2	0.8
Total	250	100.0
<b>Drugs history</b>		
No	224	89.6
Steroids and others	4	1.6
Others	22	8.8
Total	250	100.0
<b>Family history</b>		
No	232	92.8
DM	14	5.6
Others	4	1.6
Total	250	100.0
<b>Smoking history</b>		
No	178	71.2
Yes	72	28.8
Total	250	100.0
<b>Alcohol history</b>		
No	246	98.4
Yes	4	1.6
Total	250	100.0
<b>Pregnancy history</b>		
No	248	99.2
Yes	2	0.8
Total	250	100.0

The breathing was vesicular for all patients. The added sounds were crepitation (15.2%), wheezing (4%) and wheezing and crepitation (4%). The PCR was positive for all patients. The mean measures of vital signs for COVID-19 patients were (95.5 beat/m) for pulse rate, BP (118.8/76.7 mmHg), RR (19.8 breath/m), temperature (37.7 C°) and SPO<sub>2</sub> (81.5%).

(Table 6)

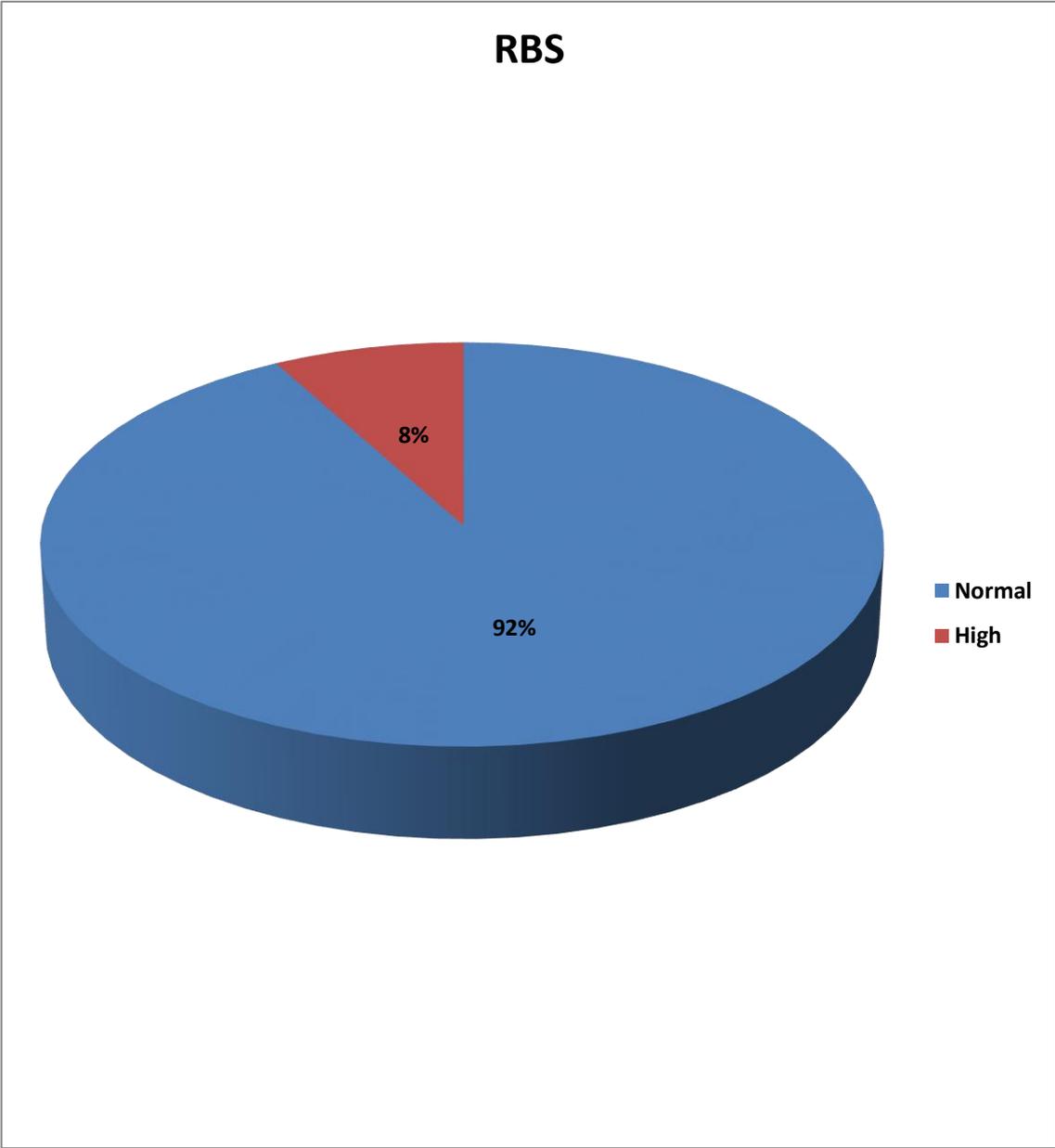
**Table 6: Examination and PCR findings of COVID-19 patients.**

Variable	No.	%
<b>Breathing</b>		
Vesicular	250	100.0
Total	250	100.0
<b>Added sounds</b>		
No	192	76.8
Wheezing	10	4.0
Crepitation	38	15.2
Wheezing and crepitation	10	4.0
Total	250	100.0
<b>PCR</b>		
Positive	250	100.0
Total	250	100.0
<b>Pulse rate</b> mean±SD (95.6±13.5 beat/m)		
<b>Blood pressure</b> mean±SD (118.8/76.7±11.6/7.2 mmHg)		
<b>Respiratory rate</b> mean±SD (19.8±5.1 breath/m)		
<b>Temperature</b> mean±SD (37.7±0.9 C°)		
<b>SPO<sub>2</sub></b> mean±SD (81.5±14.4 %)		

The mean measures of investigations for COVID-19 patients were RBS (115 mg/dl), HbA1c (6.5%), CT scan chest occupancy (37.6%), CRP (48.7 mg/dl) and D-dimer (490.1 ng/ml). The hyperglycemia was detected among 8% of COVID-19 patients. (*Table 7 and Figure 4*)

**Table 7: Investigations findings of COVID-19 patients.**

<b>Variable</b>	<b>Mean</b>	<b>SD</b>
<b>RBS (mg/dl)</b>	115	41.7
<b>HbA1c (%)</b>	6.5	1.1
<b>D-dimer level (ng/ml)</b>	490.1	613.1
<b>C-reactive protein (mg/dl)</b>	48.7	46.7
<b>CT scan chest (%)</b>	37.6	25.8
<b>Total</b>	250	100.0

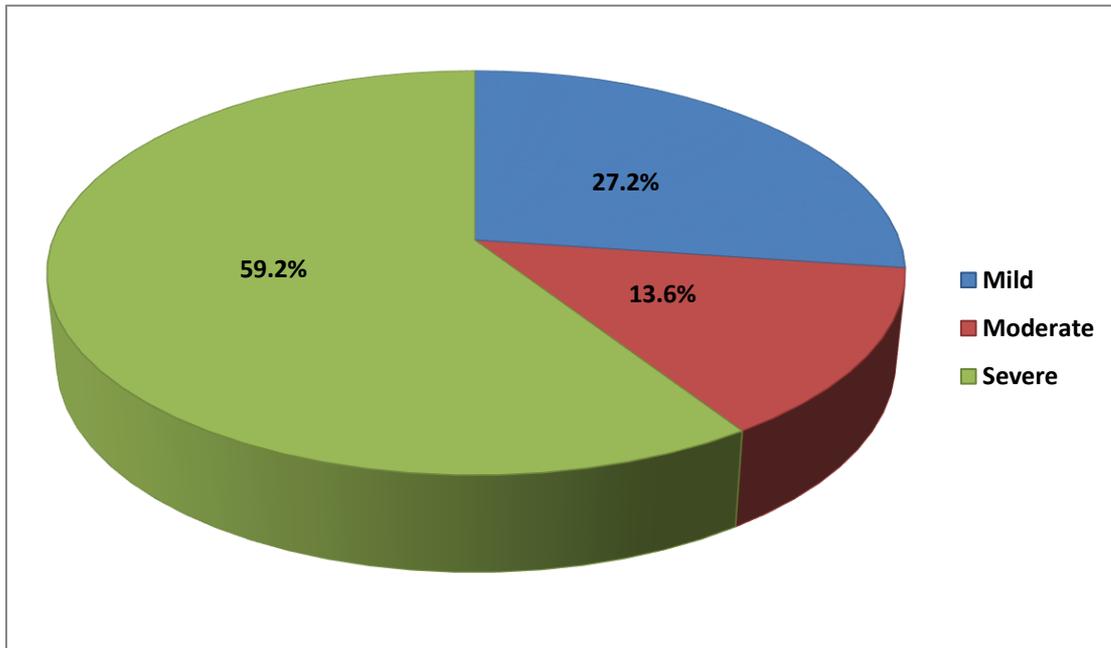


**Figure 4: Prevalence of hyperglycemia among COVID-19 patients.**

The COVID-19 severity of patients was classified into; mild (27.2%), moderate (13.6%) and severe (59.2%). (*Table 8 and Figure 5*)

**Table 8: COVID-19 severity distribution.**

Variable	No.	%
<b>COVID-19 severity</b>		
Mild	68	27.2
Moderate	34	13.6
Severe	148	59.2
Total	250	100.0



**Figure 5: COVID-19 severity.**

There was a highly significant association between increased age of patients and COVID-19 severity ( $p < 0.001$ ), 100% of patients with age of 80-90 years had severe COVID-19 disease.

No significant differences were observed between patients with different COVID-19 severity regarding gender ( $p = 0.5$ ). (**Table 9**)

**Table 9: Distribution of demographic characteristics according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Age</b>							<0.001* <sup>S</sup>
20-29 years	26	76.5	6	17.6	2	5.9	
30-39 years	22	47.8	8	17.4	16	34.8	
40-49 years	8	27.6	6	20.7	15	51.7	
50-59 years	6	17.1	6	17.1	23	65.7	
60-69 years	4	9.1	6	13.6	34	77.3	
70-79 years	2	5.0	2	5.0	36	90.0	
80-90 years	0	-	0	-	22	100.0	
<b>Gender</b>							0.5* <sup>NS</sup>
Male	42	25.0	24	14.3	102	60.7	
Female	26	31.7	10	12.2	46	56.1	

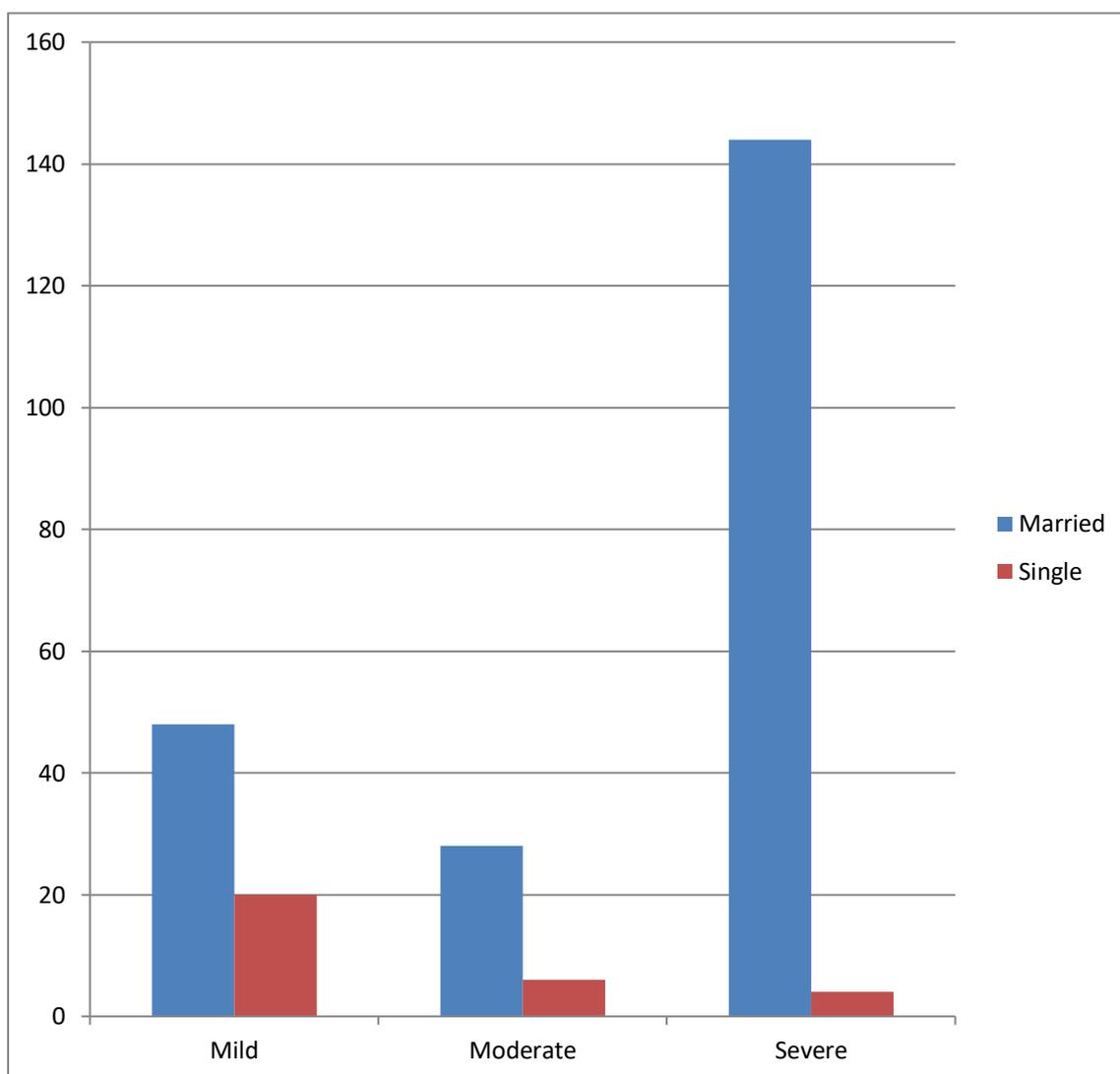
\* Chi square test, NS=Not significant, S=Significant.

No significant differences were observed between patients with different COVID-19 severity regarding residence (p=0.1). There was a highly significant association between unemployed patients (retired and housewives) and COVID-19 severity (p<0.001). A highly significant association was observed between married patients and COVID-19 severity (p<0.001). (Table 10 and Figure 6)

**Table 10: Distribution of social characteristics according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Residence</b>							0.1* NS
Urban	66	27.7	34	14.3	138	58.0	
Rural	2	16.7	0	-	10	83.3	
<b>Occupation</b>							<0.001* S
Public servant	42	48.8	10	11.6	34	39.5	
Student	8	66.7	4	33.3	0	-	
Self employed	8	21.1	6	15.8	24	63.2	
Retired	2	5.6	4	11.1	30	83.3	
Housewife	8	10.3	10	12.8	60	76.9	
<b>Marital status</b>							<0.001** S
Married	48	21.8	28	12.7	144	65.5	
Single	20	66.7	6	20.0	4	13.3	

\* Fishers exact test, \*\*Chi-square test, NS=Not significant, S=Significant.



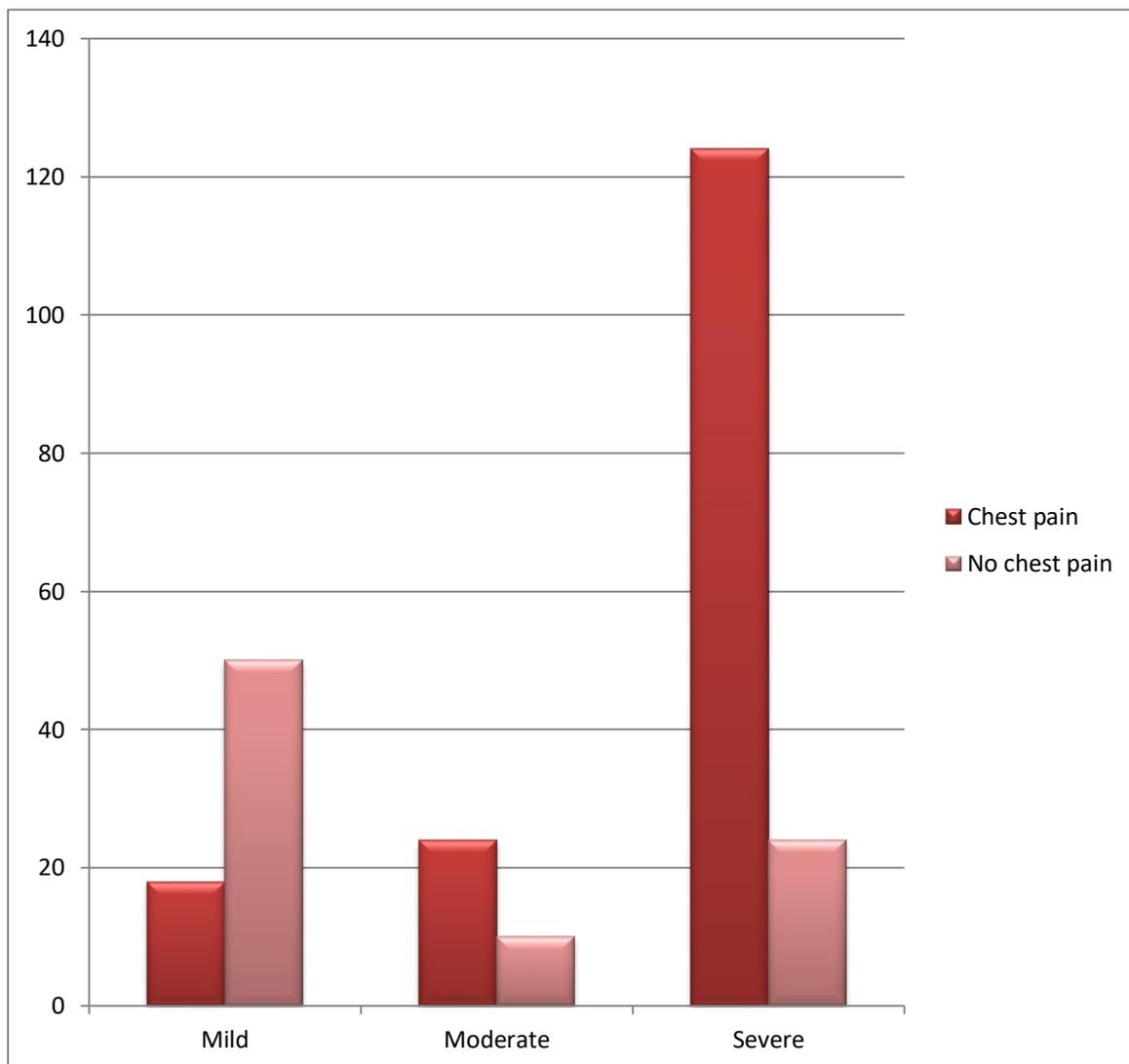
**Figure 6: Distribution of marital status according to COVID-19 severity.**

No significant differences were observed between patients with different COVID-19 severity regarding cough complaint ( $p=0.1$ ). There was a significant association between fever, loss of smell and loss of taste with mild COVID-19 severity ( $p=0.01$ ,  $p=0.004$  and  $p=0.01$ , respectively). A highly significant association was observed between dyspnea and chest pain with severe COVID-19 severity ( $p<0.001$ ). (*Table 11 and Figure 7*)

**Table 11: Distribution of clinical complaints according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Fever</b>							0.01* <sup>S</sup>
Yes	64	30.8	28	13.5	116	55.8	
No	4	9.5	6	14.3	32	76.2	
<b>Cough</b>							0.06* <sup>NS</sup>
Yes	66	28.9	32	14.0	130	57.0	
No	2	9.1	2	9.1	18	81.8	
<b>Loss of smell</b>							0.004* <sup>S</sup>
Yes	32	41.0	8	10.3	38	48.7	
No	36	20.9	26	15.1	110	64.0	
<b>Loss of taste</b>							0.01* <sup>S</sup>
Yes	28	41.2	8	11.8	32	47.1	
No	40	22.0	26	14.3	116	63.7	
<b>Dyspnea</b>							<0.001* <sup>S</sup>
Yes	14	7.5	28	15.1	144	77.4	
No	54	84.4	6	9.4	4	6.3	
<b>Chest pain</b>							<0.001* <sup>S</sup>
Yes	18	10.8	24	14.5	124	74.7	
No	50	59.5	10	11.9	24	28.6	

\* Chi-square test, NS=Not significant, S=Significant.



**Figure 7: Distribution of chest pain according to COVID-19 severity.**

There was a highly significant association between sweating and severe COVID-19 disease (p<0.001). (*Table 12*)

**Table 12: Distribution of endocrine symptoms according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Endocrine symptoms</b>							<0.001* <sup>S</sup>
No	40	46.5	10	11.6	36	41.9	
Thirst	16	19.5	10	12.2	56	68.3	
Sweating	0	-	0	-	4	100.0	
Thirst and polyurea	4	100.0	0	-	0	-	
Thirst, polyurea and sweating	2	25.0	2	25.0	4	50.0	
Thirst and sweating	6	9.1	12	18.2	48	72.7	

\* *Fishers exact test, S=Significant.*

There was a significant association between positive past medical history like HT and thyroid diseases and COVID-19 severity (p=0.002). A highly significant association was observed between positive drugs history and COVID-19 severity (p<0.001). No significant differences were observed between patients with different COVID-19 severity regarding family history

(p=0.08), smoking (p=0.2) and alcohol history (p=0.5). There was a significant association between positive pregnancy and moderate COVID-19 severity (p=0.002). (*Table 13*)

**Table 13: Distribution of clinical history according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Past medical history</b>							0.002* <sup>S</sup>
No	62	33.7	26	14.1	96	52.2	
HT	6	9.4	8	12.5	50	78.1	
HT and thyroid diseases	0	-	0	-	2	100.0	
<b>Drugs history</b>							<0.001* <sup>S</sup>
No	68	30.4	34	15.2	122	54.5	
Steroids and others	0	-	0	-	4	100.0	
Others	0	-	0	-	22	100.0	
<b>Family history</b>							0.08* <sup>NS</sup>
No	64	27.6	30	12.9	138	59.5	
DM	2	14.3	2	14.3	10	71.4	
Others	2	50.0	2	50.0	0	-	
<b>Smoking history</b>							0.2** <sup>NS</sup>
No	48	27.0	28	15.7	102	57.3	
Yes	20	27.8	6	8.3	46	63.9	
<b>Alcohol history</b>							0.5* <sup>NS</sup>
No	66	26.8	34	13.8	146	59.3	
Yes	2	50.0	0	-	2	50.0	
<b>Pregnancy</b>							0.002* <sup>S</sup>
No	68	27.4	32	12.9	148	59.7	
Yes	0	-	2	100.0	0	-	

\* Fishers exact test, \*\*Chi-square test, NS=Not significant, S=Significant.

A highly significant association was observed between sounds of wheezing and crepitation with severe COVID-19 disease ( $p < 0.001$ ). (*Table 14*)

**Table 14: Distribution of examination findings according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Added sounds</b>							$<0.001^{*S}$
No	68	35.4	28	14.6	96	50.0	
Wheezing	0	-	0	-	10	100.0	
Crepitation	0	-	6	15.8	32	84.2	
Wheezing and crepitation	0	-	0	-	10	100.0	

\* *Fishers exact test, S=Significant.*

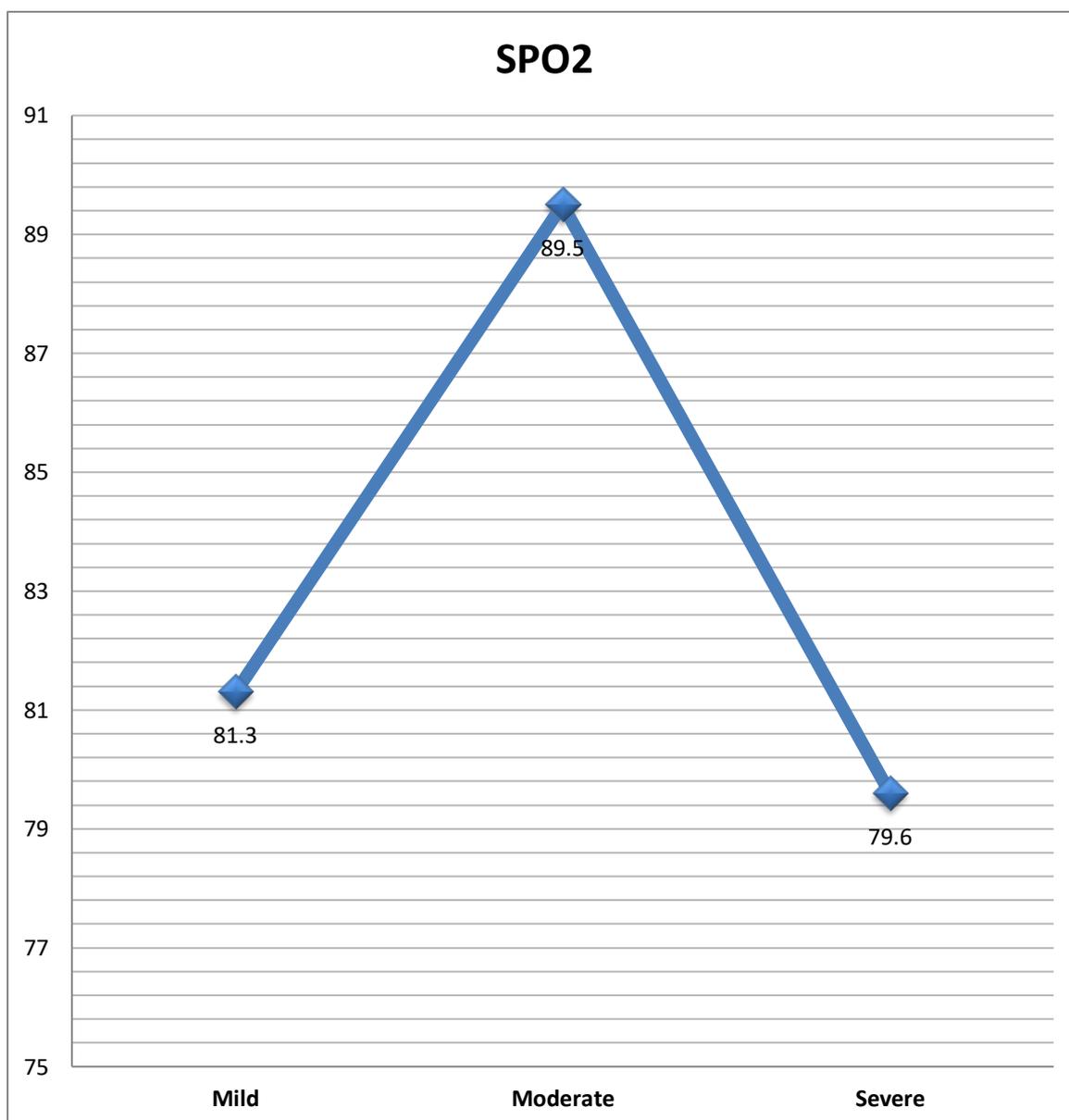
No significant differences were observed between patients with different COVID-19 severity regarding blood pressure ( $p=0.4$ ). Means of pulse rate and respiratory rate were significantly increased among patients with severe COVID-19 disease ( $p=0.002$ ,  $p < 0.001$ , respectively).

Mean temperature was significantly higher among patients with moderate COVID-19 disease (p=0.02). The mean SPO<sub>2</sub> was significantly lower among patients with severe COVID-19 disease (p=0.001). (*Table 15 and Figure 8*)

**Table 15: Distribution of investigations measures according to COVID-19 severity.**

Variable	COVID-19 severity			P
	Mild	Moderate	Severe	
	Mean±SD	Mean±SD	Mean±SD	
Pulse rate (beat/m)	91.2±9.8	93.7±10.4	98±15	0.002* <sup>S</sup>
BP (mmHg)	118/76±12/5	121/77±9/4	118/76±11/8	0.4* <sup>NS</sup>
RR (breath/m)	14.6±3	17.1±2.4	22.8±3.8	<0.001* <sup>S</sup>
Temperature (C°)	37.8±0.4	37.9±0.6	37.5±1.1	0.02* <sup>S</sup>
SPO <sub>2</sub> (%)	81.3±23.2	89.5±2.5	79.6±9.1	0.001* <sup>S</sup>

\* One-way ANOVA analysis, NS=Not significant, S=Significant.



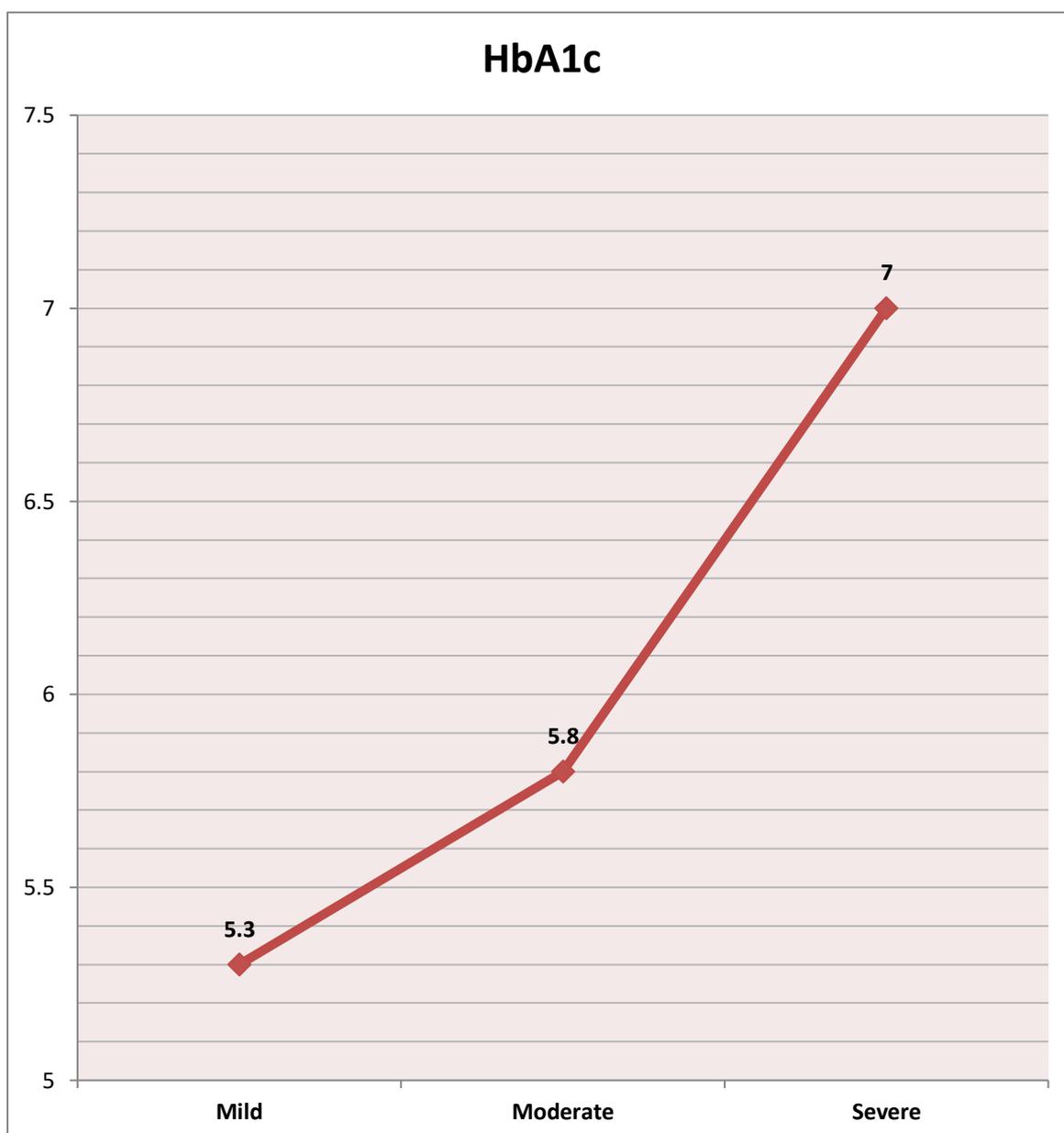
**Figure 8: Distribution of SPO<sub>2</sub> according to COVID-19 severity.**

Means of RBS and HbA1c were significantly increased among patients with severe COVID-19 disease ( $p < 0.001$ ). Means of CT scan chest occupancy, CRP and D-dimer levels were significantly increased among patients with severe COVID-19 disease ( $p < 0.001$ ). (*Table 16 and Figure 9*)

**Table 16: Distribution of investigations measures according to COVID-19 severity.**

Variable	COVID-19 severity			P
	Mild	Moderate	Severe	
	Mean±SD	Mean±SD	Mean±SD	
RBS (mg/dl)	100.8±15.4	118.1±13.2	129.3±74	<0.001* <sup>S</sup>
HbA1c (%)	5.3±0.2	5.8±0.2	7±1.1	<0.001* <sup>S</sup>
D-dimer level (ng/ml)	222.2±198.1	661±1186	573.9±505.8	<0.001* <sup>S</sup>
CRP (mg/dl)	15.5±11.3	60±67	61.3±43.9	<0.001* <sup>S</sup>
CT scan chest (%)	14.7±19.6	31.9±24.9	49.3±20.5	<0.001* <sup>S</sup>

\* One-way ANOVA analysis, NS=Not significant, S=Significant.



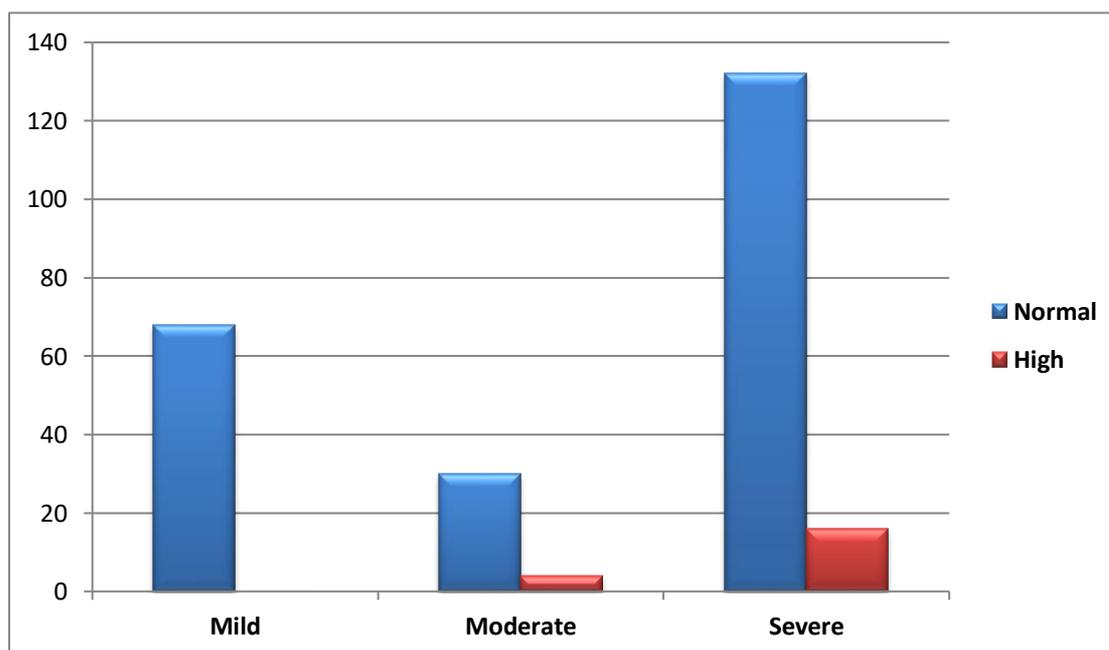
**Figure 9: Distribution of HbA1c according to COVID-19 severity.**

A significant association was observed between high blood sugar level and severe COVID-19 disease ( $p=0.01$ ). (*Table 17 and Figure 10*)

**Table 17: Distribution of blood sugar level according to COVID-19 severity.**

Variable	COVID-19 severity						P
	Mild		Moderate		Severe		
	No.	%	No.	%	No.	%	
<b>Blood sugar</b>							0.01* <sup>S</sup>
Normal	68	29.6	30	13.0	132	57.4	
High	0	-	4	20.0	16	80.0	

\* Chi-square test, S=Significant.



**Figure 10: Distribution of blood sugar level according to COVID-19 severity.**

## **DISCUSSION**

Earlier literatures of COVID-19 disease recognized the role of diabetes mellitus in the inflammatory response of disease development. Thereafter, the hyperglycemia, regardless of insulin resistance or diabetes mellitus, showed many adverse effects on the course and outcome of COVID-19 disease. On other hand, the effect of COVID-19 inflammation of the pancreatic  $\beta$  cells lead to newly diagnosed diabetes mellitus (50).

Present study showed that prevalence of hyperglycemia among studied COVID-19 non-diabetic patients was (8%). In Iraq, a study carried out by Sami and Wais reported that hyperglycemia prevalence of 8.4% among diabetic patients is accompanied with severe course of COVID-19 disease required intensive care admission (51). The prevalence rate of hyperglycemia in our study is lower than prevalence of (14%) reported by Haymana et al (52) nationwide retrospective cohort study on 12,817 non-diabetic patients.

Our study prevalence is also lower than results of Zhang et al (53) study in China which reported that (12.5%) of non-diabetic patients had hyperglycemia. Another study carried out in USA by Mamtani et al (54) on 403 COVID-19 patients, showed that (20.6%) of patients with no history of diabetes had hyperglycemia. This low prevalence of hyperglycemia among COVID-19 patients in our study might be attributed to differences in sample size and inclusion criteria between different studies in addition to differences in severity of COVID-19 disease between those studies. However, our study finding is consistent with reports of recent Iraqi study conducted by Al-Kuraishi et al (50) which documented that the corona virus is infecting causing damage to pancreas and inhibiting insulin secretion and development of hyperglycemia among non-diabetic patients. Hyperglycemia relation to inflammation status of COVID-19 is clear among diabetic and non-diabetic patients especially if the patients were obese or pre-diabetic.

There is a bidirectional relationship between chronic inflammation and hyperglycemia.

Additionally, the hyperglycemia in ill-patients resulted from stress-induced insulin resistance and stimulated glucose production. The changes in immune system like cytokines and chemokines changes, leukocytic changes and elevated apoptosis rates mainly among obese and diabetic patients referring to the role of inflammation in hyperglycemia development (55,

56). However, the high blood sugar level is accompanied with insulin resistance and increased inflammatory cytokines levels especially in acute infections such as COVID-19 disease (57, 58). A recent Chinese study (59) reported that blood glucose control for COVID-19 patients lead to reduction of serum levels of inflammatory markers, increased C-reactive protein and lactic dehydrogenase sensitivity.

Another recent Chinese study on 174 confirmed COVID-19 patients stated that inflammatory markers levels were highly increased among diabetic patients as compared to non-diabetic and lead to poorer prognosis (60) Mirzaei et al (61) study in Iran reported that patients with chronic viral infection, pneumonia, lung inflammation and short hospitalization were at high risk of hyperglycemia and insulin resistance. The hyperglycemia leads to stimulation of oxidative stress, lowering the immune system function, impairment of endothelial function, apoptosis stimulation and lowering the antioxidant. It also leads to decrease the intracellular bactericidal activity, stimulation of inflammation and maximizing the risk of lung disorders, cardiovascular diseases, renal failure and mortality (61).

In current study, 59.2% of COVID-19 cases were severe. This finding is higher than results of Abbas et al (62) prospective study in Iraq which reported that (37.7%) of COVID-19 hospitalized cases in Baghdad center were severe and critically ill patients. This high severity proportion might be due to fact that our center is receiving most of cases in Kirkuk province, while in Baghdad (Capital) many centers are available.

The current study found a significant association was observed between high blood sugar level and severe COVID-19 disease ( $p=0.01$ ). This finding is in agreement with many literatures such as Sachdeva et al (63) study in India and Kapoor et al (64) study in USA which reported that hyperglycemia among patients with COVID-19 diseases is related to severe course of the disease and poor outcomes. A recent interventional study carried out in Southern Iraq by Al-Ibrahimi and Nihad (65) revealed that the in-hospital mortality of COVID-19 patients was reduced after their treatment with Metformin. In our study, the mean HbA1c level was significantly increased among patients with severe COVID-19 disease ( $p<0.001$ ). This finding coincides with results of Wang et al (66) retrospective study in China which found that increased HbA1c level was directly linked to inflammation, low oxygen saturation, hypercoagulability and mortality in COVID-19 patients.

The present study showed a highly significant association between increased age of patients and COVID-19 severity ( $p < 0.001$ ). This finding is consistent with results of Al-Hijaj et al (67) record-based observational study in Iraq which found that advancing in age increasing severity of COVID-19 disease. Our study found a highly significant association between unemployed patients and COVID-19 severity ( $p < 0.001$ ). This finding is inconsistent with results of Mutambudzi et al (68) study in UK which stated that essential workers are at high risk of severe COVID-19 disease. This inconsistency might be attributed to effect of elderly age not the occupation as most of unemployed patients in our study were older in age. Our study also showed a highly significant association between married patients and COVID-19 severity ( $p < 0.001$ ). This finding is similar to results of Nkire et al (69) study in Canada which reported that marital status had an effect on severity and outcome of COVID-19 diseases as stress and social behavior had impact on health in general.

The current study found that fever, loss of smell and loss of taste were associated with mild COVID-19 cases, while dyspnea and chest pain were associated with severe COVID-19 cases. These findings are in agreement with results of Nabavi et al (70) study in Iran which revealed that COVID-19 symptoms with oxygen saturation and CT scan are helpful in

prediction of the disease severity. Our study found a significant association between positive past medical history like HT and thyroid diseases and COVID-19 severity ( $p=0.002$ ).

Consistently, Fathi et al (71) systematic review and meta-analysis study reported that clinical co-morbidity is regarded as the common risk factor for severity and mortality of COVID-19 disease. In present study, there was a significant association between positive pregnancy and moderate COVID-19 severity ( $p=0.002$ ). Similarly, Adhikari et al (72) study in USA revealed that most of pregnant women with COVID-19 diseases developed mild to moderate illness.

The endocrinal symptoms like sweating were significantly related to severe COVID-19 disease ( $p<0.001$ ). This finding coincides with results of Zhang et al (73) study in China which reported the night sweats as first symptom of COVID-19 pneumonia and severe form of disease. Our study also showed highly significant association was observed between sounds of wheezing and crepitation with severe COVID-19 disease ( $p<0.001$ ). Wang et al (74) study in China documented that the added sounds are indicators of pulmonary pathological changes and severity of COVID-19 disease. In current study, means of pulse rate and respiratory rate were significantly increased among patients with severe COVID-19

disease. These findings are in agreement with results of many studies like Junarta et al (75) study in USA and Miller et al (76) study in Australia. The mean SPO<sub>2</sub> was significantly lower among patients with severe COVID-19 disease (p=0.001). This finding is consistent with results of Gul et al (77) study in USA. Our study revealed that mean SPO<sub>2</sub> was significantly lower among patients with severe COVID-19 disease (p=0.001). This finding is consistent with results of Mejía et al (78) study in Peru which reported that low oxygenation among COVID-19 patients predicts the mortality. The current study found that means of CRP and D-dimer levels were significantly increased among patients with severe COVID-19 disease (p<0.001). These findings are in agreement with results of Ullah et al (79) study in USA which found that high levels of CRP and D-dimer levels among hospitalized COVID-19 patients are predictable of mortality. In present study, mean chest CT scan score was significantly higher among severe COVID-19 cases (p<0.001). This finding is consistent with results of Hafez study (80) in Egypt which reported that assessing chest CT scan score is essential in detecting severity of COVID-19 disease.

## CONCLUSION

There is a significant proportion of non-diabetic patients with COVID-19 presented with severe forms of the disease. Elevated random blood sugar and glycated hemoglobin (HbA1c) levels were found to be strong predictors of disease severity, suggesting that hyperglycemia, even in non-diabetic individuals, may play a critical role in the progression of COVID-19. Several demographic and clinical risk factors were associated with more severe illness, including advanced age, unemployment, marital status, existing comorbid conditions, and pregnancy.

Clinically, symptoms such as dyspnea, chest pain, excessive sweating, and the presence of abnormal lung sounds (wheezing and crepitations) were commonly observed among patients with severe disease. These symptoms were often accompanied by elevated pulse and respiratory rates, as well as reduced blood oxygen saturation. Laboratory and imaging findings further supported the identification of severe cases. Increased levels of D-dimer and C-reactive protein (CRP), in conjunction with higher chest CT severity scores, were significantly associated with more advanced stages of the illness. Together, these clinical, biochemical, and radiological markers provide valuable insight into the early identification and management of patients at risk of developing severe COVID-19.

## **RECOMMENDATIONS**

It is recommended that physicians be encouraged to routinely monitor both blood glucose and hemoglobin A1c levels in non-diabetic patients diagnosed with COVID-19, as these parameters may serve as early indicators of disease severity. Special attention should be given to the management of hyperglycemia in non-diabetic individuals, particularly in severe cases, to reduce the risk of complications and improve clinical outcomes. Additionally, there is a need to support further large-scale, multi-center national studies to better understand the prevalence and clinical implications of hyperglycemia among non-diabetic COVID-19 patients across different regions of the country.

### **Ethical Clearance:**

Ethical approval for the study was obtained from the Iraqi Board of Medical Specializations. Additionally, institutional permission was secured from hospital authorities, and verbal informed consent was obtained from all participating patients before data collection commenced.

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Nil.

**Conflicts of interest:**

There are no conflicts of interest.

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