



Clinical course and outcome in diabetic patients with COVID-19

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Abstract

Introduction: As diabetes is highly prevalent worldwide, understanding particular dimensions of COVID-19 infection in diabetic patients is of significant importance.

Objectives: The present research aimed to evaluate the outcome of diabetic patients with COVID-19 infection, and the clinical and biochemical characteristics in survived and non-survived patients.

Patients and Methods: The present single-center, cross-sectional study examined laboratory and clinical features of 160 patients with diabetes who had moderate to severe criteria. The obtained data were categorized as survived or non-survived patients and then we compared the clinical characteristics in two groups.

Results: In this study, 160 diabetic patients (75 men and 85 women) admitted with moderate to severe Covid-19 were evaluated. The mean age of studied patients was 51-90 years old, with diabetes duration of 5 to 15 years. One hundred thirty-one patients (81.9%) survived, but twenty-nine patients (18.1%) did not survive. Regarding the comparison of symptoms, only the loss of consciousness on admission was higher in non-survived patients; however, a majority of the non-survivors have been admitted to ICU, 23 (79.3%) and 26 (89.6%) needed invasive mechanical ventilation; in comparison to survived patients also had a shorter duration of hospital stay (5.5 ± 5.1 versus 8.4 ± 6.1 days). Non-survivors more probably suffer from high blood pressure [23 (79.3%) patients versus 80 (61%) patients] and chronic kidney disease [20 (69%) patients versus 9 (6.9%) patients; $P < 0.001$]. Glycated hemoglobin (HbA1c) of more than 9%, and high fasting blood sugar, severe inflammatory response, hepatic, renal, and coagulation impairment was higher in non-survived than those who survived.

Conclusion: Multifactorial parameters result in the poor prognosis in diabetic patients; therefore, it is critical for identifying the key clinical, as well as laboratory characteristics of COVID-19 cases that lead to severe disease and increase the risk of death.

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Introduction

In December 2019, a novel coronavirus disease (COVID-19) had been identified in Wuhan, China, a pandemic and contagious disease that led to high mortality and became a significant worldwide public health concern (1). As diabetes is highly prevalent worldwide, understanding particular dimensions of COVID-19 infection in diabetic patients is of significant importance. Diabetic patients face the greater risks of being infected due to deficiencies in innate immunity which influences neutrophil chemotaxis, cell-mediated immunity, and phagocytosis (2). In fact, diabetic patients showed poorer outcomes in the earlier epidemics of H1N1 (influenza A) and SARS-CoV (severe acute respiratory syndrome coronavirus) epidemics (3,4). However, the most prevalent

Key point

In our cross-sectional study on 160 diabetic patients admitted with moderate to severe COVID-19 infection, we found poor controlled diabetes, concurrent hypertension and chronic kidney disease were associated with severe COVID-19 infection and increase the risk of death.

comorbidities with worse consequences have been observed in diabetic patients, cardiovascular diseases, and hypertension, or high blood pressure (5). Elevation of blood glucose level is one of the vital risk factors for adverse outcomes and predicted a worse prognosis in hospitalized COVID-19 patients (6). The clinical course of COVID-19 infection in diabetic patients varies with the milder symptoms that occur at the first stage;

however, they face the increased risks of fast progression to severe pneumonia, uncontrolled cytokine storm, as well as the hypercoagulable state that involves in the poorer prognosis of the disease (7).

Objectives

We aimed to study the outcome of diabetic patients with COVID-19 infection, and the clinical and biochemical characteristics in survived and non-survived patients.

Patients and Methods

Study design

The present cross-sectional research has been performed in patients with diabetes with COVID-19 infection admitted to Loghman Hakim hospital, Tehran, Iran, from February to the end of July 2020. Patients with moderate to severe criteria have been admitted according to the inclusion criteria;

1) The reverse transcription polymerase chain reaction (RT-PCR) method has determined the presence of COVID-19 infection in the respiratory specimens; 2) Outputs of chest CT had met the standards to diagnose COVID-19; 3) Diabetes has been defined as a self-reported medical history of diabetes and the utilization of anti-diabetic medicines.

Moreover, exclusion criteria were 1) Missing data on the clinical and laboratory characteristics; 2) New-onset diabetes which has been based on the high random plasma glucose, and normal HbA1c levels that were categorized as stress hyperglycemia. Additionally, patients with the previous inflammatory, and malignant disorders were excluded from the study.

The disease severity has been staged based on the WHO's interim guidance on 13 March 2020 to manage COVID-19 (8).

Moderate case; adult or adolescent with the clinical signs of pneumonia such as cough, fever, fast breathing, and dyspnea do not have any symptoms of severe pneumonia-like $SpO_2 \geq 90\%$ on the room air.

Severe case; adult or adolescent having the clinical symptoms of pneumonia-like cough, fever, fast breathing and dyspnea, as well as each of the following symptoms, including severe respiratory distress, respiratory rate > 30 breaths/min and $SpO_2 < 90\%$ on room air; patients with loss of consciousness, shock, or respiratory failure require mechanical ventilation, admitted to the intensive care unit (ICU).

Information about patients was included in the checklist containing gender, body mass index (BMI), age, chronic comorbidities (hypertension, cardiovascular disease, chronic kidney disease, and chronic pulmonary disease), duration of diabetes, drug-taking history for treating diabetes, and clinical symptoms, as well as signs on admission time such as diarrhea, cough, fever, chest pain, nausea, headache, anorexia, fatigue, decreased sense of smell, and myalgia). Furthermore, (blood pressure, pulse

rate, respiratory rate, temperature, saturation O_2 , and level of consciousness), hospitalization duration, ICU admission, and invasive mechanical ventilation were recorded.

Besides, laboratory tests performed consisted of a complete blood count, fasting blood sugar, random blood sugar level, glycated hemoglobin (HbA1c), liver assessment, renal function and serum lipids, and coagulation testing, lactate dehydrogenase, D-dimer, high-sensitivity C-reactive protein (hs-CRP), and ferritin.

All patients were treated with standard protocol for the treatment of COVID-19 pneumonia, antidiabetic drugs stopped and substituted with insulin at admission. The study outcomes were categorized as survived or non-survived patients. We accordingly compared the clinical characteristics of diabetic patients' outcome with moderate to severe COVID-19 categorizations.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Shahid Beheshti University of Medical Sciences approved this study. The institutional ethical committee at Shahid Beheshti University of Medical Sciences approved all study protocols (IR.SBMU.RETECH.REC.1399.076). Accordingly, written informed consent was taken from all participants before any intervention and at the time of hospital admission.

Statistical analysis

Distribution of patients based on prognosis and quantitative variables using independent t-test and qualitative variables performed the chi-square test and Fisher's exact tests for evaluating the association between variables performed. The total analysis was executed by SPSS version 23. Moreover, the level of significance has been regarded to be $P < 0.05$ for each test.

Results

According to this research, 160 diabetic patients (75 men and 85 women) admitted with moderate to severe Covid-19 were evaluated. The mean age of studied patients was 51-90 years old. The duration of diabetes was 5 to 15 years.

Among 160 infected patients, 28 patients (17.5 %) had a history of exposure to COVID-19 infection. The drugs had been used for controlling diabetes, hypertension, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, insulin or oral agents and statin as shown in [Table 1](#).

Hypertension (64%), cardiovascular disease (29.4%), chronic kidney disease (18.1%), have been the most co-existing co-morbidity.

It should be noted that the most common clinical symptoms of the patients have been as follows; cough (53.7%), fatigue (49.4%), fever (66.9%), dyspnea (48.1%), chills (26.8%), diarrhea (28.1%), and nausea (18.1%). Just 20.6% of patients reported a decreased sense of smell, and

Table 1. Basic characteristics of diabetic cases with the COVID-19 infection

Parameters	Total (n=160)	Percent
Clinical Characteristics on Admission		
Gender		
Male/ Female	75/85	46.9/53.1
Comorbidities		
HTN	103	64.0
Cardiovascular disease	47	29.4
Chronic kidney disease	29	18.1
Chronic pulmonary disease	4	2.5
Drug history		
Insulin	77	48
Oral Agent	83	52
ARB/ACEI	102	63.7
Statin	86	53.7
Cigarette	23	14.4
Alcohol	0	0.0
Opium	14	8.8
Exposure to disease	28	17.5
Symptoms		
Fever	107	66.9
Chills	42	26.3
Sore throat	5	3.1
Myalgia	23	14.4
Cough	86	53.7
Dyspnea	77	48.1
Chest pain	10	6.3
Decreased sense of smell	33	20.6
Headache	2	1.3
Nausea	29	18.1
Diarrhea	45	28.1
Loss of consciousness	45	28.1
Fatigue	79	49.4

HTN, hypertension; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.

28.1% of patients presented with loss of consciousness at the beginning of the first visit.

Among the total, only 30.2% of patients (49 patients) were initially admitted with a diagnosis of diabetic ketoacidosis, however 103 people (64%) needed ICU admission and 66 patients (41.2%) underwent invasive mechanical ventilation. One hundred thirty-one patients (81.9%) survived, but regrettably, twenty-nine patients (18.1%) did not survive. The distribution of patients based on prognosis and comparison of clinical and biochemical parameters of survived or non-survived patients have been listed in Tables 2 and 3.

Non-survived patients had a higher mean age than survived patients (80.4 ± 9.5 versus 73.4 ± 22.4 years; $P < 0.001$). The prognosis was worse in the male, 75.9% ($P < 0.001$). Moreover, any differences have been not observed in the duration of diabetes, body mass index (BMI), as well as the previous history of anti-diabetic,

antihypertensive drugs.

Non-survivors more probably suffer from the high blood pressure [(23 (79.3%) patients versus 80 (61%) patients)] and chronic kidney disease [20 (69%) patients versus 9 (6.9%) patients], ($P < 0.001$). There were no differences in smoking, alcohol, opium habit among patients.

In a comparison of symptoms, only the loss of consciousness on admission was higher in non-survived patients (62.1% versus 20.6%; $P < 0.001$). However, the symptoms of fever, chills, and diarrhea were higher in survived patients ($p < 0.0001$).

At admission time, temperature and heart rate were higher, and systolic blood pressure was significantly lower in non-survived patients.

A majority of the non-survivors have been admitted to the ICU, 23 (79.3%) and 26 (89.6%) needed invasive mechanical ventilation. In addition, in comparison to survived patients, the non-survivors had a shorter duration of hospital stay (5.5 ± 5.1 versus 8.4 ± 6.1 days), which indicated worse progression in these patients. Clearly, in comparison to the survivors, the non-survivors exhibited greater neutrophil counts (82.7 ± 6.4 versus $74.1 \pm 13.5\%$), lower lymphocyte count (12.7 ± 5.7 versus $28.5 \pm 4.4\%$), and lower hemoglobin levels (11.6 ± 2.4 versus 12.9 ± 2.1 g/dL). There was no difference in cholesterol, triglyceride level, and random blood glucose level between patients in the two groups, however in terms of fasting blood sugar level, which was statistically significant (235.5 ± 123.5 versus 148.9 ± 52.9 mg/dL; $P < 0.001$) in non-survived patients. Totally, in 45 (34.4%) patients, HbA1c level, shows they were adequately controlled (HbA1c $< 7\%$).

In the non-survived group, two people had HbA1c below 7%, which was not comparable. HbA1c was more than 9%, which was considerably higher in non-survivors than those who survived (50% versus 3.8%).

The following laboratory parameters were higher in patients who died than in patients who survived and were statistically significant ($P < 0.05$); serum creatinine level (2.6 ± 1.8 versus 1.3 ± 0.4 mg/dL), aspartate transaminase levels (113 ± 25 versus 40.6 ± 24 U/L), alanine aminotransferase levels (69.6 ± 63.5 versus 36.9 ± 34.9 U/L), lactate levels (21.2 ± 13.6 versus 15.3 ± 6.6 U/L), lactate dehydrogenase levels (622.9 ± 108.5 versus 349.2 ± 247.9 U/L), prothrombin time (14.9 ± 2.6 versus 13.1 ± 1.1 seconds), D-dimer level (1.3 ± 0.8 versus 0.8 ± 0.5 $\mu\text{g/mL}$). Although erythrocyte sedimentation rate (55.6 ± 27.4 versus 49.1 ± 20.7 mm/h) and hs-CRP (44.8 ± 27.5 versus 38.3 ± 21 mg/L) were higher in non-survived patients than who survived, however, these differences did not show any statistical significance ($P = 0.1$).

Discussion

This present study evaluated diabetic patients' outcomes with moderate to severe COVID-19 infection and compared the clinical characteristics of survived or non-survived patients. Among all patients, 18.1 percent did

Table 2. Demographic and clinical characteristics of survivors and non-survivors in patients with COVID-19 with diabetes on admission to hospital

Parameters	Survivor, n= 131 (100)	Non-survivor, n=29 (100)	Total (100)	P value
Clinical characteristics on admission				
Age	73.4±22.4	80.4±9.5		0.001
Gender				
Male	53(40.5)	22(75.9)	75(46.9)	0.001
Female	78(59.5)	7(24.1)	85(53.1)	
BMI	29.8±11.0	29.5±9		0.877
Duration of DM	8.6±5.6	10.1±4.6		0.142
Drug history				
Insulin	61(46.5)	16(55)	77(48)	0.569
Oral agent	70(53.5)	13(45)	83(52)	0.516
ARB/ACEI	86(65.6)	16(55)	102(63.7)	0.169
Statin	70(53.4)	16(55)	86(53.7)	0.154
Comorbidities				
HTN	80(61)	23(79.3)	103(64)	0.001
Cardio vascular disease	40(30.5)	7(24)	47(29.4)	0.151
Chronic kidney disease	9(6.9)	20(69.0)	29(18.1)	0.001
Cigarette	23(17.6)	0(0.0)	23(14.4)	0.015
Alcohol	0(0.0)	0(0.0)	0(0.0)	-
Opium	14(10.7)	0(0.0)	14(8.8)	0.075
Exposure to disease	26(19.8)	2(6.9)	28(17.5)	0.112
Symptoms				
Fever	97(74.0)	10(34.5)	107(66.9)	0.001
Chills	42(32.1)	0(0.0)	42(26.3)	0.001
Sore throat	5(3.8)	0(0.0)	5(3.1)	0.586
Myalgia	15(11.5)	8(7.6)	23(14.4)	0.038
Cough	70(53.4)	16(55.1)	86(53.7)	1.000
Dyspnea	66(50.4)	11(37.9)	77(48.1)	0.305
Chest pain	8(6.1)	2(6.9)	10(6.3)	1.000
Decreased sense of smell	28(21.4)	5(17.2)	33(20.6)	0.801
Headache	2(1.5)	0(0.0)	2(1.3)	1.000
Nausea	23(17.6)	6(20.7)	29(18.1)	0.790
Diarrhea	45(34.4)	0(0.0)	45(28.1)	0.001
Loss of consciousness	27(20.6)	18(62.1)	45(28.1)	0.001
Fatigue	62(47.3)	17(58.6)	79(49.4)	0.309
Vital signs on admission				
Temperature	37.6±0.8	37.9±0.7		0.048
PR	81.9±35.4	95.8±11.8		0.046
RR	21.5±11.4	32.1±17.6		0.055
SBP	130.9±20.6	103.1±21.3		0.000
DBP	80.5±17.0	81.1±26.1		0.926
Oxygen saturation	79.8±6.5	71.1±13.4		0.002
Length of hospital admission	8.4±6.1	5.5±5.1		0.012
Ketoacidosis	40(30.5)	9(31)	49(30.2)	0.113
Hypoglycemia	14(10.7)	0(0.0)	14(8.8)	0.075
ICU Admission	80(61)	23(79.3)	103(64)	0.001
Invasive mechanical ventilation treatment	40(30.5)	26(89.6)	66(41.2)	0.001

HTN, hypertension; BMI, body mass index; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ICU, intensive care unit; PR, pulse rate; RR, respiratory rate; SBP, systolic blood pressure; DBP, diastolic blood pressure.

not survive. Recent studies of COVID-19 conducted on diabetic patients, suggest that the outcome of disease correlated to the critical or severe varied between 14% and 32% in diverse investigations (9-13).

Additionally, Wang et al (11), Wu et al (12) and Chen et al (5) reported a significant association of the COVID-19 severity with diabetes. However, in the meta-analysis

on the eight studies conducted by Yang et al (14), the odds ratio (OR) of the severe COVID-19 has been not significantly greater in the diabetic cases (OR, 2.07; 95% CI, 0.89 to 4.82). We noticed that most of non-survived patients with diabetes were older and were male compared with survived patients. The obtained results consistent with other reports (5,15,16), revealed the specific mechanism

Table 3. The biomedical values of survivors and non-survivors in patients with COVID-19 with diabetes on admission to hospital

	Normal range	Surviver, n= 131 (100)	Non-surviver, n=29 (100)	P value
Laboratory examination on admission				
Leukocyte count, 10 ³ /dL	4.8-10.8	9.2±1.9	10.5±4.5	0.108
Hemoglobin, g/dl	12-15	12.9±2.1	11.6±2.4	0.007
Platelet count, 10 ³ /μL	140-450	390±79	450±78	0.043
Neutrophil count, 10 ³ /μL	20-65	74.1±13.5	82.7±6.4	0.000
Lymphocyte count, 10 ³ /μL	11-30	28.5±4.4	12.7±5.7	0.000
Fasting blood sugar, mg/dL	* <100	148.9±52.9	235.5±123.5	0.012
Random blood sugar, mg/dL	* <180	313.7±0.7	339.6±164.3	0.628
Glycated hemoglobin (HbA1c), %				
<7	*	45 (34.4)	2 (6.8)	0.001
7-7.9	*	56 (42.7)	6 (21.4)	0.001
8-8.9	*	26 (19.8)	7 (25.0)	0.001
≥9	*	4 (3.1)	14 (50.0)	0.001
Blood urine nitrogen, mg/dL	8-23	49.5±36.9	100.5±99.3	0.011
Creatinine, mg/dL	0.7-1.3	1.3±0.4	2.6±1.8	0.000
Aspartate aminotransferase, U/L	15-30	40.6±24.7	113.0±25	0.005
Alanine aminotransferase, U/L	15-30	36.9±34.9	69.6±63.5	0.008
Erythrocyte sedimentation rate, mm/H	<20	49.0±20.7	55.6±21.4	0.135
C-reactive protein, mg/L	<5	38.3±21.0	44.8±27.5	0.162
Triglyceride, mg/dL	<150	364.1±74.8	180.7±115.9	0.829
Cholesterol, mg/dL	<200	210.2±38.4	200.3±20.2	0.507
Low-density lipoprotein, mg/dL	<100	123±43.3	128.3±27.1	0.791
High-density lipoprotein, mg/dL	F>50, M>40	50.8±21.2	46.3±3.5	0.227
Total bilirubin, mg/dL	0.1 - 1.2	1.0 ± 0.8	0.7±0.3	0.031
Direct bilirubin, mg/dL	< 0.3	0.3±0.3	0.2 ± 0.2	0.069
Lactate, nmol/L	<20	15.3±6.6	21.1±13.6	0.005
Lactate dehydrogenase, U/L	135-200	349.2±247.9	622.9±108.5	0.000
Prothrombin time, s	10-14	13.1±1.1	14.9±2.6	0.000
Partial thromboplastin time, s	22-35	34.4±25.6	43.1±14.7	0.073
International normalized ratio, μg/L	0.8-1.2	1.1±0.1	1.8±0.2	0.003
Ferritin, μg/L	30-250	612.2±239.0	719.0±201.5	0.184
D-dimer, μg/mL	<0.5	0.8±0.5	1.3±0.8	0.030

*In diabetic patients, normal range fasting blood sugar <130, Random blood sugar <180, and HbA1c <7% were considered.

for the men's susceptibility to COVID-19 in which the ACE2 expression in males has been approximately three times more than females(17).

Furthermore, the fatality rate of our study was particularly high in diabetic patients with concomitant morbidities, hypertension, and chronic kidney disease.

Besides, more serious outcomes are significantly associated with concomitant conditions such as cardiovascular diseases, diabetes, high blood pressure, chronic obstructive pulmonary disease, and obesity (5,14,18,19). The high frequency of diabetes in older patients and those with serious chronic medical conditions are at the highest risk levels for complications from COVID-19 infection, explaining the fatal outcomes.

There are few data regarding the effects of antidiabetic or antihypertensive medicines for the course of COVID-19 disease. In the present study, medicine control for diabetes,

hypertension showed a similar prognosis in survived and non- survived patients.

According to this research hypertension and chronic kidney disease were the strongest predictor of COVID-19-related death in diabetic cases. Since, high blood pressure would be frequently treated with ACE suppressors or angiotensin receptor blockers that theoretically may result in increasing the risk of severe infection in COVID-19 (20), however withdrawal of these drugs may be harmful in certain high-risk patients with underlying cardiovascular and kidney diseases (9,11,21,22). Therefore, continued treatment in otherwise stable conditions is recommended (23). Most of the studied patients were overweight and had the same prognosis, but in other studies, the mortality was higher in morbid obese patients (BMI >40 kg/m²) (13,14,24).

According to this study, the clinical presentation

of COVID-19 infection in survived or non-survived patients had a similar pattern. The only difference is in the decreased level of consciousness, which was higher in non-survived patients.

Upon the initiation of the symptoms, the physicians can be aided for identifying cases with poorer prognosis. According to the present study, the overall rate of loss of consciousness, abnormal vital signs, and severe hypoxia was higher in non-survived patients, like other studies (10,13,14).

As the same as the earlier research, in cases showing poor prognosis, more likely needed for ICU admission and invasive mechanical ventilation and median survival duration from the hospital admission has been considerably lessened in cases showing good prognosis (6,14,16,25).

In comparison to the diabetic survivors, the non-survivors exhibited more severe inflammatory response (higher levels of the neutrophil count, lower levels of lymphocyte count, elevated lactate dehydrogenase and lactate levels), hepatic, renal, and coagulation impairment (prolonged prothrombin time and D-dimer), which is consistent with other related studies (12,13). However, we could not measure other inflammatory cytokines such as tumor necrosis factor α , IL-6, in this study.

Although the level of CRP was higher in non-survived patients, this difference was not statistically significant. Perhaps, the low-grade chronic inflammations would already characterize the diabetes condition, and when there are higher viral loads, diabetic cases may be endangered through the capacity for raising the acute immune responses (7).

In the current study, people with diabetes with rapid deterioration (septic shock, disseminated intravascular coagulopathy, acute respiratory distress syndrome) indicated more prolonged prothrombin duration and greater D-dimer concentration, lactate dehydrogenase, lactate level, prolonged prothrombin time, which could justify the increased risk of pro-coagulative and cytokine storm state; exposing them to more severe adverse effects (16,26).

Hence, it is necessary to control glycemia in diabetic patients COVID-19-infected, although there is not enough information on the correlation of mortality with the level of blood glucose (4,16,27). The outputs observed in other infections such as influenza H1N1 and SARS indicated that cases with poorer control on the glycemia, experience greater risks of complications and mortality (25, 28). Furthermore, the level of HbA1c >9% is correlated with a 60% greater risks of hospitalization, as well as pneumonia-associated severity in the course of the bacterial infections (29).

A cohort analysis of the above 5500 cases with COVID-19 in the UK reported that poorer control of glycemia prior to the hospital admission had been shown in the HbA1c concentration related to the increased risks

in-hospital mortalities (3).

This study observed people who have well-controlled diabetes (HbA1c <7%) displayed lower mortality rates, and poorly controlled diabetes (HbA1c >9%) associated with severe disease, higher inflammatory response, and higher mortality situations.

However, the level of random blood sugar at the time of referral was not associated with prognosis, perhaps due to stress-related hyperglycemia. Fasting glucose levels have been associated with a more inadequate prognosis, which is in line with the other recent studies on COVID-19 (25).

Hyperglycemia in earlier phases of disease can particularly contribute to the determination of the prognosis seriousness (27, 30).

Moreover, Wang et al hypothesized that infection of SARS-CoV-2 in diabetic cases can stimulate the conditions for stress and enhance secretion of the hyperglycemic hormones like glucocorticoids, as well as catecholamine that leads to the higher level of the blood glucose, diabetic consequences and abnormal glucose variability, which cause the increased mortalities and morbidities in such cases (31).

Moreover, the higher blood glucose levels on admission were associated with inflammatory response and an abnormal coagulopathy, leading to severe COVID-19 disease and death (32).

Conclusion

It has been found that the weaker prognosis of diabetic cases is multifactorial; older age, male gender, comorbidities, in particular hypertension, chronic kidney disease, poor glycemic control, and pro-inflammatory and pro-coagulation states possibly involve in risks of more serious consequences. Therefore, it is critical to identify key laboratory and clinical characteristics of the COVID19 cases that propose severe disease.

Limitations of the study

This investigation had some limitations. One of this research's limitations was the small sample size on one hospital center of COVID-19 in Tehran, Iran.

In general, patients with moderate to severe conditions were evaluated. This study did not have complete findings in cardiac biomarkers and did not have the conditions to check for inflammatory cytokines. Although all patients were treated by insulin infusion or subcutaneous basal-bolus, the present study did not evaluate the therapeutic effect of insulin during hospitalization and its effect on mortality, similar to other intervention studies due to incomplete data bank.

It is recommended that additional research with the large sample size in several hospitals needs to carry out. Also, the contribution of the control of glycemia with mortality rate, prior to the hospital admission, upon the hospital admission, as well as the course of treatments in hospitals should be evaluated.

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Authors' contribution

ZD, IAD, FS, SH, SS and MS conducted the research. ZD and LG assisted in the preparation of this paper. ZD and LG procured the resulting paper. The resulting paper has been read by each author and then signed.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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