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Original Article

Predictors of COVID-19 related death in diabetes patients: A case-control study in Iran

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ABSTRACT

Background: Identifying the predictors of COVID-19 related death in diabetes patients can assist physicians for detecting risk factors related to the worse outcome in these patients. In this study we investigated the predictors of the death in patients with diabetes compared with non-diabetic COVID-19 patients.

Methods: In the present case-control study, the case group were diabetic patients with COVID-19 and the control group included Non-diabetic COVID-19 patients. The data source regarding the demographic characteristics, clinical symptoms, laboratory, and radiological findings on admission as well as the complications, treatment, and outcomes during hospitalization were gathered from their medical record through two trained nurses. Adjusted and unadjusted odds ratios (OR) estimate were calculated using the simple and multiple logistic regression through backward model.

Results: The mean (SD) age of the case group was higher than that of the control group; [65.24 (12.40) years vs. 59.35 (17.34) years, respectively ($P < 0.001$)]. Results of the adjusted logistic regression model showed that, advanced age (+60 year) (OR = 5.13, P = 0.006), addiction (OR = 5.26, P = 0.033), high level of Blood urea nitrogen (OR = 5.85, $P < 0.001$), and high level of Alkaline Phosphatase (OR = 3.38, P = 0.012) in diabetic patients were significantly associated with increase the odds of death in COVID-19 patients.

Conclusion: We found that in COVID-19 patients with diabetes; advanced age, addiction, high level of BUN and Alp and in non-diabetic COVID-19 patients advanced age, dyspnea, high level of BUN and SGOT were associated with increase risk of death in these patients.

1. Introduction

Diabetes is one of the most common non-communicable diseases worldwide and there is evidence of its substantial increasing trend in recent years [1]. Several studies have revealed a higher vulnerability to some infectious diseases in diabetic people [2,3]. Decreased T cell−mediated immune response and impaired neutrophil functionin diabetics can explain this higher susceptibility [2].

Alongside severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS), coronavirus disease 2019)COVID-19(is another common type of coronavirus that infect

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humans [4]. The role of diabetes in increasing of mortality and morbidity in patients with SARS have been shown previously [5]. Also, noticeable proportion of identified COVID-19 patients are diabetic. In such a way that, the rate of diabetes and COVID-19 comorbidity is range from 20 to 50% in different global regions [6]. Published studies showed that some underlying diseases such as hypertension and diabetes mellitus are important risk factors for the fatality of COVID-19 patients [7–9].

Although, studies have been designed to identify death-related factors in COVID-19 patients. However, most of them are conducted on the total COVID-19 cases, regardless of having an underlying disease or not, or the investigated variables were rare. Identifying the predictors of death in diabetic COVID-19 patients helps in better management of them, and assist physicians for detecting risk factors which contributes to the severity and mortality of COVID-19 in these patients. This study was conducted in order to identify the predictors of the worse outcome in patients with diabetes in whom COVID-19 was confirmed compared with non-diabetic COVID-19 patients.

2. Materials and method

In the present case-control study, we identified all patients admitted to Sina Hospital and Beheshti Hospital in Hamadan province, the west of Iran, which was assigned to admit COVID-19 adult patients. Patients recruited from January 2020 to January 2021.

The Ethics Committee of the Hamadan University of Medical Sciences approved this study (IR.UMSHA.REC.1399.841). In this study, patients with positive real time reverse transcriptase polymerase chain reaction (RT-PCR) on samples from upper respiratory nasopharyngeal swabs were enrolled to the study.

The case group included diabetic patients with COVID-19 and the control group included Non-diabetic COVID-19 patients. Accordingly, all 420 diagnosed diabetic patients with confirmed COVID-19 in the above mentioned time period were included and considered as case group and for increase the statistical power of the study, compared them with 1260 non-diabetic patients with COVID-19, as controls group. Controls were selected at the same time and from the same hospital in order to overcome some potential confounders such as quality of care and type of prescription drugs.

The data source regarding the demographic characteristics, clinical symptoms, laboratory, and radiological findings on admission as well as the complications, treatment, and outcomes during hospitalization were gathered from their medical record through two trained nurses and was modified according the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) [10].

The variables registered included demographic data, epidemiological information, comorbidities (chronic cardiac disease, chronic pulmonary disease, cancer, hypertension and chronic liver disease), baseline laboratory tests result (hemoglobin lymphocyte count, platelet count), signs and symptoms at admission (fever, cough, dyspnea, myalgia and headache) and outcome including mortality in hospital.

2.1. Statistical analysis

2.1.1. Logistic regression (LR)

LR is an exceedingly popular classical statistical technique used for classifications type prediction problems, has traditionally been the choice of many studies to determine the relationship between target variable of with a set of independent variables [11]. The model can be present as follows:

$$\log(\frac{\pi}{1-\pi}) = \alpha + \sum_{i=1}^{k} \beta_i x_i$$

In this model's are factors, α and β_i 's are regression coefficients that state the measure of effect size. (x) indicate the probability of success and given a specific value of covariates and $\pi/1-\pi$ indicate the odds ratio of classifying the response [12]. The result induces the Odds ratio (OR) of death in diabetic patients with COVID-19 in one group compared to non-diabetic patients with COVID-19.

We used the chi-square test to compare categorical variables and the *t*-test to compare the continuous variables. Adjusted and unadjusted odds ratios (OR) estimate were calculated using the simple and multiple logistic regression through backward model. All statistical analyses were performed at a significance level of 0.05, using Stata software, version 16 (StataCorp, College Station, TX, USA).

3. Results

The mean (SD) age of the case group was higher than that of the control group; [65.24 (12.40) years vs. 59.35 (17.34) years, respectively ($P < 0.001$)]. In addition, the proportion of females was significantly higher in case than in control (57.1% versus 43.6%; $P < 0.001$). The details of cases and controls, including demographic characteristics, epidemiological information, comorbidities, signs and symptoms at admission and laboratory tests results are shown in Table 1. As shown, two groups were heterogenic in regards of gender, headache and fever sign, cardiovascular and hypertension co-morbidity, and ESR, BUN, BS, NA, K, HCT and Hb markers ($P < 0.05$).

The effect of various potential risk factors for mortality of COVID-19 in diabetic AND non-diabetic patients is given in Tables 2 and 3 using crude (Table 2) and adjusted (Table 3) OR.

Results of the adjusted logistic regression model (Table 3) showed that, advanced age (+60 year) (OR = 5.13, P = 0.006), addiction (OR = 5.26, P = 0.033), high level of BUN (OR = 5.85, $P < 0.001$), and high level of Alp (OR = 3.38, P = 0.012) in diabetic patients and advanced age (+60 year) (OR = 4.69, $P < 0.001$), Dyspnea (OR = 2.46, $P < 0.001$), high level of BUN (OR = 3.65, $P < 0.001$) and high level of SGOT (OR = 2.51, $P < 0.001$) in non-diabetic patients were significantly associated with increase the odds of death in COVID-19 patients.

4. Discussion

In this study we analyzed the demographic characteristics, epidemiological information, comorbidities, signs and symptoms at admission and laboratory tests results of COVID-19 patients with diabetes compared COVID-19 patients without diabetes and identified the risk factors associated with in-hospital death of these patients. In this study we found that in COVID-19 patients with diabetes advanced age, addiction, high level of BUN and Alp and in non-diabetic COVID-19 patients advanced age, dyspnea, high level of BUN and SGOT were associated with increase risk of death in these patients.

Similar to our study, in previous studies advaned age has been considered as a risk factor of death in non-diabetic COVID-19 patients and also in COVID-19 patients with diabete type 1 and 2 diabetes [13]. In Cheng et al. study age older than 60 years was identified as a independent risk factors for serious disease in SARS-CoV-2 infection [14]. Tehrani and collagenous revealed that advanced age contribute to a fatal outcome in hospitalized COVID-19 patients [15]. It has been shown that high mortality rate of elderly patients with COVID-19 is mainly due to the frequent

Table 1
Comparison of baseline characteristics of the patients in the case and control groups.

Variable	Case (n = 420)		Control (n = 1260)		*P*-value
	No	%	No	%	
Demographics Characteristic					
Gender					<0.001*[a]
Male	180	42.9	711	56.4	
Female	240	57.1	549	43.6	
Habitat					0.534
rural	67	16.0	201	16.0	
urban	353	84.0	1059	84.0	
Smoking status					0.086
Nonsmoker	397	94.5	1157	91.8	
Smoker	23	5.5	103	8.2	
Injecting drug use					0.094
No	397	94.5	1160	92.1	
Yes	23	5.5	100	7.9	
Admission signs and symptoms					
Headache					<0.001*[a]
No	369	87.9	1001	79.5	
Yes	51	12.1	258	20.5	
Fatigue					0.500
No	406	96.7	1225	97.3	
Yes	14	3.3	34	2.7	
Myalgia					0.374
No	232	55.2	664	52.7	
Yes	188	44.8	595	47.3	
Diarrhea					0.272
No	381	90.7	1118	88.8	
Yes	39	9.3	141	11.2	
Nausea					0.490
No	316	75.2	968	76.9	
Yes	104	24.8	291	23.1	
Vomiting					0.534
No	330	78.6	1007	80.0	
Yes	90	21.4	252	20.0	
Abdominal Pain					0.404
No	405	96.4	1203	95.5	
Yes	15	3.6	57	4.5	
Chest pain					0.331
No	390	92.9	1151	91.3	
Yes	30	7.1	109	8.7	
Sputum					0.563
No	417	99.3	1254	99.5	
Yes	3	0.7	6	0.5	
Sweat					0.432
No	411	97.9	1224	97.1	
Yes	9	2.1	36	2.9	
Fever					0.014*[a]
No	213	50.7	552	43.8	
Yes	207	49.3	708	56.2	
Chills					0.067
No	238	56.7	649	51.5	
Yes	182	43.3	611	48.5	
Dry cough					0.776
No	240	57.1	710	56.3	
Yes	180	42.9	550	43.7	
Sore Throat					0.280
No	409	97.4	1213	96.3	
Yes	11	2.6	47	3.7	
Sputum Cough					0.717
No	345	82.1	1025	81.3	
Yes	75	17.9	235	18.7	
Urinary symptoms					0.085
No	402	95.7	1227	97.4	
Yes	18	4.3	33	2.6	
Vertigo					0.818
No	406	96.7	1215	96.4	
Yes	14	3.3	45	3.6	
Constipation					0.832
No	412	98.1	1238	98.3	
Yes	8	1.9	22	1.7	
Weakness					0.349
No	226	53.8	711	56.4	
Yes	194	46.2	549	43.6	
Anorexia					0.574
No	269	64.0	826	65.6	
Yes	151	36.0	434	34.4	
Awareness					0.038*[a]
No	400	95.2	1226	97.3	
Yes	20	4.8	34	2.7	
loss of taste and smell					0.137
No	379	90.2	1106	87.8	
Yes	41	9.8	154	12.2	
Dyspnea					0.499
No	177	42.1	507	40.3	
Yes	243	57.9	752	59.7	
Stomach ache					0.299
No	413	98.3	1247	99.0	
Yes	7	1.7	13	1.0	
Comorbidities					
cardiovascular diseases					<0.001*[a]
No	298	71.0	1048	86.0	
Yes	122	29.0	176	14.0	
Hypertension					<0.001*[a]
No	184	43.8	892	70.8	
Yes	236	56.2	368	29.2	
cancer					0.697
No	410	97.6	1234	97.9	
Yes	10	2.4	26	2.1	
Pulmonary Disease					0.529
No	364	86.7	1092	86.7	
Yes	56	13.3	168	13.3	
Liver diseasee					0.881
No	416	99.0	1249	99.1	
Yes	4	1.0	11	0.9	
Continuous variables	**Mean**	**SD**	**Mean**	**SD**	***P*-value**
vital signs					
Number of Breaths	19.59	3.70	19.93	4.08	0.128
Body Temperature	37.24	0.71	37.29	1.05	0.367
Diastolic	78.64	12.46	75.94	10.70	<0.001*[b]
Systolic	126.44	20.98	120.46	17.72	<0.001*[b]
Heart Rate	92.80	15.02	93.04	36.38	0.892
Laboratory parameters					
ESR	49.69	29.78	40.92	28.86	<0.001*[b]
BUN	24.18	19.43	20.07	15.25	<0.001*[b]
BS	217.03	121.15	124.82	49.89	<0.001*[b]
CR	1.28	0.81	1.33	3.70	0.803
PT	13.73	3.31	13.65	4.05	0.717
CPK	191.32	295.26	248.34	461.13	0.063
SGPT or ALT	37.54	63.43	43.31	112.04	0.336
SGOT	44.86	118.85	53.22	192.29	0.419
Alp	214.95	140.58	203.64	105.23	0.104
PTT	34.25	12.56	35.57	12.64	0.086
K	4.29	0.56	4.15	1.08	0.019*b
NA	136.45	3.99	137.60	3.76	<0.001*b
Plat	196.68	75.44	198.59	89.93	0.697
HCT	41.70	5.48	42.49	5.75	0.014*b
Hb	13.55	1.97	13.93	2.10	<0.001*b
LDH	576.70	338.13	580.85	324.60	0.838
Lym	23.00	13.17	23.49	12.26	0.494
NEUT	72.73	13.85	72.06	13.29	0.386

SD: standard deviation, [a] Chi-Square Test, [b] T- Test, *Significant at the level of P < 0.05. ESR: Erythrocyte Sedimentation Rate, BUN: Blood Urea Nitrogen, BS: Blood Sugar, CR: Blood creatinine, PT: Prothrombin Time, CPK: Creatine Phosphokinase, ALT: Alanine Aminotransferase, SGOT: Serum Glutamic-Oxaloacetic Transaminase, Alp: Alkaline Phosphatase Level Test, PTT: Partial Thromboplastin Time, K: Potassium, NA: Sodium, PLT: Blood Platelets, HCT: Hematocrit, HB: Hemoglobin, LDH: Lactate Dehydrogenase, lym: Lymphocyte, NEUT: Neutrophils.

occurrence of multiple comorbidities including but not limited to hyperglycemia [16].

We observed that non-diabetic COVID-19 patients with dyspnea were significantly more likely to die than patients without dyspnea. Dyspnea is a sign of respiratory disease, so can be an important risk factor for progression COVID-19 to advanced stages [17]. Shi et al.

Table 2
Association between covid-19 mortality and potential risk factors in diabetic and non-diabetic patients using unadjusted odds ratio.

Characteristic demographics	Diabetes N = 420		Unadjusted Odds Ratio (95% CI)	*P* value	Non- Diabetes N = 1260		Unadjusted Odds Ratio (95% CI)	*P* value
	Alive	Dead			Alive	Dead		
Age (year)								
<60	128(38.2)	9(10.6)	–	–	581(55.0)	38(18.8)	–	–
>=60	207(61.8)	76(89.4)	18.64 (1.57, 221.71)	0.021*	475(45.0)	164(81.2)	13.44 (4.93, 36.64)	<0.001*
Gender								
Male	138(41.2)	42(49.4)	–	–	582(55.1)	128(63.4)	–	–
Female	197(58.8)	43(50.6)	0.61 (0.11, 3.16)	0.560	474(44.9)	74(36.6)	0.62 (0.28, 1.36)	0.231
Residence								
Rural	53(15.8)	14(16.5)	–	–	171(16.2)	29(14.4)	–	–
urban	282(84.2)	71(83.5)	70.10 (2.19, 240.74)	0.016*	885(83.8)	173(85.6)	3.78 (1.29, 11.06)	0.015*
Smoking status								
Nonsmoker	316(94.3)	81(95.3)	–	–	973(92.1)	182(90.1)	–	–
Smoker	19(5,7)	4(4.7)	0.07(0.01, 0.47)	0.020*	83(7.9)	20(9.9)	1.12 (0.28, 4.49)	0.871
Injecting drug use								
No	320(95.5)	77(90.6)	–	–	974(92.2)	184(91.1)	–	–
Yes	15(4.5)	8(9.4)	23.94 (1.22, 471.14)	0.037*	82(7.8)	18(8.9)	1.78 (0.42, 7.53)	0.436
Admission signs & symptoms								
Headache								
No	291(86.9)	78(91.8)	–	–	828(78.4)	172(85.6)	–	–
Yes	44(13.1)	7(8.2)	0.59 (0.05, 6.92)	0.675	228(21.6)	29(14.4)	2.37 (0.99, 5.64)	0.052
Fatigue								
No	326(97.3)	80(94.1)	–	–	814(77.1)	153(76.1)	–	–
Yes	9(2.7)	5(5.9)	31.43 (1.21, 81.91)	0.038*	48(23.9)	290(23.1)	0.38 (0.05, 2.77)	0.342
Myalgia								
No	179(53.4)	53(62.4)	–	–	540(51.1)	124(61.7)	–	–
Yes	156(46.6)	32(37.6)	0.38 (0.06, 2.34)	0.295	516(48.9)	77(38.3)	1.89 (0.92, 3.86)	0.0812
Diarrhea								
No	302(90.1)	79(92.9)	–	–	937(88.7)	180(89.6)	–	–
Yes	33(9.9)	6(7.1)	1.75 (0.16, 19.67)	0.649	119(11.3)	21(10.4)	3.23 (1.13, 9,18)	0.028*
Nausea								
No	247(73.7)	69(81.2)	–	–	814(77.1)	153(76.1)	-	–
Yes	88(26.3)	16(18.8)	1.46 (0.06, 37.59)	0.819	242(22.9)	48(23.9)	2.63 (0.84, 8.25)	0.097
Vomiting								
No	258(77.0)	72(84.7)	–	–	845(80.0)	160(79.6)	–	–
Yes	77(23.0)	13(15.3)	0.16 (0.01, 6.50)	0.329	211(20.0)	41(20.4)	0.85 (0.26, 2.83)	0.794
Fever								
No	168(50.1)	45(52.9)	–	–	456(43.2)	96(47.5)	–	–
Yes	167(49.9)	40(47.1)	0.22 (0.02, 2.44)	0.216	600(56.8)	106(52.5)	3.90 (0.99, 15.42)	0.052
Chills								
No	186(55.5)	52(61.2)	–	–	529(50.1)	120(59.4)	–	–
Yes	149(44.5)	33(38.8)	17.37 (1.08, 28.04)	0.044*	527(49.9)	82(40.6)	0.20 (0.05, 0.78)	0.021*
Dry cough								
No	187(55.8)	53(62.4)	–	–	594(56.3)	116(57.4)	–	–
Yes	148(44.2)	32(37.6)	0.99 (0.24, 4.36)	0.8987	462(43.8)	86(42.6)	0.81 (0.38, 1.73)	0.578
Urinary symptoms								
No	327(97.6)	75(88.2)	–	–	1032(97.7)	193(95.5)	–	–
Yes	8(2.4)	10(11.8)	209.32 (7.57, 578.953)	0.002*	24(2.3)	9(4.5)	1.04 (0.19, 5.53)	0.969
Vertigo								
No	325(97.0)	81(95.3)	–	–	1016(96.2)	197(97.5)	–	–
Yes	10(3.0)	4(4.7)	5.42 (0.19, 160.43)	0.329	40(3.8)	5(2.5)	2.46 (0.40, 15.01)	0.331
Constipation								
No	329(98.2)	83(97.6)	–	–	1040(98.5)	196(97.0)	–	–
Yes	6(1.8)	2(2.4)	53.99 (0.72, 404.86)	0.070	16(1.5)	6(3.0)	7.66 (0.82, 71.62)	0.074
Anorexia								
No	210(62.7)	59(69.4)	–	–	702(66.5)	123(60.9)	–	–
Yes	125(37.3)	26(30.6)	0.16 (0.03, 0.92)	0.040*	354(33.5)	79(39.1)	0.52 (0.24, 1.07)	0.077
loss of taste and smell								
No	298(89.0)	81(95.3)	–	–	921(87.2)	185(91.6)	–	–
Yes	37(11.0)	4(4.7)	0.09 (0.01, 1.31)	0.079	135(12.8)	17(8.4)	1.04 (0.31, 3.49)	0.948
Dyspnea								
No	147(43.9)	30(35.3)	–	–	453(42.9)	54(26.9)	–	–
Yes	188(56.1)	55(64.7)	1.88 (0.40, 8.74)	0.422	603(57.1)	147(73.1)	4.36 (1.99, 9.55)	<0.001*
Comorbidities								
Cardiovascular diseases								
No	249(74.3)	49(57.6)	–	–	931(88.2)	151(74.8)	–	–
Yes	86(25.7)	36(42.4)	2.39 (0.44, 13.19)	0.316	125(11.8)	51(25.2)	1.44(0.59, 3.53)	0.420
Hypertension								
No	154(46.0)	30(35.3)	–	–	770(72.9)	120(59.4)	–	–
Yes	181(54.0)	55(64.7)	0.23 (0.24, 2.12)	0.193	286(27.1)	82(40.6)	1.61 (0.73, 3.52)	0.231
Pulmonary Disease								
No	294(87.8)	70(82.4)	–	–	924(87.5)	166(82.2)	–	–
Yes	41(12.2)	15(17.6)	2.19 (0.27, 17.63)	0.460	132(12.5)	36(17.8)	0.42 (0.14, 1.30)	0.133
vital signs								

Table 2 (*continued*)

Characteristic demographics	Diabetes N = 420		Unadjusted Odds Ratio (95% CI)	*P* value	Non- Diabetes N = 1260		Unadjusted Odds Ratio (95% CI)	*P* value
	Alive	Dead			Alive	Dead		
Body Temperature								
<37	167(49.9)	42(49.4)	–	–	500(47.3)	98(48.8)	–	–
>=37	68(50.1)	43(50.61)	2.81 (0.42, 18.99)	0.290	556(52.7)	103(51.2)	1.06 (0.53, 2.14)	0.859
Systole Bp								
<140	247(73.7)	68(80.0)	–	–	886(83.9)	171(84.7)	–	–
>=140	88(26.3)	17(20.0)	3.27 (0.10, 104.92)	0.502	170(16.1)	31(15.3)	1.09 (0.24, 5.07)	0.913
Diastolic Bp								
<90	254(75.8)	70(82.4)	–	–	884(83.7)	171(84.7)	–	-
>=90	81(24.4)	15(17.6)	0.06 (0.01, 3.38)	0.169	172(16.3)	31(15.3)	0.42 (0.09, 1.84)	0.250
laboratory parameters								
ESR								
Normal	153(49.0)	30(38.5)	–	–	580(60.0)	92(47.9)	–	–
Abnormal	159(51.0)	48(61.5)	0.15 (0.02, 1.05)	0.056	385(39.9)	100(52.1)	1.19 (0.56, 2.55)	0.647
BUN								
<20	224(67.1)	18(21.2)	–	–	785(74.5)	57(28.4)	–	–
>=20	110(32.9)	67(78.8)	52.03 (4.35, 62.68)	0.002*	268(25.5)	144(71.6)	6.57 (3.80, 14.04)	<0.001*
BS								
70–105	34(12.0)	8(10.5)	–	–	335(44.3)	36(22.0)	–	–
>=105	249(88.0)	68(89.5)	2.69 (0.05, 14.44)	0.623	421(55.7)	128(78.0)	1.23 (0.57, 2.64)	0.589
PT								
<13	98(34.0)	20(24.7)	–	–	272(30.3)	53(27.6)	–	–
>=13	190(66.0)	61(75.3)	0.04 (0.01, 0.49)	0.012*	625(69.7)	139(72.4)	1.86 (0.79, 4.34)	0.153
CPK								
Normal	126(61.5)	39(75.0)	–	–	423(64.0)	94(75.8)	–	–
Abnormal	79(38.5)	13(25.0)	0.82 (0.14, 4.67)	0.824	238(36.0)	30(24.2)	1.37 (0.60, 3.04)	0.426
SGPT								
<37	241(77.5)	54(64.3)	–	–	710(72.7)	111(56.9)	–	–
>=37	70(22.5)	30(35.7)	1.56 (0.21, 11.299)	0.662	257(27.3)	84(43.1)	1.38 (0.59, 3.16)	0.457
SGOT								
<45	279(85.8)	51(61.4)	–	–	840(81.3)	96(48.5)	–	–
>=45	46(14.2)	32(38.6)	1.09 (0.12, 10.05)	0.940	193(18.7)	102(51.5)	3.85 (1.63, 9.09)	0.002*
Alp								
<270	251(86.6)	52(66.7)	–	–	762(85.7)	140(76.9)	–	–
>=270	39(13.4)	26(33.3)	21.65 (1.66, 28.08)	0.019*	127(14.3)	42(23.1)	0.45 (0.18, 1.11)	0.085
K								
3.5–5.1	11(3.4)	6(7.1)	–	–	56(5.5)	17(8.6)	–	–
=<3.5	300(92.3)	69(82.1)	0.02 (0.01, 1.16)	0.059	932(91.6)	166(83.8)	0.13 (0.03, 0.63)	0.011*
>=5.1	14(4.3)	9(10.7)	0.04 (0.01, 4.98)	0.191	30(2.9)	15(7.6)	0.07 (0.01, 0.57)	0.012*
NA								
136–145	156(48.3)	47(56.6)	–	–	332(32.7)	93(47.0)	–	–
>=136	167(51.7)	36(43.4)	0.97 (0.17, 5.50)	0.974	682(67.3)	105(53.0)	0.95 (0.46, 1.97)	0.897
LLDH								
<942	251(90.6)	46(67.6)	–	–	816(90.5)	88(54.7)	–	-
>942	26(9.4)	22(32.4)	12.21 (0.69, 213.85)	0.087	86(9.5)	73(45.3)	5.36 (2.19, 13.07)	<0.001*

*Significant at the level of P < 0.05.

ESR: Erythrocyte Sedimentation Rate, BUN: Blood Urea Nitrogen, BS: Blood Sugar, CR: Blood creatinine, PT: Prothrombin Time, CPK: Creatine Phosphokinase, ALT: Alanine Aminotransferase, SGOT: Serum Glutamic-Oxaloacetic Transaminase, Alp: Alkaline Phosphatase Level Test, PTT: Partial Thromboplastin Time, K: Potassium, NA: Sodium, PLT: Blood Platelets, HCT: Hematocrit, HB: Hemoglobin, LDH: Lactate Dehydrogenase, lym: Lymphocyte, NEUT: Neutrophils.

reported that presence of dyspnea was a risk factors for death in SARS-CoV-2 infection [18].It has been reported in several studies that COVID-19 patients with dyspnea had a higher risk for hospitalization, ICU addmission, mechanical ventilation, severe disease, disease progression and mortality than those without dyspnea [19–22].

Other finding of present study showed that addiction is a risk factor of death in COVID-19 patients with diabetes. It may be because patients with diabetes are at higher risk of receiving polypharmacy than patiens without diabetes. So, addicted patiens with diabetes have increased risks of adverse drug events [23]. In this regard, Baillargeon et al. indicated that COVID-19 patients with substance use are at greater risk for adverse outcomes [24]. Wang et al. found COVID-19 patients with substance use especially opioids use are at increased risk for adverse outcomes [25].

In present study, high BUN levels was another rsik factor of COVID-19 related death in diabetic and non-diabetic patients. Recently, there is a lot of evidence of increase in COVID-19 mortality rate in patients with higher serum BUN levels [26]. According to Pazoki et al. study, kidney damage indicators, including serum creatinine and blood urea nitrogen (BUN) is linked with higher mortality in COVID-19 patients [27]. A meta-analysis conducted by Shao and collagenous on 40 studies and 25,278 patients revealed a positive relationship between BUN levels and mortality rate in patients with COVID-19 [28].

In our study, high ALP and SGOT (AST) levels respectively in diabetic and non-diabetic patients were associated with increased risk of COVID-19 related death. Both of these enzymes are indicators of liver damage and dysfunction, which can be seen in more than half of patients with COVID-19 [29]. It has been shown that the SARS-CoV-2 virus may also bind to ACE2 on cholangiocytes and induce a systemic inflammatory response leading to liver injury [30]. Also, it has been suspected that some detrimental effects on liver injury is mainly due to certain medications used during COVID-19 hospitalization [31]. In agreement with our findings, Pazoki et al. showed that high serum levels of ALP and AST was a risk factor of in-hospital mortality and disease severity in diabetic patients with confirmed or clinically suspected COVID-19

Table 3
Association between covid-19 mortality and potential risk factors in diabetic and non-diabetic patients using adjusted odds ratio.

Characteristic demographics	Diabetes N = 420		Adjusted Odds Ratio (95% CI)	*P* value	Non- Diabetes N = 1260		Adjusted Odds Ratio (95% CI)	*P* value
	Alive	Dead			Alive	Dead		
Age (year)								
<60	128	9	–	–	581	38	–	–
>=60	207	76	5.13 (1.61, 16.39)	0.006	475	164	4.69 (2.71, 8.13)	<0.001
Residence								
Rural	53	14	–	–	171	29	–	–
urban	282	71	1.79 (0.61, 5.25)	0.289	885	173	1.89 (0.99, 3.57)	0.052
Smoking status								
Nonsmoker	316	81	–	–	973	182	–	–
Smoker	19	4	0.29 (0.06, 1.39)	0.121	83	20	2.42 (0.99, 5.89)	0.052
addiction								
No	320	77	–	–	974	184	–	–
Yes	15	8	5.26 (1.14, 24.19)	0.033	82	18	0.63 (0.24, 1.73)	0.342
Admission signs & symptoms								
Fatigue								
No	326	80	–	–	814	153	–	–
Yes	9	5	2.59 (0.52, 12.89)	0.246	48	290	0.47 (0.10, 2.14)	0.326
Diarrhea								
No	302	79	–	–	937	180	–	–
Yes	33	6	1.75 (0.16, 19.67)	0.649	119	21	1.46 (0.74, 2.90)	0.274
Chills								
No	186	52	–	–	529	120	–	–
Yes	149	33	1.21 (0.55, 2.69)	0.638	527	82	1.03 (0.65, 1.61)	0.912
Anorexia								
No	210	59	–	–	702	123	–	–
Yes	125	26	0.54 (0.24, 1.24)	0.146	354	79	0.88 (0.56, 1.38)	0.579
Dyspnea								
No	147	30	–	–	453	54	–	–
Yes	188	55	1.44(0.75, 3.19)	0.371	603	147	2.46 (1.52, 3.98)	<0.001
laboratory parameters								
BUN								
<20	224	18	–	–	785	57	–	–
>=20	110	67	5.85 (2.54, 13.52)	<0.001	268	144	3.65 (2.28, 5.85)	<0.001
PT								
<13	98	20	–	–	272	53	–	–
>=13	190	61	0.97 (0.42, 2.17)	0.923	625	139	0.96 (0.59, 1.58)	0.885
SGOT								
<45	279	51	–	–	840	96	–	–
>=45	46	32	2.65 (0.99, 7.03)	0.050	193	102	2.51 (1.56, 4.04)	<0.001
Alp								
<270	251	52	–	–	762	140	–	–
>=270	39	26	3.38 (1.31, 8.75)	0.012	127	42	1.34 (0.77, 2.32)	0.300

*Significant at the level of P < 0.05.
BUN: Blood Urea Nitrogen, PT: Prothrombin Time, SGOT: Serum Glutamic-Oxaloacetic Transaminase, Alp: Alkaline Phosphatase Level Test, K: Potassium, LDH: Lactate Dehydrogenase.

[27]. Shen et al. reported a similar findings [32]. However, liver damage and increased levels of liver enzymes in serum including AST and ALP is also reported in the diabetic patients in Islam et al. study [33].

Limitations of this study include the following: first, due to the retrospective nature of the study, we could not assess all clinical and laboratory information such as d-dimer for all patients. Secondly, in this study we included only hospitalized patients with relatively severe symptoms and patients with mild or moderate symptoms were not assessed in the present study.

5. Conclusion

We found that in COVID-19 patients with diabetes; advanced age, addiction, high level of BUN and Alp and in non-diabetic COVID-19 patients advanced age, dyspnea, high level of BUN and SGOT were associated with increase risk of death in these patients.

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Declaration of competing interest

The authors claimed no conflict of interest.

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