Original Article

Diabetes Mellitus And Covid-19

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Abstract

Background and Purpose: according to the studies that have been conducted so far, the corona virus has more severe clinical consequences in diabetic patients than in non-diabetic cases; Therefore, the present study was conducted with the aim of investigating the severity of the disease and mortality in patients infected with the Coronavirus between these 2 groups.

Materials and Methods: In this cross-sectional-analytical study, the clinical records of 185 hospitalized patients with a positive laboratory diagnosis of Covid-19 were reviewed from February 14 to February 26, 2020. The patients were divided into 2 non-diabetic (95 people) and diabetic (90 people) groups, and their clinical symptoms and blood biochemical parameters were compared.

Results: Based on the results, most of the patients were male and compared to non-diabetic patients, the diabetic group was significantly older (P=0.01). In this study, the disturbance in paraclinical factors such as d-dimer, BUN, VBG and lymphopenia in diabetic patients was significantly higher than in the control group, which indicates the need for more care in diabetic patients.

Conclusion: it is suggested to follow health protocols for people with land diseases, be more careful., therefore, more extensive research with larger sample sizes is needed to achieve more accurate results.

Keywords: Diabetes Mellitus, Covid-19, Clinical Symptoms and Blood Biochemical Parameters.

INTRODUCTION

The Covid-19 pandemic started out as a viral respiratory infection in Wuhan in December 2019. Now at the 4th quarter of 2021, it has affected all the world. The disease has claimed millions of lives and many more has been diagnosed with it. Despite introduction of successful vaccines, vaccination coverage has been subpar due to financial problems in some countries and due to antivaccine movements and public distrust in some others (1-3). Therefore, we are observing countries confronting large numbers of patients. There has been a massive surge in research and literature dedicated to understanding different aspects of the virus and the correlated disease. Many risk factors affecting the prognosis of disease and are identified and many more are being investigated. A significant number of tools and test have been developed to assess the severity of the disease and predict the outcome.

One of the most prevalent non-communicable disease of the world is diabetes mellitus. It is identified by high levels of blood sugar and affects nearly all systems in patients' body. DM has been shown to affect the mortality and later morbidity of covid-19 patients and is considered an age-independent risk factor for severe disease (4-6).

It has been estimated that nearly triple increase in mortality is expected in DM patients compared to normal population without DM. (OR= 3.62; 95% CI 2.11–6.2) (3) the mechanism is thought to downregulation of both humoral and innate immune system (through neutrophils and T-cells). In diabetic patients with SARS and COVID-19 viral clearance may take longer. This may be due to the association of the disease with higher levels of ACE2 expression but it is also hypothesized that virus binding and fusion are also due to the amount of glycosylated ACE2 receptor rather than the amount of ACE2, alone (7). The covid-19

disease is thought to affect glucose regulation in patients. The mechanisms of such effects have not been fully understood (8).

In our study we aim to further investigate the properties of relation between diabetes and covid. We aim to understand the relationship between diabetes control and exact laboratory results obtained during patients' presence in hospital. Furthermore, this study could guide us further in exploring subgroups of patients who would benefit the most from alternative and novel therapeutic methods (5).

Material and Method

The subjects were selected from the patients admitted to wards with the covid-19 diagnosis. They were selected among those admitted to the bohlool hospital in gonabad from august to December 2020. The diagnosis was made by either CT scan or PCR results. The criteria for inpatient admission were according to the national guideline on covid-19 management issued by the ministry of health and medical education. It includes patients with o2 saturation of 93% or lower or those with high risk of complication. Our exclusion criteria were dissatisfaction with participating in the study, Existence of an underlying disease other than diabetes mellitus, Patients under 20 years.

The patient selection process was divided into two parts. First the case group which was selected from our pool of patients using simple random sampling. Presence of DM was ascertained by patient history. 95 patients were included in the final selection. Later the control group was selected with cluster sampling in order to account for other pre-existing conditions.

First, the subjects were assessed for baseline parameters. Later, using the medical records their ongoing clinical and laboratory outcomes were assessed and compared. The results were then analyzed by a statistician. The details of the statistical analysis are included in the appendix. Body temperature was measured by manual mercury thermometer.

Fever was defined as WHO definition of temperature of 37.3 and above as a sign of the disease. Dizziness was defined as any symptom that can range from transient weakness to severe imbalance that makes normal functioning impossible.

Diarrhea was defined as Excretion of watery stools more than 3 times a day. (WHO definition)

Severe case was defined as SpO2 <94% on room air at sea level, a respiratory rate >30 breaths/min, PaO2/FiO2 <300 mm Hg, or lung infiltrates >50%. VBG was obtained by trained nurses and was analyzed by the same blood gas analyzer.

Blood pressure data are obtained on the day of admission using a manual manometer, calibrated at the beginning of the study Patients were intubated based on their clinical status and o2 saturation.

Results

The baseline parameters assessed in our subjects were as follows: age, sex, past medical history of malignancy or other chronic medical conditions and previous history of covid-19 infection. Due to the time limitation of our study and limited number of patients that could be enrolled there is considerable age and sex difference in both groups. The only statistically significant comorbidity was cardiovascular disease. (p value<0.001) A summary of the baseline parameters can be found in the table1. Other baseline parameters were similar in both groups

Table 1: Demographic characteristics of the participants

	No. (%) Total (n =185)	Non-diabetes (n = 90)	Diabetes (n = 95)
Age, median (IQR), y	61 (42-75)	45 (30-60)	72 (61-80)
Male	81 (43.8)	47 (52.2)	34 (35.8)
Female	104 (56.2)	43 (47.8)	61 (64.2)

One of the most important vital signs to in every covid patient is body temperature, as it can be an indicator of virus activity. Our recorded fever data is grouped into 4 categories based on the traditional cut off points of 37.3, 38 and 39. Shortness of breath was the most common symptom. There was a remarkable difference between two group with nearly double the number of patients in Dm group (p value=0.002) Fatigue was remarkably higher in our case group with 30 patients compared to 7 in control group (p value<0.001). interestingly myalgia was observed in control group with 27 patients in control vs 3 patients in DM group (p value<0.001). Reported chills were similar in both groups (p value=0.395). number of people who reported having coughs had a recognizable difference but the statistically it was not significant (p value=0.72). A similar situation was also seen with headache (p value=0.092) nausea and vomiting was similar in both groups (p value=0.749) diarrhea was higher in DM group but not by a significant margin (p value=0.216).

The more uncommon symptoms were also analyzed; sore throat was rare among both groups and no significant difference was seen (p value=0.798). Report of dizziness was much higher in DM group versus control group with 14 patient's vs 4(p value=0.018). Chest pain was relatively uncommon in both groups and no significant difference was detected (p value=0.748)

Hospitalization period was oddly lower in DM group compared to control group with 4 and 5 days respectively.

Severe cases were rare among our population but we had 4 severe case with DM group compared to only one in control group. No patient from control group was intubated while 5 patients required mechanical ventilations during their hospitalization.

A summary of our lab variables results is visible in table 2. The most prominent variables that showed significant difference was D-dimer and blood pressure with p values of 0.005 and less than 0.001 respectively.

Interestingly there were a number of variables that did not show the expected results despite being some of the most common features of the COVID-19 or DM. Lymphopenia, ESR and LDH was such examples.

Table 2: Comparison of para-clinical factors in two groups

		Normal Range	Median (IQR)			
			Total (n = 185)	**Non-diabetes (n = 90)**	**Diabetes (n = 95)**	P-Value
CBC	WBC	4000 - 11000	7200 (4700-10100)	5750 (3900-8000)	9150 (6500-11400)	<0.001
	Hb	14 – 17.5	14 (13-15)	14 (13-14.2)	14.5 (13-15)	0.456
	Lymph	1500 – 5000	1300 (880-2000)	1200 (800-1780)	1300 (900-2500)	0.241
	Neut	1500 – 8000	4900(3100-7200)	3840 (2500-5800)	5900 (3600-8300)	<0.001
	Plt	150000 – 450000	222000(167000-274500)	198500 (149000-255000)	241000 (188000-293000)	0.001
Coagulation	PT	12 – 14	13.4 (13-14.5)	13 (12.8-14.4)	13.5 (13.1-14.5)	0.095
	PTT	24 – 40	31 (26.5-37.5)	31 (28.5-38)	29.5 (24.5-36)	0.236
	INR	< 1.1	1.08 (1-1.18)	1.05 (1-1.18)	1.09 (1.05-1.18)	0.135
	TPI1 mis	0 – 0.5				
	D-dimer	< 0.5	730 (540-1410)	630 (320-910)	1045 (600-1970)	0.005
	ESR	< 15	25 (12-44)	19.5 (10.5-37)	31 (15-60)	0.007
	ALT	< 41	21 (13-33)	23 (15-36)	17 (11.7-29.2)	0.039
	AST	< 37	29 (20-38)	29(21-38)	28(17-38)	0.504
	ALP	80 - 306	175 (140-217)	161 (132-196)	188 (156-250)	0.003
	Alb	3.5 – 5.5	5 (4-5)	4 (4-4.5)	5 (4.5-5)	0.393
	Bill Total	< 1.2	1 (1-4)	4.5 (1-5)	4 (1-4)	0.667
	Bill Direct	0.1 – 0.3	0.25 (0.2 – 0.4)	0.2 (0.14-0.3)	0.28 (0.2-0.44)	0.015
	CPK	Male: 39 – 308 Female: 26 – 192	80 (54-134) 59 (38 - 94)			
	BUN	8 – 24	16 (12-22)	14 (11-16.9)	19 (14-28.1)	<0.001
	Cr	0.7 – 1.4	1 (0-1)	1 (0-1)	1 (0.25-1.25)	0.454
	Ferritin	Male: 24 to 336 Female: 11 to 307	167 (85 - 336) 73 (47-128)			
	Mg	1.5 – 2.8	2 (1.8 – 2.2)	2.1 (1.8-2.2)	1.9 (1.7-2.2)	0.436
	Na	135 – 145	136 (133 - 138)	136 (133-138)	136 (131-138)	0.465
	K	3.5 – 5.5	3.8 (3.5 – 4.1)	3.7 (3.4-4)	3.9 (3.6-4.2)	0.029
VBG	pH mis	7.35 – 7.45				
	PCO2	40 – 52	40.2 (35.4 – 45.6)	38.3 (34.6-41.9)	42.4 (35.9-49)	0.005
	HCO3	21.8 – 26.9	23.9 (21.3 – 25.9)	24 (21.2-25.8)	27 (23.7-30.6)	0.477
	SPO2	< 90%	94 (91-96)	95 (93-96)	92 (90-95)	<0.001
Blood Pressure	SBP	< 120 mm	137 (122 – 159)	125 (117-144.7)	145 (127-170)	<0.001
	DBP	< 80 mm	83 (78 - 93)	80 (75-89)	88 (80-98)	0.002
	HR	60 - 100	97.5 (82.5 – 111.5)	98(84 -113)	96 (78.5-111.5)	0.241

DISCUSSION

The aim of this retrospective study is to investigate the clinical outcomes of patients with COVID-19 in diabetics in comparison with non-diabetic patients. The results of the present study showed that the hospitalized diabetic and non-diabetic patients with COVID-19 showed almost the same clinical symptoms, laboratory findings and imaging (CT scan of the chest). In addition, there was no significant difference in the mortality rate between the two groups of diabetic patients and non-diabetic patients with COVID-19. Based on many retrospective studies, age and male gender are among the epidemiological factors effective in causing adverse clinical results in both diabetic and non-diabetic patients with COVID-19. According to the results of the present study, diabetic patients with COVID-19 They were about 20 years older than the non-diabetic group, which is consistent with the results of previous studies, although all age groups are susceptible to contracting COVID-19, but elderly people with underlying diseases, including diabetes, are more susceptible to contracting SARS-COV-2. (1-3). This situation can be the result of the effects of aging on the function of T cells and B cells, which help the accumulation of inflammatory biomarkers (4). In

addition, similar to other studies, the majority of patients hospitalized in our hospital were men in both diabetic and non-diabetic groups (3). Studies show that the main reason for men's greater sensitivity to COVID-19 is the higher prevalence of smoking () and the greater expression of angiotensin-converting enzyme 2 (5-8) in men. Diabetes Mellitus due to its association with other metabolic disorders, as a key factor in the occurrence of severe clinical consequences in patients infected with different types of corona virus; It is known as MERS, COV-SARS and COVID-19 (6). The results of the present study show a significant difference between the two groups in terms of co-morbidities such as IHD, HTN, history of COPD and liver diseases (7). According to studies, the expression of 2-ACE receptor in different organs (lung, kidney and liver) is increased in patients with glucose and lipid disorders (8). However, our results showed that there is no significant difference in the mortality rate between the two groups. It should be mentioned that in our study, diabetic patients did not have a history of asthma or smoking, this fact may have prevented the irreparable consequences of corona virus on organ damage, and led to a lower number of deaths in the group of diabetic COVID-19 patients. According to studies, high FBS is an important and independent factor in causing adverse clinical outcomes and death of diabetic patients infected with corona virus (). Also, the increase in blood glucose level, due to the release of blood sugar-increasing hormones, leads to an increase in inflammatory biomarkers in diabetic patients suffering from the disease - COVID-19 (9-13). The mentioned causes lead to disruption in the inflammatory biomarkers of blood circulation, disrupting the immune response of diabetic patients in comparison with non-diabetic people (13-15). According to previous studies, we found that the level of FBS in diabetic patients with corona virus is significantly higher than non-diabetic patients. However, based on the evaluation of inflammatory biomarkers, despite the increase in the serum CRP level and the slight increase in the WBC count in diabetic patients, no significant difference was observed between this group and the non-diabetic group, the present results are in line with the study of Liu et al. Another case is the relationship between inflammatory conditions and the increase in the ratio of neutrophils to lymphocytes (NLR). Based on this, the increase in NLR has a direct relationship with the severity of COVID-19 in patients with diabetes (16-18). Also, in the analysis of laboratory findings, including AST, ALT, LDH, bilirubin, creatine phosphokinase, troponin, creatinine, BUN and ions, there was no statistical difference between the two groups of patients. However, the blood ALP level was higher in diabetic patients compared to the non-diabetic group. ALP in most of the members The body exists and its increase is usually attributed to the liver and bones (18). Although in another study on COVID-19 patients, liver aminotransferases, total bilirubin and the aforementioned biochemical indices were significantly higher in diabetic patients than in non-diabetic patients (19), Due to the retrospective nature of the present study and its related limitations, more studies are needed to clarify the involvement of liver, myocardium and kidney cells caused by COVID-19 in diabetic and non-diabetic patients.

CONCLUSION

In this study, the disturbance in para-clinical factors such as d-dimer, BUN, VBG and lymphopenia in diabetic patients was significantly higher than in the control group, which indicates the need for more care in diabetic patients. Therefore, it is suggested to follow health protocols for people with land diseases, be more careful.

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