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Diversity in Clinical Spectrum and Outcomes of COVID-19 in Diabetic vs Non-Diabetic Patients: A Retrospective Comparative Study.

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Abstract: Coronavirus disease 19 (COVID-19) has caused substantial morbidity and mortality worldwide. It is an infectious disease caused by SARS-CoV-2. COVID-19 has had a particularly catastrophic impact on individuals with pre-existing health conditions, especially diabetes mellitus. The objective of the study was to provide an overview of the clinical spectrum and outcomes of COVID-19 patients in both diabetic and non-diabetic admitted patients. It was a retrospective, observational study done over the period of ten months from April 2020 to January 2021 in a private hospital of Karachi. The study enrolled 348 COVID-19-admitted patients, which comprised 212 diabetic patients and 136 non-diabetic patients. After completing bio-data, we gathered clinical characteristics of this viral illness, and then observed how their laboratory parameters were affected and finally, the consequences of the altered biochemical parameters were observed in both the diabetic and non-diabetic groups. Most of the admitted patients of COVID-19 were diabetic and had comorbidities. Mostly, COVID-19 admitted patients had diabetes (60.9%), this segment of patients also had hypertension (66.9%), cardiovascular disturbances (47.6%) and chronic kidney disease (17.4%), in clinical features, and cough was found commonly in non-diabetic. On laboratory parameters, HbA1c, hemoglobin, leukocyte count, creatinine, urea nitrogen, and pro-BNP had significant p-value 0.05 or less. As far as disease treatment is concerned, the need for dialysis for diabetic patients was found to be significantly higher (10.5%), while other treatment needs were found to be statistically insignificant. Statistics pertaining to outcomes of disease in diabetics versus non-diabetics were also not found statistically significant.

Keywords: COVID-19, SARS-CoV-2, diabetes

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Introduction

In the past the pandemic situation corona virus disease 2019 (COVID-19) has emerged as one of the greatest challenges faced by all humanity in the world. People suffering from diabetes and related co-morbidities are at increased risk of complications and COVID-19-related mortality [1].

A new coronavirus disease (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread across the globe since its outbreak in December 2019 at Wuhan, China. This led the World Health Organization to declare it a pandemic [2].

It is transmissible through respiratory secretions from one person to another. This virus comes in contact with body through mucous membrane of the upper respiratory tract; afterward it affects lungs

[3]. In most of the cases it appears as mild illness while some people develop respiratory compromise and progress to severe disease characterized by septic shock or respiratory and/or multi-organ failure. Patients who were severely affected by this viral illness and mortality is more pronounced in patients of advanced age, male sex and having underlying health problems like cardiovascular disease, obesity and/or diabetes type I or type II, Some studies have proven that presence of cardiovascular diseases and diabetes mellitus are common in covid-19 admitted patients in ICUs [4-6].

One retrospective study stated that patients with COVID-19 who have diabetes and satisfactory glucose control have a lower risk of mortality compared with patients with poor glycemic control [7]. Another study found that COVID-19 diabetic patients with poorly controlled blood glucose may be associated with poor disease out comes [8].

In a contemporary study concluded that in diabetic patients admitted to hospital with COVID-19, the in-hospital mortality rate four-fold higher (28.8%) than that of patients with normal glucose level (6.2%) [9].

Method

This was a single centered, retrospective, observational type study. We enrolled all the admitted patients of Covid-19 illness during the period of 10 months who fulfilled inclusion criteria, that was age > 18, admitted with diagnosis of COVID-19 according to WHO guidelines without discrimination of severity of disease [10]. Age <18, those not diagnosed with covid-19 and pregnant ladies were excluded; we reviewed their bio-data, clinical record, laboratory details through specially designed Performa. Data collected included age, sex, BMI, known history of Diabetes (had recent Hba1c value > 6.5% [11], or patient was on hypoglycemic medication) hypertension, chronic kidney disease, chronic liver disease, chronic pulmonary disease, cerebro-vascular disease, and cardiovascular disease. Clinical symptoms at presentation like fever, fatigue, generalized weakness, diarrhea, headache, and cough, shortness of breath, chest pain, nausea and vomiting. Laboratory details were collected on admission, HBA1c, hematological parameters, kidney and liver function test, inflammatory markers, cholesterol levels and cardiac enzymes. Documented the Primary outcomes (discharged home or mortality). Lastly, Gathered patient management protocol during admission which were Secondary outcomes (Mechanical ventilation, dialysis, length of stay) of this viral illness. The study was approved by Institutional review board of Tabba Heart Institute (Reference no. THI/IRB/SQ/04-05-2021/088).

Statistical analysis

All data were entered and analyzed using SPSS version 22.0. The qualitative variables were presented as frequencies and percentages. Quantitative variables by mean $\pm$ SD Chi-square test were applied for categorical variables and student`s t-test for quantitative variables; p value of 0.05 or less was considered statistically significant.

Result

Table 1: Our study enrolled total 348 covid-19 suffering hospitalized patients. The mean age was 62 years, included 253 males and 95 females. Among them 204 patients had hypertension, 148 were having cardiovascular disease and 42 were suffering chronic kidney disease. Mostly patients were diabetics 212, and less numbers were non-diabetic 136.

The most common presenting symptoms of this illness were fever (74%), shortness of breath (61%) and cough (46.5%), but some patients presented with other symptoms too. Most of the sufferers were having complains less than 5 days (49.7%) and their hospital stay was short < 5 days (42.8%). During management of this hazardous viral illness 85% needed Glucocorticoid therapy, 76% supplemented

with oxygen, antiviral injection applied to 61% patients, application of noninvasive ventilation to 23.5% and invasive ventilation to 16% in total.

Table 1. Bio-data, Clinical presentation, Management and Outcomes of COVID-19 in Diabetics Vs Non-Diabetic

Population: COVID 19 Patients	**Total no. N=348**	**N=212, with Diabetes**	**N=136, without Diabetes**	**P values**
	- - - - - - - No. / [a]Mean, % / (Range) - - - - - - - -			
Demographic Information				
Age in years	62[a], (27 to 95)	62[a], (35 to 90)	62[a], (27 to 95)	0.95
Gender				
Female	95, 27%	53,25%	42, 31	0.23
Male	253, 73	159, 75	94, 69	0.23
BMI	29[a], (18 to 53)	29[a], (18 to 53)	28[a], (20 to 48)	0.27
Height in cm	162[a], (82 to 200)	163[a], (141 to 200)	162[a], (82 to 182)	0.24
weight in kg	76[a], (41 to 130)	77[a], (45 to 128)	73[a], (41 to 130)	0.02
Clinical presentation				
Fever	259, 74.43%	162, 76.42%	97, 71.32%	0.29
Fatigue	14, 4.02%	10, 4.72%	4, 2.94%	0.41
Generalized weakness	35, 10.06%	22, 10.38%	13, 9.56%	0.80
Headache	4, 1.15%	3, 1.42%	1, 0.74%	0.56
Diarrhea	34, 9.77%	21, 9.91%	13, 9.56%	0.92
Cough	162, 46.55%	86, 40.57%	76, 55.88%	0.02
Shortness of Breath	213, 61.21%	134, 63.21%	79, 58.09%	0.34
chest pain	49, 14.08%	30, 14.15%	19, 13.97%	0.96
nausea and vomiting	11, 3.16%	5, 2.36%	6, 4.41%	0.29
Any Other				
abdominal pain	2, 0.57%	1, 0.47%	1, 0.74%	0.47
Flu	4, 1.15%	1, 0.47%	3, 2.21%	0.47
Sore throat	4, 1.15%	2, 0.94%	2, 1.47%	0.47
Duration of COVID-19 illness				
above 10 days	84, 24.14%	45, 21.23%	39, 28.68%	0.23
between 5 to 10 days	91, 26.15%	60, 28.30%	31, 22.79%	0.23
less than 5 days	173, 49.71%	107, 50.47%	66, 48.53	0.23
Other Disease/Co-morbidities information				
Hypertension	204, 58.62%	142, 66.98%	62, 45.59%	0.00
Cardio-vascular disease	148, 42.53%	101, 47.64%	47, 34.56%	0.02

Cerebrovascular disease	13, 3.74%	8, 3.77%	5, 3.68%	0.96
Chronic Kidney Disease	42, 12.07%	37, 17.45%	5, 3.68%	0.00
Chronic pulmonary disease	22, 6.32%	15, 7.08%	7, 5.15%	0.47
Chronic Liver disease	6, 1.72%	5, 2.36%	1, 0.74%	0.26
Treatment of COVID-19 **illness**				
Length of hospital stay				
above 10 days	111, 31.90%	74, 34.91%	37, 27.21%	0.22
between 5 to 10 days	88, 25.29%	48, 22.64%	40, 29.41%	0.22
less than or up to 5 days	149, 42.82%	90, 42.45%	59, 43.38%	0.22
Antiviral therapy	215, 61.78%	126, 59.43%	89, 65.44%	0.26
Glucocorticoid therapy	296, 85.06%	179, 84.43%	117, 86.03%	0.68
Dialysis	29, 8.33%	23, 10.85%	6, 4.41%	0.03
Oxygen inhalation	266, 76.44%	163, 76.89%	103, 75.74%	0.80
NIV	82, 23.56%	50, 23.58%	32, 23.53%	0.99
IMV	57, 16.38%	39, 18.40%	18, 13.24%	0.20
Outcomes of patient's admission				
Discharge home	282, 81.03%	167, 78.77%	115, 84.56%	0.18
Mortality	66, 18.97%	45, 21.23%	21, 15.44%	0.18

An immense portion of study population was diabetic patients. As compared to non-diabetic patients, there were non-significant changes in age and gender but diabetic patients had statistically significant excessive weight with a mean weight 77 kg. Clinical presentation of COVID-19 was more or less similar in both groups but only cough was statistically significant which was found more in non-diabetic individuals. Diabetic patients found themselves to have more hypertension and more of them had chronic kidney disease.

During management of COVID-19 in these two groups, no difference was found except the need of dialysis which was more in diabetic patients. Primary Outcomes i.e. discharge to home and mortality was not found to be statistically significant.

Table 2. Investigational Parameters of COVID-19 in Diabetics Vs Non-Diabetics

Population: COVID 19 Patients	**Total no. N=348**	**N=212, with Diabetes**	**N=136, without Diabetes**	**P values**
	- - - - - - - Mean, (Range) - - - - - - -			
Laboratory parameters				
HbA1c %	7.80, (4.5 to 16.3)	8.51, (4.5 to 16.3)	6.25, (4.9 to 11.3)	0.00
Leukocyte count (109/L)	10.02, (2.1 to 37.2)	10.4, (3.1 to 37.2)	9.44, (2.1 to 24.2)	0.07
Lymphocytes (109/L)	15.66, (0.8 to 93)	15.35, (0.8 to 93)	16.14, (1.8 to 42.7)	0.51
Neutrophils (109/L)	76.73, (8.3 to 96)	77.13, (8.3 to 96)	76.1, (11.6 to 95)	0.48

Hemoglobin (g/dL)	12.59, (4.9 to 17.2)	12.32, (4.9 to 17.2)	13.02, (9.1 to 17.1)	0.00
CRP (mg/L)	121.10, (0.6 to 550)	127.12, (0.6 to 550)	111.71, (0.7 to 411)	0.23
LDH (U/L)	757.01, (11 to 3210)	758.54, (11 to 2665)	754.64, (172 to 3210)	0.94
Platelets (109/L)	269.81, (75 to 779)	270.91, (88 to 779)	268.1, (75 to 742)	0.82
Serum ferritin (ng/ml)	1297.79, (10.86 to 33511)	1396.58, (10.86 to 33511)	1144.79, (28 to 16875.5)	0.36
ESR (mm/hr)	24.75, (7 to 66)	21, (8 to 46)	27, (7 to 66)	0.73
D-dimer (mg/L)	2.19, (0.1 to 135)	2.92, (0.1 to 135)	1, (0.1 to 8.3)	0.07
ALT (u/l)	50.18, (5 to 506)	45.8, (5 to 506)	57.44, (6 to 214)	0.05
Alkaline phosphatase (u/l)	98.85, (17 to 373)	92.48, (17 to 373)	109.42, (25 to 348)	0.11
Albumin (g/dl)	3.33, (2.2 to 4.2)	3.34, (2.5 to 4.2)	3.3, (2.2 to 4.1)	0.86
Total Bilirubin (mg/dl)	0.54, (0.1 to 2.9)	0.49, (0.1 to 1.7)	0.63, (0.19 to 2.9)	0.06
LDL (mg/dL)	82.31, (25 to 304)	82.7, (25 to 304)	81.36, (25 to 154)	0.91
Cholesterol (mg/dL)	145.46, (67 to 369)	145.63, (76 to 369)	145.05, (67 to 223)	0.96
Triglyceride (mg/dL)	159.58, (9.1 to 1130)	158.43, (44 to 579)	162.48, (9.1 to 1130)	0.93
Creatinine (mg/dl)	1.44, (0.4 to 11.8)	1.6, (0.4 to 11.8)	1.19, (0.4 to 11)	0.01
Uric acid (mg/dL)	3.01, (0.6 to 9.3)	3.07, (0.6 to 9.3)	2.88, (0.8 to 5.9)	0.89
Urea nitrogen (mg/dL)	51.72, (9 to 255)	58.45, (9 to 255)	41.22, (11 to 172)	0.00
Procalcitonin (ng/ml)	2.68, (0.02 to 79)	3.22, (0.02 to 79)	1.82, (0.02 to 72.6)	0.18
Pro-BNP (pg./ml)	484.55, (0.03 to 10840)	581.26, (0.1 to 10840)	291.14, (0.03 to 2927)	0.01
Cardiac Troponin I (ng/ml)	4266.07, (0.1 to 294488)	5977.62, (0.1 to 294488)	1157.74, (0.2 to 29377)	0.07

In Table 2 among laboratory parameters HbA1c, leukocyte count, hemoglobin, creatinine, urea nitrogen pro-BNP were observed being high in diabetic as compared to non-diabetic.

Table 3. Bio-data, Co-morbidities and Management of COVID-19 in Survivors Vs Non Survivors

Population: COVID 19 Patients	**Total no. N=348**	**N=282, Survivors**	**N=66, Non-Survivors**	**P values**
	- - - - - - - no. / [a]Mean, % / (Range) - - - - - - -			
Demographic Information				
Age in years	62[a], (27 to 95)	61[a], (27 to 90)	68[a], (50 to 95)	0.00
Gender				
Female	95, 27.3%	79, 28.01%	16, 24.24%	0.54

Male	253, 72.7%	203, 71.99%	50, 75.76%	0.54
Diabetics	212, 60.92%	167, 59.22%	45, 68.18%	0.18
Duration of Covid-19 illness				
above 10 days	84, 24.14%	77, 27.3%	7, 10.61%	0.01
between 5 to 10 days	91, 26.15%	73, 25.89%	18, 27.27%	0.01
less than 5 days	173, 49.71%	132, 46.81%	41, 62.12%	0.01
Other Disease/Co-morbidities information				
Hypertension	204, 58.62%	158, 56.03%	46, 69.7%	0.04
Cardio-vascular disease	148, 42.53%	105, 37.23%	43, 65.15%	0.00
Cerebrovascular disease	13, 3.74%	10, 3.55%	3, 4.55%	0.70
Chronic Kidney Disease	42, 12.07%	29, 10.28%	13, 19.7%	0.03
Chronic pulmonary disease	22, 6.32%	18, 6.38%	4, 6.06%	0.92
Chronic Liver disease	6, 1.72%	3, 1.06%	3, 4.55%	0.05
Length of hospital stay				
above 10 days	111, 31.9%	71, 25.18%	40, 60.61%	0.00
between 5 to 10 days	88, 25.29%	78, 27.66%	10, 15.15%	0.00
less than or up to 5 days	149, 42.82%	133, 47.16%	16, 24.24%	0.00
Treatment of COVID-19 illness				
Antiviral therapy	215, 61.78%	162, 57.45%	53, 80.3%	0.00
Glucocorticoid therapy	296, 85.06%	233, 82.62%	63, 95.45%	0.00
Dialysis	29, 8.33%	10, 3.55%	19, 28.79%	0.00
Oxygen inhalation	266, 76.44%	200, 70.92%	66, 100%	0.00
NIV	82, 23.56%	43, 15.25%	39, 59.09%	0.00
IMV	57, 16.38%	13, 4.61%	44, 66.67%	0.00

In Table 3 out of the total 348 admitted patients of COVID-19, the majority were survivors 282 while 66 patients were non-survivors. Non-survivors were advanced in age, with a mean age of 68 years, and both the duration of illness and the length of hospital stay were found to be statistically significant. Patients who did not survive had more co-morbidity like hypertension, cardiovascular disease, and chronic kidney disease. In hospital management they needed extensive treatment as antiviral 80.3%, glucocorticoid therapy 95.4%, dialysis 28.7%, oxygen inhalation 100%, NIV 59% and IMV 66.6%.

Discussion

This study covered the whole clinical spectrum of this viral illness and at last it's outcome in all admitted patients. As it has been established prevalence of diabetes is alarmingly increasing in Pakistan factors are mainly genetic and sedentary lifestyle. Prevalence of generalized obesity was 57.9% and central obesity was 73.1% in Pakistan [12]. Our study also found most of the admitted COVID-19 patients were diabetic. It is believed that whatever may be the underlying cause, people who are having Diabetes mellitus are at an increased risk of severe and fatal COVID 19 disease. This

viral illness also makes patients more susceptible to hyperglycemia, this hyperglycemia changes immune and inflammatory responses, affecting people with COVID-19 and perhaps its deadly outcomes [13].

A Chinese study enrolled 1099 confirmed covid-19 patients in which 173 had severe disease; in those patients the presence of any coexisting illness was more common among patients with severe disease than with non-severe disease (38.7% vs. 21.0%) [14]. In our retrospective analysis, we found no significant changes in clinical presentation of both groups, about co- morbidities hypertension 66.9% and chronic kidney disease 17.4% were more in diabetic covid-19 patients. One other study also found diabetic individuals having more co-morbidity as compared to non-diabetic like hypertension 77.5%, renal diseases 13.6%, and liver problems [15]. We did not find significant labs changes expect Hemoglobin, leukocyte count, Creatinine, urea nitrogen pro-BNP these were found to be high in diabetic patients.

During hospital stay diabetic individuals did not need extra management as compared to non-diabetic, but they needed more dialysis. Mortality between diabetic and non-diabetic patients was not found to be statistically significant. In one prime study of China which studied 72,314 cases of this viral illness calculated higher mortalities in diabetic patients (7.3%) [16]. In one meta-analysis in which they analyzed total of 6452 patients from 30 studies, concluded that diabetes mellitus is related with higher mortality, severe COVID-19, ARDS, and disease advancement in patients with COVID-19 [17].

Strengths and limitations

The strength of our study comprises a good sample size of COVID-19 patients which were admitted in specially designed COVID-19 ward. It was a retrospective single-center observational study. Second there was lack of glycemic control stratification. Diabetes mellitus is a chronic disease and most of the patients had other co-morbidities too, so isolated effect of diabetes on this viral illness could not be determined. At last the potential for unmeasured confounding variable remains present.

Conclusion

Diabetic and non-diabetic patients shared the majority of clinical traits, test parameters and management of COVID- 19. Their outcomes were also largely similar. Non-survivors experienced a more complicated hospital course. Therefore, patients with co-morbid conditions were more vulnerable to infections and its complication. There is always a need to develop preventive and treatment strategies for these high-risk individuals to reduce morbidity and mortality.

Ethics Approval and Consent to Participate

The study was approved by Institutional review board of Tabba Heart Institute. (Reference no. THI/IRB/SQ/04-05-2021/088), it is a Retrospective study, therefore patient consent not applicable.

Human and Animal Rights

Not applicable

Consent for Publication

Not applicable

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

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Conflict of Interest
All authors declared that they have no potential conflict of interest.

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