

ORIGINAL ARTICLE

Severity and Mortality of Covid-19 in Patients with Diabetes MellitusMALIK FAYYAZ HUSSAIN AWAN¹, SARWAR MALIK², FATIMA QAYYUM³, QAISAR ALI⁴, ASAD MUNIR⁵, AIMAN ALTAF⁶¹Fellow endocrinology Capital Hospital CDA Islamabad²Consultant physician endocrinologist Capital Hospital CDA Islamabad³Fellow endocrinology Capital Hospital CDA Islamabad⁴PGR Pulmonology Ayub Teaching hospital Abbottabad^{5,6}MBBS, House Officer Shaikh Zayed Hospital, LahoreCorrespondence to: Malik Fayyaz Hussain Awan, Email: drfayaz92@gmail.com, Cell: +92 310 9373913**ABSTRACT**

Background: Covid-19 infection appeared as rapidly spreading cases of acute respiratory disease in Wuhan city of China that became pandemic. It was brought to the notice of WHO on December 31, 2019. Diabetes mellitus is one of the biggest health problems and fast growing emergencies of the 21st century. Diabetic patients with who got infected with Covid-19 have more chance of in hospital treatment need, intensive care unit care requirement, intubation and death.

Objective: The objective of this study was to know the severity and mortality of covid-19 in patients with diabetes mellitus.

Study Design: This was a descriptive case series study.

Study Setting: It was done in the Covid-19 isolation and ICU unit of Ayub Teaching Hospital Abbottabad from May 2020 to October 2021.

Methods: Using non-probability consecutive sampling, 189 diabetic patients were enrolled. Sample included all covid-19 patients having diabetes that received indoor treatment during this period. All patients from both genders with age > 18 years were included. Patients with malignancy or on immunosuppressants for more than 1 month were excluded. Patients who were maintaining oxygen saturation at room air/facemask/nasal prongs were labelled as having non-severe disease while patient who needed CPAP or assisted ventilation were labelled as having severe covid-19 disease. All patients who died during admission were documented as covid-19 related mortality. Patients were labelled as diabetic who were known diabetic and taking diabetes treatment. Data was collected on a structured pro forma. Statistical program SPSS version 16.0 was used for the analysis of data.

Results: In this study, mean age was 61.29 ± 11.73 years. There were 40.2% male and 59.8% female patients. 86.2% patients were not-vaccinated, 3.7% patients were partially vaccinated and 10.1% patients were fully vaccinated. Hypertension was most common comorbidity (42.3%) and only CKD was significantly associated with increased mortality. 43.92% patients had non-severe illness while 56.08% patients had severe illness. The overall mortality of illness was 48.15% while it was 84.9% in patients with severe illness.

Practical implication: These published publications provide a variety of various estimations and impact amounts due to the numerous different study designs and demographics. A comprehensive and methodical study is required because of the unpredictability of the situation. So that we conducted this study to assess the severity and mortality of covid-19 in patients with diabetes mellitus

Conclusion: Our study concluded that severity and mortality of covid-19 was high in diabetic patients with high fasting & random sugar levels, pack smoking years and low oxygen saturation.

Keywords: Covid-19, diabetes mellitus, severity, mortality. Severity and mortality of Corona virus infectious disease-19 in patients with diabetes mellitus

INTRODUCTION

Covid-19 is a phrase that quotes for corona virus disease of 2019. It is a viral illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It came to notice as a rapidly spreading illness of respiratory tract Wuhan City, China. It was brought to the notice of World Health Organization (WHO) on December 31, 2019. World Health Organization (WHO) had given the name of covid-19 to this illness on Feb 11, 2020.¹ It is infection of respiratory tract that present with fever, cough, dyspnea, body aches, nasal congestion, runny nose, sore throat or diarrhea. The symptoms of disease appear within 14 days of infection. The illness varies from asymptomatic to mild or severe disease. It is categorized accordingly as uncomplicated illness, pneumonia, ARDS, sepsis and septic shock. Covid-19 is diagnosed through polymerase chain reaction (PCR) done on nasopharyngeal/oropharyngeal swab, antigen testing on nasopharyngeal/oropharyngeal swab, antibodies titer in blood and covid-19 pneumonia can be diagnosed by using High resolution computerized tomography (HRCT) chest.² 608.33 million confirmed cases were reported around the globe with 6.5 million deaths. In Pakistan, 1.57 million cases reported with 30,604 deaths till now.³

Diabetes mellitus is one of the biggest health issues and fast growing emergencies of the 21st century. The worldwide increase in number of diabetes cases has caused rise in health care expenses.⁴ 537 million people are having diabetes as per estimate in 2021 and it will reach to 643 million by 2030, and 783 million by 2045. A high percentage (45%) of people remains undiagnosed.^{2,5} Different studies showed that diabetes is present in 5-20% of

patients infected with Covid-19.⁶ Patients with diabetes who got infected with Covid-19 have more chance of in hospital treatment, admission to intensive care unit and assisted ventilation requirement. Patients with diabetic have more deaths due to Covid-19 infection. Covid-19 patients who have good glycaemic control are at lesser chance of death as compared to patients with poor control. Many research studies suggested the independent association of diabetes with Covid-19-related mortality.⁷

There are many postulated pathogenic mechanisms of diabetes related higher severity and mortality including modulation of immune response, presence of associated illnesses and angiotensin converting enzyme 2 (ACE2) expression modulators. Risk of severe to critical illness is 14 to 32% in covid-19 patients with diabetes. An overall mortality ratio of covid-19 was reported as 2.3% in comparison to 7.3% for diabetes patients.⁷

The objective of the study is to assess the severity and mortality of covid 19 in patients with diabetes As this is an under addressed aspect in the treatment & care of covid-19 patients in our region and outcome will lead to device meaningful interventions at planning, management and care provision level.

MATERIALS AND METHODS

This study was descriptive case series. It was conducted in the Covid-19 isolation and ICU unit of Ayub Teaching Hospital Abbottabad from May 2020 to October 2021. Through non-probability consecutive sampling, 189 diabetic patients were included in study. All patients with age >18 years, who were admitted during this period were included. Those patients who

were diagnosed cases of malignancy or taking immunosuppressant drugs for more than 1 month were excluded from the study. Patients were labelled as diabetic when diabetes mellitus was known from their history or from their previous documents, they were already on anti-diabetic medications, they had raised blood glucose (>200 mg/dl) on presentation or on previous laboratory reports. Covid-19 was diagnosed by using PCR on nasopharyngeal swab and high resolution computerized tomography (HRCT) chest. Patients who were maintaining oxygen saturation at room air/facemask/nasal prongs were labelled as non-severe while patient who needed CPAP or assisted ventilation were labelled as have severe covid-19 disease. All patients who died during admission were documented as covid-19 related mortality.

Data was collected on a systematic pro forma after approval from hospital administration and permission from Ethical Committee of the institution. Informed consent was taken from every conscious patient and from the attendants of unconscious patient after full explanation of study work. Detailed history was taken regarding diabetes, antidiabetic medication use, previous sugar test reports, co-morbidities' presence & duration. Blood samples were taken for evaluation of the glycemic control(fasting and random blood sugar). Nasopharyngeal swab was taken for covid-19 PCR (if not done before admission) and HRCT chest was done if indicated.

Statistical program SPSS version 16.0 was used for data entry and analysis. Gender, presence or absence of co-morbidities, need for ICU care & ventilation, covid-19 severity and mortality were presented as frequencies and percentages. Age, blood sugar levels, diabetes duration, comorbidities' duration, inflammatory markers level, cell counts, ALT , creatinine, duration of stay in hospital was reported in terms of mean ± standard deviation. Covid-19 severity and mortality was stratified by its type, gender and age. Post stratification Chi-square test was applied at 5% level of significance.

RESULTS

In our study, 189 patients of diabetes mellitus who were admitted with Covid-19 were enrolled having ages more than 18 years. The mean age was 61.29 ± 11.73 years. There were 76 (40.2%) male and 113 (59.8%) female. Out of 189, 2 (1.1%) patients had type 1 DM and 187(98.7 %) had type 2 DM. 163(86.2%) patients were not-vaccinated, 7(3.7%) patients were partially vaccinated and 19(10.1%) patients were fully vaccinated. 146(77.2%) patients have positive PCR while 43(22.8%) patients have negative Covid - 19 PCR (diagnosed on HRCT chest). Hypertension was most common co-morbidity and was 42.3 %. Smoking was present in 23.3%, ischemic heart disease was present in13.2%, kidney disease was present in 5.8% and chronic respiratory illness was present in 2.7%. 83(43.92%) patients had non-severe Covid-19 while 106(56.08%) patients had severe Covid-19. The mortality of Covid-19 was (48.15%) 91 (Results shown in table1).

ICU care was required by 107(56.6%) patients and only 84(44.4%) patients received ICU care. 106 patients were admitted in ICU due to severe covid-19 while 1 patient was admitted due to acute decompensation of chronic kidney disease and need of hemodialysis. Out of 106 patients of severe covid-19 admitted in ICU, 91 patients required assisted ventilation but due to limited resources, it was available for only 16 patients. Out of 16 patients who received assisted ventilation only one patient survived. Out of 91 covid-19 patients who died, 1 patient died during management of renal failure with non-severe covid disease. Mortality in severe covid-19 was 84.9% (90/106) while overall in hospital covid-19 mortality was 48.14% (91/189) (results shown in table 2).

Gender, age, type & duration of diabetes, vaccination status and presence & duration of comorbidities except CKD were not significantly associated with severity and mortality of covid-19. CKD which was significantly associated with increased mortality. Severity and mortality was significantly associated with high average fasting sugar, high random sugar, pack years of smoking, low oxygen saturation and have more stay duration in hospital (shown in table 3 & 4).

Table 1: Demographic profile and their severity and mortality

S.No	Variable	Frequency	Percentage	Covid severity P-value	Covid mortality P-value	
1	Gender	Female	113	59.8	0.809	0.676
		Male	76	40.2		
2	Age groups	20-40	10	5.3	0.309	0.104
		40-60	89	47.1		
		60-75	71	37.6		
		>70	19	10		
3	Type of diabetes	Type 1 diabetes	2	1.1	0.897	0.958
		Type 2 diabetes	187	98.9		
4	Vaccination status	Not vaccinated	163	86.2	0.231	0.125
		Partially vaccinated	7	3.7		
		Fully vaccinated	19	10.1		
5	Covid-19 PCR	Positive	146	77.2		
		Negative	43	22.8		
6	HRCT chest	Not done	74	29.2		
		Done and positive	115	60.8		
7	Hypertension	Present	81	42.8	0.239	0.108
		Absent	108	57.2		
8	Smoking	Present	44	23.3	0.532	0.646
		Absent	145	76.7		
9	Ischemic heart disease	Present	25	13.2	0.203	0.672
		Absent	164	86.8		
10	Chronic kidney disease	Present	11	5.8	0.040	0.174
		Absent	178	94.2		
11	Chronic lung disease	Present	5	2.7	0.591	0.858
		Absent	184	97.3		
12	Severity of Covid-19	Non-Severe	83	43.92		
		Severe	106	56.08		
13	Mortality	Discharged	98	51.85		
		Deaths	91	48.15		

Table 2: ICU care and covid-19 severity and mortality

S.no		Non-severe	Severe	Discharged	Deaths	
1	ICU care required for the patients	Yes	1	106	16	91
		No	82	0	82	0
2	ICU care received by the patient	Yes	1	83	15	69
		No	82	23	83	22
3	Patient required assisted ventilation	Yes	0	91	1	90
		No	83	15	97	1

Table 3: Covid-19 severity

	Severity of Covid-19		N	Mean	P value
	Non-severe	Severe			
Age of the Patients	Non-severe	Severe	83	60.30±12.20	0.309
	Severe	Non-severe	106	62.06±11.36	
Duration of diabetes	Non-severe	Severe	83	7.07±5.98	0.728
	Severe	Non-severe	106	7.34±6.07	
Average fasting blood sugar levels during admission*	Non-severe	Severe	83	177.19±38.52	0.001*
	Severe	Non-severe	106	199.20±51.08	
Average random blood sugar during admission*	Non-severe	Severe	83	289.94±63.32	0.031*
	Severe	Non-severe	106	311.16±69.03	
Duration of hypertension in the patients	Non-severe	Severe	83	3.65±5.85	0.073
	Severe	Non-severe	106	2.30±4.42	
Pack years of smoking*	Non-severe	Severe	83	0.98±2.68	0.014*
	Severe	Non-severe	106	2.50±5.06	
Duration of ischemic heart disease in patients	Non-severe	Severe	83	0.37±1.40	0.805
	Severe	Non-severe	106	0.42±1.45	
duration of chronic kidney disease	Non-severe	Severe	83	0.07±0.287	0.345
	Severe	Non-severe	106	0.035±0.228	
duration of chronic lung disease in patients	Non-severe	Severe	83	0.11±0.699	0.526
	Severe	Non-severe	106	0.21±1.28	
maximum Oxygen saturation on most invasive Modality*	Non-severe	Severe	83	92.90±2.230	0.000*
	Severe	Non-severe	106	76.90±12.82	
Total stay in hospital till the end of treatment*	Non-severe	Severe	83	6.86±4.56	0.002
	Severe	Non-severe	106	9.71±7.24	

Table 4: Covid-19 mortality

	End treatment result of the patients		N	Mean	P value
	Discharged	Death in hospital			
Age of the Patients	Discharged	Death in hospital	98	59.95±12.0	0.104
	Death in hospital	Discharged	91	62.73±11.30	
Duration of diabetes	Discharged	Death in hospital	98	7.31±6.0	0.879
	Death in hospital	Discharged	91	7.17±6.0	
Average fasting blood sugar levels during admission*	Discharged	Death in hospital	98	180.63±40.20	0.007*
	Death in hospital	Discharged	91	199.12±52.20	
Average random blood sugar during admission*	Discharged	Death in hospital	98	290.31±61	0.014*
	Death in hospital	Discharged	91	314.26±71.7	
Duration of hypertension in the patients	Discharged	Death in hospital	98	3.49±5.70	0.098
	Death in hospital	Discharged	91	2.25±4.4	
Pack years of smoking*	Discharged	Death in hospital	98	1.12±2.84	0.015*
	Death in hospital	Discharged	91	2.62±5.30	
Duration of ischemic heart disease in patients	Discharged	Death in hospital	98	0.31±1.30	0.398
	Death in hospital	Discharged	91	.49±1.56	
duration of chronic kidney disease	Discharged	Death in hospital	98	0.082±0.33	0.076
	Death in hospital	Discharged	91	0.017±0.12	
duration of chronic lung disease in patients	Discharged	Death in hospital	98	0.092±0.65	0.333
	Death in hospital	Discharged	91	0.24±1.38	
maximum Oxygen saturation on most invasive Modality*	Discharged	Death in hospital	98	92.82±2.70	0.000*
	Death in hospital	Discharged	91	74.34±11.92	
Total stay in hospital till the end of treatment*	Discharged	Death in hospital	98	7.51±5.12	0.033
	Death in hospital	Discharged	91	9.48±7.37	

DISCUSSION

In our study, mean age was 61.29 ± 11.73 years including 76 (40.2%) male and 113 (59.8%) female. Corona G et al reported mean age of 60.9±8.2 years and 57.7±13.5% were male.⁸ Mean age was similar to our study but female patients were more in our study. Woolcott O et al reported 52.1% male patients with mean age of 44 years.⁹ Patients in our study had higher mean age and female patients. In our study 2 (1.1%) patients had type 1 DM and 187(98.7 %) had type 2 DM. Study done by Tamura et al reported similar % of type 1(2.65%) and type 2 diabetes (97.35%) m in studied population.¹⁰ In our study, 163(86.2%) patients were not-vaccinated, 7(3.7%) patients were partially vaccinated and 19(10.1%) patients were fully vaccinated. Butt et al reported that 18.7% peoples were not-vaccinated.¹¹ In comparison to this study, we have very less population vaccinated, may be due to availability of vaccine a later stages of study duration. Ashby et al. study showed 79% patients unvaccinated, 7% had single dose vaccination, and 14% had second-dose vaccination.¹²

The vaccination status results of this study were comparable to our study. Li et al showed that 15.1% patients were not-vaccinated, 7.3% were partially vaccinated, 63.6% were fully vaccinated and 14.0% received a booster dose.¹³ These differences in vaccination status may be due to availability or other safety concerns. In our study, hypertension was present in 42.3%, ischemic disease was 12.22%, chronic lung disease was 2.63%, chronic kidney disease was 5.75% and smoking was present in 23.3%. Hypertension was most common comorbidity. Corona et al (40.8%), Sanyaolu et al, Tamura et al (31.5%) and Woolcott et al.

(14.2%) showed hypertension as most common comorbidity.^{8, 14, 10, 9}

Our study showed that severity and mortality related to covid-19 was not associated with age, gender, type of diabetes, covid-19 vaccination status, associated co-morbidities like hypertension, ischemic heart disease, chronic lung disease and their duration. Corona et al. also reported that age and gender were not associated with increased mortality.¹ Study of Iccarino et al. reported that hypertension is not significantly associated with covid-19 mortality.¹⁵ The results of both these studies are consistent with our study. Zhao et al. showed that COPD is strongly associated with mortality in covid-19 patients.¹⁶ De Almeida-Pititto et al reported that cardiovascular disease and hypertension are strongly associated with increased Covid-19 severity and mortality.⁷ Pranata et al. demonstrated that hypertension was associated with covid-19 severity and mortality.¹⁷ Wang et al. reported that comorbidities like hypertension, diabetes, COPD, cardiovascular disease, and cerebrovascular disease are significantly associated with covid-19 severity and mortality.¹⁸ The result of these studies are contrary to our study where hypertension, COPD and cardiovascular disease are not significantly associated with covid-19 severity and mortality which may be due to geographical or ethnic differences. Our study showed that high average fasting sugar, high random blood sugar, high smoking pack year and low oxygen saturation values has statistically significant association with covid-19 severity and mortality. Zhu et al. reported that well-controlled blood glucose was associated with lower mortality compared to patients with poorly controlled blood glucose during stay in hospital.¹⁹ These results

were similar to our study. Data from a British hospital and Bode et al. showed that there is higher mortality risk in patients with uncontrolled diabetes.^{20,21} High blood glucose on admission lead to worse prognosis.^{22, 23, 24}

Chances of disease severity and mortality are higher in diabetic patients. [25] Presence of diabetes can be best prognosis predictor of covid-19 related outcome.^{26, 27} Singh AK et al reported that uncontrolled hyperglycemia and low oxygen saturation in diabetic patients is associated with higher mortality.²⁸ Results of all these studies are consistent to our study and show presence of diabetes and uncontrolled hyperglycemia are associated with increased severity and mortality.

CONCLUSION

This study concludes that severity and mortality of covid-19 patients was high in diabetics, especially with poor glycemic control, pack smoking years and low oxygen saturation.

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