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Original Article

Outcomes in Critical COVID 19 Infection Affected by Pre-Existing Diabetes Mellitus

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Abstract

Objective: To determine the effect of pre-existing diabetes mellitus on disease course in COVID-19 infection.

Methods: This retrospective observational study was done from Jan 2021 to August 2021. We included patients with COVID-19 infection having a positive PCR for SARS-CoV-2. Exclusion criteria included missing data or a negative PCR for SARS-CoV-2. Patients were selected using consecutive sampling. Length of stay and death within hospital were compared amongst diabetic and non- diabetic patients.

Results: The 279 patients were aged 52.53± 11.31 years. Of these, 216 (77.42%) were males and 92 (32.97%) had diabetes. They remained admitted for 10.18± 3.13 days. The period of hospitalization was similar in diabetics and non- diabetics (10.70± 3.51 days vs 9.92± 2.91 days; p=0.052). Amongst the diabetics, 43(46.74%) died in hospital in comparison with 53 (39.55%) non- diabetics (p=0.002). The risk of in-hospital death in diabetics was 1.673 (95% CI 1.207 - 2.319).

Conclusion: Diabetes mellitus is linked with greater risk of death, longer duration of hospital stay and higher need for critical care and novel therapy in COVID-19 infection.

Keywords: hospital stay, mortality, pandemic, pneumonia

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Introduction

The ongoing COVID 19 pandemic is a huge global challenge caused by SARS-CoV.[1] Corona virus is RNA enveloped virus broadly distributed in human, birds and animals that causes diseases involving respiratory, gastrointestinal and neurological systems.[1] There are six species known to cause diseases in humans, some of which frequently cause common cold, whereas others are zoonotic in origin and could even lead to severe/ critical illness.[1] A study done in China during the early phase of COVID-19 pandemic revealed that diabetes mellitus was one of the most common co-morbidities in patients with SARS-CoV infection.[2] It also increased the risk of acquiring this disease as well as the severity of infection, leading to a higher morbidity and mortality. The potential mechanisms for this cause and effect relationship include an exaggerated inflammation and deregulated immune response, angiotensin converting enzyme 2 (ACE 2) expressions and abnormal activity, vascular dysfunction and thrombotic states, anti-diabetic drugs interaction with ACE 2 expression.[3] We now have very strong proof to suggest that diabetic patients have a much higher chance of developing complications such as acute respiratory distress syndrome necessitating shifting to critical care units and also having higher chances of death due to COVID-19 infection.[4] Diabetes mellitus could thus be used as a marker of severity of disease and could even foretell the outcomes.

In many other illnesses, we have ample evidence to suggest that our patients behave differently from those in developed countries because of ethnic, racial and environmental factors. At the time of this study was planned, it was not clear whether this would hold true for COVID 19 infection as well. We therefore carried out this study to compare in-hospital mortality, duration of hospital stay, need for intensive/ critical care and novel therapy for COVID-19 infection in diabetic and non-diabetic patients. The results would help us to identify and manage the patients with greater risk of high mortality, hospital stay, need for intensive care and novel therapy.

Methods

This retrospective observational study was done on patients with COVID-19 pneumonia treated indoor from Jan 2021 to August 2021. Ethics Review Committee of this hospital ratified the study protocol beforehand. A positive PCR for SARS-CoV-2 was required to establish the diagnosis of COVID-19 infection. Sample size calculation was done using EpiTools Epidemiological Calculators. There was a requirement for a minimum of 117 patients, including 59 diabetics and 118 non- diabetic patients. This estimation was based on statistics from a study by Hui et al, in which mortality rates of 80% and 58% were quoted for diabetic and non- diabetic patients with severe COVID-19 infection respectively.[5] Ratio of sample sizes was set at 2, power 80% and confidence level of 95% with a 2 tailed test.

Patients with negative PCR for SARS-CoV-2, incomplete data and leaving against medical advice were excluded from the study. Physical medical notes of all patients with severe/critical disease who satisfied the selection criteria were consecutively evaluated. Clinical disease severity was gauged using World Health organization interim guidance on clinical management of COVID-19.6 Length of stay and death within hospital as well as need for intensive/ critical care and novel therapies were compared amongst diabetic and non-diabetic patients. Data was analyzed using SPSS version 24. Independent samples t-test and Chi square tests were used for comparison of continuous and categorical variables respectively, with a level of significance set at <5%.

Results

There were 279 patients aged 52.53± 11.31 years. Of these, 216 (77.42%) were males and 92 (32.97%) had diabetes. The most prevalent co-morbidity in our cohort was hypertension, as shown in Figure 1. They remained admitted for 10.18±3.13 days. The period of hospitalization was similar in diabetics and non- diabetics (10.70 ± 3.51 days vs 9.92± 2.91 days; p=0.052). Overall mortality rate was 34.41% (96 patients). Amongst the diabetics, 43 (46.74%) expired in hospital. Of the 187 non-diabetics, 53 (39.55%) expired. This difference

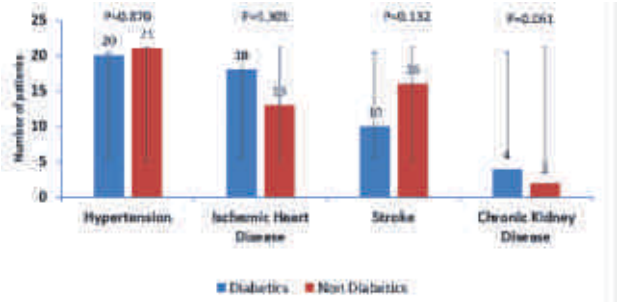

Figure 1: *Frequency of Co-Morbidities*

was statistically significant (p=0.002). Hazard ratio for in- hospital death amongst diabetics was 1.673 (95% CI 1.207, 2.319). Requirement for intensive care was similar amongst diabetics (38; 41.30%) and non- diabetics (68; 36.36%) (p=0.424). Need for novel therapies amongst the two groups is shown in Table I.

Table 1: *Need for Novel Therapy*

Type of novel therapy	Diabetics (n=92)	Non-diabetics (n=187)	p value
Plasma exchange	25 (27.17%)	39 (20.86%)	0.238
Remdesivir	55 (59.78%)	146 (78.07%)	0.001
Tocilizumab	21 (22.83%)	21 (11.23%)	0.011

Discussion

In this study, we studied the effect of type 2 diabetes mellitus on COVID-19 infection in terms of in hospital mortality, duration of stay in hospital, need for intensive care and novel therapies. Our results showed that the fatality ratio was higher in diabetics in contrast to non-diabetics. There was a trend towards longer hospital stay in diabetic patients, though this was statistically insignificant. The need for intensive care and novel therapies was also higher in this group pf patients. Diabetes mellitus results in high morbidity and death in patients infected by SARS-CoV. The different mechanisms responsible for this phenomenon include exaggerated inflammation and deregulated immune response, angiotensin converting enzyme 2 (ACE 2) expressions and abnormal activity, vascular dysfunction and thrombotic states, anti-diabetic drugs interaction with ACE 2 expression.[4]

The most prevalent co-morbidity in our cohort was hypertension. This is similar to what has been reported elsewhere in the recent past. As an example, in a metanalyses of seven studies involving 1576 patients, Yang et al have documented hypertension to be the commonest comorbid condition, present in in 21% patients.[7] Similar statistics have been reported in many other studies as well.[8] Mortality rate in our cohort was high in diabetics as compared to non-diabetics. Amongst 7337 patients in Hubei (China), Zhu et al have described a death rate of 7.8% amongst patients with type 2 diabetes mellitus and 2.7% in those without diabetes. The former group had 1.49 times higher risk of dying from the disease.[9] Similarly, amongst 1122 American patients, Bode et al have documented mortality rates of 28.8% amongst patients with diabetes mellitus or uncontrolled hyperglycemia as compared to and 6.2% in euglycemic patients. The interplay between these two pandemics (type 2 diabetes mellitus and COVID-19) has been highlighted in detail in a narrative review by Azar et al.[11]

The duration of hospital stay was equal amongst diabetic

and non- diabetic patients. Bode et al have reported a longer duration of hospital stay (average 5.7 days) in patients with poorly controlled diabetes suffering from COVID-19 infection as compared to 4.3 days amongst those without diabetes in United States.[10] Amongst 461 patients from Wuhan (China) reported upon by Zhang et al, the median duration of admission to hospital was higher in diabetic patients (16 versus 12 days).[12]

A higher proportion of diabetic patients in our study required intensive care. This is not surprising as similar statistics have been reported previously.[13] As per the results of Roncon et al, amongst 1372 COVID-19 patients from Italy, those with type 2 diabetes had 2.79 times higher chances of requiring admission to critical care units.[14] We used remdesivir and tocilizumab more frequently in patients with co-existent diabetes mellitus. This might simply be a reflection of more severe disease in this sub-groups of patients. The deregulated inflammatory response, increased vascular permeability, thromboembolic states and oral hypoglycemic medications interaction in patients with co-existent type 2 diabetes and COVID-19 infection are responsible for their disease severity, thus increasing the need for novel therapy in diabetics.[3]

In our study, gender bias could not be eliminated as most of the patients in our cohort were males but different throughout the globe have shown that mortality rate is high amongst males due to SARS-CoV is high is compared to females. Study of Williamson EJ showed that risk of mortality due to COVID-19 was 2 times higher in males as compared to females.[15] Our study had certain limitations. It was a retrospective study so that proving a cause-and-effect relationship remains difficult. Patients with incomplete data were excluded from the study, which reduced our sample size significantly. Other limitations include an inability to correlate the outcomes with the level of glycemic control. We also did not consider other confounding factors responsible for mortality in our cohort.

Conclusion

Pre-existing diabetes is associated with higher mortality rates, longer duration of hospital stay, high need of intensive care and novel therapy in COVID-19 infection.

Disclosure

This data was presented in the 19th Pakistan Endocrine Society Annual Conference held at Islamabad in November 2021, and subsequently published as an abstract in Khyber Medical University Journal.[16]

Conflict of Interest: *None*

Funding Source: *None*

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