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Original article:

Relation of diabetes mellitus with mortality in COVID 19 hospitalized patients: A retrospective study

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Abstract:

Introduction: Diabetes mellitus (DM) is a chronic metabolic condition. It causes many changes in the normal functioning of the body. There are reports that COVID 19 mortality is more in those with comorbid diabetes mellitus. The study aims to find the association between DM and COVID19 mortality.

Methods: This is a retrospective cohort study conducted in a tertiary care hospital dedicated to COVID19 treatment. A total of 332 patients admitted during the month of august 2020 were analyzed. Data was analyzed using R language to meet the study objectives.

Results: There is significant association between age ($p < 0.001$), diabetes mellitus (0.010), random blood sugar ($p= 0.007$) and HbA1C ($p < 0.001$) with the COVID19 mortality. As age ($r= -0.300$), RBS ($r= -0.146$) and HbA1c ($r= -0.322$) levels increase there is more chances of mortality. Similarly, the diagnosis of diabetes mellitus ($r= -0.136$) is correlated with increased chances of mortality.

Conclusions: The study finds a link between the presence of diabetes mellitus and mortality associated with COVID19. There are other variables which need to be taken into consideration along with diabetes mellitus in the mortality.

Keywords: diabetes mellitus, mortality, COVID 19, SARS-CoV-2.

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1. Introduction:

Coronaviruses belong to a Coronavidridae family and are named after their 'crown-like' appearance in electron microscope. They transmit by airborne droplets, which get deposited in the nasal mucosa and replicate in cells of ciliated epithelium. Once in the host body, they cause symptoms resembling common cold.[1] In the past they were associated with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). The current virus implicated is a novel one, hence called as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 or COVID 19).[2]

It was identified as the causative agent of respiratory infection in Wuhan city of China. The infection spread like a wild fire and within few days crossed continents. With thirteen fold speed of spread and number countries being affected tripled, the World health organization (WHO) declared the COVID 19 as pandemic.[3] India noted a steady increase in the cases starting from 28th of January 2020, reaching peak daily new cases of more than 90,000 in a single day during August-September 2020. The cases started to decline in the succeeding months to less than 20,000 per day in December 2020.[4]

COVID 19 being a novel virus, our understanding about the disease characteristics was limited in the beginning. As the cases started increasing, so was our knowledge about the disease. Many risk factors were found to be associated with prognosis and outcome. Among the different risk factors, diabetes mellitus was thought to be associated with poorer outcomes. Research done elsewhere has found an association between diabetes mellitus and COVID 19 mortality. But there are a lot of variations in presentation and outcomes in different geographic regions making these findings not generalisable to our Indian population. We have learnt and still learning about multiple facets of COVID 19 infection. To the best of our knowledge similar studies are scarce in our Indian population. This study is an attempt to fill this gap.

2. Methods and Materials:

2.1. Aims of the study: To study the association of diabetes mellitus with mortality in COVID 19 hospitalized patients.

2.2. Study details: We conducted a retrospective cohort study. The study was started after obtaining the approval from the ethics committee, patients admitted during the month of august 2020, with the positive diagnosis for COVID19 were included. During the time of admission, a brief history of diabetes mellitus is noted down and patients were subjected to a battery of investigations as a routine protocol. These tests include the random blood sugars (RBS), HbA1c (only in those who mention as diabetic), liver function tests and serum creatinine. Patients were also subjected to variety of other tests like inflammatory markers, arterial blood gas analysis etc, but as our study objective was to see the diabetes mellitus association with the mortality, these were not included.

2.3. Statistical analysis: The data obtained from the case sheets were tabulated in to Microsoft excel sheet. The excel sheet was then analyzed using R language version 4.0.3[5] and R studio[6] was used as Integrated development environment (IDE). R is an open source software used for statistical analysis. The packages used were "summaryTools"[7], "dplyr"[8] and "DescTools"[9]. The data was analyzed to obtain mean, standard deviation, range and percentages where ever necessary for tabulation. As the data was not normally distributed, non-parametric tests

like wilcoxsan sign rank test, kruskal wallis test, fischer exact test and spearman (point biserial method) correlation were used. The p value of 0.05 was considered as significant with 95% confidence interval.

3. Results:

A total of 332 admitted patients were included in the study. The mean age of the sample was 49 years with the minimum being 12 years and the maximum being 86 years. Males constitute 70% of the sample. The mean Random Blood Sugar (RBS) was 190 mg/dl with a range of 52 mg/dl to 587 mg/dl. Among the patients, 179 (54%) had a diagnosis of diabetes mellitus at the time of admission and 32 (9.6%) had expired due to COVID 19 related mortality.

Comparison of variables with COVID19 outcome (Table 1): There is significant association between the variables: age, diabetes mellitus, random blood sugars (RBS) and HbA1C with the mortality.

Table 1: Comparison of variables with COVID19 outcome.

Sl. No	**Variable**		**Outcome**		**p- value**
			Death	**Discharged**	
1	Age (years)	< 20	0	5 (1.7%)	< 0.001*
		21 – 35	0	69 (23%)	
		36 – 50	5 (15.6%)	87 (29%)	
		51 – 65	15 (46.9%)	103 (34.3%)	
		> 65	12 (37.5%)	36 (12%)	
2	Gender	Male	24 (75%)	208 (69.3%)	0.644
		Female	8 (25%)	92 (30.7%)	
3	Diabetes Mellitus	Present	24 (75%)	156 (52%)	0.010*
		Absent	8 (25%)	144 (48%)	
4	RBS (mg/dl)		211.80 (73.6)	184 (101.6)	0.007*
5	HbA1C		7.6 (0.51)	6.3 (0.23)	< 0.001*

Test used: Wilcoxsan sign rank and Kruskall wallis, *p < 0.05 is considered significant

Correlation between the variables and the COVID19 mortality (Table 2): The COVID19 outcome is a categorical variable hence spearman point biserial correlation was used. Outcome which was either death or discharge was recoded as “0” or “1” respectively and analysed. Based on this; as age, levels of RBS and HbA1C increase there is more chances of COVID19 related mortality. Similarly the diagnosis of diabetes mellitus is associated with increase in COVID19 mortality.

Table 2: Correlation of variables with the COVID19 outcome

Sl. no	Variable	Correlation coeff (r)	p- value
1	Age	-0.300	<0.001*
2	RBS	-0.146	0.007*
3	Diabetes Mellitus	-0.136	0.012*
4	HbA1C	-0.322	< 0.001*

Test used: spearman point biserial, *p < 0.05 was considered significant

4. Discussion:

Diabetes mellitus is one of the major risk factor contributing to the COVID 19 adverse outcomes. In the study we found nearly half of the deaths occurring in the age group of 51 to 65 years, which is in line with a study done in Hong Kong, who found that mortality rates among those aged above 75 years was higher than mortality due to cardio vascular and cancer.[10] In the study, mortality was 13% among those diagnosed to have diabetes mellitus and 5% among non diabetics. Previous studies have found that the history of diabetes in presence of other influenza infections increases the mortality to nearly two to three times. [11,12] Recent studies among COVID 19 infections, have found the presence of diabetes to be associated with odds ratio ranging from 2.85 to 3.14 with mortality. [13,14]

In the study, mean blood sugar levels were elevated among the diabetics (257 mg/dl versus 102 mg/dl among non diabetics) as well as those in whom the end outcome was death. This indicates elevated blood sugar could have contributed to the adverse outcome. Zhang et al [14], found that even a mild elevation in fasting sugar levels (100 mg/dl to 124 mg/dl is associated with increase in mortality. There is also a negative correlation between blood sugar levels and HbA1c levels with the mortality. Wu et al [15] reported that higher rates of acute respiratory distress syndrome (ARDS) among diabetics. Previous studies have discussed various factors regarding this association; first, diabetes patients usually have other co morbid diseases like hypertension, cardio vascular disease and kidney injuries; second, diabetes patients also have poor immune response, increase in pro inflammatory reactions and metabolic abnormalities which could have contributed to the worse outcome; third, diabetics are easily susceptible to co infections. [15,16]

In the study we found HbA1c among those who have expired to be 7.6 versus 6.3 among discharged. These findings are similar with the study done by Liu et al [17], who have compared the HbA1c between diabetes and non diabetes. They found mean HbA1c levels of 8.1 among diabetics and 6.3 among non-diabetics. In our study, there is a relatively higher HbA1c levels among those who have succumb to death due to COIVD19 than those were discharged. HbA1c is an indicator of the glycemic control and reflects the glycemic history over the past two to three months. There are studies which indicate that this is also linked with long term diabetes related complications especially with coronary heart disease.

Conclusions:

The study finds that the presence of diabetes mellitus is associated with increase in mortality among COVID 19 infected patients. Further studies should focus on robust study design to establish the cause and effect relationship in our population.

Limitations:

The study has concentrated on the association of diabetes mellitus and mortality in COVID 19 patients. We were unable to collect information on the type, duration and medications being used for of the management for diabetes mellitus because of the restrictions in managing the cases. We did not include inflammatory markers in the study which would have given a bigger picture in our understanding.

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