

Original Article

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Diabetes Mellitus Associated with Outcome of COVID-19 Patients.

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Abstract:

Introduction: COVID-19 is a highly infectious disease spreading all over the world since its appearance causing enormous sufferings and loss of human life specially among those who have suffered from Diabetes Mellitus.

Material & method: This retrospective cohort study was conducted among purposively selected 133 COVID-19 patients in which 39 were exposed to DM and 94 were not-exposed to DM who were admitted in CMH, Dhaka from July 2020 to June 2021 with the objective to find out the association of Diabetes Mellitus with the mortality and morbidity outcome of COVID-19 patients within 90 days of discharge from Hospital. The data were collected by telephonic interview and from medical record.

Result: The study revealed that the mean age of the respondents were 48.01 years, 80.5% were male. It was seen from the study that among all the respondents 95.5% were survivor and 4.5% were non-survivor. Among the exposed 87.2% were survivor and among the non-exposed 89.9% were survivor. Among the exposed more than half (51.3%) were ≥ 60 years age group, 48.7% were military retired personnel, 61.5% had family income TK < 25,000. On 14th and 28th day of admission among exposed 94.9% and 30.8% and among non-exposed 83.0% and 21.3% were not cured respectively. Before attaining 28th day of admission among exposed 12.8% and among non-exposed 1.1% were non-survivor. Regarding ICU support among exposed 30.8% and among non-exposed 10.6% required ICU support during treatment, whereas among exposed 33.3% and among non-exposed 6.4% were critical patients. Among exposed 48.7% required oxygen, 17.9% needed ventilator support whereas among non-exposed 23.4% required oxygen and 4.3% needed ventilator support. Among exposed HTN, CHDs and CKDs were 61.5%, 7.7% and 12.8% whereas among non-exposed it was 21.3%, 3.2% and 1.1% respectively. The risk exposure outcome among ≥ 60 years age group were higher among exposed (RR:2.05, 95% CI 1.33-3.17). Morbidity outcome among exposed on 14th, 28th and 90th day were higher (RR:2.05, 95% CI 1.33-3.173), (RR: 1.485, 95% CI 0.847-2.603) and (RR:1.190, 95% CI 0.371-3.820) respectively. Need of Oxygen were higher among exposed (RR:1.445, 95% CI 1.064-1.961). Association in regards to HTN, CHDs and CKD were also higher among exposed which were (RR:1.87, 95% CI 1.321-2.656), (RR: 1.433, 95% CI 0.639-3.214) and (RR:4.394, 95% CI 0.732-26.376) respectively.

Conclusion: Health education measures should be taken to prevent and control the morbidity and mortality outcome of COVID-19 patients with special attention to those who are aged, and suffering from DM, HTN and CKD. However, to draw comprehensive inferences on this study, further research on representative sample size in this field is recommended.

Keywords: Diabetes mellitus, outcome, COVID-19.

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Introduction:

COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a newly emergent coronavirus, that was first recognized in Wuhan, Hubei province, China, in December 2019. SARS-CoV-2 is a positive-sense single-stranded RNA virus that is contagious in humans.

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It is the successor to SARS-CoV-1, the strain that caused the 2002–2004 SARS outbreak. Epidemiology and virologic studies suggest that transmission mainly occurs from both symptomatic and asymptomatic people to others by close contact through respiratory droplets or by direct contact with infected persons, or by contact with contaminated objects and surfaces or by aerosols, i.e. in enclosed spaces indoors, crowded and inadequately ventilated spaces,

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where infected persons spend long periods of time with others, which may include restaurants, choir practices, fitness classes, nightclubs, offices and places of worship, or during aerosol-generating procedures. Clinical and virologic studies that have collected repeated biological samples from confirmed patients demonstrate that shedding of SARS-CoV-2 is highest in the upper respiratory tract (URT) (nose and throat) early in the course of the disease, within the first 3 days from onset of symptoms. A study of 77 infector-infectee transmission pairs observed the highest viral load in throat swabs at the time of symptom onset, suggesting infectiousness peak on or before symptom onset with an estimated 44% (95% confidence interval, 30–57%) of onward infections happening during the pre-symptomatic phase of the index case.¹

The disease has a wide range of clinical manifestations from asymptomatic stage to severe form of respiratory illness. Mild to moderate cases shows fever, headache, cough, breathlessness, sore throat, general weakness, loss of smell and taste etc. In those patients that do become symptomatic, most people with COVID-19 develop only mild (40%) or moderate (40%) disease, approximately 15% develop severe disease that requires oxygen support, and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiorgan failure, including acute kidney injury and cardiac injury. Older age, smoking and underlying noncommunicable diseases (NCDs), such as diabetes, hypertension, cardiac disease, chronic lung disease and cancer, have been reported as risk factors for severe disease and death, and multivariable analyses have confirmed older age, higher sequential organ failure assessment (SOFA) score and D-dimer > 1 µg/L on admission were associated with higher mortality.² COVID-19 is associated with mental and neurological manifestations, including anxiety, depression, sleep problems, headache, dizziness, impaired sense of smell or taste, myalgias, delirium/encephalopathy, agitation, stroke, hypoxic ischemic brain injury, seizures, coma, meningo-encephalitis and Guillain-Barré syndrome. Anxiety and depression appear to be common amongst people hospitalized for

COVID-19. In many cases, neurological manifestations have been reported even without respiratory symptoms.

Diabetes is a chronic disease that occurs when the pancreas is no longer able to make insulin, or when the body cannot make good use of the insulin it produces. Insulin is a hormone made by the pancreas, that acts like a key to let glucose from the food we eat pass from the blood stream into the cells in the body to produce energy. All carbohydrate foods are broken down into glucose in the blood. Insulin helps glucose get into the cells. Not being able to produce insulin or use it effectively leads to raised glucose levels in the blood (known as hyperglycaemia). Over the long-term high glucose levels are associated with damage to the body and failure of various organs and tissues.³ There are three main types of diabetes – type 1, type 2 and gestational DM.

The objective of the study was to find out the association of Diabetes Mellitus with morbidity and mortality outcome of COVID-19 patients within 90 days after discharge from Combined Military Hospital, Dhaka.

Inclusion Criteria of exposed/non-exposed were:

1. COVID-19 admitted patients within 90 days after discharged from CMH, Dhaka
2. Age between 22 to 81 years
3. Well enough to undertake minimum 20 minutes interview.
4. Those who gave informed written consent to participate in the study.

Exclusion criteria of exposed/non-exposed

1. Psychologically abnormal patients
2. Severely ill patients
3. Who did not respond to a phone call on three separate occasion.

Methods & materials

This was a retrospective cohort study. Combined Military Hospital (CMH), Dhaka was selected for the study place to carry out the research. Ethical approval of the research proposal was achieved from the Protocol approval Committee, Armed Forces Medical Institute (AFMI). All Armed Forces Personnel and their families get treatment here including retired personnel. The organization is situated on the

western side of AFMI and Armed Forces Institute of Pathology (AFIP), Dhaka Cantonment which is well road communicated and easily accessible by the researcher. As this organization is situated nearby, it is easy for the researcher to collect data from the place. The duration of study period was one year commencing from 01 January 2021 to 31 December 2021.

The study populations were admitted RT-PCR laboratory confirmed cases COVID-19 patients within 90 days after discharge from CMH, Dhaka. This includes all Armed Forces COVID-19 patients (Army, Navy Air Force) including their families and patients [Civilian Non-Entitled (CNE) patients and Relative Entitled (RE) patients] those who were admitted to Combined Military Hospital, Dhaka. Purposive sampling technique was adopted for the study. Total 133 sample size were selected for the study. Data were collected from the patient's file, electronic medical record (EMR) and by interviewing of the participant by a pre-tested questionnaire at the day 28 and day 90. The collected data throughly edited through checking and rechecking for quality control. Coding, editing, cleaning and categorization were done as required. Collected data then be transferred to variable sheet of SPSS programme and data analysis was done by computer with the help of " Statistical package for Social Science" (SPSS software, version 23.0).

Results

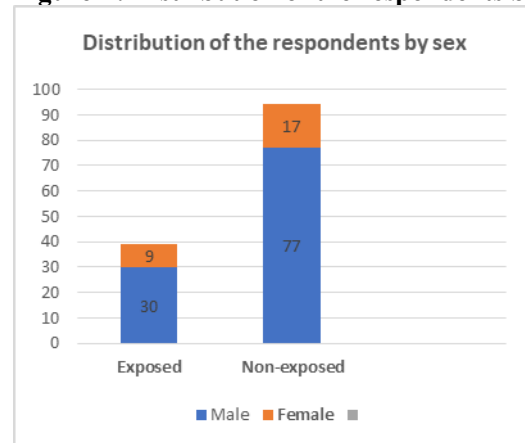
This retrospective cohort study was conducted to find out the association between Diabetes Mellitus and outcome of COVID-19 among the 133 admitted RT-PCR laboratory confirmed positive COVID-19 patients within 90 days after discharge from CMH, Dhaka.

Table-1: Distribution of the respondents by age (n=133)

| Age group (Years) | Exposed f (%) | Non-Exposed f (%) | Total f (%) | Significance P< 0.05 |
|-------------------|---|---|--|---|
| 20-29 | 0(0.0%) | 16(17.0%) | 16(12.0%) | χ ² =28.83 df=4 p=.000 |
| 30-39 | 2(5.1%) | 25(26.6%) | 27(20.3%) | |
| 40-49 | 5(12.8%) | 15(16.0%) | 20(15.0%) | |
| 50-59 | 12(30.8%) | 25(26.6%) | 37(27.8%) | |
| 60 and above | 20(51.3%) | 13(13.8%) | 33(24.8%) | |
| Total | 39(100%) | 94(100%) | 133(100%) | |
| Statistics | Mean±SD= 58±13.90 years Minimum 22, Maximum 81 yrs | Mean±SD= 43.87±13.90 years. Minimum 22, Maximum 81 yrs | Mean±SD= 48.01±14.16 years Minimum 22, Maximum 81 yrs | |

Table-1 shows that among the 133 respondents the age ranged from 22 to 81 years and maximum were 37 (27.8%) in 50-59 age group and minimum were 16 (12%) in 20-29 age group among the population. Among the exposed maximum were 20 (51.3%) in 60 and above age group and minimum were 2 (5.1%) in 30-39 age group. On the other hand, among non-exposed maximum were 25 (26.6%) in each 30-39 and 50-59 age group and minimum were 13 (13.8%) in the 60 and above age group. The Mean age of the respondents were 48 years with the standard deviation 14.16 years. Among exposed and non-exposed Mean age were 58 and 43.87 years respectively. The association between age and exposure status were statistically highly significant (RR:2.05, 95% CI: 1.33-3.173, P=.000).

Figure-1: Distribution of the respondents by sex



Among the respondents male were 107 (80.5%) and female were 26 (19.5%). Among exposed male were 30 (76.9%) and female were 9 (23.1%). Among Non-exposed male were 77 (81.9%) and female were 17 (18.1%).

Table-2: Comparison of outcome on 90th Day between exposed and non- exposed

| Outcome at 90 th day | Exposed f (%) | Not Exposed f (%) | Total f (%) | Significance P< 0.05 |
|---------------------------------|-----------------|-------------------|------------------|-------------------------------------|
| Cured | 35(89.74%) | 90(95.7%) | 125(95.4%) | $\chi^2=1.79$ $df=1$ $p=.181$ |
| Not Cured | 4(10.76%) | 4(4.3%) | 8(4.6%) | |
| Total | 39(100%) | 94(100%) | 133(100%) | |

Table-3 Comparison of mortality outcome among exposed and non-exposed

| Mortality outcome | Exposed f (%) | Not Exposed f (%) | Total f (%) | Significance P< 0.05 |
|-------------------|--------------------|--------------------|---------------------|--------------------------------------|
| Survivor | 34(87.18%) | 93(98.9%) | 127(95.49%) | $\chi^2=8.844$ $df=1$ $p=.008$ |
| Non-Survivor | 5(12.82%) | 1(1.1%) | 6(4.51%) | |
| Total | 39 (100.0%) | 94 (100.0%) | 133 (100.0%) | |

Table-3 reveals that among the respondent 127 (95.49%) were survivor and 6 (4.51%) were non-survivor. Among exposed 34 (87.18%) were survivor and 5 (12.82%) were non-survivor whereas among non-exposed it was 93 (98.9%) and 1 (1.1%) respectively. The association between mortality outcome and exposure status was statistically significant (RR: 0.372, 95% CI: 0.198-0.699, p=.008)

Table-4: Comparison among exposed and non-exposed on placement of ward in Hospital

| Placement in Ward | Exposed f (%) | Not Exposed f (%) | Total f (%) | Significance P<.05 |
|-------------------|-----------------|-------------------|------------------|--------------------------------------|
| General ward | 26(66.7%) | 83(88.3%) | 109(82.0%) | $\chi^2=8.739$ $df=2$ $p=.013$ |
| HDU | 1(2.6%) | 1(1.1%) | 2(1.5%) | |
| ICU | 12(30.8%) | 10(10.6%) | 22(16.5%) | |
| Total | 39(100%) | 94(100%) | 133(100%) | |

Table-4 shows that regarding the stay at Hospital during treatment maximum 109 (82.0%) were in General ward and minimum 2 (1.5%) were in HDU. Among exposed maximum 26 (66.7%) were in General ward and minimum 1 (2.6%) were in HDU, whereas 12 (30.8%) were treated in ICU. Among non-exposed maximum 83 (88.3%) were in General ward and 1 (2.6%) were in ICU and 10 (10.6%) were placed in ICU. The result was statistically highly significant (p=.013)

Table-5: Relative Risk between exposed and non-exposed by selected risk factors

| Variables | RR | 95% CI |
|---|-------|--------------|
| Age ≥60 years <60 years | 2.05 | 1.33-3.173 |
| Condition on 14 th day Not Cured Cured | 2.896 | 0.769-10.985 |
| Condition on 28 th day Cured Not Cured | 1.485 | 0.847-2.603 |
| Condition on 90 th day Cured Not Cured | 1.190 | 0.371-3.820 |
| Mortality outcome Survivor/Non-survivor Yes No | 0.372 | 0.198-0.699 |
| Need of Oxygen Yes No | 1.445 | 1.064-1.961 |
| Need of Ventilator support Yes No | 0.398 | 0.243-0.652 |
| HTN Yes No | 1.87 | 1.321-2.656 |
| CHDs Yes No | 1.433 | 0.639-3.214 |
| CKD Yes No | 4.394 | 0.732-26.376 |

The risk of exposure outcome among the age group ≥60 years was higher (RR:2.05, 95% CI 1.33-3.173). Morbidity outcome on 14th day on 28th and 90th day were higher among exposed (RR: 2.896, 95% CI 0.769-10.985) (RR: 1.485, 95% CI 0.847-2.603) and (RR:1.190, 95% CI 0.371-3.820) respectively. Need of Oxygen were also higher among exposed (RR:1.445, 95% CI 1.064-1.961). Comorbidity HTN, CHDs and CKD also were higher among exposed which

were (RR:1.87, 95% CI 1.321-2.656), (RR: 1.433, 95% CI 0.639-3.214) and (RR:4.394, 95% CI 0.732-26.376) respectively.

Discussions:

Study conducted by Farhana A et al in southern part of Bangladesh on Clinical characteristics and short-term outcomes after recovery from COVID-19 in patients with and without diabetes in Bangladesh in 2020. Variation in clinical characteristics, contact history, comorbidities, treatment patterns, and immediate post COVID complications were investigated by the rechargers. There were 734 COVID-19 patients in this study of which 19.8% of patients had diabetes and 76% of the COVID-19 patients were male. Among biochemical parameters, plasma glucose, D-dimer, and Troponin-I levels were significantly elevated amidst the cohort with diabetes. The frequency of patients requiring insulin increased threefold during infection with SARS CoV-2. 1.4% patients developed new onset of diabetes mellitus. A number of COVID-19 patients with diabetes have been suffering from post-recovery complications including pain, discomfort, and sleep disturbances. They concluded that individuals with diabetes have experienced a severe manifestation of COVID-19 and post disease complications.⁴

In another study conducted by Ahmed NU et al. on the clinical characteristics of 201 patients diagnosed and admitted with COVID-19 in Combined Military Hospital, Dhaka. The objectives of the study were to evaluate the clinicopathologic profile of COVID-19 positive Bangladeshi patients and also to see their clinical outcome within defined period. Among them 180 (90%) were male and 21 (10%) female. Most patients were from 26-35 years age group which was 71 (35.5%); then from 16-25 years age group 54 (27%), from 35-45 years 49 (24.5%), 8 patients (4%) below 15 years, 9 (4.5%) from 46-55 years, 10 (5%) from 56-65 yrs. Mean age is 32.2 ± 2 . Among the patients 21 had multiple comorbidities like DM, HTN, IHD, ESRD ON MHD, bronchial asthma and pheochromocytoma. Regarding clinical presentation, 67 (33.5%) patients presented with only one symptom, 125 (62.5%) had multiple symptoms, 9 (4.5%) were asymptomatic. Fever

was the dominant presenting feature and 154 (77%) patients presented with fever. Other presentations were cough 71 (35.5%), headache 27 (13.5%), myalgia 25 (12.5%), sore throat 25 (12.5%), malaise 15 (7.5%), respiratory distress 11 (5.5%). Rare symptoms were nasal obstruction (10), backache (7), diarrhea (6), abdominal pain (4), chest pain (4), palpitation (3), burning whole body (2), and toothache (2). All patients were discharged 10 days course of treatment. Discharge criteria were two negative RT-PCR 24 hours apart.⁵

Another Study conducted by Mowla SGM et al at Dhaka Medical College Hospital in 2020. Among the total participants (n=100), mean age was 41.7 ± 16.3 years, 63% were male and 60% patients had positive contact history. Appearance of symptom to hospital admission time was a median of 6 days (range 1 to 21 days) and mean hospital stay was 7.77 ± 5.62 days. Predominant presenting symptoms were fever (69%), cough (54%), breathlessness (41%), fatigue (40%), anorexia (26%) and diarrhea (19%). Hypertension (21%), diabetes mellitus (16%), heart diseases including ischemic heart disease (IHD) (8%) and renal diseases including chronic kidney disease (CKD) (8%) were frequent comorbidities. Ten out of hundred patients died. Older age ($p=0.001$), male sex ($p=0.007$), smoking ($p=0.001$), breathlessness ($p=0.001$) and presence of comorbidities ($p < 0.05$) were significantly associated with mortality.⁶

Another study conducted by Saha A et al. at southern part of Bangladesh on Clinical characteristics and outcomes of COVID-19 infected diabetic patients admitted in ICUs of the southern region of Bangladesh in 2020 and found that the prevalence of diabetes was high among 51-70 years old patients. All the diabetic patients had at least one other comorbidity, with a significantly higher incidence of hypertension (53.4% vs 27.5%, $P < 0.05$). Prevalence of male patients (74/88; 84.1%) was slightly higher among diabetic patients than the non-diabetic patients (60/80; 75%). Even though not significant, Kaplan-Meier survival curve showed that COVID-19 patients with diabetes had a shorter overall survival time than those without

diabetes. In subgroup analysis, diabetic patients were classified into insulin-requiring and non-insulin-requiring groups based on their requirement of insulin during the stay in ICU. COVID-19 infected diabetic patients requiring insulin have high risk of disease progression and shorter survival time than the non-insulin required group.⁷

A study carried out in Italy by Shang J et al in 2021 showed that 96% of patients that died in hospitals had previous comorbidities, with type 2 diabetes being second highest amongst other non-communicable diseases (NCDs). A meta-analysis that assessed the prevalence of comorbidities among COVID-19 patients revealed that of the 1576 cases studied, diabetes was one of the most prevalent comorbidities, which occurred in 9.7% of the cases, after hypertension (21.1%).⁸ The study also showed that diabetic patients had a significantly higher incidence of bilateral pneumonia (86.9%, $P = .020$). In terms of complications and clinical outcomes, the incidence of respiratory failure (36.9% vs 24.2%, $P = .022$), acute cardiac injury (47.4% vs 21.2%, $P < .01$), and death (20.2% vs 8.0%, $P = .001$) in the diabetes group was significantly higher than that in the nondiabetic group.⁸

Alkundi A et al. conducted a study in 2020 showed that diabetes was found to be a strong predictor of a length of stay (LOS) in hospital. Data identified an association between older age of diabetic COVID-19 patients and lower probability of survival. In general, all age groups are susceptible to encounter COVID-19 infection, however, older patients and individuals with pre-existing medical conditions such as diabetes found to be more vulnerable to severe outcomes including death. study showed that COVID-19 patients with diabetes who are suffering from DKA were more likely to non-survive compared to the ones without DKA.⁹

Another study in China in 2020 found that nearly half of the patients had comorbidity where HTN was the most common followed by DM and coronary heart disease (CHD). The study also established the association between increased age and death of the COVID-19

patients. study showed that severe patients were older and had comorbidities including HTN (30.0%), DM (12.1%) and cardiovascular diseases (9%).¹⁰

In another study in West Court Union Hospital in Wuhan, China of the 258 hospitalized patients (63 with diabetes) with COVID-19, the median age was 64 years (range 23–91), and 138 (53.5%) were male. Patients with diabetes were more likely to develop severe or critical disease conditions with more complications, and had higher incidence rates of antibiotic therapy, non-invasive and invasive mechanical ventilation, and death (11.1% vs. 4.1%).¹¹

Conclusion

This retrospective Cohort study was designed to find out the association between exposed (suffering from Diabetes Mellitus) and non-exposed (not suffering from Diabetes Mellitus) with morbidity and mortality outcome of COVID-19. DM has already become a worldwide epidemic and the study revealed that DM had association with the mortality and morbidity outcome of this newly discovered COVID-19. The association between age and exposure status was statistically significant. Among the exposed type 2 DM were more than type1 DM. There was no significant difference with Sign/symptom of COVID-19 between exposed and non-exposed. Requirement of ICU and ventilator support, oxygen therapy and overall duration of stay in Hospital were more among exposed than non-exposed. Comorbidities like HTN, CHDs, CKDs and cancer were more dominant in the exposed group than non-exposed.

The study predicts that among the exposed those who are aged, having retirement from service and have comorbidities are more prone to develop severe morbidity and mortality outcome with COVID-19. As such, there is a need for population and community-wide policy intervention for controlling DM which will help to live a healthy life and increase the operational capabilities of our population. In the long run it will help us to improve socioeconomic development of the country.

Conflict of interest: No conflict of interest was involved in this study.

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