Original Article

Clinical Characteristics of Non-Survivors of Coronavirus Disease 2019 (COVID-19)

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Abstract

Introduction: The pattern of infection and mortality rates of coronavirus disease 2019 (COVID-19) has varied significantly amongst the countries. There is scarcity of data regarding characteristics of non-survivors ofCOVID-19 in Bangladesh. The purpose of this study was to delineate demographics, clinical characteristics and treatment of Bangladeshi individuals who died due to COVID-19.

Methods: This prospective observational study included all confirmed symptomatic and asymptomatic COVID-19 positive non-survivors from April 2020 to July 2023at the National Heart Foundation Hospital & Research Institute of Bangladesh. Demographic and clinical characteristics of COVID-19 positive non-survivors were evaluated.

Results: During this study period, 2506 patients were enrolled. Of whom 100 (4.0%) were non-survivors and included in this study. The mean age of the non-survivors was 62.94 ± 13.43 years. Male were predominant (71.0% vs 29.0%). Healthcare personnel (HCP) were 2.0% and non-HCP were 98.0%. Cardiovascular disease (88.0%) was the commonest comorbidity followed by hypertension (70%), chronic kidney disease (70.0%), diabetes mellitus (61.0%), dyslipidemia (43.0%), smoking (38.0%), and obesity (27.0%) among non-survivors. Most of the patients (94.0%) had multiple comorbidities. Most of the non-survivors were unvaccinated (56%). Shortness of breath (82.0%), fever (77.0%), cough (52.0%), and fatigue (32.0%) were the most common symptoms. Asymptomatic non-survivors were 2.0%, 39 (39%) had mild disease; one (1.0%) had moderate disease; 45 (45%) had severe disease, and 13 (13%) had critical ill form of disease.

Conclusion: In our study, the mortality rate in patients with COVID-19 was 4.0%. Most of deceased were older in age, male, unvaccinated, had multiple co-morbidities and more severe disease.

Key Ward: COVID-19, non-survivors, demographics, clinical characteristics, treatment.

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Introduction

The global spread of coronavirus disease 2019 (COVID-19) has emerged as one of the most significant public health crises of the 21st century. The estimated global mortality rate for COVID-19 is approximately 3.4%, which exceeds earlier projections of around 2% [1], yet remains considerably lower than the fatality rates associated with Middle East Respiratory Syndrome (MERS) at 34% [2] and Severe Acute Respiratory Syndrome (SARS) at 10% [3]. Reported COVID-19 mortality rates vary widely-from 3.14% to as high as 61.51%-depending on disease severity and other contributing factors [4–21]. This variation can be attributed to several influences, including geographic differences, viral mutations, stage of infection (early or advanced), severity of illness, pre-existing health conditions [9], disparities in data reporting systems [11], socioeconomic conditions [17], vaccination status, and the overall capacity of healthcare systems. A number of clinical and demographic factors have been recognized as strong predictors of adverse outcomes and mortality, including advanced age, male sex, and comorbidities such as hypertension, diabetes, cardiovascular diseases, chronic kidney or liver disease [22]. Socioeconomic determinants such as poverty, reliance on public transportation, lack of health insurance, low levels of education, and crowded living conditions-which hinder effective social distancing-have also been linked to higher rates of in-hospital deaths among COVID-19 patients [23–26]. However, limited data is available regarding the mortality

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patterns, associated risk factors, and predictors of death in lower- and middle-income countries, such as Bangladesh. This study, therefore, seeks to explore the demographic profiles, clinical features, and treatment patterns of individuals in Bangladesh who succumbed to COVID-19.

Materials and methods

Study design, setting, and population

This prospective observational study was carried out from April 2020 to July 2023 in the non-COVID tertiary cardiac care hospital at National Heart Foundation Hospital & Research Institute, Dhaka, Bangladesh. All admitted patients, who subsequently got diagnosed as COVID positive & health care personnel of this hospital, who become COVID positive and have not survived were enrolled in this study. The study was approved by the Ethics Review Committee of National Heart Foundation Hospital & Research Institute (N.H.F.H. & R.I./4-14/7/AD-1105) and written informed consent was obtained from all non-survivors or non-survivor's attendance after confirmation of COVID-19 diagnosis as soon as possible.

Definition and variables

We studied all symptomatic and asymptomatic confirmed COVID-19 positive non-survivors and analyzed baseline variables, comorbidities, clinical presentation, treatment, and severity of COVID-19. Baseline information included gender, age, risk factors and co-morbidities (hypertension, diabetes, smoking, dyslipidemia, obesity, cardiovascular disease, chronic obstructive pulmonary disease /bronchial asthma (COPD/BA), chronic kidney disease). The degree of severity of COVID-19 were classified as mild, moderate, severe, and critical ill [27,28]. Participants were considered partially vaccinated (PV) if received one dose of vaccine, fully vaccinated (FV) if received two doses of vaccine and boosted if received three doses of vaccine.

Statistical analysis

Continuous variables illness described using the mean and standard deviation. Discrete variables were expressed as frequency rates and percentage. All analyses were performed using SPSS statistical software version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 2506 COVID-19 patients were enrolled during this period. Of whom 100 (4.0%) patients deceased and included in the study. The mean age of the non-survivors was 62.94 ±13.43 years and most of them were aged ≥50 years (86%). Individuals >65 years was 37% and <65 % years 63%. Most of the non-survivors were male (71.0% vs 29.0%). Non-Healthcare personnel (HCP) were more deceased than HCP (98.0% vs 2.0%). Baseline characteristics of COVID-19 non-survivors are presented in Table 1. Cardiovascular disease (88.0%) was the most common comorbidity followed by hypertension (70.0%), chronic kidney disease (70.0%), diabetes mellitus (61.0%), dyslipidemia (43.0%), smoking (38.0%), obesity (27.%), and COPD/BA (10%).Most of the patients (94.0%) had more than one comorbidity and only 5.0% patients had one comorbidity (Figure 1). Most of the patients had heart disease in addition to COVID-19 diagnosis (89.0%) and only 11.0% patients had COVID-19 alone.

Table 1: Baseline characteristics of non-survivors of COVID-19 (n-100)

Variables	Mean±SD/n(%)
Age (Mean±SD) year	62.94 ±13.43
Age category	
<50 years	14(14%)
≥50 years	86(86%)
Gender	
Male	71(71.0%)
Female	29(29.0%)
Patient category	
HCP	2(2.0%)
Non-HCP	98(98.0%)
Risk factors & comorbidities	
HTN	70(70.0%)
DM	61(61.0%)
Cardiovascular disease	88(88.0%)
Dyslipidemia	43(43.0%)
Smoking	38(38.0%)
CKD	70(70.0%)
Obesity	27(27.0%)
COPD/BA	10(10.0%)
Number of comorbidities	
0	01(1.0%)
1	05(5.0%)
>1	94(94.0%)
Unvaccinated	56(56%)
Diagnosis	
COVID-19 only	11(11.0%)
COVID-19 with heart disease	89(89.0%)

COVID-19: coronavirus disease 2019; HCP: healthcare personnel; non-HCP: non-healthcare personnel; SD: standard deviation; DM: diabetes mellitus; COPD: chronic obstructive pulmonary disease; BA: Bronchial asthma; CKD: chronic kidney disease.

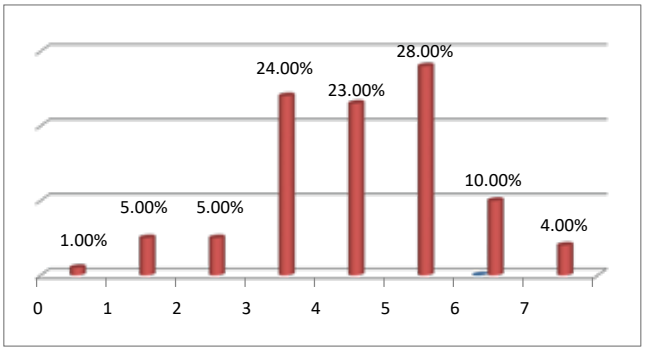


Figure 1: Number of comorbidities of non-survivors of COVID-19. COVID-19: coronavirus disease 2019.

Most of the non-survivors were unvaccinated (56%), 1% PV, 11% FV, 7% boosted and 25% died before development of vaccine. Most of the non-survivors were symptomatic (98.0%). Shortness of breath (82.0%), fever (77.0%), cough (52.0%), and fatigue (32.0%) were the most common symptoms. Clinical characteristics of non-survivors of COVID-19 are presented in Table 2.

Table 2: Clinical characteristics of non-survivors of COVID-19 (n=100)

Variables	**n(%)**
Clinical presentation	
Symptomatic	98(98.0)
Asymptomatic	2(2.0)
Fever	77(77.0)
Cough	52(52.0)
Sore throat	05(5.0)
Shortness of breath	82(82.0)
Diarrhoea	01(1.0)
Anosmia	02(2.0)
Fatigue	32(32.0)
Headache	08(8.0)
Bodyache	19(19.0)
Anorexia	12(12.0)
Nausea	03(3.0)
Vomiting	04(4.0)
Abdominal pain	01(1.0)
Numbness	01(1.0)
Dizziness	14(14.0)
Generalized itching	02(2.0)

COVID-19: coronavirus disease 2019.

Oxygen therapy (low flow, high flow) was given when required. Twelve patients required high-flow nasal cannula. Prone positioning was advised for all patients. Treatment outline is given in Table 3. Twenty-eight (28.0%) non-survivors received ivermectin. Only 2 (2.0%) non-survivors received favipiravir (1600 mg on day 1 followed by 600 mg 12 hourly from day 2 to day 10) and 27 (27.0%) non-survivors received remdesivir (200 mg IV infusion [within 30 min-2 hours] on day 1 followed by 100 mg infusion within [30 min to 2 hours] from day 2 to day 5).

Regarding antibiotic therapy, 40 (40.0%) non-survivors were treated with a single antibiotic and 54 (54.0%) non-survivors were given double antibiotic therapy. Most of the non-survivors (74.0%) received intravenous antibiotic, 13% (13) combination of oral & intravenous and only 7.0% (7) received oral antibiotic therapy alone. Around 38 (38.0%) non-survivors were also treated with methylprednisolone and dexamethasone for 3–7 days.Low molecular weight heparin was used in 84.0% (84) patients followed by newer oral anticoagulants (rivaroxaban).

Table 3: Distribution of treatment of non-survivors with COVID-19 (n=100)

Variables	**n(%)**
Antibiotics	
IV	74(74.0)
Oral + IV	13(13.0)
Oral	07(7.0)
Not received	06(6.0)
Antibiotics	
Single	40(40.0)
Double	54(54.0)
Not received	06(36.0)
Steroids	38(38.0)
Favipiravir	02(2.0)
Remdesivir	27(27.0)
Ivermectin	28(28.0)
Hydroxy-chloroquine	01(1.0)
Enoxaparine	84(84.0)
Rivaroxaban	84(84.0)

COVID-19: coronavirus disease 2019; IV: intravenous.

Among deceased, only 2 (2.0%) were asymptomatic; 39 (39%) had mild disease; one (1.0%) had moderate disease; 45 (45%) had severe disease, and 13 (13%) had critical ill form of disease (Table 4). As most of the non-survivors (89%) had cardiovascular diagnosis in addition to COVID-19, they developed more cardiovascular complications: acute left ventricular failure (70.0%); cardiogenic shock (45.0%), arrhythmias (5%); conduction disturbance (8%).

Table 4: Disease Severity of non-survivors of COVID-19 (n=100)

Variables	**n (%)**
Disease severity	
Asymptomatic	02(2.0)
Mild	39 (39.0)
Moderate	01 (1.0)
Severe	45(45.0)
Critical ill	13(13.0)
In-hospital cardiogenic shock	45(45.0%)
In-hospital acute LVF	70(70.0%)
In-hospital conduction disturbance	08(8.0%)
In-hospital arrhythmias	05(5.0%)

COVID-19: coronavirus disease 2019; LVF: left ventricular failure.

Discussion

In this study, the observed mortality rate among COVID-19 patients was 4.0%, which is in line with several reports that have estimated case fatality rates between 3.14% and 6.3% [4–8]. However, other studies have documented significantly higher mortality rates, ranging from 6.91% to 61.51% [9–21]. These discrepancies can be attributed to varying study populations, ranging from asymptomatic individuals to those with severe or critical illness. Notably, in our cohort, 2% of deceased individuals were asymptomatic.

The mean age of the non-survivors in our study was 62.94 ±13.43 years and male were predominant. Most of the non-survivors (86%) were aged ≥ 50 years. The prevalence of cardiovascular disease (CVD), hypertension, chronic kidney disease, diabetes mellitus, dyslipidemia, smoking, and obesity were higher among non-survivors as our hospital is tertiary care cardiac hospital. Abohamr et al. [5] studied 768 hospitalized COVID-19 patients and mortality rate was 4.27%. The mean age of the deceased was 47.6 ± 15.6 years and 86.5% were male. Obesity, smoking and diabetes mellitus were predictors of mortality. In a systematic review and meta-analysis including 14 studies with 29,909 COVID-19 infected patients and 1445 cases of death (mortality 4.8%) showed older age (≥65 years old), male gender, hypertension, CVD, diabetes, COPD and cancer were associated with greater risk of death from COVID-19 infection [6].

Zhang et al. [7] retrospectively analyzed 432 patients from two centers of Hubei province, China which showed mortality rate 5.09% and identified 5 predictors of mortality among the overall population of COVID-19 patients: low hemoglobin, high CK-MB (creatine kinase-MB), high LDH (lactate dehydrogenase), high PCT (procalcitonin), and high CT (computed tomography) score. Sausa et al. [8] aimed to identify the risk factors associated with mortality and survival of COVID-19 cases in a state of the Brazilian Northeast among 2070 people that tested positive to COVID-19 and of them 6.3% (131) died. The mortality risk was 3.7 times higher in the elderly (aged ≥60 years), 19.3 times higher in people with CVD, 14.3 times higher in people with diabetes, 32.6 times higher in people with neurological disease and 9.9 times higher in people with renal disease. Such a risk was 3.0 times higher in hospitalized people and 3.5 times higher in people admitted to ICU.

In a retrospective study from COVID-19 dedicated hospital in Bangladesh of the 3115 patients 282 (9.05%) died [10]. The mean age of deceased was 56.7 ± 14.9 years. Approximately three-fourths (61.3%) of deceased patients were male. Older age, male sex, rural residence, history of smoking, and chronic kidney disease were found to be important predictors of mortality. Another retrospective Bangladeshi study included 50 hospitalized COVID-19 patients and of them 07 (14.0%) died. The mean age of the non-survivors was 51.57±13.89 years. Older age, higher Sequential Organ Failure Assessment (SOFA) score, and elevated fibrinogen level at admission were risk factors for death [12]. Higher mortality rate in two Bangladeshi studies may be due to inclusion of hospitalized patients only as we included both hospitalized and non-hospitalized patients.

A retrospective cohort study in the New York City metropolitan area included 6493 COVID-19 patients and of them 858 (13.2%) patients died. The median age of the deceased was 76 years. Olderage, male sex, hypotension, tachypnea, hypoxia, impaired renal function, elevated D-dimer, and elevated troponin were associated with increased in-hospital mortality [11]. An Indonesian retrospective study observed 17.18% (78) death among 454 COVId-19 patients [13]. The highest mortality rate occurred in the age group ≥60 years (35; 51.47%) and male were 66.67%. Hypertension, cardiovascular disease, and diabetes were the most common comorbidity inpatients death due to COVID-19. More than half of the patients had two or more comorbidities. A systematic review and meta-analysis of 42 studies including 423,117 patients showed that the pooled prevalence of mortality among hospitalized patients with COVID-19 was 17.62% [14]. Acute kidney injury, COPD, diabetes, hypertension, CVD, cancer, increased D-dimer, male gender, older age, current smoker, and obesity are clinical risk factors for a fatal outcome associated with coronavirus.

Mesas et al. [15] in a comprehensive systematic review and meta-analysis included 60 studies, with a total of 51,225 patients (12,458 [24.3%] deaths) from hospitals in 13 countries. A mean age ≤60 years, dyspnoea, smoking, kidney disease, hypertension, malignancy, diabetes, pulmonary disease, decreased platelet count, decreased haemoglobin concentration, increased interleukin-6 and increased cardiac troponin I were more markedly associated with mortality. A cross-sectional analytic observational study enrolled 69 patients with 21 (30%) of them were non-survivors [16]. Age >52 years, dyspnea, hypertension, anemia, thrombocytopenia and neutrophil-lymphocyte ratio (NLR) >3.13 were associated with increased mortality of COVID-19 patients.

Olivas-Martinez et al. [17] in a prospective cohort study included 800 adult hospitalized severe confirmed COVID-19 pneumonia patients and from those 241 died (30.1%). The main risk factors associated with in-hospital mortality were male gender, obesity and oxygen saturation < 80% on admission. A descriptive cross-sectional study involving a cohort of 375 COVID-19 hospitalized patients and 129 patients were died [18]. Age greater than 50 years, presence of multiple underlying diseases, dyspnea, acute confusion, saturation of peripheral oxygen below 94% and oxygen demand exceeding 5 L per minute demonstrated independent predictive value for mortality.

In a retrospective case series, among a cohort of 799 patients, 113 who died and 161 who recovered with a diagnosis of covid-19 were analyzed [19]. The median age of deceased patients was 68 years and male were more predominant in deceased patients (73%). Hypertension, cardiovascular disease, and cerebrovascular disease were much more frequent among deceased patients. Dyspnea, chest tightness, and disorder of consciousness were more common in deceased patients. A prospective study in Peru by Valladares-Garrido et al. [20] analyzed 301 hospitalized COVID-19 patients and 41.3% of them died. Older age, ICU admission, obese, impaired consciousness and thrombocytopenia were associated with mortality in patients with COVID-19.

In a meta-analysis of a total of 58 studies with 122,191 patients from different countries were analyzed. The pooled prevalence rate (PR) of mortality among the hospitalized COVID-19 patients was 18.88%. Highest mortality was found in Europe (PR 26.85%) followed by North America (PR 21.47%) and Asia (PR 14.83%). Older age (> 65 years), male gender, ICU patients, obesity, hypertension, diabetes, cardiovascular disease and cancer had a high risk for mortality [29].

Ruiz-Quinonez et al. [30] retrospectively analyzed185 deceased individuals with confirmed diagnoses of COVID-19. The mean age of the deceased was59.53±12.50 (range 24–86) years and the majority were individuals of 65+ years (36.7%, n = 58). Almost similar mean age of deceased individuals was also found in our study. A study in China reported that the mortality rate of COVID-19 patients aged older than 59 years was around 5.1 times higher than that in patients aged 30–59 years [31]. There was a male predominance (60.1%). The most common comorbidities were diabetes (60.63%), hypertension (59.57%) and obesity (43.61%). The most frequent symptoms were dyspnea (88.77%), fever (71.42%) and dry cough (64.28%) which were almost similar to our study [Shortness of breath (82.0%), fever (77.0%), cough (52.0%), and fatigue (32.0%)]. The main drugs used for treating COVID-19were azithromycin (60.6%), hydroxychloroquine (53.0%) and oseltamivir (27.3%). Twenty eight (28.0%) non-survivors received ivermectin. 2.0% favipiravir, 27.0%remdesivir in our study. Most of the non-survivors (74.0%) received intravenous antibiotics.

In our study, most of the non-survivors had severe forms of disease; 45% severe disease and 13% critical ill forms of disease. In contrast to our study, Zhang et al. [7] showed all deceased had severe type and critical types of disease (72.7% and 27.3%, respectively). COVID-19 vaccination is associated with decreased mortality caused by COVID-19, severity of COVID-19 and hospitalization duration [32]. The unvaccinated group had the highest proportion of deaths (5.2% vs. 1.4% and 0.3% in FV and boosted groups, respectively). Also in our study, most of the non-survivors were unvaccinated (56%), 1% PV, 11% FV, 7% boosted and 25% died before development of vaccine.

Limitation

Our study has several limitations. Firstly, study conducted in non-COVID-dedicated cardiac hospital. Secondly, wave-based mortality was not assessed. Thirdly, both hospitalized and non-hospitalized patients were included. Finally, the influence of treatment on mortality of COVID-19 was not assessed.

Conclusion

In current study, the mortality rate in patients with COVID-19 was 4.0%. Most of deceased were older in age, male, unvaccinated, had multiple co-morbidities (cardiovascular disease, hypertension, chronic kidney disease, diabetes mellitus, dyslipidemia, smoking, and obesity) and more severe disease.

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