RISK FACTORS OF FATAL COVID-19 CASES: REPORT FROM TWO COVID HOSPITALS OF CHATTOGRAM, BANGLADESH

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Abstract

Background: Predictors for severe COVID-19 infection have not been well defined especially in Bangladeshi patients. This study was aimed to investigate the association between clinical and laboratory parameters and the mortality from COVID-19 infections in patients admitted in two Government Hospitals in Chattogram, Bangladesh.

Materials and methods: This prospective observational study included 178 confirmed COVID-19 (By reverse transcription polymerase chain reaction test) patients aged ≥ 18 years, admitted in Chittagong Medical College Hospital and Chittagong General Hospital, Chattogram, Bangladesh. Socio-demographic and clinical characteristics on admission were recorded. Patients were categorized as survivors (Improved and discharge, n=148) and deceased (Expired in hospital, n=30). Analyses were performed using SPSS version 23.0.

Results: Median age for deceased cases and for survived cases were 57.5 and 55 years respectively with male predominance in both groups. Majority of the patients were from urban area (65.2%) and from upper lower (42.7%) socio-economic class. In univariate analysis mortality was associated with being from upper or middle socio-economic class, presence of hypertension, diabetes, pre-existing renal disease (p=0.004) and having difficulty breathing at admission. Moreover, compared to the survivors, deceased cases were associated with lower levels oxygen saturation, lymphocytes, elevated levels of leukocytes, neutrophil to-lymphocyte ratio, D-dimer and ferritin at admission.

Conclusions: Factors associated with mortality in this study might improve our understanding of COVID19 progression and provide baseline data to compile or improve the prediction models for the estimation of COVID-19 prognosis in Bangladesh.

Key words : COVID-19; Mortality; Risk factor; Chattogram.

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Submitted on : 04.10.2020
Accepted on : 06.12.2020

Introduction

Coronavirus Disease-19 (COVID-19) is an acute respiratory viral infection related to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] The disease outbreak started in China in late December 2019 and quickly spread to the rest of the world, resulting in a pandemic affecting 215 countries and territories worldwide so far.[1,2] As of September 15, the total number of patients with COVID-19 had risen sharply to 29,522,468 patients globally, with 934,165 deaths and a mortality rate of 4%.[2] There was a slow spread initially in Bangladeshafter declaration of the first case on March 8, 2020.[3] However, later on cases are in sharp rise in Bangladesh like elsewhere with a total 341,056 cases with 4802 death as of September 15, 2020.[4]

COVID-19 has a seemingly variable clinical presentation and progression. According to data from China, an estimated 10–15% of mild cases progress to severe and 15–20% of severe cases go on to become critical, with many of those in the latter category requiring treatment in Intensive Care Units (ICU).[5] Though 99% of the active cases till date is in mild form 1% critical cases creating a huge burden over the existing overburden health care system of Bangladesh.[3] Among patients with similar clinical characteristics and with similar treatment regiments, there may be a diversity in clinical outcomes.[6] Therefore, the development and use of an accurate predictor for COVID-19 prognosis will be beneficial for the clinical management of patients with COVID-19 and will help reduce the mortality rate.

Though several published meta-analysis reports

are already available describing different predictors associated with poor clinical outcomes in patients with COVID-19, unfortunately neither of theses reports included any study from Bangladesh.[7-9] It is probably due to the lacking of published clinical data on COVID-19 in Bangladesh. Contemplating this background we have set out to identify risk factors associated with unfavorable outcome in a cohort of COVI-19 patients admitted in two COVID hospital of Bangladesh.

Materials and methods

This prospective observational study was conducted in two Government COVID Hospital of Bangladesh, Chittagong Medical College Hospital and Chattogram General Hospital. Patients with confirmed COVID19 (Positive real-time reverse transcriptase–polymerase chain reaction assay of a nasopharyngeal swab) were included in this study. Patients were treated as per the institutional guideline. Relevant lab reports were noted and finally in hospital outcome was recorded. Case definition and severity categorization was done in accordance with the national guideline.[10]

Data were collected through interview administered semi structured questionnaire and check list. We collected demographic data (Age, sex, residential location and socio-economic class) clinical data (Symptoms on admission, comorbidities, and some laboratory parameters) and outcome (Improved and discharged or died in hospital).

Statistical analyses were performed with Statistical Package for the Social Sciences version 23.0 for Windows. Patients were categorized according to their outcome (Deceased and survived groups). Categorical variables were summarized as frequencies and percentages. Continuous data were expressed as median and Interquartile Range (IQR) as they are not normaly distributed. Mann–Whitney U tests were used to compare continuous data and Chi-square or Fisher's exact tests were used to compare categorical variables. Only univariate analysis were conducted in the study p <0.05 was considered as statistical significance.

The study was approved by the Ethical Review Committee of Chittagong Medical College (Memo NO.: CMC/PG/2020/106) on September 13, 2020. The study was conducted in accordance with Declaration of Helsinki ethical principles for medical research involving human subjects. Informed consent was obtained from competent patients before enrollment. In patients who were unable to give fully informed consent, assent was obtained from a legal representative.

Results

Of 178 laboratory-confirmed admitted cases, 30 patients had died and 148 recovered and discharged. Median (IQR) age for entire cohort was 55 (45-65) years, for deceased cases 57.5 (45.8-65.0) years and for survived cases 55 (45-65) years. Though the median age was comparatively higher in deceased cases compared to survived cases, the difference failed to reach statistical significance (p=0.69). Most the infected patients were male (72.5%). There was no statistically significant difference in outcomes with reference to gender (p=0.74). There was no representation from the lower socio-economic class in this cohort, indicating low rate hospitalization in this group. Majority of the patients were from upper lower (42.7%) followed by lower middle socio-economic class (34.3%). Death rate was significantly higher in upper and upper middle socio-economic class in this study (Table I).

Table I : Socio-demographics characteristics of the patients stratified by outcome (n=178).

Characteristics	Total (n=178)	Survived (n=148)	Deceased (n=30)	p value
Age (Years)				
Median (IQR)	55 (45-65)	55 (45-65)	57.5 (45.8-65.0)	0.690†
<60 years	108 (60.7)	90 (60.8)	18 (60.0)	0.946*
≥ 60 years	70 (39.3)	58 (39.2)	12 (40.0)	
Sex				
Male	129 (72.5)	108 (73.0)	21 (70.0)	0.740*
Female	49 (27.5)	40 (27.0)	9 (30.0)	
Area of residence				
Urban	116 (65.2)	97 (65.5)	19 (63.3)	0.817*
Rural	62 (34.8)	51 (34.5)	11 (36.7)	
Socio-economic class[a]				
Upper	10 (5.6)	7 (4.7)	3 (10.0)	
Upper middle	31 (17.4)	22 (14.9)	9 (30.0)	
Lower middle	61 (34.3)	48 (32.4)	13 (43.3)	0.011*
Upper lower	76 (42.7)	71 (48.0)	5 (16.7)	
Lower	0 (0)	0 (0)	0 (0)	

Within parentheses are percentages over column total of respective variable, [a]Based on Kuppuswamy's socio-economic status scale 2020 with slight modification[11], IQR, interquartile range, p values were either reached from †Mann Whitney U test or *Chi-square test.

Table II shows that, more than half of the patients (63.5%) had at least one co-morbidity and the most frequent co-morbidities was hypertension (51.7%) followed by diabetes (46.6%). Compared with survivors, deceased cases showed a higher rate of co-morbidities including hypertension (70% vs 48%) diabetes (63.3% vs. 43.3%) and chronic kidney disease (16.7% vs. 3.4 %). Regarding smoking though compared to survivors, deceased cases showed a higher rate of smokers (46.7% vs. 30.4%) the difference was not statistically significant (p=0.084).

Table II : Frequency of co-morbidities and symptoms in patients stratified by outcome (n=178).

Variables	Total (n=178)	Survived (n=148)	Deceased (n=30)	p value*
Comorbidities				
At least one comorbidity	113 (63.5)	90 (60.8)	23 (76.7)	0.098
Hypertension	92 (51.7)	71 (48.0)	21 (70.0)	0.028
Diabetes mellitus	83 (46.6)	64(43.2)	19(63.3)	0.044
COPD/Asthma	17 (9.6)	14 (9.5)	3 (10.0)	0.926
Ischemic heart disease	10(5.6)	8 (5.4)	2 (6.7)	0.842
Chronic kidney disease	10(5.6)	5 (3.4)	5 (16.7)	0.004
Stroke	3 (1.7)	3 (2.1)	0 (0)	0.982
Tuberculosis	2 (1.1)	1 (0.7)	1 (3.3)	0.309
On immunosuppressive	2(1.1)	1 (0.7)	1 (3.3)	0.309
Pregnancy	2 (1.1)	1 (0.7)	1 (3.3)	0.309
Smoking habit				
Smokers[a]	59 (33.1)	45 (30.4)	14 (46.7)	0.084
Non-smokers	119 (66.9)	103 (66.9)	16 (53.3)	

[a]Included both past and current smokers, COPD: Chronic Obstructive Pulmonary disease, *p values were reached from either Chi-square test or Fisher's exact test.

Fever, cough, difficult breathing and fatigue were the most frequent clinical symptoms with 126 (70.8%), 116 (65.2%), 89 (50%) and 85 (47.8%) cases, respectively (Table III). Compared with survived cases, deceased cases were more likely to experience difficulty of breathing (p = 0.002) at admission (Table III).

Table III : Frequency of symptoms in patients stratified by outcome (n=178).

Symptoms	Total (n=178)	Survived (n=148)	Deceased (n=30)	p value*
Fever	126 (70.8)	101 (68.2)	25 (83.3)	0.097
Cough	116 (65.2)	96 (64.9)	20 (66.7)	0.847
Difficult breathing	89 (50.0)	66 (44.6)	23 (76.7)	0.002
Weakness/ fatigue	85 (47.8)	67 (45.3)	18 (60.0)	0.140
Throat pain	27 (15.2)	22 (14.9)	5 (16.7)	0.814
Diarrhea	25 (14.0)	23 (15.5)	2 (6.7)	0.202
Muscle ache	21 (11.8)	15 (10.1)	6 (20.0)	0.091
Headache	21 (11.8)	17 (11.5)	4 (13.3)	0.821
Chest pain	18 (10.1)	15 (10.1)	3 (10.0)	0.941
Runny nose	18 (10.1)	14 (9.5)	4 (13.3)	0.824
Altered smell/ taste	16 (9.0)	13 (8.8)	3 (10.0)	0.739
Shivering	14 (7.9)	12 (8.1)	2 (6.7)	0.724
Others[a]	17 (9.6)	13 (8.8)	4 (13.3)	0.314

[a]Other symptoms: abdominal pain 13 (7.3%) Vomiting 8 (4.5%) dizziness 7 (3.9%) red eye 5 (2.8%) *p valueswere reached from either Chi-square test or Fisher's exact test.

The results of the peripheral blood test of the patients on the day of hospital admission are listed in Table IV. It should be noted that, it was not possible to document all the laboratory parameters for each included case and so there are variable number of missing values for each laboratory parameters. Absolute WBCs and neutrophil counts were significantly higher in the deceased cases than in the survived cases (6.2 vs. 5.1, p= 0.002 and 4.3 vs. 3.1, p< 0.001, respectively) whereas the absolute lymphocyte count was significantly lower in the deceased cases than in the survived cases (0.8 vs. 1.2, p< 0.001). The median NLR of the deceased cases was higher than that of the survived cases (6.6 vs. 3.3, p< 0.001). No significant differences in haemoglobin and platelet count were found. D-dimer was significantly elevated in the deceased cases (0.7 vs. 0.4, p< 0.001) and similar trend was also observed for ferritin level between two groups.

Table IV : Laboratory parameters in patients stratified by outcome.

Symptoms	Total	Survived	Deceased	p value*
SpO_2, %	95 (80–97)	96 (95–98)	80 (80–86)	<0.001
WBCcount,$\times 10^9$ /l	5.4 (3.1–7.3)	5.1 (3.1–7.0)	6.2 (3.4–8.8)	0.002
Neutrophils, $\times 10^9$ /l	3.6 (2.6–5.0)	3.1 (2.4–4.3)	4.3 (2.9–5.9)	<0.001
Lymphocytes, $\times 10^9$ /l	1.0 (0.6–1.4)	1.2 (0.9–1.8)	0.8 (0.5–1.0)	<0.001
NLR	4.7 (0.9–9.5)	3.3 (1.0–3.4)	6.6 (2.1–11.1)	<0.001
Haemoglobin, g/l	11.2 (10.1-14.2)	11.1 (10.7–13.4)	11.9 (10.2-13.8)	0.200
Platelet count, $\times 10^9$ /l	197 (116-277)	203 (123-283)	188 (107-269)	0.642
D-dimer, g/ml	0.6 (0.3–1.3)	0.4 (0.2–0.8)	0.7 (0.5–1.9)	<0.001
Ferritin, median, g/l	841 (504–1240)	632 (394–1045)	965 (573–1364)	0.069

Data were expressed as Median (Interquartile rage), SpO_2, peripheral capillary oxygen saturation, WBC: White Blood Cell, NLR: Neutrophil to-Lymphocyte Ratio, *p values were reached from Mann Whitney U-tests.

Discussion

Though detection rate of COVID-19 is in decreasing trends since 1 September 2020 in Bangladesh, the case fatality rate was not declining in accordance with the detection rate.[12] On 3 April, 2020 first COVID-19 case was declared in Chattogram city of Bangladesh in a 67-year-old male who was diabetic and hypertensive.[13] As of 16 September 2020 total COVID-19 cases in Chattogram district was 2nd highest in Bangladesh followed by Dhaka.[12] From 3rd April onwards most of the COVID-19 cases of Chattogram district were admitted in Chittagong General Hospital and Chittagong Medical College Hospital.[12] So, we believed that this study among the COVID-19 confirmed patients admitted in these two hospitals, would give good insight about the epidemiological and clinical characteristics of COVID-19 patients of Chattogram as well as Bangladesh.

According to the data of the present series median age of the hospitalized COVID-19 infected patients was 55 years which is in agreement with other studies conducted in Chaina and Iran but was lower than the previous reports from Bangladesh.[14-17] Male predominance of the present study was in agreement with other studies conducted in and around our country.[14-17] Hypertension (21%) and diabetes (16%) remains the most common comorbidities found in patients of the present study like the world as well as Bangladesh.[14,15,18-22] In the present study 63.5% of the patients had at least one comorbidity and suggested that co-morbidity may be one of the most significant factors influencing hospitalization with COVID-19 in these two hospitals.The initial reports from China described fever, dry cough, breathing difficulties, headache and pneumonia as the typical clinical symptoms of COVID-19.[1,23,24] Patients of the current study also got admitted predominantly with fever (70.8%) cough (65.2%) breathlessness (50%) and fatigue (47.8%). These frequencies of the symptoms also comply with the CDC interim clinical guideline.[25]

In contrast to the previous studies from Bangladesh, the present study did not observe any significant association between older age and male gender for severe disease in patients with COVID-19.[14,15] However, it is in agreement with the meta-analysis which reported that age and gender were not the independent predictive factor for poor outcome.[9] It is well established that, with regard to respiratory infections, people from deprived backgrounds have been noted to have both a higher incidence of disease as well as a more severe infection.[26] However, the current study demonstrated that, none of the hospitalized patients were from lower socio-economic class. Around 84% of the patients who died were from either upper or middle socioeconomic class. Khan et al. compared the outcome of hospitalized COVID-19 patients in low and high SES group and reported that, the SES does not have any impact on outcome of hospitalized patients with COVID-19.[27] Regarding symptoms breathlessness was the only symptom significantly associated with mortality in the present study. Though this is in agreement with other reports, other symptoms like anorexia, fatigue were also revealed to be associated with severe form of diseasein other report.[9,28] World Health Organization, in a recent review stated that the available evidence suggests that smoking is associated with increased severity of disease and death in hospitalized COVID-19 patients.[29] Though similar trend was also observed in the present study the association was not statistically significant probably attributable to small sample size and non probability sampling technique.

Regarding laboratory parameters absolute WBC count, neutrophil counts, D-dimer level and ferritin level were significantly higher in the deceased cases than in the survived cases, whereas the absolute lymphocyte count was significantly lower in the deceased cases than in the survived cases in the present study. These are in accordance with the existing evidences.[8,9,28] One of the important finding of the current study was that, the median NLR of the deceased cases was significantly higher than that of the survived cases ($p < 0.001$). Recent evidences supported that NLR is one of the most useful factor affecting the incidence of severe COVID-19.[14,30] In a resource constrain setting like ours this index would be more useful diagnostic tool to identify patients with the most serious COVID-19 infection.

Limitations

The study has some limitations including small sample size collected conveniently from two government level hospitals. In addition, certain crucial

factors that might play an important role in the pathogenesis of COVID-19, including secondary infection, treatment and immunological status were not assessed.

Conclusions

This study identified few factors that are associated with COVID-19 related mortality in a group of patients from Bangladesh. This might improve our understanding of COVID-19 progression and provide baseline data to compile or improve the prediction models for the estimation of COVID-19 prognosis in our setting.

Recommendations

Findings are available which indicate that COVID-19 can result in prolonged illness even among persons with milder outpatient illness, including young adults.[31] Future longitudinal studies are desirable to reveal such long-term impacts of SARS-CoV-2 infection in our country.

Acknowledgments

Prof. MA Sattar, Prof. Aniruddha Ghose, Prof. Ranjan Kumar Nath, Dr. Md. Abdur Rob of Chittagong Medical College, Chattogram.

Contribution of authors

FUA: Conception, design, data analysis, interpretation of data drafting and final approval.

BC: Data collection, drafting and final approval.

HMHM: Data collection, data analysis, drafting and final approval.

PC: Data collection, interpretation of data, drafting and final approval.

FKP: Data collection, drafting and final approval.

RAB: Data analysis, critical revision and final approval.

SP: Conception, critical revision and final approval.

Disclosure

All the authors declared no competing interest.

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