Predictors of Outcome in Hospitalized Adult COVID-19 Patients Admitted to a Tertiary Hospital in Chattogram

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Abstract

Background: The COVID-19 pandemic emerged as a major public health emergency affecting the healthcare services all over the world. It is essential to analyze the epidemiological and clinical characteristics of patients with COVID-19 in different parts of our country. This study highlights clinical experience in managing patients with COVID-19 at a tertiary care centre in southeastern Bangladesh.

Materials and methods: Clinical characteristics and outcomes of consecutive 199 adult patients admitted to Chittagong Medical College Hospital, Chattogram, Bangladesh, from February 1 to March 31, 2021 were studied in this prospective observational study. The diagnosis of SARS-CoV-2 infection was confirmed by real-time reverse transcriptase polymerase chain reaction (RT-PCR) on throat and/or nasopharyngeal swabs. All patients were managed according to the hospital's consensus protocol and in accordance with National Guidelines on clinical management of COVID-19.

Results: The median age of the patients was 57 years (Range: 20-102 years) and 118 (59.3%) were male. One hundred and thirty two (67.3%) patients had associated comorbid condition and diabetes (44.7%) and hypertension (33.3%) were the most common. Majority (57.3%) was classified as having moderate severity and mortality of 10.1% (20 patients) was observed. Elderly age (>60 years), diabetes mellitus, elevated levels of D-dimer and neutrophil-lymphocyte ratio were the predictors of mortality.

Conclusions: These findings suggest that the mortality rate in elderly COVID-19 patients with comorbidity is high and neutrophil-lymphocyte ratio could be a cost effective predictor of mortality in our context.

Key words: COVID-19; Outcomes; Predictors.

Introduction

The World Health Organization (WHO) reported more than 323 million confirmed cases of SARS-CoV-2 infection and more than 5.5 million deaths globally, with Bangladesh contributing to more than 1.6 million confirmed patients and over 28 thousand deaths as of 16 January 2022.[1,2] There was a slow spread initially in Bangladesh after declaration of the first case on March 8 2020and gradually COVID-19 has engulfed the entire country in accordance with the global scenario.[3] Patients with SARS-CoV-2 infection may have mild-to-asymptomatic illness, but some rapidly progress to Acute Respiratory Distress Syndrome (ARDS) Multi-Organ Dysfunction Syndrome (MODS) and death.[4] Roughly 20% of cases lead to clinically complex and severe conditions. Older adults aged more than 60 years of age with comorbid conditions are the most vulnerable group.[4,5] Recent studies have also indicated that COVID-19's clinical spectrum may vary worldwide across diverse ethnic backgrounds and geographical locations.[6,7]

It is pertinent to identify the clinical and demographic characteristics of patients considering the novelty and substantial heterogeneity of the illness across the world. Understanding regional features are always important. Although previous studies detailed the clinical presentation of hospital-admitted reverse transcription–PCR (RT-PCR) positive patients with COVID-19, very few originate from Bangladesh and few are still from the Southeastern part of Bangladesh.[8-14] Therefore, the present study was undertaken to describe the clinical features and outcome and to identify the predictors of clinical outcome, as early identification would be paramount in optimal utilization of medical resources in managing these high risk-patients.

Materials and methods

This prospective observational study was conducted at the Chittagong Medical College Hospital, a COVID dedicated government hospital, Chattogram, Bangladesh, from February

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1 to March 31, 2021. Individuals admitted in the COVID block of this hospital were screened. Consecutive adult patients (>18 years) who tested positive on RT-PCR assay for SARS-CoV-2 on a throat and/or a nasopharyngeal swab were included in the study. Pregnant women were excluded. 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.

A written informed consent was taken in person from patients by the treating team while consent was obtained from a legal representative in case the patient was unable to consent himself/herself. Demographic details, medical history including comorbidities, and vital parameters were recorded at admission to the hospital. Baseline laboratory parameters, treatment details and clinical outcomes were also collected. Case definition and severity categorization was done in accordance with the national guideline. Patients were treated as per the institutional guideline.[15]

Statistical analyses were performed with Statistical Package for the Social Sciences version 23.0 for Windows. Patients were categorized according to their outcome (Survivor and non-survivor groups). Categorical variables were summarized as frequencies and percentages. Continuous data were expressed as median and Interquartile Range (IQR) as they are not normally 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.Logistic regression was applied for multivariate analysis for both demographic and clinical characteristics as well as laboratory parameters. Variables significantly associated with mortality during univariate analysis were directly considered as predictors of mortality and others were excluded from multivariate analysis. p value <0.05 was considered as statistically significant.

Results

During the study period, 199 consecutive patients were diagnosed to have COVID-19 and were included in the study. The baseline demographic and clinical characteristics of these patients are summarized in Table I. The median age of the patients was found to be 57 years (Range: 20-102 years) and 118 (59.3%) were male. One hundred and thirty two (67.3%) patients had associated comorbid condition of varying severity. These included diabetes in 88 (44.7%) hypertension in 67 (33.3%) and chronic obstructive pulmonary disease in 15 (7.5%) patients. Fifty eight patients (29.1%) had multiple comorbidities. Majority (57.3%) were classified as having moderate severity. Around 90% of the patients improved and other 20 (10.1%) died in hospital (Table I).

Table I Baseline characteristics and clinical outcomes of COVID-19 patients (n=119)

Characteristics	Frequency	Percentage (%)
Age (Years)		
Median (Range)	57 (20-102)	
<60 years	121	60.8
≥60 years	78	39.2
Sex		
Male	118	59.3
Female	81	40.7
Comorbidities		
None	67	33.7
One comorbidity	74	37.2
More than one comorbidity	58	29.1
Diabetes mellitus	88	44.7
Hypertension	67	33.3
COPD/Asthma	15	7.5
Ischemic heart disease	12	6.0
Chronic kidney disease	10	5.0
Stroke	8	4.0
Tuberculosis	7	3.5
On immunosuppressive	5	2.5
Clinical severity		
Mild	37	18.6
Moderate	114	57.3
Severe	12	6.0
Critical	36	18.1
Clinical outcome		
Improved and Discharged	179	89.9
Expired in hospital	20	10.1

At admission, leucocyte counts had increased in 35patients (17.6%) and were below the normal range in ten (5.0%) patients. High neutrophilto-lymphocyte ratio (NLR) (≥ 3.5) was observed in 74 (37.2%) patients. Twenty three (11.6%) patients had thrombocytopaenia and 38 (19.1%) had anemia. Ninety nine (49.7%) patients had high C-reactive protein, 128 (64.3%) had raised D-dimer, and 101 (50.8%) had increased ferritin (Table II).

Table II Baseline laboratory parameters of COVID-19 patients (n=199)

Parameters	Frequency	Percentage (%)
Haemoglobin, g/l		
Median (IQR)	12.7 (11.6-13.9)	
Decreased	38	19.1
WBC count,×10^9 /l		
Median (IQR)	7.6 (6.2-9.6)	
Increased	35	17.6
Decreased	10	5.0
NLR		
Median (IQR)	2.35 (1.48-5.7)	
Increased	74	37.2
Platelet count, ×10^9 /l		
Median (IQR)	305 (224-486)	
Increased	30	15.1
Decreased	23	11.6
CRP		
Median (IQR)	2.1 (0.8-5.4)	
Increased	99	49.7
D-dimer, g/ml		
Median (IQR)	0.94 (0.5-1.9)	
Increased	128	64.3
Ferritin, median, g/l		
Median (IQR)	90 (40.5-200.5)	
Increased	101	50.8

NLR: Neutrophil to-Lymphocyte Ratio.

Table III depicts that there was a significant difference in the median age of survivors and non-survivors of COVID-19 (p<0.001). Hypertension and diabetes were significantly more common among non-survivors as compared to survivors. Regarding laboratory parameters, It is evident from table II that median values of leucocyte count, NLR and D-dimer levels were significantly higher among non-survivors as compared to survivors.

Table III Association between baseline clinical and laboratory characteristics with in-hospital outcome

Characteristics	Survivor (n=179)	Non-survivor (n=20)	p value
Age (Years)			
Median (IQR)	55 (41-59)	60 (56-71)	<0.001†
<60 years	115 (64.2)	6 (30.0)	0.003*
≥60 years	64 (35.8)	14 (70.0)	
Sex			
Male	105 (58.7)	13 (65.0)	0.584*
Female	74 (41.3)	7 (35.0)	
Comorbidities			
Diabetes mellitus	74 (41.3)	14 (70.0)	0.014*
Hypertension	55 (30.7)	12 (60.0)	0.002*
COPD/Asthma	12 (6.7)	3 (15.0)	0.183**
Ischemic heart disease	10 (5.6)	2 (10.0)	0.431*
Chronic kidney disease	9 (5.0)	1 (5.0)	0.995**
Stroke	8 (4.5)	0 (0.0)	0.115**
Tuberculosis	6 (3.4)	1 (5.0)	0.704**
On immunosuppressive	4 (2.2)	1 (5.0)	0.917**
Laboratory parameters			
Haemoglobin, g/l	11.1 (10.7–13.4)	11.9 (10.2-13.8)	0.200†
WBC count,×10^9 /l	6.1 (3.1–8.0)	7.2 (3.4–9.8)	0.002†
NLR	3.3 (1.0–3.4)	6.6 (2.1–11.1)	<0.001†
Platelet count, ×10^9 /l	203 (123-283)	188 (107-269)	0.642†
CRP	2.0 (0.8-5.1)	2.2 (0.9-5.6)	0.112†
D-dimer, g/ml	0.4 (0.2–0.8)	0.7 (0.5–1.9)	<0.001†
Ferritin, median, g/l	632 (394–1045)	965 (573–1364)	0.069†

Within parentheses are percentages over column total of respective variable, IQR, Interquartile range, p values were either reached from †Mann Whitney U test or *Chi-square test or **Fisher's exact test.

Table IV depicts that among demographic and clinical parameters, older age group (AOR=4.12, 95%CI: 1.11-20.12) and diabetes (AOR=2.47, 95% CI: 1.35-6.19) were found as significant predictors of mortality in our patients. Amongst laboratory parameters, D-dimer level (AOR=7.24, 95% CI: 1.16-45.16) and NLR (AOR=1.67, 95%CI: 1.11-11.20) were significant predictors of mortality.

Table IV Predictors of in-hospital mortality in COVID-19

Variables	COR (95% CI)	AOR (95% CI)
Age group		
≤60 years	Reference	Reference
>60 years	10.01 (5.12-29.11)	4.12 (1.11-20.12)
Comorbidity (present v/s absent)		
Diabetes mellitus	5.81 (2.91-17.71)	2.47 (1.35-6.19)
Hypertension	6.77 (2.52-18.21)	2.39 (0.65-8.83)
WBC count,×10^9 /l	5.01 (1.81-13.22)	1.34 (0.31-6.65)
NLR 4.01 (2.01-9.57)	1.67 (1.11-11.20)	
D-dimer, µg/ml	16.04 (4.99-51.54)	7.24 (1.16-45.16)

COR: Crude Odds Ratio, AOR: Adjusted Odds Ratio, CI: Confidence Interval.

Discussion

Through univariate and multivariate analysis, we identified some demographic, clinical and laboratory parameters as predictors of mortality among the hospitalized patients with COVID-19. The study observed many similar and few contrasting findings when compared with national and international studies.

According to the data of the present series median age of the hospitalized COVID-19 infected patients was 57 years which is in agreement with other studies conducted in and around our country.[16-18] In the present study, advanced age was found to be a significant predictor of mortality. Similar observations were made from the studies carried out in India and New York.[19,20] Accelerated inflammation and immune senescence have been shown to be associated with worse clinical outcomes in elderly COVID-19 patients.[21]

Majority of our patients were males. Male predominance of the present study was in agreement with other studies conducted in and around our country.[9-14,19] The gender distribution was similar in survivor and non-survivor group. A preliminary Chinese study investigated the role of gender in COVID-19 and found that while males and females had the same prevalence; males had higher mortality as compared to women.[22] In another study from Iran, male gender was significantly associated with the risk of death among COVID-19 patients.[23] These findings are in contrast to the findings of our study. However, our results were in agreement with the findings of Chauhan et al. from India.[19]

Comorbidities like diabetes, hypertension, obesity, etc. have been associated with poor COVID-19 outcomes.[24] Among the comorbidities mentioned in table I, only diabetes mellitus was found to be independently associated with an increased risk of mortality. Similar findings have been observed during the COVID-19 outbreak in United States.[25] Diabetes creates a hyperinflammatory state and impairs innate and cell-mediated immunity, which may predispose patients to the cytokine storm known to occur in severe COVID-19.[26]

We observed significantly higher level of total leucocyte count, NLR, and D-dimer among the non-survivors than survivor. However, in regression analysis only D-dimer and NLR were revealed as independent predictor of in-hospital mortality. D-dimer has been found to be an important prognostic factor for mortality in COVID-19 patients.[19,27] Raised D-dimer levels is associated with increased mortality in patients without any evidence of pulmonary thromboembolism or deep vein thrombosis.[28] Recent evidences supported that NLR is one of the most useful factor affecting the incidence of severe COVID-19.[17,18] 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 single government hospital. In addition, certain crucial factors that might play an important role in the pathogenesis and outcome of COVID-19, including secondary infection, treatment and immunological status were not assessed.

Conclusions

Older age, diabetes mellitus, elevated D-dimer, and NLR at baseline are the risk factors for COVID-19 related mortality. This study identified few factors that were 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

In the light of the limitations of the present study, we recommend further multicentre studies with a larger patient cohort to inform clinicians, public health researchers and policymakers regarding the local nature of COVID-19 in Chattogram, Bangladesh.

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Contribution of authors

RB-Conception, designing, Acquision of data, Interpretation of data, drafting the article and final approval.

MNK- Design, acquision of data, analysis,critical revision of content and final approval.

EEU -Conception, drafting and final approval.

MHA- Design, interpretation of data, critical revision and final approval.

MC- Interpretation of data, drafting of article and final approval.

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Disclosure

All authors declared no competing interest.

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