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Clinical and radiological characteristics of adult hospitalized coronavirus disease-2019 patients of Dhaka, Bangladesh

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Abstract: The severity of Coronavirus disease-2019 (COVID-19) varies among individuals and some influential factors leads to critical infections and death. This study aimed to assess various clinical data of hospitalized patients and identify the determinants of critical COVID-19 infection. This was a cross-sectional study among hospitalized COVID-19 patients confirmed by reverse transcription polymerase chain reaction (RT-PCR). Data was collected from a single Centre between January to April 2021 by experienced physicians of Ad-din Medical College Hospital. All of the laboratory tests were performed by technical experts and the data was analyzed by Statistical package for the social sciences software. Among the study participants 25% were Intensive care unit (ICU) patients and the mean age of them were higher (59 years) than non-ICU (55 years) patients. Our analysis has identified diabetes mellitus (AOR=2.5, 95%CI: 1.1-5.4) and ischemic heart disease (AOR=3.1, 95%CI: 1.1-8.9) as significant predictor of critical outcome (ICU admission). Anemia (AOR=3.3, 95%CI: 1.5-7.4), lymphopenia (AOR=2.9, 95%CI: 1.2-7.1), and thrombocytopenia (AOR=4.2, 95%CI: 2.7-12.9) was also associated critical outcome. Biomarkers of kidney injury (creatinine, blood urea nitrogen), liver damage (alanine transaminase, aspartate aminotransferase, fibrinogen) and electrolyte imbalance (sodium and potassium level) were also significantly associated with critical infection. A higher d-dimer level (≥ 2.5) was the most important predictor (AOR=11.5, 95%CI: 5.4-24.6) of critical COVID 19 infections. The study has revealed socio-demographic, comorbidity, and radiological risk factors of critical COVID-19 infections. The identified risk factors would be considered for decision making during the treatment process.

Keywords: COVID-19; comorbidity; biomarkers; critical infection; Bangladesh

1. Introduction

Since the inception of coronavirus disease 2019 (COVID-19) pandemic, more than five million people were died worldwide due to this highly infectious disease (Johns Hopkins Coronavirus Resource Center, 2021; Shang *et al.*, 2020). Severely infected patients required hospitalization which would bring extremely high burden due to substantial hospital management and treatment cost. Moreover, the critically ill patients required Intensive

care unit (ICU) support which imposed a large economic burden and a huge number of death cases (Di Fusco *et al.*, 2021; Ghaffari Darab *et al.*, 2021). Therefore, country's health system faces a significant stress in terms of manpower and financing (Ghaffari Darab *et al.*, 2021).

Respiratory viral disease have a highly infectious nature, virulence and pathogenicity and historically associated with a huge mortality (Piret & Boivin, 2021). Similarly, COVID-19 is also highly infectious and the severity of disease depends on host virus interaction and various characteristics of host such as comorbidity, lifestyle, immunity, etc. (Burrell *et al.*, 2017; Kash & Taubenberger, 2015). Like other respiratory viruses, it uses the same means of transmission as influenza, which was started in 1889 and continued as a public health threat due to its intermittent style of pandemic outbreaks (Noor & Maniha, 2020).

The ongoing COVID-19 pandemic has appeared as less dreadful compared to the Spanish influenza in terms mortality (Lin *et al.*, 2020). However, due to high infectious rate of viral strains, around 260 million people worldwide have been infected until 20 November 2021. Including other South Asian countries, Bangladesh has also faced several waves of COVID-19 with around 1.6 million cases and twenty-eight thousand death (Johns Hopkins Coronavirus Resource Center, 2021).

Majority of COVID-19 patients face mild to moderate symptoms and only about 5% requires hospitalization those are the main medical resources consumer. Smaller portion become critically ill and requires ICU admission mostly due to septic shock, respiratory failure, organ damage, etc. (Gao, 2020). The mortality rate of ICU patients was also observed high in various countries such as, 28% in United States of America (Nguyen *et al.*, 2021), 27% in Italy (Grasselli *et al.*, 2020), 45% in Kuwait (Ayed *et al.*, 2020), and 11.67% in Bangladesh (Halim *et al.*, 2021). According to recent observations, the death rate due to COVID-19 infections has been decreasing around the world (Ledford, 2020).

To decrease the mortality due to COVID-19, it is important to control the risk factors for severe infection. The association between socio-demographic factors, comorbidities with critical covid infections has widely been studied (Halim *et al.*, 2021). Various laboratory biomarkers have also been discussed in studies conducted various parts of the world (Samprathi & Jayashree, 2021). Biomarkers for Anemia, lymphopenia, leukocytosis, kidney injury, liver damage, damage in body tissues, electrolyte imbalance etc. are also important in the outcome of COVID-19 patients (Hashem *et al.*, 2021; Samprathi & Jayashree, 2021). In Bangladesh, radiological data is very much limited and no study has compared the variation of biomarkers between ICU and non-ICU patients. Few studies were conducted focusing biomarkers of specific damage, however, the comprehensive study focusing multiple types of biomarkers yet not conducted. Therefore, the aim of this study was to assess the various types of clinical and radiological characteristics of COVID-19 patients and determine the factors associated with critical infection.

2. Materials and Methods

2.1. Study design

This was a single Centre based cross-sectional study among hospitalized adult COVID 19 patients in Dhaka city. The report was prepared following the strengthening the reporting of observational studies in epidemiology (STROBE) checklist for cross sectional studies. All the patients were confirmed COVID-19 positive by reverse transcription polymerase chain reaction (RT-PCR) assay and had available health records for the study.

2.2. Study setting

The study site was the Ad-din Medical College Hospital, which is one of the largest privately facilitated tertiary level hospitals in Dhaka City. Data was collected from hospital premises between January to April 2021 by experienced physicians. After hospitalization of patients, all of the laboratory tests were performed by technical experts immediately after instructed by respective physicians.

2.3. Study participants, sampling and data collection

The participants were confirmed COVID-19 patients admitted in the Ad-din Medical College Hospital. During the study period around 30 COVID 19 patients admitted each day in the hospital. As this is a single Centre hospital-based study among COVID-19 patients, there was a high-risk selection bias. To control this, one of every ten patients admitted were systematically selected for the study. Patients less than 18 years old and those were not interested were excluded from the study. During the study period the complete data of 323 COVID-19 patients was collected and among them 82 patients were admitted to intensive care unit (ICU) after the recommendations from physician. Data with incomplete information were excluded from the analysis.

2.4. Tools and variables

The laboratory reports and clinical records were checked by experienced medical doctors and extracted for the analysis. The laboratory data includes biomarkers for anemia, lymphopenia, leukocytosis, kidney injury, liver damage, damage in body tissues, electrolyte imbalance etc. Patients' socio-demographic characteristics, and various comorbidities were also extracted for the analysis. Among the comorbidities, diabetes mellitus (DM), hypertension, hypothyroidism, malignancy, asthma, and ischemic heart disease (IHD) were analyzed. Some other complications discussed in this study were bacterial co-infection, acute respiratory distress syndrome (ARDS) and septic shock etc.

2.5. Statistical analysis

Based on the outcome, patients were categorized into ICU patients and non-ICU patients. The collected data were entered in Microsoft excel-2013 and statistical analysis was performed by IBM Statistical package for the social sciences (SPSS) version-25 software. The descriptive analysis of categorical variables was performed by frequency, percentage and continuous variables were reported as means with standard deviation. Association between continuous variables and outcome was analyzed by Mann-Whitney U test. Association among categorical variables were analyzed Pearson's chi-square test, Fisher's exact test when appropriate. Statistically significant variables were subjected to multiple logistic regression analysis to identify the predictors of critical COVID-19 infection.

2.6. Ethical consideration

Each of the steps of this study was completed following the Helsinki Declaration (1964). Patient's data were maintained confidential. Informed consent was taken from each of the study participants.

3. Results

A total of 323 COVID-19 patients were included in the analysis and among them 82 (25%) were transferred to ICU with the recommendations of respective physician. The mean age of ICU patients (58.5 years) was higher than the non-ICU patients (55.5 years) and the variation was statistically significant ($p=0.04$). We categorized the patients into three age group such as young (≤ 40 years), middle aged (41-60 years) and older aged (>60 years). Majority of our participants were from middle aged group. The prevalence of ICU patients was increased with the increase of age such as, 5.9% among young, 26.9% among middle aged, 28.7% among older aged patients and the association was statistically significant ($p=0.02$). The majority (70.6%) of our study participants were male and the prevalence of ICU admission was significantly higher among male compared to female ($p=0.02$). We also analyzed blood group of COVID-19 patients, where 'A' and 'B' blood group had higher ICU admission rate than 'AB' and 'O' Blood group (Table 1).

About 49% of our study participants were diabetic and a significantly higher proportion of diabetic (31%) patients were subjected ICU admission compared to non-diabetic (20%) patients ($p=0.02$). A higher proportion of hypertension patients were also admitted to ICU. A high proportion (61%) of hospitalized patients has asthma problem. Around 3% of the COVID-19 patients also had malignancy and hyperthyroidism was present in 5% patients. Around 12% of our study participants had pre-existing IHD which is also significantly associated with more severe condition or ICU admission ($p=0.03$). Around 33% patients had inter-district travel history within 15 days of symptom. Analysis also indicates, the chance of ICU admission increases with the increase days prior to hospitalization (Table 1).

One of the major objectives this study was to assess various types of biomarkers related to COVID-19 infection. Blood hemoglobin level was found low for 47.7% cases, which is also highly prevalent among ICU patients compared to non-ICU patients ($p=0.01$). The mean White blood cell (WBC) count was $8.5 \times 10^9/L$, which is slightly higher among ICU patients and the mean neutrophils count was $6.4 \times 10^9/L$, which is also slightly higher among ICU patients. The difference of lymphocytes count was significantly associated with critical infection ($p=0.005$), the mean lymphocyte count of ICU patients was $1.17 \times 10^9/L$, which is lower than non-ICU patients. The platelet count was also significantly lower ($p=0.01$) among ICU patients ($202 \times 10^9/L$) compared to non-ICU patients. The men d-dimer was observed very high among high among ICU patients ($3.6 \mu\text{g/ml}$) whereas the reference range is $<2.5 \mu\text{g/ml}$. Our data suggests that 21% hospitalized patients had acute kidney infection (AKI) which is even higher among ICU patients (42%). The biomarker of kidney injury, such as, creatinine, blood urea nitrogen (BUN) was significantly higher among ICU patients. We have also analyzed several biomarkers of liver damage and the mean value of fibrinogen ($p=0.001$), alanine transaminase (ALT) ($p=0.001$), and aspartate aminotransferase (AST) ($p=0.003$) was also significantly higher among ICU patients (Table 2).

The mean lactate dehydrogenase (LDH) level was observed slightly lower among ICU admitted patients. Septic shock was also observed 52% hospitalized patients with COVID-19 and the proportion is significantly higher among critically infected patients. The mean sodium and potassium level of critically ill patients were lower than the non-ICU patients and variation was statistically significant. Proportion of bacterial co-infection was also higher among critically ill patients (Table 2).

Our multiple logistics regression analysis indicates, DM (AOR=2.5, 95%CI: 1.1-5.4) and IHD (AOR=3.1, 95%CI: 1.1-8.9) as significant predictor of critical infection. It is also evident that, with the increase of age, the risk of critical infection increases and female has significantly lower risk of developing critical infection (AOR=0.1, 95%CI: 0.04-0.3). Presence of anemia (AOR=3.3, 95%CI: 1.5-7.4), lymphopenia (AOR=2.9, 95%CI: 1.2-7.1), and thrombocytopenia (AOR=4.2, 95%CI: 2.7-12.9) was also associated with ICU admission. Indicator of liver damage such as, ALT (AOR=13.39, 95%CI: 5.0-35.8) was also significantly associated with critical infection. A higher D-dimer level (≥ 2.5) was the most important predictor (AOR=11.5, 95%CI: 5.4-24.6) of critical infections (Table 3).

Table 1. Descriptive statistics of socio-demographic and pre-existing comorbidity related factors.

Variables	All patients, N=323	ICU, n = 82	Non-ICU, n = 241	p value
Age, Mean (SD)	56.25 (12.03)	58.54 (8.7)	55.47 (12.9)	0.04*
Age group, n (%)				
< 40 years	34 (10.5)	2 (5.9)	32 (94.1)	0.02*
41-60 years	169 (52.3)	45 (26.9)	122 (73.1)	
>60 years	120 (37.2)	35 (28.7)	87 (71.3)	
Sex, n (%)				
Male	228 (70.6)	67 (29.4)	161 (70.6)	0.02*
Female	95 (29.4)	15 (15.8)	80 (84.2)	
Blood group, n (%)				
A	78 (24.15)	24 (30.8)	54 (69.2)	0.16
AB	43 (13.31)	11 (25.6)	32 (74.4)	
B	104 (32.2)	30 (28.8)	74 (71.2)	
O	98 (30.34)	17 (17.3)	81 (82.7)	
RH factor, n (%)				
Negative	24 (7.43)	8 (33.3)	16 (66.7)	0.35
Positive	299 (92.57)	74 (24.7)	225 (75.3)	
Diabetes mellitus, n (%)				
Diabetic	158 (48.9)	49 (31.0)	109 (69)	0.02*
Non-diabetic	165 (51.1)	33 (20.0)	132 (80)	
Hypertension, n (%)				
Yes	139 (43.03)	35 (25.18)	104 (74.82)	0.29
No	184 (56.97)	44 (23.91)	140 (76.09)	
Asthma, n (%)				
Absent	198 (61.3)	44 (22.2)	154 (77.8)	0.10
Present	125 (38.7)	38 (30.4)	87 (69.6)	
Malignancy, n (%)				
Absent	314 (97.2)	78 (24.8)	236 (75.2)	0.18
Present	9 (2.8)	4 (44.4)	5 (55.6)	
Hypothyroidism, n (%)				
Absent	306 (94.7)	76 (24.8)	230 (75.2)	0.34
Present	17 (5.3)	6 (35.3)	11 (64.7)	
Ischemic heart disease, n (%)				
Absent	285 (88.2)	67 (23.5)	218 (76.5)	0.03*
Present	38 (11.8)	15 (39.5)	23 (60.5)	
Travel history (≤ 15 days before infection), n (%)				
No	216 (66.9)	50 (23.1)	166 (76.9)	0.19
Yes	107 (33.1)	32 (29.9)	75 (70.1)	
Days prior to hospitalization, Mean (SD)	4.98 (1.82)	5.22 (1.54)	4.81 (1.84)	0.08

Table 2. Descriptive statistics of clinical and radiological findings on hospital admission.

Variables	All patients, N=323	ICU, n = 82	Non-ICU, n = 241	p value
Anemia, n (%)				
Absent	169 (52.3)	32 (18.9)	137 (81.1)	0.01*
Present	154 (47.7)	50 (32.5)	104 (67.5)	
Haemoglobin (g/L), Mean (SD)	130.05 (24.64)	125.22 (23.44)	131.69 (24.87)	0.03*
WBC (x10 ⁹ /L), Mean (SD)	8.52 (2.31)	8.77 (2.4)	8.44 (2.27)	0.85
Neutrophils (x10 ⁹ /L), Mean (SD)	6.39 (1.39)	6.45 (1.49)	6.36 (1.36)	0.82
Lymphocytes (x10 ⁹ /L), Mean (SD)	1.29 (0.40)	1.17 (0.28)	1.33 (0.43)	0.005*
Platelets (x10 ⁹ /L), Mean (SD)	223.48 (59.01)	202.01 (39.7)	230.78 (62.7)	0.01*
D-dimer (µg/ml), Mean (SD)	2.82 (1.34)	3.57 (1.67)	1.84 (0.83)	0.001*
Acute kidney injury, n (%)				
Absent	255 (78.95)	53 (20.8)	202 (79.2)	0.01*
Present	68 (21.05)	29 (42.6)	39 (57.4)	
Creatinine (mg/dL), Mean (SD)	1.63 (1.3)	2.086 (1.64)	1.47 (1.12)	0.001*
BUN (mg/dL), Mean (SD)	30.12 (17.16)	42.4 (24.5)	25.94 (12.7)	0.001*
Fibrinogen (g/L), Mean (SD)	6.27 (1.34)	6.88 (1.26)	6.06 (1.3)	0.001*
Albumin (g/L), Mean (SD)	25.49 (2.24)	25.23 (1.3)	25.58 (2.48)	0.31
ALT (IU/L), Mean (SD)	41.1 (15.2)	53.33 (15.32)	36.92 (12.66)	0.001*
AST (IU/L), Mean (SD)	46.7 (12.2)	50.317 (12.63)	45.5 (11.9)	0.003*
CRP (mg/L), Mean (SD)	93.9 (44.9)	91.2 (38.5)	94.86 (46.95)	0.98
LDH (IU/L), Mean (SD)	448.08 (168.1)	442.63 (159.3)	449.93 (171.2)	0.81
Acute respiratory distress syndrome, n (%)				
No	175 (54.2)	42 (24.0)	133 (76.0)	0.74
Mild	39 (12.1)	10 (25.6)	29 (74.4)	
Moderate	58 (17.96)	18 (31.0)	40 (69.0)	
Severe	51 (15.8)	12 (23.5)	39 (76.5)	
Septic shock, n (%)				
Absent	155 (47.99)	30 (19.4)	125 (80.6)	0.017*
Present	168 (52.01)	52 (31.0)	116 (69.0)	
Sodium (mEq/L), Mean (SD)	133.6 (9.1)	131.79 (6.39)	134.17 (9.8)	0.01*
Potassium (mmol/L), Mean (SD)	3.4 (0.5)	3.06 (0.56)	3.51 (0.43)	0.001*
Bacterial co-infection, n (%)				
No	259 (80.2)	61 (23.6)	198 (76.4)	0.13
Yes	64 (19.8)	21 (32.8)	43 (67.2)	

Table 3. Multiple logistic regression analysis of statistically significant factors of ICU admission.

Associated factor	AOR	95% CI		P value
		LCI	UCI	
Age (>60 years)	6.94	1.17	40.63	0.03*
Age (41-60 years)	9.91	1.66	58.48	0.01*
Age (<40 years)	Reference			
Gender (female)	0.11	0.04	0.31	0.001*
Preexisting diabetes mellitus (yes)	2.48	1.13	5.44	0.024*
Preexisting ischemic heart disease (yes)	3.06	1.05	8.92	0.04*
Anemia (yes)	3.29	1.46	7.41	0.004*
Lymphocytopenia (yes)	2.93	1.21	7.13	0.02*
Thrombocytopenia (yes)	4.16	2.68	12.89	0.002*
D-Dimer level (abnormal)	11.55	5.42	24.62	0.001*
Acute kidney infection (yes)	2.109	0.93	4.78	0.07
ALT level (abnormal)	13.39	5.01	35.86	0.001*
Fibrinogen level (abnormal)	2.59	0.45	19.12	0.35
Experienced septic shock (yes)	1.25	0.56	2.78	0.58

4. Discussion

In this cross-sectional study, we have described the clinical and radiological characteristics of adult hospitalized confirmed COVID-19 patients. We have evaluated patients' sociodemographic variables, comorbidity status, various biomarkers of blood, kidney, and liver infections, etc. Moreover, we have also analyzed how these variables are associated with more severe infection or ICU admission.

Our study has analyzed various comorbidity related risk factors, where we identified DM and IHD as significant predictor of ICU admission. Similar to previous data, there was a high prevalence of DM among hospitalized COVID-19 patients (Alguwaihes *et al.*, 2020; Mithal *et al.*, 2021). DM is also associated with higher death rate and lower survival time (Alguwaihes *et al.*, 2020). Cardiovascular problems have always been a significant predictor in hospital mortality and patients with coronavirus infection is associated with higher risk of aggravation and mortality (Agarwal *et al.*, 2020; Islam *et al.*, 2020).

Among the severe COVID 19 patients' hematological abnormalities such as anemia, thrombocytopenia, lymphopenia are common features. Anemia has been discussed as an independent predictor of critical outcome in COVID-19 which usually affects elderly and can negatively influence patients' quality of life (Anai *et al.*, 2021; Bergamaschi *et al.*, 2021). According to our analysis low hemoglobin level is an independent predictor for severe outcome of COVID-19 infection and more than three times increases the risk of ICU admission. Some studies have assessed whether lymphopenia is a reliable predictor for COVID-19 severity or not. Lee *et al.* concluded that, lymphopenia might be a strong indicator for clinical use during the management of COVID-19 patients (Lee *et al.*, 2021). Low platelet count or thrombocytopenia is a common scenario of COVID-19 as the virus is able affect bone marrow cells, however severe thrombocytopenia is rarely reported (Bomhof *et al.*, 2020; Yang *et al.*, 2005). Previously conducted studies revealed that, critically ill COVID-19 patients had lower platelet count compared to non-severe disease (Bomhof *et al.*, 2020; Jiang *et al.*, 2020). Following previous studies, a lower platelet count is associated with more than four times increased risk of ICU admission.

Human kidney is a target for COVID-19 virus, therefore, many patients died with COVID-19 have serious viral load in kidneys (Batlle *et al.*, 2020; Legrand *et al.*, 2021). The risk of AKI is also significantly higher among critical cases compared to non-severe cases (Liu *et al.*, 2021). Study also identified that, patients with abnormal count of biomarkers are associated with increased death of hospitalized patients (Cheng *et al.*, 2020). These findings are also corroborated with our analysis.

We have analyzed liver biochemistry values of patients and abnormal values was significantly associated with more severe outcome. Previously conducted studies also identified abnormal values of liver biomarkers as common among COVID-19 patients. Moreover, COVID-19 patients with pre-existing severe liver injury are at significant higher risk of critical infection and death (Marjot *et al.*, 2021). Our analysis also suggests, without pre-existing liver problem COVID-19 patients show abnormal results in biochemical test indicates direct impacts of COVID-19.

Studies have point out hypokalemia and hyponatremia as common biomarkers in patients with severe COVID-19 infections (Lippi *et al.*, 2020). We have also analyzed Hyponatremia and hypokalemia of hospitalized COVID-19 patients and observed a significantly higher prevalence among critically ill patients. Another study also confirmed the association of Hyponatremia and hypokalemia with the severity of COVID-19 infection (Lippi *et al.*, 2020). The aged peoples are usually more vulnerable to electrolytic imbalance due to the pathophysiological changes; therefore, an improved monitoring is required during the treatment process (Schlanger *et al.*, 2010).

Studies have reported d-dimer value as an initial accurate biomarker for severe COVID-19 infection and an early increase of 3 to 4-fold rise in D-dimer is significantly associated with poor prognosis (Poudel *et al.*, 2021). Moreover, various comorbidities such as diabetes, stroke, hypertension and pregnancy would trigger high d-dimer levels (Rostami & Mansouritorghabeh, 2020). Our findings are also similar to previous observations and identified d-dimer as the most important predictor. We would like to suggest the incorporation of D-dimer into routine investigation to assess the risk of critical infection.

Our study was completed with several limitations in terms of study design, sample size, and representativeness. First of it was a cross-sectional study and data was collected only once from the patients. A follow up study during the hospital days and after discharge is necessary for more useful findings. We have analysed data of single hospital, therefore, could not represent the common scenario of Bangladesh. A more comprehensive study with substantial sample size is required in hospitals located in various regions in Bangladesh. Moreover, we didn't analyse the final status (death or discharged) of hospitalized patients due to incomplete information. Besides these limitations, our study has generated important findings regarding various types of biomarkers related to COVID-19 infection and also identified some important predictors of ICU admission.

5. Conclusions

The study has revealed socio-demographic, comorbidity, and radiological risk factors of critical COVID-19 infections. Our analysis has successfully assessed various types of biomarkers related to critical infection which will guide researchers of similar field. The identified risk factors would be considered for decision making during the treatment process. Some important biomarkers such as d-dimer, complete blood count test, kidney and liver function test should be incorporated in routine investigation of infected as well as post COVID-19 patients in Bangladesh.

Conflict of interest

None to declare.

Authors' contributions

A.H.M. Khairul Imam Suman and Mohammad Morshad Alam equally contributed in research design, data analysis, and manuscript writing; A.H.M. Khairul Imam Suman, Khadija Begum, Kaniz Rahman and Saiful Bahar Khan involved in data collection and data entry. All authors have read and approved the final manuscript.

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