IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 6 Ser.10 (June. 2020), PP 38-53
www.iosrjournals.org

Demographic and Clinical Presentation of CoVid19 Patients in Bangladesh- A Single Center Experience

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Abstract

Background

Corona virus disease 2019 (COVID-19) is a declared global pandemic. Since December, 2019, Wuhan, China, has experienced an outbreak of corona virus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). Epidemiological and clinical characteristics of patients with COVID-19 have been reported & well described in different articles from different countries. This epidemic of Corona virus Disease 2019 (COVID-19) leading to a Public Health Emergency of International Concern (PHEIC). No systematic reviews on COVID-19 have been published to date. No articles depicting this pandemic have been published to date in Bangladesh. There are multiple parameters of the clinical course and management of the COVID-19 that need optimization in our country. A hindrance to this development is the vast amount of misinformation present due to scarcely sourced manuscript preprints and social media. This study aims to present basic sciences of SARS-CoV-2, clinical presentation and disease course of COVID-19, public health interventions, and current epidemiological developments in our country.

Methods

In this retrospective, single centre cohort study, we included all adult inpatients (≥18 years old) with laboratory confirmed COVID-19 from Evercare Hospital (Dhaka, Bangladesh) who had been discharged or had died by May 31, 2020. The study population was divided into two groups. Group I: includes patients who survived from CoVid 19 disease & Group II: includes patients who died from CoVid 19 disease. Demographic, clinical, treatment, and laboratory data, including serial samples for viral RNA detection, were extracted from electronic medical records and compared between the groups.

Results

50 patients from Evercare Hospital were included in this study, of whom 43 were discharged and 07 died in hospital. Mean age of group-I was 34.63±13.96 & that of group-II was 51.57±13.89. Among them 34 (68%) were male & 16 (32%) were female. 14 (28%) patients had a comorbidity, with smoking being the most common (25 [50%] patients), followed by diabetes (14 [28%] patients), ischaemic heart disease (13 [26%] patients) and hypertension (10 [20%] patients). Among the socio-economic condition majority of the study population belongs to middle class & majority had higher secondary education level which was statistically significant. Among the cardiac markers mean Creatine Kinase level was 68.34±98.31 which was statistically significant. Imaging profile of the study population was statistically significant. Among the DIC profile of the study population mean fibrinogen level was 298.02±135.95 which was statistically significant. Serum albumin & S. ALT levels were 3.28±0.55 & 66.16±94.69 respectively which were also significant. Among the septic markers of the study population the mean CRP & LDH levels were 3.56±6.26 & 241.44±210.39 respectively, which were statistically significant. Mean Sequential organ failure & qSOFA scores were 2.00±2.73 & 0.88±0.66 respectively which were also significant. Mean duration of viral shedding was 13.86±7.80. The longest observed duration of viral shedding in survivors was 28 days.

Conclusion
The potential risk factors of older age, high SOFA score, and fibrinogen could help clinicians to identify patients with poor prognosis at an early stage. Prolonged viral shedding provides the rationale for a strategy of isolation of infected patients and optimal antiviral interventions in the future.
Keywords: *CoVid19, SARS-CoV-2, Severe Acute Respiratory Syndrome, Pandemic, ARDS, Remdesevir, Hydroxychloroquine, Plasma Therapy, Public Health Emergency of International Concern.*

Date of Submission: 03-06-2020 Date of Acceptance: 18-06-2020

I. Introduction:

In December, 2019, Wuhan city, the capital of Hubei province in China, became the centre of an outbreak of pneumonia of unknown cause[1]. By Jan 7, 2020, Chinese scientists had isolated a novel corona virus, severe acute respiratory syndrome corona virus 2 (SARS-CoV-2; previously known as 2019-nCoV), from these patients with virus-infected pneumonia, [2, 3] which was later designated corona virus disease 2019 (COVID-19) in February, 2020, by WHO.[4]

On January 30, 2020, the World Health Organization (WHO) declared COVID-19 outbreak as the sixth public health emergency of international concern (PHEIC), and on March 11, 2020, the WHO announced COVID-19 as *pandemic*. [5] On April 9, 2020, nearly 1 436 198 cases of 2019- novel coronavirus recorded out of which 85 522 died with a case fatality rate (CFR) of 5.95%. The WHO evaluated the global risk of COVID-19 as very high. In the coming days and weeks, the amount of events, fatalities, and affected countries is projected to increase sharply.[6]

Although the outbreak is likely to have started from a zoonotic transmission event associated with a large seafood market that also traded in live wild animals, it soon became clear that efficient person-to-person transmission was also occurring.[7] The clinical spectrum of SARS-CoV-2 infection appears to be wide, encompassing asymptomatic infection, mild upper respiratory tract illness, and severe viral pneumonia with respiratory failure and even death, with many patients being hospitalized with pneumonia in Wuhan.[8–10] Although some case series have been published, many patients in these series remained hospitalized at time of publication. To our knowledge, no previous studies have been done among patients with definite outcomes. The estimation of risk factors for severe disease and death in these earlier case series are therefore not very robust. Additionally, details of the clinical and virological course of illness have not yet been well described.

COVID-19 is thought to be expanding in Bangladesh. The first case of COVID-19 was reported from Dhaka on March 8, 2020, with estimated population of Bangladesh as 161.4 million[11,12]. Successively, the virus spreads into various regions nationwide and has currently become epidemic. Within 92 days, on June 9, 2020, the Bangladesh's tally has reached 71,675 confirmed cases of COVID-19, 15,337 patients have recovered, and 975 have died.[12]

This short communication is conducted to shed light on the epidemic of coronavirus in the country. Here, we present details of all patients admitted to the Evercare Hospital in Dhaka, Bangladesh —with laboratory- confirmed COVID-19 and a definite clinical outcome (death or discharge/ recovered) as of May 31, 2020. We aim to explore risk factors of in-hospital death for patients and describe the clinical course of symptoms, viral shedding, and temporal changes of laboratory findings during hospitalisation.

II. Methods

Study design and participants

This retrospective cohort study included two cohorts of adult inpatients (≥18 years old) from Evercare Hospital (Dhaka, Bangladesh). All adult patients who were diagnosed with COVID-19 according to WHO interim guidance were screened, and those who died or were discharged between March 01, 2020 (i.e., when the first patients were admitted), and May 31, 2020, were included in our study. Our study enrolled all adult in patients who were hospitalized for COVID-19 and had a definite outcome (dead or discharged). Before April 20, 2020, SARS-CoV-2 RNA detection results were not available in the electronic medical records, from which data for this study were obtained retrospectively[8].

The study was approved by the Research Ethics Commission of Evercare Hospital.

Data collection

Epidemiological, demographic, clinical, laboratory, treatment, and outcome data were extracted from electronic medical records using a standardized data collection form, which was a modified version of the WHO/International Severe Acute Respiratory and Emerging Infection Consortium case record form for severe

acute respiratory infections. All data were checked by two physicians (MHK and AMI) and a third researcher (RUA) adjudicated any difference in interpretation between the two primary reviewers.

Laboratory procedures

Methods for laboratory confirmation of SARS-CoV-2 infection have been described elsewhere[8]. Briefly, one institution— the Institute of Epidemiology, Disease Control and Research (IEDCR), Bangladesh — was responsible for SARS-CoV-2 detection in respiratory specimens by next-generation sequencing or real-time RT-PCR methods. From April 20, 2020, SARS-CoV-2 RNA was detected by Evercare Hospital Dhaka. Nasopharyngeal-swab specimens were obtained for SARS-CoV-2 PCR re-examination every other day after clinical remission of symptoms, including fever, cough and dyspnoea, but only qualitative data were available. The criteria for discharge were absence of fever for at least 3 days, substantial improvement in both lungs in chest CT, clinical remission of respiratory symptoms, and two nasopharyngeal-swab samples negative for SARS-CoV-2 RNA obtained at least 24 hours apart.

Routine blood examinations were complete blood count, coagulation profile, serum biochemical tests (including renal and liver function, creatine kinase, lactate dehydrogenase, and electrolytes), myocardial enzymes, serum ferritin, and procalcitonin. Chest radiographs or CT scan were also done for all inpatients. Frequency of examinations was determined by the treating physician.

Definitions

Fever was defined as axillary temperature of at least 37.3°C. Sepsis and septic shock were defined according to the 2016 Third International Consensus Definition for Sepsis and Septic Shock[8]. Secondary infection was diagnosed when patients showed clinical symptoms or signs of pneumonia or bacteraemia and a positive culture of a new pathogen was obtained from lower respiratory tract specimens (qualified sputum, endotracheal aspirate, or bronchoalveolar lavage fluid) or blood samples after admission[8]. Ventilator-associated pneumonia was diagnosed according to the guidelines for treatment of hospital-acquired and ventilator-associated pneumonia[13]. Acute kidney injury was diagnosed according to the KDIGO clinical practice guidelines[14] and acute respiratory distress syndrome (ARDS) was diagnosed according to the Berlin Definition[15]. Acute cardiac injury was diagnosed if serum levels of cardiac biomarkers (e.g., high sensitivity cardiac troponin I) were above the 99th percentile upper reference limit, or if new abnormalities were shown in electrocardiography and echocardiography[8]. The illness severity of COVID-19 was defined according to the National Guidelines on Clinical Management of Coronavirus Disease 2019 (CoVid-19) (Version 6.0)[16]. Coagulopathy was defined as a 3-second extension of Prothrombin time or a 5-second extension of activated partial thromboplastin time. Hypoproteinaemia was defined as blood albumin of less than 25 g/L. Exposure history was defined as exposure to people with confirmed SARS-CoV-2 infection or history of travelling from CoVid19 disease prevalence countries during the outbreak.

Statistical analysis

Continuous and categorical variables were presented as mean ± SD and n (%), respectively. We used the $\chi 2$ test or t-test to compare differences between survivors and non-survivors where appropriate. To explore the risk factors associated with in-hospital death, uni-variable and multi-variable logistic regression models were used. Considering the total number of deaths (n=07) in our study and to avoid over fitting in the model. Previous studies have shown blood levels of d-dimer and Sequential Organ Failure Assessment (SOFA) scores to be higher in critically ill or fatal cases, whereas lymphopenia and cardiovascular disease have been less commonly observed in non-critical or surviving patients with SARS-COV-2 infection[8-9,17]. Similar risk factors, including older age, have been reported associated with adverse clinical outcomes in adults with SARS and Middle East respiratory syndrome (MERS)[4,18]. Some laboratory findings, including alanine aminotransferase (ALT), lactate dehydrogenase, high-sensitivity cardiac troponin I, creatine kinase, d-dimer, and serum ferritin, might be unavailable in emergency circumstances. Therefore, we chose lymphocyte count, d-dimer, SOFA score, coronary heart disease, and age as the five variables for our multivariable logistic regression model.

We excluded variables from the uni-variable analysis if their between-group differences were not significant, if their accuracy was unconfirmed (e.g., exposure, which was self-reported), if the number of events was too small to calculate odds ratios, and if they had co-linearity with the SOFA score.

We compared patient characteristics and used a generalized linear model to adjust for possible differences in patients' characteristics and treatment between the two study groups.

A p value of less than 0.05 was considered statistically significant. Statistical analyses were done using the SPSS software (version 23), unless otherwise indicated.

III. Result

5783 adult patients were hospitalized in Evercare Hospital from March 01, 2020 to Jan 31, 2020. Among them 50 patients were SARS-COV-2 infection confirmed by RT-PCR and thus were included in the

study & analyzed. The study population was divided into two groups. Group I: includes patients who survived from CoVid -19 disease & Group II: includes patients who died from CoVid -19 disease.

Table I: Age distribution of the study population (n=50)

Age group (years)	Group-I (n=43)		Group-II (n=7)		p value
	Number	%	Number	%	
20-30	18	41.9	0	0.0	
31-40	16	37.2	2	28.6	
41-50	4	9.3	2	28.6	
51-60	2	4.7	0	0.0	
61-70	2	4.7	2	28.6	
71-80	0	0.0	1	14.3	**0.005^{s}**
81-90	1	2.3	0	0.0	
Mean ± SD	**34.63±13.96**		**51.57±13.89**		

Unpaired t-test was done.
S means significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Age distribution table of the study population showed that the individuals of group-II were more aged than the other groups (mean age having 34.63±13.96 & 51.57±13.89 respectively). Most of the study population belonged to 20-30 years age group then 31-40 years groups. Above 40 years only 14 out of 50 (28%) were observed. Significant differences were found between different age groups.

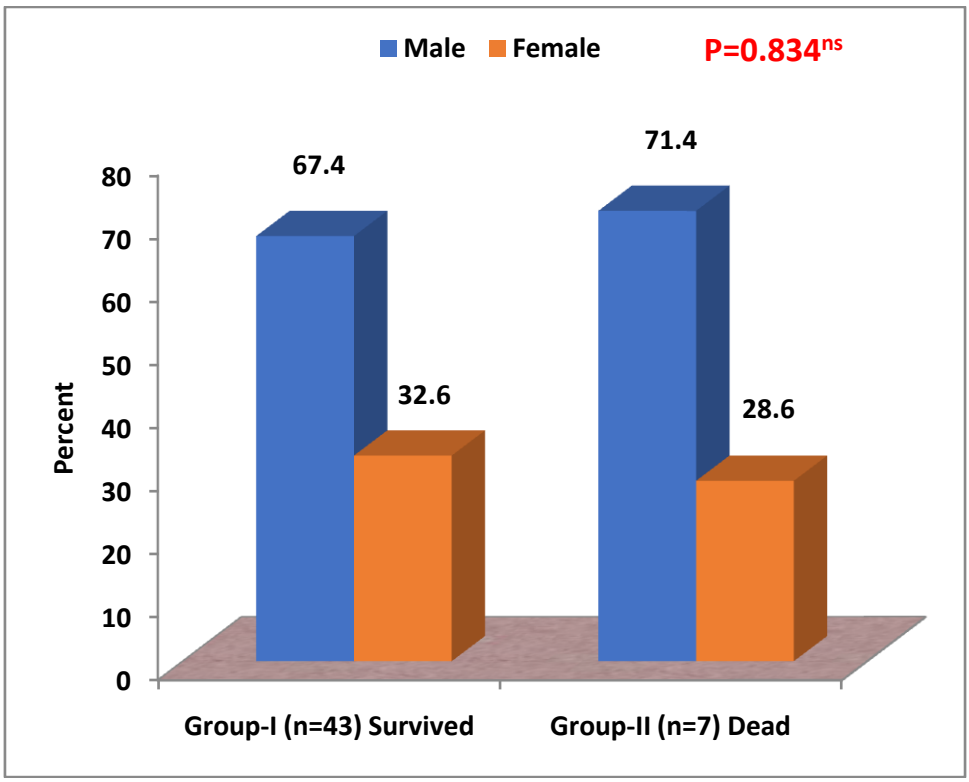

Figure 1: Bar diagram shows sex distribution of the study population (n=50).
ns means not - significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

The above bar diagram shows the sex distribution among the study group. Overall, the number of male cases was predominant (68% as compared to females 32%). But no statistical significance was observed.

Table II: Anthropometric status of the study population (n=50)

Parameters	Group-I (n=43)	Group-II (n=7)	p value
BMI	24.71±3.90	25.84±1.76	**0.224^{ns}**
BSA	1.67±0.17	1.71±0.15	**0.602^{ns}**

Unpaired t-test was done to measure the level of significance.

ns means not - significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Anthropometric distribution table of the study population showed that the individuals of group II were little obese than the other groups. No significant differences were found between different groups.

Table III: Demographic status of the study population (n=50)

Demographic Parameters		Outcome of Disease				p value
		Group-I (n=43)		Group-II (n=7)		
		Number	%	Number	%	
Socio-Economic Condition	Low	2	4.7	0	0.0	**0.243^{ns}**
	Middle	34	79.1	4	57.1	
	Upper	7	16.3	3	42.9	
Educational Status	No	1	2.3	0	0.0	**0.023^{s}**
	Secondary	2	4.7	0	0.0	
	Higher Secondary	24	55.8	0	0.0	
	Masters	16	37.2	7	100.0	

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05). s means Significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Demographic distribution table of the study population showed that the disease was more prevalent in middle class & with higher secondary educational status people. No significant differences were found in socio-economic condition of the study groups. But there was significant difference was seen in the educational status of the study groups.

Table IV: Risk factors analysis of the study population (n=50)

Risk Factors		Group-I (n=43)		Group-II (n=7)		p- Value
		Number	%	Number	%	
Hypertension	Yes	6	14	4	57.1	**0.008^{s}**
	No	37	86	3	42.9	
Diabetes	Yes	9	20.9	5	71.4	**0.006^{s}**
	No	34	79.1	2	28.6	
Smoker	Yes	22	51.2	3	42.9	**0.684^{ns}**
	No	21	48.8	4	57.1	
Dyslipidaemia	Yes	7	16.3	4	57.1	**0.016^{s}**
	No	36	83.7	3	42.9	
BA/ COPD	Yes	4	9.3	0	0	**0.400^{ns}**
	No	39	90.7	7	100	
Previous IHD	Yes	8	18.6	5	71.4	**0.003^{s}**
	No	35	81.4	2	28.6	
CKD	Yes	1	2.3	2	28.6	**0.007^{s}**
	No	42	97.7	5	71.4	
Any Malignancy	Yes	1	2.3	0	0	**0.684^{ns}**
	No	42	97.7	7	100	
Transplantation or Immune Suppressive Medication	Yes	4	1	9.3	14.3	**0.684^{ns}**
	No	39	6	90.7	85.7	

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05). s means Significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Risk factor analysis table of the study population showed that the smoking was more prevalent in the study groups followed by diabetes, ischaemic heart disease & hypertension. But only hypertension, diabetes, dyslipidaemia, previous ischaemic heart disease & CKD were statistically significant whereas others were not.

Table V: Renal profile of the study population (n=50)

Renal Profile	Group-I (n=43)	Group-II (n=7)	p value
Creatinine	0.97±0.20	2.32±2.19	**0.54^{ns}**

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05). s means Significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Renal profile analysis table of the study population showed that the mean serum creatinine level of group-II was higher than that of group-I, i.e. 2.32±2.19 & 0.97±0.20 respectively. There was no statistical significance was observed among the different groups.

Table VI: Cardiac Biomarkers profile of the study population (n=50)

Cardiac Biomarkers Profile	Group-I (n=43)	Group-II (n=7)	p value
hs Troponin-I	143.76±619.17	369.93±878.66	**0.533^{ns}**
Creatine Kinase	41.98±34.31	230.29±187.36	**0.038^{s}**
BNP	177.81±817.37	366.88±727.55	**0.547^{ns}**

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05). s means Significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Cardiac biomarkers analysis table of the study population showed that only serum creatine kinase level (68.34±98.31) was statistically significant among the groups for myocarditis but other markers like high sensitive Troponin-I (hs Trop-I) & BNP were not statistically significant.

Table VII: Imaging profile of the study population (n=50)

Imaging Profile	Outcome of Disease				p value
	Group-I (n=43)		Group-II (n=7)		
	Number	%	Number	%	
Normal	30	69.8	0	0.0	**0.001^{s}**
Consolidation	1	2.3	1	14.3	
Ground Glass Appearance	1	2.3	2	28.6	
Pulmonary Infiltrate	11	25.6	4	57.1	

Unpaired t-test was done to measure the level of significance.
s means significant (P<0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Imaging profile analysis table of the study population revealed that pulmonary infiltration (41.35%) was predominant in the study groups followed by ground glass appearance & normal (15.45% & 15% respectively). The imaging features were highly significant among the different study groups.

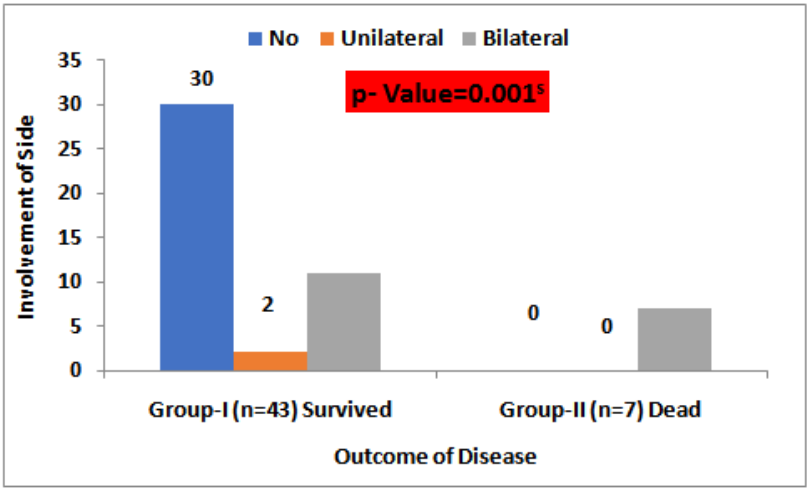

Figure 2: Bar diagram showing involvement of sides in imaging of the study population (n=50).

ns means not - significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

The above bar diagram showed that bilateral involvement in imaging was more prevalent in both groups. Overall, statistical significance was observed among the study groups.

Table VIII: DIC profile of the study population (n=500)

DIC Profile	Group-I (n=43)	Group-II (n=7)	p Value
d-Dimer	533.90±926.49	1891.37±2003.06	**0.125^{ns}**
Fibrinogen	271.12±109.70	463.26±172.22	**0.025^{s}**
APTT	29.62±3.92	30.01±4.92	**0.845^{ns}**
Prothrombin Time	12.93±1.20	14.03±1.40	**0.086^{ns}**

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05). s means Significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

DIC biomarkers analysis table of the study population showed that only serum fibrinogen level was statistically significant among the groups but other markers like d-Dimer, APTT & Prothrombin Time were not statistically significant.

Table XIX: Septic Marker profile of the study population (n=50)

Septic Marker Profile	Group-I (n=43)	Group-II (n=7)	p Value
CRP	2.07±4.34	12.77±8.60	**0.016^{s}**
Procalcitonin	1.59±5.89	0.21±0.13	**0.132^{ns}**
Ferritin	313.49±352.27	5913.29±12036.17	**0.264^{ns}**
LDH	206.02±186.21	459.00±233.59	**0.028^{s}**

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05). s means Significant. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Septic biomarkers analysis table of the study population showed that serum CRP & LDH levels were statistically significant among the groups but other markers like Procalcitonin & Ferritin were not statistically significant.

Table XX: LFT profile of the study population (n=50)

LFT Profile	Group-I (n=43)	Group-II (n=7)	p Value
S. Albumin	3.40±0.49	2.56±0.34	**0.001^{s}**
S. ALT	44.49±15.83	199.29±217.79	**0.001^{s}**

Unpaired t-test was done to measure the level of significance.
LFT means Liver Function Test. s means significant (P<0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Liver function test analysis table of the study population showed that individuals belonging to group-II were hypoalbuminic & also had altered liver level of serum ALT (Alanine Transaminase). Statistical analysis showed the mean levels of both S. Albumin & S. ALT were both highly significant.

Table XXI: SOFA Score profile of the study population (n=50)

SOFA Profile	Group-I (n=43)	Group-II (n=7)	p Value
SOFA	1.05±1.21	7.86±1.95	**0.001^{s}**
qSOFA	0.74±0.58	1.71±0.49	**0.001^{s}**

Unpaired t-test was done to measure the level of significance.
SOFA means Sequential Organ Failure Assessment. s means significant (P<0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

SOFA analysis table of the study population showed that individuals belonging to group-II were more SOFA & qSOFA scores. Statistical analysis showed the mean levels of both SOFA & qSOFA were statistically highly significant (p<0.05).

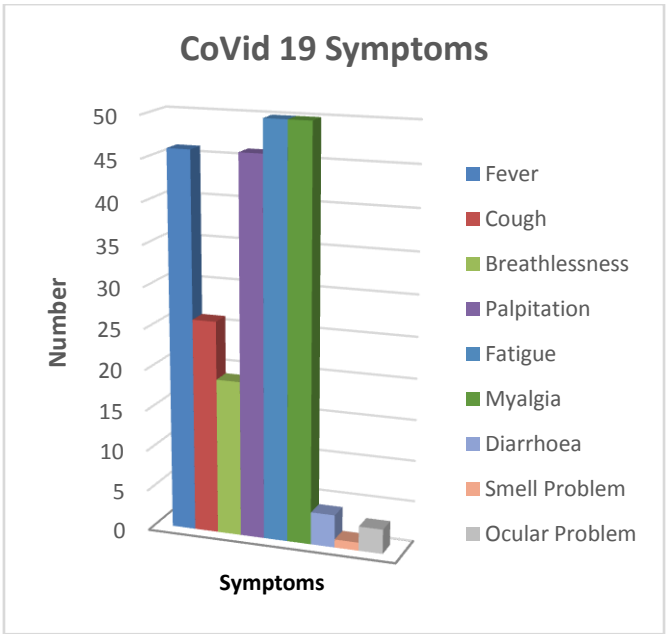

Figure 3: Bar diagram depicting symptomatology of the study population (n=50).

The above bar diagram showed the symptomatology of the study population which depicted that fatigue, myalgia, fever & cough were predominant symptoms.

Table XXII: Fever duration of the study population (n=50)

	Group-I (n=43)	Group-II (n=7)	p Value
Fever Duration (in days)	3.12±2.81	6.14±1.46	0.008[s]

Unpaired t-test was done to measure the level of significance.
s means significant (P<0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Fever duration analysis table of the study population showed that individuals belonging to group-II had comparatively long duration of fever (6.14±1.46) than that of group-I (3.12±2.81). Statistical analysis showed fever duration was statistically significant.

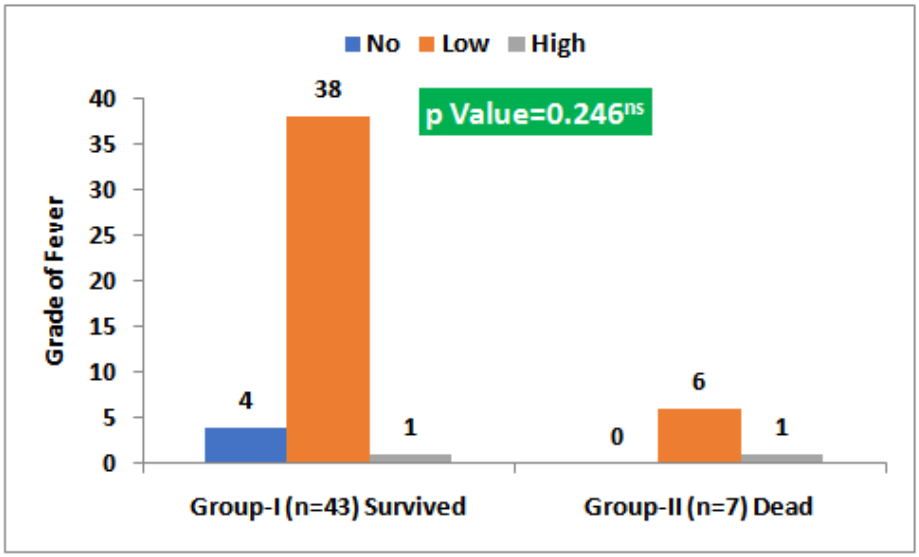

Figure 4: Bar diagram depicting fever grade of the study population (n=50).

Unpaired t-test was done to measure the level of significance.
s means significant (P>0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

The above bar diagram showed the fever grading of the study population which depicted that most patients had low grade of fever. But the grading of fever was not statistically significant (p>0.05).

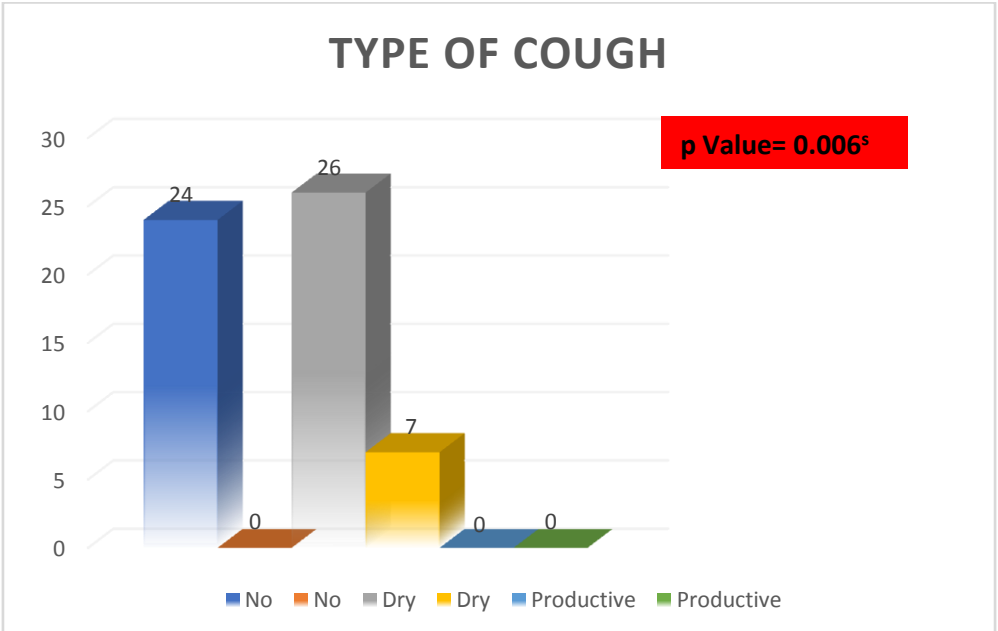

Figure 5: Bar diagram depicting type of cough of the study population (n=50).

Unpaired t-test was done to measure the level of significance.
s means significant (P<0.05).

The above bar diagram showed the type of cough among the study population which depicted that most patients had dry cough. Analysis showed type of cough was statistically significant (p<0.05).

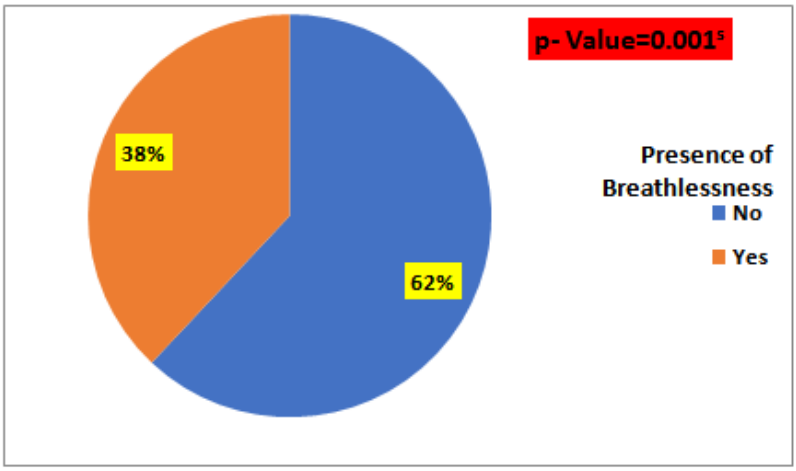

Figure 4: Pie chart depicting fever grade of the study population (n=50).

s means significant (P<0.05).

The above pie chart showed that breathlessness was seen in significant number (38%) of study population. Analysis showed breathlessness was a significant (p<0.05) symptom.

If we consider the contact history of the study population, majority of them had contact (86%) but all of them had no H/O travelling abroad (100%). Statistical analysis showed no significance (p>0.05).

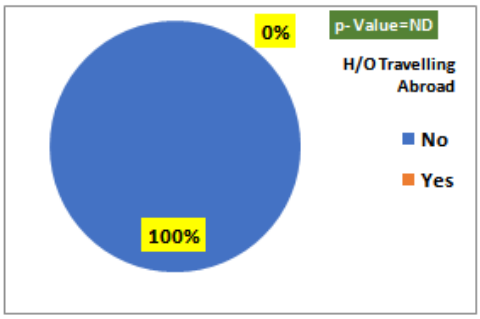

Figure 5: Pie chart showing H/O travelling abroad of the study population (n=50)

ND means not detected

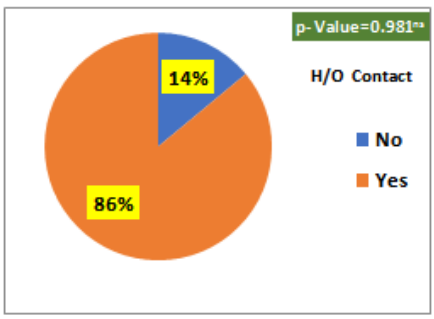

Figure 6: Pie chart showing H/O contact of the study population (n=50)

ns means not – significant (p>0.05)

If we consider atypical symptoms of the study population, like diarrhoea, smell problem or ocular problem; only smell problem was statistically significant (p<0.05).

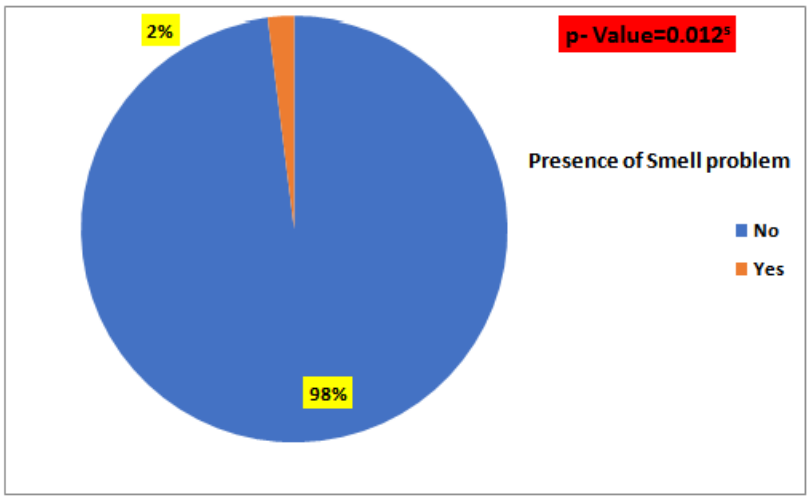

Figure 6: Pie chart showing presence of smell problem of the study population (n=50)

s means significant (P<0.05).

If we consider severity of disease majority of group-I patients had mild form of disease (38), on the other hand in group-II majority (6) had moderate form of disease. The analysis was statistically significant (p<0.05).

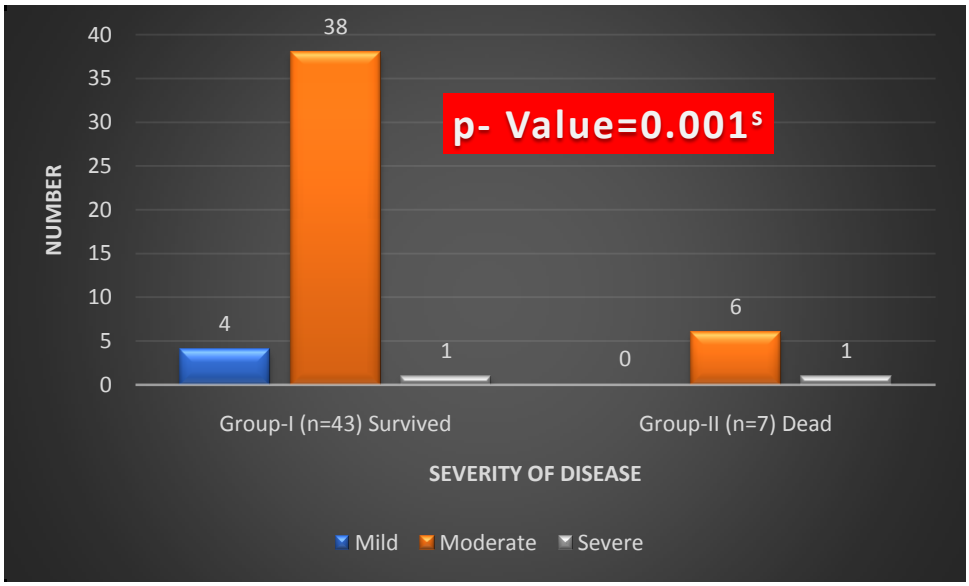

Figure 7: Bar chart showing severity of disease of the study population (n=50)

Table XXIII: CURB 65 score of the study population (n=50)

CURB65 Score	Outcome of Disease				p Value
	Group-I (n=43)		Group-II (n=7)		
	Number	%	Number	%	
0	15	34.9	0	0.0	**0.001ˢ**
0-1	27	62.8	0	0.0	
3-5	1	2.3	7	100.0	

Chi-square (λ^2)-test was done to measure the level of significance.
s means significant (P<0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

CURB65 score analysis table of the study population showed that majority of the individuals (27; 62.8%) belonging to group-I had score within 0-1 but all the individuals (7; 100%) belonging to group-II had score within 3-5. Statistical analysis showed CURB65 score of the study groups was statistically significant (p<0.05).

Table XXIV: Time of illness onset to hospital admission of the study population (n=50)

		Group-I (n=43)	Group-II (n=7)	p Value
Time	**Days**	6.35±3.30	10.57±2.44	**0.002^{s}**

Unpaired t-test was done to measure the level of significance.
s means significant (P<0.05).

The above table showed group-II people had delayed hospital admission from illness onset than the group-I people. Analysis showed the difference was statistically significant (p<0.05).

Table XXV: Critical Care Parameters of the study population (n=50)

Critical Care Parameters Profile	Group-I (n=43)	Group-II (n=7)	p Value
RR	19.72±2.67	23.14±2.48	**0.009^{s}**
Temp	99.49±0.97	100.76±0.78	**0.004^{s}**
SPO_2	96.81±3.25	85.57±4.24	**0.001^{s}**
Calculated PaO_2:FiO_2	576.28±123.73	430.29±130.04	**0.025^{s}**

Unpaired t-test was done to measure the level of significance.
s means significant (P<0.05). RR means respiratory rate. Temp means temperature. SPO_2 means saturation of oxygen. PaO_2 means partial pressure of oxygen. FiO_2 means fraction of inhaled oxygen.

The above table showed group-II people had worse critical care parameters than that of group-I people. Analysis showed the differences were statistically significant (p<0.05).

Table XXVI: Complication profile of the study population (n=50)

Types of Complication	Group-I (n=43)		Group-II (n=7)		p value
	Number	%	Number	%	
Sepsis	4	9.3	5	71.4	**0.001^{s}**
Respiratory Failure	1	2.3	7	100	**0.001^{s}**
ARDS	1	2.3	7	100	**0.001^{s}**
Heart Failure	3	7	2	28.6	**0.077^{ns}**
Shock	1	2.3	5	71.4	**0.001^{s}**
Coagulopathy	7	16.3	3	42.9	**0.103^{ns}**
Acute Cardiac Injury	2	4.7	2	28.6	**0.031^{s}**
Acute Kidney Injury	2	4.7	3	42.9	**0.002^{s}**
Major Bleeding Episode	-	-	-	-	**ND**
Secondary Infection	4	9.3	3	42.9	**0.018^{s}**
Hypoproteinaemia	26	60.5	7	100	**0.041^{s}**
Acidosis	2	4.7	7	100	**0.001^{s}**
ICU Admission	2	4.7	7	100	**0.001^{s}**
Need of Ventilatory Support	1	2.3	7	100	**0.001^{s}**

Chi-square (λ^2)-test was done to measure the level of significance.
s means significant (P<0.05), ns means not – significant & ND means not- detectable. Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Complication analysis table of the study population showed that majority of the individuals had some forms of complications. Group-II people had more complications than group-I subjects.

Table XXVII: Duration of hospital stay of the study population (n=50)

	Group-I (n=43)	Group-II (n=7)	p Value
Hospital Stay (in days)	**12.00±5.60**	**17.00±7.19**	**0.121^{ns}**

Unpaired t-test was done to measure the level of significance.
ns means not- significant (P>0.05).

The above table showed group-II people had more hospital stay than that of group-I people. But the difference was not statistically significant (p>0.05).

Table XXVIII: Baseline medication profile of the study population (n=50)

Baseline Medication	Outcome of Disease				p Value
	Group-I (n=43)		Group-II (n=7)		
	Number	%	Number	%	
No	14	32.6	2	28.6	**0.144^{ns}**
Statin	2	4.7	1	14.3	
ACEi/ARB + Statin	3	7.0	3	42.9	
Systemic Steroids	1	2.3	0	0.0	
Hydroxychloroquine	20	46.5	1	14.3	
Systemic Steroids + Hydroxychloroquine	2	4.7	0	0.0	

Chi-square (λ^2)-test was done to measure the level of significance.
ns means not - significant (P>0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Baseline medication analysis table of the study population showed that majority of the individuals (20; 46.5%) belonging to group-I had taken Hydroxychloroquine prior to hospital admission & majority of the individuals (3; 42.9%) belonging to group-II had H/O ACEi/ARB & Statin ingestion. A significant number of individuals also had no H/O medication intake prior to admission in both groups (32.6% & 28.6% respectively. Statistical analysis showed no statistical significance (p>0.05) among the study groups.

Table XXIX: Treatment profile of the study population (n=50)

Treated with	Outcome of Disease				p-Value
	Group-I (n=43)		Group-II (n=7)		
	Number	%	Number	%	
No Specific Treatment	1	2.3	0	0.0	**0.001^{s}**
Hydroxychloroquine	1	2.3	0	0.0	
Hydroxychloroquine + Azithromycine + Doxycycline	1	2.3	0	0.0	
Hydroxychloroquine + Doxycycline	26	60.5	0	0.0	
Hydroxychloroquine + Ivermactine	1	2.3	0	0.0	
Hydroxychloroquine + High Flow Oxygen Therapy	0	0.0	1	14.3	
Azithromycine	2	4.7	0	0.0	
Doxycycline	6	14.0	0	0.0	
Doxycycline + Remdesivir + Ivermactine + Corticosteroids	0	0.0	1	14.3	
Doxycycline + Plasma Therapy + Corticosteroids + High Flow Oxygen Therapy	2	4.7	1	14.3	
Doxycycline + Corticosteroids	0	0.0	1	14.3	
Doxycycline + Corticosteroids+ High Flow Oxygen Therapy	0	0.0	1	14.3	
Doxycycline + Corticosteroids+ High Flow Oxygen Therapy	0	0.0	1	14.3	
Doxycycline+ High Flow Oxygen Therapy	0	0.0	1	14.3	
Corticosteroids	2	4.7	0	0.0	
High Flow Oxygen	1	2.3	0	0.0	

Chi-square (λ^2)-test was done to measure the level of significance.
s means significant (P<0.05). Group-I: CoVid19 Survived, Group-II: CoVid19 Dead.

Treatment analysis table of the study population showed that majority of the individuals (26; 60.5%) belonging to group-I were treated with Hydroxychloroquine & Doxycycline combination and most of the individuals (7; 100%) belonging to group-II were treated with multiple drugs. Statistical analysis showed statistical significance (p<0.05) among the study groups.

Table XXX: Time duration of development of complications of the study population (n=50)

	Outcome of Disease	
Complications	**Mean ± SD**	**p-Value**
Sepsis	10.57±7.66	**0.022^{s}**
ARDS	16.00±2.94	**0.001^{s}**
ICU Admission	10.00±2.45	**0.001^{s}**
Death or Discharge	18.86±5.27	**0.034^{s}**

Unpaired t-test was done to measure the level of significance.
s means significant (P<0.05).

The above table showed development of different complications of the study people. It showed sepsis (10.57±7.66) & ICU admission (10.00±2.45) occurred the earliest, but death or discharge (18.86±5.27) & development of ARDS (16.00±2.94). They were statistically significant (p<0.05).

Table XXXI: Multivariate regression analysis of the risk factors of the study population (n=50)

Parameter	β	p-value
HTN	63.971	**.000**[s]
DM	-2.497	.268[ns]
F/H of CAD	-11.473	**.008**[s]
Smoker	-.430	.790[ns]
Dyslipidaemia	2.292	.533[ns]
B. Asthma/ COPD	-1.023	.719[ns]
Previous IHD	5.485	**.062**[s]
Chronic Kidney Disease	-15.277	**.000**[s]
Any Malignancy	9.025	.119[ns]
H/O Transplant or any Immunosuppressive Medications	-5.996	**.073**[s]

s means significant (P<0.05). ns means not – significant (p>0.05).

Above table showed the multivariate regression analysis of the risk factors of the study population. It showed **hypertension**, **family H/O CAD**, **previous H/O ischaemic heart disease**, **chronic kidney disease** & **H/O transplant or any immunosuppressive medications** were major significant risk factors for the disease outcome.

IV. Discussion:

This retrospective cohort study identified several risk factors for death in adults in Dhaka who were hospitalized with COVID-19. In particular, older age, higher C- reactive protein levels, fibrinogen level, and higher SOFA score on admission were associated clinical outcome that is discharge or death. Additionally, elevated levels of blood high-sensitivity cardiac troponin I, and lactate dehydrogenase and lymphopenia were more commonly seen in severe COVID-19 illness. Sustained viral detection in throat samples was observed in both survivors and non-survivors. Previously, older age has been reported as an important independent predictor of mortality in SARS and MERS[19,20] .The current study confirmed that increased age was associated with death in patients with COVID-19. Previous studies in macaques inoculated with SARS-CoV found that older macaques had stronger host innate responses to virus infection than younger adults, with an increase in differential expression of genes associated with inflammation, whereas expression of type I interferon beta was reduced[21]. The age-dependent defects in T-cell and B-cell function and the excess production of type 2 cytokines could lead to a deficiency in control of viral replication and more prolonged pro-inflammatory responses, potentially leading to poor outcome[22].

SOFA score is a good diagnostic marker for sepsis and septic shock, and reflects the state and degree of multi-organ dysfunction[23, 24]. Although bacterial infections are usually regarded as a leading cause of sepsis, viral infection can also cause sepsis syndrome. Previously, we determined that sepsis occurred in nearly 40% of adults with community-acquired pneumonia due to viral infection[25]. In the current study, we found that about 18% of patients developed sepsis. Additionally, we found that 86% of patients had white blood cell count below 11.0×10^9 per L or procalcitonin below 0.25 ng/mL, and no bacterial pathogens were detected in these patients on admission. Sepsis was a common complication, which might be directly caused by SARS-CoV-2 infection, but further research is needed to investigate the pathogenesis of sepsis in COVID-19 illness.

Cardiac complications, including new or worsening heart failure, new or worsening arrhythmia, or myocardial infarction are common in patients with pneumonia. Cardiac arrest occurs in about 3% of inpatients with pneumonia[26]. Risk factors of cardiac events after pneumonia include older age, pre-existing cardiovascular diseases, and greater severity of pneumonia at presentation[27]. Coronary heart disease has also been found to be associated with acute cardiac events and poor outcomes in influenza and other respiratory viral infections[26–28]. In this study, increased high-sensitivity cardiac troponin I during hospitalisation was found in more than half of those who died. About 90% of inpatients with pneumonia had increased coagulation activity, marked by increased d-dimer concentrations[29]. In this study, we found d-dimer greater than 1 μg/mL is associated with fatal outcome of COVID-19. High levels of d-dimer have a reported association with 28-day mortality in patients with infection or sepsis identified in the emergency department[30]. Contributory mechanisms include systemic pro-inflammatory cytokine responses that are mediators of atherosclerosis directly contributing to plaque rupture through local inflammation, induction of pro coagulant factors, and haemodynamic changes, which predispose to ischaemia and thrombosis[31–33]. In addition, angiotensin converting enzyme 2, the receptor for

SARS-CoV-2, is expressed on myocytes and vascular endothelial cells[34,35]. So there is at least theoretical potential possibility of direct cardiac involvement by the virus. Of note, interstitial mononuclear inflammatory infiltrates in heart tissue has been documented in fatal cases of COVID-19, although viral detection studies were not reported[36].

The level and duration of infectious virus replication are important factors in assessing the risk of transmission and guiding decisions regarding isolation of patients. Because coronavirus RNA detection is more sensitive than virus isolation, most studies have used qualitative or quantitative viral RNA tests as a potential marker for infectious coronavirus. For SARS-CoV, viral RNA was detected in respiratory specimens from about a third of patients as long as 4 weeks after disease onset[37]. Similarly, the duration of MERS-CoV RNA detection in lower respiratory specimens persisted for at least 3 weeks[38,39], whereas the duration of SARS-CoV-2 RNA detection has not been well characterized. In the current study, we found that the detectable SARS-CoV-2 RNA persisted for a median of 21 days in survivors and that it was sustained until death in non-survivors. This has important implications for both patient isolation decision making and guidance around the length of antiviral treatment. In severe influenza virus infection, prolonged viral shedding was associated with fatal outcome and delayed antiviral treatment was an independent risk factor for prolonged virus detection[40]. Similarly, effective antiviral treatment might improve outcomes in COVID-19.

V. Conclusion:

We concluded that older age, higher SOFA score, and elevated fibrinogen level at admission were risk factors for death of adult patients with COVID-19. The prolonged viral shedding provides the rationale for testing novel coronavirus antiviral interventions in efforts to improve outcomes.

VI. Limitations:

To the best of our knowledge, this is the first retrospective cohort study among patients with COVID-19 in Bangladesh who have experienced a definite outcome. Although, some limitations were acknowledged by the study team:

1. Not all laboratory tests were done in all patients, including IL-6. Therefore, it`s role might be underestimated in predicting in-hospital death, as it was a retrospective study.
2. Patients were sometimes transferred late in their illness to the hospital. Lack of effective anti- virals, inadequate adherence to standard supportive therapy, and high-dose corticosteroid & other non-proven anti CoVid drug use might have also contributed to the poor clinical outcomes in some patients.
3. The estimated duration of viral shedding is limited by the frequency of respiratory specimen collection, lack of quantitative viral RNA detection, and relatively low positive rate of SARS-CoV-2 RNA detection in throat-swabs[41].
4. By excluding patients still in hospital as of May 31, 2020, and thus relatively more severe disease at an earlier stage, the case fatality ratio in our study cannot reflect the true mortality of COVID-19.
5. Last but not least, interpretation of our findings might be limited by the sample size due to single center involvement. However, by including all adult patients in multiple hospitals for COVID-19, we believe our study population would be representative of cases diagnosed and treated in Bangladesh.

Acknowledgements:

The research team greatly appreciates Mr. Tofiel Ahmed, for his co-operation and help during the data analysis and computer processing of the manuscript.

Conflict of interest disclosure:

The authors have nothing to disclose.

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Dr. Mahmood Hasan Khan, et. al. "Demographic and Clinical Presentation of CoVid19 Patients in Bangladesh- A Single Center Experience." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(6), 2020, pp. 38-53.