Original Article

Clinical Profile and Short-term Outcomes of COVID-19 Patients in a Dedicated Intensive Care Unit of Bangladesh: A Single Centre Experience

Shahjad Hossain Md. Al Momen[1], Afroza Akhter[2], Md. Mazharul Anwar[3], Chandrashekhar Karmakar[4], Md Harun Ur Rashid[5], Rumana Sultana[6], Abul Khayer Nazrul[7]

[1]Assistant Professor, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital, Dhaka, [2]Classified Specialist in Gynaecology and Obstetrics, Combined Military Hospital (CMH), Dhaka, [3]Assistant Professor, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital, Dhaka, [4]Consultant, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital, Dhaka, [5]Registrar, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital, Dhaka, [6]Consultant, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital, [7]Medical Officer, Department of Anaesthesiology and Intensive Care Medicine, Kurmitola General Hospital

Corresponding Author: E-mail: shahjaddr@gmail.com

Abstract

Introduction: The COVID-19 pandemic emerged as a major public health crisis and was confirmed to have spread to Bangladesh since March 2020. A large number of hospitalized patients with COVID-19 pneumonia require intensive care for respiratory support due to hypoxic respiratory failure. Bangladesh is greatly facing multiple challenges to combat the surging pandemic due to lack of experiences and insufficient medical resources. Reports describing patients admitted to the ICU with COVID-19 in Bangladesh are very limited. Objective of this study was to determine the clinical characteristics and outcomes of the COVID-19 patients admitted at the dedicated intensive care unit of Kurmitola General Hospital, Dhaka for better characterization of COVID-19 infection in critically ill patients in a resource limited setting.

Materials and Methods: *All the RT-PCR confirmed COVID-19 patients aged >15 years who had been admitted to the dedicated COVID intensive care unit of Kurmitola General Hospital, Dhaka from April 2020 to October 2020 were included in this retrospective cross-sectional study. The protocol was approved by the Ethical and Scientific Committee of the institute. The demographic, clinical and treatment data of all participants were collected and evaluated and mode of treatments were compared between survivor and non-survivor groups. The statistical analysis was carried out using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA).*

Results: *A total of 294 critically ill COVID-19 patients were admitted to the ICU of Kurmitola general hospital between April, 2020 to October, 2020. The mean (±SD) age of the patients was 57.4 (±13.1) years, male participants were predominant (71.1%), 74.5% patients had positive contact history, common presenting problems were fever (94.5%), cough (83.6%), dyspnoea (80.9%), diarrhoea (60.2%) and chest pain (42.8%). Frequency of different associated co-morbidities like hypertension (49.3%), diabetes mellitus (50.3%), cardiac diseases (34.0%), renal diseases (17.7%), bronchial asthma (33.3%), COPD (40.1%), CVD (24.1%) and obesity (24.1%) were high. The mean (±SD) length of ICU stay of the patients was 7.0 (±4.1) days; 11.6% patients required mechanical ventilation; 63.6% of ICU patients died and 36.4% recovered in the specified time period. HFNC was provided to 62.6% patients in survivor group and 56.1% in non-survivor group, 31% of non-survivor patients required non-invasive ventilator support. Requirement of mechanical ventilation was significantly higher among the non-survivor group (18.7%) than survivor group (p <o.oo1). Use of convalescent plasma therapy was significantly higher in survivor group (29.0%) than the non-survivor group (18.7%) (p=0.043). No significant differences regarding anti-viral, monoclonal antibody and anticoagulant therapy were observed between both groups.*

Conclusion: *This retrospective cross-sectional study represented the clinical characteristics and treatment outcomes of the critically ill COVID-19 patients at ICU of Kurmitola General Hospital, Dhaka, Frequency of positive contact history and presence of co-morbidities were high. Death rate was significantly high among the patients who required mechanical ventilation. Patients of survivor group were significantly benefited from convalescent plasma therapy. Larger, multicenter, prospective studies with extended follow-up should be conducted to verify the study findings.*

Key words: *COVID-19, Clinical feature, outcome, Intensive care unit, Bangladesh*

(JBSA 2021; 34(1):12-19)

Introduction:

The COVID-19 was declared as pandemic disease by World Health Organization (WHO) on 11th March, 2020 which is a potentially severe acute respiratory infection caused by a novel evolving severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. The first human cases of COVID-19 were reported by officials in Wuhan City, China, in December 2019[2] and since then eventually the entire world is working to address this rapidly evolving and emerging situation.

The virus was confirmed to have spread to Bangladesh in March 2020. Since then, the pandemic has spread day by day over the whole nation and the number of affected people has been increasing. Till November 2020, total of 26,65,131 people had been tested for COVID-19. Among them 4, 49, 760 were tested confirmed, 3,64,611 recovered and number of deaths was 6,416[2].

COVID-19 has a seemingly variable clinical presentation and progression, presenting with mild infection to severe disease to fatal illness[3]. Recent reports suggested that approximately 14 to 29% of hospitalized patients with COVID-19 pneumonia require intensive care, primarily for respiratory support in the setting of hypoxic respiratory failure, with acute respiratory distress syndrome (ARDS) developing in 33% of hospitalized patients at a median time from symptom onset of 8 days[4].

Lack of experience in combating such a pandemic and insufficient medical resources have led to a difficult situation in controlling disease transmission to a large extent in Bangladesh. Most of the hospitals in the country are not fully ready to cope with the expected surge in COVID-19 patients[5]. Currently, treatment for COVID-19 is being provided in total 33 Government and non-government hospitals nationwide which includes a total of 4530 general beds, 368 ICU beds and 343 mechanical ventilators and other testing and treatment facilities[1].

A better characterization of COVID-19 infection in critically ill patients is important for appropriate management and allocation of resources in intensive care setting and there is great scarcity of these data in our country. Objective of this study was to determine the clinical characteristics and outcomes of the patients admitted in COVID dedicated intensive care unit of Kurmitola General Hospital, Dhaka hospital to enhance the insight regarding epidemiology and management of critically ill COVID-19 patient in a resource limited setting.

Materials and Methods:

In this retrospective cross-sectional study, a total of 294 RT-PCR confirmed critically ill COVID-19 patients aged >15 years were included who had been admitted to the dedicated COVID intensive care unit of Kurmitola General Hospital, Dhaka from April 2020 to October 2020. Data were collected in structured data collection sheets through consecutive sampling from the ICU patient registrars. The protocol was approved by the Ethical and Scientific Committee of the Kurmitola General Hospital (KGH). The demographic data (age, sex, contact history, etc.), clinical data (symptoms on admission, comorbidities etc.) and treatment data (oxygen delivery methods, medication and adjuvant therapies etc.) were collected from all participants and mode of treatments were compared between survivor and non-survivor groups. The statistical analysis was carried out using the Statistical Package for Social Sciences version 22.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Qualitative variables were expressed as frequency and percentage. Quantitative variables were expressed as mean ± standard deviation. Chi-square test and Fisher's exact test were performed to measure the level of significance in different treatment modalities. A "p" value <0.05 was considered as significant.

Results:

A total of 294 RT-PCR confirmed COVID patients were admitted to the ICU of Kurmitola General Hospital between April, 2020 to October,2020. Table-I showed the distribution of the admitted patients according to age. The mean (±SD) age of the patients was 57.4 (±13.1) years. Maximum (28.6%) patients belonged to 51 to 60 years' age group, followed by 24.5% patients aged between 61 to 70 years, 18.7% patients aged more than 70 years, 17.3% patients belonged to 41-50 years' age group and remaining 10.8% patients aged between 15 to 40 years.

Table I *Distribution of the patients according to age (n=294)*

Age (years)	Frequency	Percent (%)
>15-20	1	0.3%
21-30	8	2.7%
31-40	23	7.8%
41-50	51	17.3%
51-60	84	28.6%
61-70	72	24.5%
>70	55	18.7%
Mean ± SD	57.4 ± 13.1	

Male patients were predominant (71.1%) than the female patients (28.9%) in the present study (Figure-1), male-female ratio was 2.5.

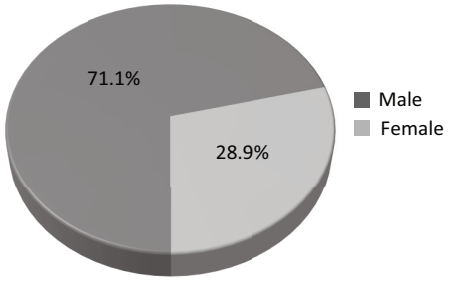

Figure 1 *Distribution of the patients according to sex (n=294)*

Among the study sample, 74.5% patients had positive contact history, 21.8% were not aware of contact and only 3.7% had no history of contact with persons having definite symptoms of Coronavirus infection (Figure-2).

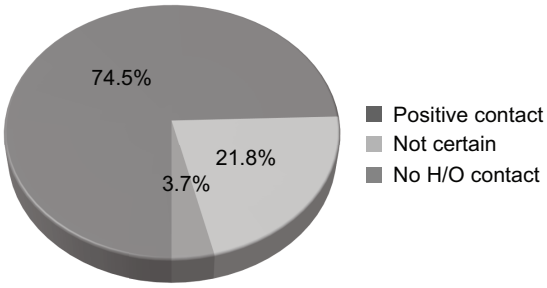

Figure 2 *Distribution of the patients according to history of contact (n=294)*

The presenting problems patients got admitted with are enlisted in Table-II. Fever (94.5%), cough (83.6%), dyspnoea (80.9%), diarrhoea (60.2%) and chest pain (42.8%) were predominant symptoms. Other less frequent symptoms were vomiting, haemorrhage, anosmia, sore throat, myalgia, rhinitis, nasal congestion, abdominal pain, altered sensorium etc.

Table II *Distribution of the patients according to presenting symptoms (n=294)*

History of contact	Frequency	Percent (%)
Fever	278	94.5%
Cough	246	83.6%
Dyspnoea	238	80.9%
Diarrhoea	177	60.2%
Chest pain	126	42.8%
Vomiting	95	32.3%
Hemorrhage (e.g. Hemoptysis)	55	18.7%
Anosmia	37	12.6%
Sore throat	35	11.9%
Myalgia	34	11.6%
Rhinitis	33	11.2%
Nasal congestion	32	10.9%
Abdominal pain	23	7.8%
Altered sensorium	7	2.4%

The frequency of different co-morbidities was high among the ICU patients, documented as hypertension (49.3%), diabetes mellitus (50.3%), cardiac diseases (34.0%), renal diseases (17.7%), bronchial asthma (33.3%), COPD (40.1%), CVD (24.1%), obesity (24.1%), liver disease (9.5%) and malignancy (8.2%) (Table-III).

Table III *Distribution of the patients according to co-morbidities (n=294)*

Co-morbidities	Frequency	Percent (%)
Hypertension	145	49.3%
Diabetes mellitus	148	50.3%
Cardiac disease	100	34.0%
Renal disease	52	17.7%
Bronchial asthma	98	33.3%
COPD	118	40.1%
Stroke	71	24.1%
Obesity	71	24.1%
Liver disease	28	9.5%
Pregnancy	0	0.0%
Malignancy	24	8.2%

The length of ICU stay of the participants are summarized in Table-IV. Most of the patients (63.3%) needed ICU support for 1 to 7 days, followed by 32.3% patients needed to stay at ICU for 8 to 15 days and rest (4.1%) patients stayed at ICU for more than 15 days. The mean (±SD) length of ICU stay of the patients was 7.0 (±4.1) days. Among them, mechanical ventilation was required for 11.6% patients and 88.4% did not require it (Table-V).

Table IV *Distribution of the patients according to ICU stay (n=294)*

ICU stay (days)	Frequency	Percent(%)
1-7	187	63.6%
8-15	95	32.3%
>15	12	4.1%
Mean ± SD	7.0 ± 4.1	

Table-V *Distribution of the patients according to use of mechanical ventilation (n=294)*

Mechanical ventilation	Frequency	Percent(%)
Used	34	11.6%
Not used	260	88.4%
Total	294	100.0%

Despite every possible effort, number of deceased patients were higher (187, 63.6%) than the number of patients who recovered (107, 36.4%) among the critically ill COVID patients in our ICU (Table-VI).

Table VI *Distribution of the patients according to disease outcome (n=294)*

Outcome information	Frequency	Percent(%)
Recovered	107	36.4%
Referred	0	0.0%
Death	187	63.6%
Total	294	100.0%

Table-VII showed the comparison of treatment modalities between the ICU survivor and non-survivor group of COVID-19 patients. Prone positioning was applied to 276 patients and was almost equally maintained in both survivor (92.5%) and non-survivor (94.7%) groups. A total of 288 patients required oxygen therapy via non re-breathing (NRB) mask; all patients of the survivor group (100.0%) used it and 96.8% patients of non-survivor group used it. High flow nasal cannula (HFNC) was provided to 172 patients, which was more used in survivor group (62.6%) than the non-survivor group (56.1%). Non-invasive ventilation was required by 81 patients, 21.5% patients of survivor group and 31.0% patients of non-survivor group were provided this. Thirty-five deceased patients (18.7%) required mechanical ventilation, where none of survivor patients required it, which was a significant observation ($p < 0.001$). All admitted patients received systemic steroid and empiric antibiotic therapy. Among 66 recipients, use of convalescent plasma therapy was observed significantly higher in survivor group (29.0%) than the non-survivor group (18.7%) ($p=0.043$). There was no significant difference regarding anti-viral, monoclonal antibody and anticoagulant therapy observed between both groups.

Table VII *Comparison of treatment modalities between the ICU survivor and non-survivor group of COVID-19 patients*

Mode of treatment	Number of patients receiving the treatment	Survivor n=107(%)	Non-survivor n=187(%)	p value
Prone positioning	276	99 (92.5%)	177 (94.7%)	0.464[a]
Oxygen delivery method				
• NRB	288	107 (100.0%)	181 (96.8%)	0.090[b]
• HFNC	172	67 (62.6%)	105 (56.1%)	0.279[a]
• Non-invasive ventilation	81	23 (21.5%)	58 (31.0%)	0.103[a]
• Mechanical ventilation	35	0 (0.0%)	35 (18.7%)	**<0.001[b]**
Medications and adjuvant therapy				
• Inj. Dexamethasone	294	107 (100.0%)	187 (100.0%)	-
• Inj. Remdesivir	132	53 (49.5%)	79 (42.2%)	0.227[a]
• Convalescent plasma therapy	66	31 (29.0%)	35 (18.7%)	**0.043[a]**
• Tocilizumab	67	25 (23.4%)	42 (22.5%)	0.859[a]
• Empiric antibiotic	294	107 (100.0%)	187 (100.0%)	-
• Anti-coagulant therapy	292	107 (100.0%)	185 (98.9%)	0.535[b]

[a]Chi-square test was done to measure the level of significance. [b]Fisher's Exact test was done to measure the level of significance. Figure within parenthesis indicates in percentage.

Discussion:

The 500 bed Kurmitola General Hospital is one of the leading COVID dedicated hospitals of Bangladesh. Since March 2020, this hospital has been providing treatment services with 275 general beds, 10 ICU beds and 10 mechanical ventilators along with testing and follow-up facilities[1]. In the present study, the clinical profile and short-term treatment outcomes of the COVID-19 patients admitted at Intensive care unit of Kurmitola General Hospital, Dhaka have been evaluated to elicit the importance of understanding the variation of regional presentations of Coronavirus infection.

The risk of severe illness with COVID-19 is believed to be increased with age, with older adults at highest risk[6]. Maximum (28.6%) patients belonged to 51 to 60 years' age group in this study. Mean (±SD) age of the patients was 57.4 (±13.1) years. This result is consistent with a large cohort in Italy (mean age 63 years)[7], but inconsistent with the earlier studies in Bangladesh[8,9,10] and India[11]. Further studies are required to explore the multidimensional presentations of this emerging disease. Reports also showed that men were more at risk for worse outcomes due to COVID-19 independent of age[13]. Male patients were predominant in this study (71.1%) than the female patients (28.9%). Similar results were found in earlier Bangladeshi studies[8,9] and in other studies worldwide[7,11,12].

The present study revealed that 74.5% patients had positive contact history, which is remarkable, though statistically not significant. Earlier in this year, 73% patients had positive contact history among 201 COVID-19 patients in a study done in Dhaka Combined Military ospital[8] and 60% patients had positive contact history in another study at Dhaka Medical College Hospital[9]. In the context of massively populated and lower-middle-income countries like Bangladesh, enforcement of social distancing is tough[5]. But as yet there are no vaccines or antiviral drugs approved for the disease, and hence, non-therapeutic interventions to control the spread of the virus are the most effective measures to control the disease[14].

The SARS-CoV-2 infection may rapidly progress to acute respiratory distress syndrome (ARDS), multi-organ dysfunction syndrome (MODS) and death[11]. Presenting symptoms like fever (94.5%), cough (83.6%), dyspnoea (80.9%), diarrhoea (60.2%) and chest pain (42.8%) were more frequent among our ICU patients. The likelihood of progressing to poorer outcomes was observed high among COVID-19 patients who had associated co-morbidities in previous studies[15,16]. The frequency of different co-morbidities were observed high among the ICU patients; hypertension (49.3%), diabetes mellitus (50.3%), cardiac diseases (34.0%), renal diseases (17.7%), bronchial asthma (33.3%), COPD (40.1%), CVD (24.1%) and obesity (24.1%). This finding suggested that public health preventive measures might have a role in reducing the risk of transmission to this vulnerable population.

The rapid spread of the virus and the high proportion of patients requiring respiratory support have placed unprecedented demand on intensive care unit services worldwide[17]. In this study, the mean (±SD) length of ICU stay of the patients was 7.0 (±4.1) days, which was somehow lesser than a study conducted among ICU patients in China (11.8 days)[18]. 63.6% of the ICU patients died and 36.4% patients recovered in the specified time period. Mortality rate among the patients requiring ICU supports for COVID-19 varied among different studies worldwide. Mortality rate was 37.7% among a large cohort in Wuhan, China[18]. A recent report from New York, USA showed that, 21% patient died among 5700 patients who required ICU support and 24.5% of them required mechanical ventilation[19]. The poor outcomes seen in various studies may be related to the disease process itself, or due to rationing of resources in overwhelmed ICUs.

Due to pandemic pressures on ICU services, there has been widespread use of advanced respiratory supports (high flow nasal cannula, non invasive ventilation, mechanical ventilation) and this may have meant that patients actually admitted to ICU are disproportionately sicker[18]. In response to rapidly progressive hypoxemia, oxygen therapy was provided for all patients in our ICU. A total of 288 patients required oxygen via non re-breathing (NRB) mask; all patients of the survivor group (100.0%) and 96.8% patients of non-survivor group used it. High flow nasal cannula (HFNC) was provided to 172 patients, which was used more by

the survivor group (62.6%) than the non-survivor group (56.1%). Non-invasive ventilation was required by 81 patients, 21.5% patients of survivor group and 31.0% patients of non-survivor group were provided this; 11.6% of ICU admitted patients required mechanical ventilation and 88.4% did not require it. Studies have reported close to 100% mortality amongst patients requiring mechanical ventilation for ARDS due to Coronavirus infection[20]. The requirement of mechanical ventilation was significantly higher among the non-survivor group (18.7%) in this study, where none of the patients from survivor group required it (p <o.oo1). Hypoxic organ damages, including the brain, heart, lung, and kidney due to ARDS; which is characterized by a rapid progression and a severe state of illness, may be a major contributory factor to increased mortality associated with mechanical ventilation[17]. Our findings should alert physicians to pay attention not only to the symptoms of respiratory failure but also to the other organ injuries as well.

Use of convalescent plasma therapy was observed significantly higher in survivor group (29.0%) than the non-survivor group (18.7%) (p=0.043) among total 66 plasma recipients. Recent studies in Bangladesh[21] and other countries[22,23] revealed convalescent plasma therapy as an evolving defensive treatment option for near-fatal cases of COVID-19. The results of analyses among >70,000 COVID-19 patients by FDA, USA and Mayo clinic also suggested that, convalescent plasma with high antibody titers may be beneficial when administered within 72 hours of COVID-19 diagnosis[24]. Although many limitations exist regarding plasma therapy, nevertheless, considering the absence of specific treatments, it remains a viable option for treating COVID-19[25,26,27].

Our study had several limitations. This was a retrospective exploratory study with relatively small sample size. We were unable to collect data on detailed physical examination and standardized laboratory investigations for all cases. Thus, disease severity of the ICU patients could not be assessed. The associations of co-morbidities with mortalities in critically ill COVID-19 patients of this study are also needed to be evaluated in further multicenter prospective studies with larger cohort and extended follow-up.

To the best of our knowledge, this is the largest retrospective cross sectional study among COVID-19 patients undergoing treatment in a dedicated COVID-19 intensive care unit of Bangladesh. There are still so many fields remained unexplored which needs attention in national and institutional level. Researchers must address unanswered questions, including the role of repurposed and experimental therapies which have potentials to offer the best chance of survival for the critically ill COVID-19 patients.

Conclusion:

This retrospective study represented the clinical characteristics and treatment outcomes of the critically ill COVID-19 patients in a dedicated COVID ICU in Bangladesh. High frequency of positive contact history and associated co-morbidities enlightened the importance of public health preventive measures in reducing the risk of transmission and disease severity to this population. Death rate was significantly high among the patients who required mechanical ventilation. Patients of survivor group were significantly benefited from convalescent plasma therapy. Further prospective studies should be conducted to verify the study findings. Collaboration at the local, regional, national, and international level with a focus on high-quality research, evidence-based practice, sharing of data and resources, and ethical integrity in the face of unprecedented challenges will be key to the success of these efforts.

Acknowledgment:

Authors acknowledge Brigadier General Dr. Jamil Ahmed, Director, Kurmitola General Hospital and the COVID-19 management team consisting of the faculty and all staffs from the departments of Anaesthesia & Intensive Care who helped in setting up of a dedicated facility for COVID-19-positive patients, and their management protocol.

References

1. National Guidelines on Clinical Management of Coronavirus Disease 2019 (COVID-19), Version 7.0, 28 May 2020, Disease Control Division, Directorate General of Health Services Ministry of Health & Family Welfare Government of the People's Republic of Bangladesh

2. WHO. Morbidity and Mortality Weekly Update (MMWU), N°39, 2020

3. Suleyman G, Fadel RA, Malette KM, Hammond C, Abdulla H, Entz A. Clinical characteristics and morbidity associated with coronavirus disease 2019 in a series of patients in metropolitan Detroit. JAMA Netw Open [Internet]. 2020; 3 (6): e2012270. JAMA. 2020;323: 2052

4. Rodríguez-Morales AJ, Balbin-Ramon GJ, Rabaan AA, Sah R, Dhama K, Paniz-Mondolfi A, Pagliano13 P, Esposito13 S. Genomic Epidemiology and its importance in the study of the COVID-19 pandemic. genomics. 2020 Jan 1; 1:3.

5. Anwar S, Nasrullah M, Hosen MJ. COVID-19 and Bangladesh: Challenges and how to address them. Frontiers in Public Health. 2020;8.

6. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/older-adults.html

7. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, Bonanomi E, Cabrini L, Carlesso E, Castelli G, Cattaneo S. Risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. JAMA internal medicine. 2020 Oct 1;180(10):1345-55.

8. Ahmed NU, Islam MA, Kabir MA, Rahman MH, Sadat SA. Clinico-Pathological Findings of Bangladeshi Covid 19 Patients with their Clinical Outcome: Study of A Cohort of 201 Cases. Journal of Bangladesh College of Physicians and Surgeons. 2020 Jun 3:37-42.

9. Mowla SG, Azad KA, Kabir A, Biswas S, Islam MR, Banik GC, Khan MM, Rohan KI, Alam MA. Clinical profile of 100 confirmed COVID-19 patients admitted in dhaka medical college hospital, Dhaka, Bangladesh. Journal of Bangladesh College of Physicians and Surgeons. 2020 Jun 9:29-36.

10. Bhuyan MA, Al Mahtab M, Ashab E, Haque MJ, Hoque SM, Huq AF, Islam MA, Choudhury N, Alia RA, Mahtab M, Khan MS. Treatment of COVID-19 Patients at a Medical College Hospital in Bangladesh. Euroasian journal of hepato-gastroenterology. 2020 Jan;10(1):27.

11. Soni SL, Kajal K, Yaddanapudi LN, Malhotra P, Puri GD, Bhalla A, Singh MP, Sehgal IS, Koushal V, Varma N, Biswal M. Demographic & clinical profile of patients with COVID-19 at a tertiary care hospital in north India. The Indian Journal of Medical Research. 2020 Nov 12.

12. Sim BL, Chidambaram SK, Wong XC, Pathmanathan MD, Peariasamy KM, Hor CP, Chua HJ, Goh PP. Clinical characteristics and risk factors for severe COVID-19 infections in Malaysia: A nationwide observational study. The Lancet Regional Health-Western Pacific. 2020 Nov 1;4:100055.

13. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, Liu S, Yang JK. Gender differences in patients with COVID-19: Focus on severity and mortality. Frontiers in Public Health. 2020 Apr 29;8:152.

14. Bootsma MC, Ferguson NM. Public health interventions and epidemic intensity during the 1918 influenza pandemic. Proc. Natl Acad. Sci. USA. 2007;104:7588-93.

15. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020;369. doi: 10.1136/bmj.m1966 .

16. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID- 19-related death using OpenSAFELY. Nature. 2020;584(7821):430–436. doi: 10. 1038/s41586-020- 2521- 4 .

17. Zhao S, Lin Y, Zhou C, Wang L, Chen X, Clifford SP, Akca O, Huang J, Chen X. Short-Term Outcomes of Patients With COVID-19 Undergoing Invasive Mechanical Ventilation: A Retrospective Observational Study From Wuhan, China. Frontiers in medicine. 2020;7.

18. Du RH, Liu LM, Yin W, Wang W, Guan LL, Yuan ML, Li YL, Hu Y, Li XY, Sun B, Peng P. Hospitalization and critical care of 109 decedents with COVID-19 pneumonia in Wuhan, China. Annals of the American Thoracic Society. 2020 Apr 7(ja).

19. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. Jama. 2020 Apr 22.

20. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y, Zhao Y. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. Jama. 2020 Mar 17;323(11):1061-9.

21. Samad N, Sodunke TE, Banna HA, Sapkota A, Fatema AN, Iskandar K, Jahan D, Hardcastle TC, Nusrat T, Chowdhury TS, Haque M. Convalescent Plasma Therapy for Management of COVID-19: Perspectives and Deployment in the Current Global Pandemic. Risk Manag Healthc Policy. 2020;13:2707-2728, https://doi.org/10.2147/RMHP.S281388

22. Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, Zhou M, Chen L, Meng S, Hu Y, Peng C. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proceedings of the National Academy of Sciences. 2020 Apr 28;117(17):9490-6.

23. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. The Lancet Infectious Diseases. 2020 Apr 1;20(4):398-400.

24. Tanne JH. Covid-19: FDA approves use of convalescent plasma to treat critically ill patients. BMJ. 2020 Mar 26;368:m1256. doi: 10.1136/bmj.m1256. PMID: 32217555.

25. Montelongo-Jauregui D, Vila T, Sultan AS, Jabra-Rizk MA. Convalescent serum therapy for COVID-19: A 19th century remedy for a 21st century disease. PLoS Pathogens. 2020 Aug 12;16(8):e1008735.

26. Wood EM, Estcourt LJ, McQuilten Z. How should we use convalescent plasma therapies for COVID-19?. Blood. 2020 Nov 17.

27. Eckhardt CM, Cummings MJ, Rajagopalan KN, Borden S, Bitan ZC, Wolf A, Kantor A, Briese T, Meyer BJ, Jacobson SD, Scotto D. Evaluating the efficacy and safety of human anti-SARS-CoV-2 convalescent plasma in severely ill adults with COVID-19: A structured summary of a study protocol for a randomized controlled trial. Trials. 2020 Dec;21(1):1-3.