Original article

Complications affecting outcome in COVID 19 patients admitted in high dependency unit Sir Ganga Ram Hospital, Lahore

Shazia Siddique[1], Muhammad Anwar[2], Asma Kamal[3], Bilal Azeem Butt[4], Khadija Muneer[4], Zia Ul Haq[5]

[1]Assistant Professor of Medicine, Fatima Jinnah Medical University/Sir Ganga Ram Hospital, Lahore, [2]Associate Professor of Paediatrics, Rashid Latif Medical College, Lahore, [3]Assistant Professor of Medicine, Services Hospital, Lahore, [4]Assistant Professor of Medicine, Fatima Jinnah Medical University/Sir Ganga Ram Hospital, Lahore, [5]Senior Registrar of Medicine, Sir Ganga Ram Hospital, Lahore

Correspondence to: Dr. Shazia Siddique, Email: doctorshazia@hotmail.com

ABSTRACT

Background: Covid 19 is a highly contagious viral infection resulting in severe acute respiratory syndrome Coronavirus (SARS-CoV-2). The objective of this study was to determine the potential complications affecting the outcome of moderate to severe COVID 19 patients admitted in HDU of Sir Ganga Ram Hospital, Lahore.

Subjects and methods: It was a prospective cohort study. The study was conducted on 108 patients admitted in the COVID HDU of Sir Ganga Ram Hospital, Lahore with positive PCR for COVID-19 having moderate to severe disease. After written consent, all the demographic data and complications like ARDS, respiratory failure, cardiac injury and liver dysfunction, acute kidney injury and sepsis/DIC were obtained through specially designed proformas data was collected through specially designed proformas and data was analysed through SPSS version 22. During hospital stay, we observed the patients for the development of complications as mentioned above. All Patients were followed up till discharge and outcome were noted in terms of discharge or death.

Results: Out of 108 admitted patients in COVID HDU, 68 were discharged, 26 were died and14 got left against medical advice. The mean age was 53.6 ± 15.94 years with 53.7% males (n=58), the most common complication during hospital stay was sepsis (31 affected with 16 deaths, 14 survived and p-value=0.000), acute kidney injury (27 affected, 13 died, 13 survived, p-value=0.002), ARDS (seen in 19 patients with 16 deaths, 3 survived and acute cardiac injury (17 affected, 9 died, 8 survived, p-value=0.005).

Conclusion: The complications like adult respiratory distress syndrome, respiratory failure, acute cardiac injury, acute kidney injury, and secondary infection had poor outcomes. This study could help clinicians to take early measures to prevent the development of complications in patients admitted in HDU.

Keywords:

Covid -19, Outcome, HDU admission criteria

INTRODUCTION

Human infections can be caused by six different coronavirus species.[1] SARS-CoV-2 and SARS-COV-1 show some phylogenetic resemblance and share common receptor angiotensin-converting enzyme 2 (ACE2).[1] Theoretically, COVID-19 may mimic SARS. SARS infected cells which expressed ACE 2 receptors were found to have elevated pro-inflammatory cytokines on autopsies.[2] Very high levels of INF-g, IL-1b, IL-6, IL-8, IL-12, and TNF-a cytokines were found in SARS patients who developed ARDS.[3-5] High mortality rates associated with epidemics of SARS (9.6%) and Middle East respiratory syndrome (34.4%) posed a major global threat in recent past.[6]

Till date (22 June 2021), globally, there have been 178,360,849 confirmed cases of COVID-19, including 3,869,384 deaths, reported to WHO. It has spread to 213 countries of the world.[7] First case of COVID 19 was reported in Pakistan on 26th February, 2020 in Karachi and till date there are more than 949,838 cases and more than 22,034 deaths.[8]

Several complications have been postulated for predicting the severity and high mortality of SARS CoV-2 including ARDS, acute cardiac injury, acute kidney injury, and sepsis.[9, 10] High risk of mortality has also been observed in patients on high dose corticosteroids.[11] In severe COVID-19 patients with lung injury, high levels of LDH have been observed postulating a possibility of association with severe disease and poor outcome.[11] Many previous studies have reported older age, hyperglycaemia, high LDH level and leucocytosis as risk factors for in hospital mortality.[11-14]

The corona pandemic has badly affected all health systems. There is a great need to identify potential complications that can predict the outcome of disease. Many previous studies were based on relatively small sample size and they were retrospective and use early data with deficient evidence.[10,14] In future such

Conflict of interest: The authors declared no conflict of interest exists.

Citation: Siddique S, Anwar M, Kamal A, Butt BA, Muneer K, Haq Z. Complications affecting Outcome in COVID 19 patients admitted in high dependency unit Sir Ganga Ram Hospital, Lahore. J Fatima Jinnah Med Univ. 2021; 15(4):161-165.

DOI: https://doi.org/10.37018/JTEG8507

identified complications that affect the final outcome can be used for making guidelines for the management of COVID-19 patients and it will help to reduce the overall mortality of COVID-19 patients. Therefore, this study is carried out to determine the potential complications affecting the outcome of moderate to severe COVID 19 patients admitted in HDU of Sir Ganga Ram Hospital, Lahore.

PATIENTS AND METHODS

A prospective, cohort study was conducted in the COVID-19 HDU of Sir Ganga Ram Hospital, Lahore in a period of three months 1st June to 31st August 2020 after the approval of synopsis by the ethical review board of Fatima Jinnah Medical University/SGRH, Lahore. Total 108 patients with positive PCR for Covid-19 not maintaining saturation above 93% at room air (criteria set by corona Expert Advisory Group, (CEAG) guidelines) were admitted in High Dependency Unit (HDU).[15] Patients with age of 18 to 90 years were included in study. Patients with autoimmune diseases, on immunosuppressant, organ transplant and pregnant females were not included in study.

All the information was collected through a specially designed proforma. On admission, demographic data (age and gender), complications like ARDS, respiratory failure, cardiac injury, liver dysfunction, acute kidney injury and sepsis were noted. During hospital stay, patients were observed for the development of complications as mentioned above. Patient were followed up till discharge and outcome were noted in terms of discharge or death.

Data was compiled in the computer and analysed using SPSS version 22 for the windows. Mean and + SD was calculated for numerical/quantitative variables like age. Frequencies in percentages were calculated for categorical data like sex, complications and outcome. Means were compared by t-test and p-value ≤0.05 was taken as significant.

RESULTS

Total 108 patients were admitted in COVID-19 HDU with mean age 53.62 ± 15.94 years. Males were 53.7% (n=58). Complications of COVID-19 assessed at time of admission were adult respiratory distress syndrome (ARDS) (23.5%), respiratory failure (84.7%), cardiac injury (21.2%), liver dysfunction (3.5%), acute kidney injury (35.3%), sepsis (44.7%). In the follow up period, the complications observed during hospitalization were ARDS (38.8%), respiratory failure (28.6%), cardiac injury (34.7%), liver dysfunction (8.2%), acute kidney injury (55.1%), sepsis (63.3%) (Table 1).

Analyzing the complications at time of admission with outcome: 20 patients had ARDS, out of which 15 died, 5 discharged (p-value=0.000). Respiratory failure, the most common complication, was observed in 72 individuals, 15 (20.8%) died, 50 (69.4%) discharged and 7 (9.7%) got LAMA. Cardiac injury was seen in 18 patients, half of them recovered (50.6%), less than half died (44.4%). Only 3 of Study population had liver dysfunction and 2 died, 1 discharged. Acute Kidney injury was recorded in 30 individuals, one third (33.3%) did not survive, nearly two third (60%) survived. Sepsis, the second commonest complication, observed in 38 individuals, death was reported in 16 (42.1%), 21 (55.3%) survived (p-value=0.001) (Table 2).

In the follow-up period, complications during hospitalization were assessed with outcome. The most frequent complication was found to be sepsis, in around 31 patients, 14 (45.2%) survived, 16 (51.6%) not survived and 1 (3.2%) got LAMA with overall p-value of 0.000. The second commonest complication was acute kidney injury, seen in 27 individuals, with equal number of discharged and deaths that is 13 and 13 respectively with 1 LAMA (p-value=0.002). ARDS was present in total 19 patients, 3 were discharged, 16 died (p-value=0.000). Respiratory failure was observed in 14 cases, 9 survived and 4 did not survive. Cardiac injury was recorded in 17 patients, more than half 9 (52.9%) died, 8 (47.1%) were discharged (p-value=0.005). The least affected organ was liver with only 4 individuals had liver dysfunction, with half recovered and half died. (Table 3).

Table 1. Complications at time of admission and hospitalizations

Complications	Complications at time of Admission			Complications during hospitalizations		
	Responses		Percent of Cases	Responses		Percent of Cases
	N	Percent		N	Percent	
ARDS	20	11.0%	23.5%	19	17.0%	38.8%
Respiratory failure	72	39.8%	84.7%	14	12.5%	28.6%
Cardiac injury	18	9.9%	21.2%	17	15.2%	34.7%
Liver dysfunction	3	1.7%	3.5%	4	3.6%	8.2%
Acute kidney injury	30	16.6%	35.3%	27	24.1%	55.1%
Sepsis	38	21.0%	44.7%	31	27.7%	63.3%
Total	181	100.0%	212.9%	112	100.0%	228.6%

Table 2. Outcome and complications at time of admission cross tabulations

Complications at time of admission	Outcome			Total	p-value
	Discharged alive n (%)	Death n (%)	Left Against Medical Advice n (%)		
ARDS	5 (25)	15 (75)	0 (0.0%)	20	0.000
Respiratory failure	50 (69.4)	15 (20.8)	7 (9.7)	72	0.127
Cardiac injury	8 (44.4)	9 (50.2)	1 (5.6)	18	0.017
Liver dysfunction	1 (33.3)	2 (66.7)	0 (0.0)	3	0.206
Acute kidney injury	18 (60)	10 (33.3)	2 (6.7)	30	0.246
Sepsis	21 (55.3)	16 (42.1)	1 (2.6)	38	0.001

Table 3. Outcome and complication during hospitalization

Complications during hospitalization	Outcome			Total	p-value
	Discharged alive n (%)	Death n (%)	Left Against Medical Advice n (%)		
ARDS	3 (15.8)	16 (84.2)	0 (0.0)	19	0.000
Respiratory failure	9 (64.3)	4 (28.6)	1 (7.1)	14	0.756
Cardiac injury	8 (47.1)	9 (52.9)	0 (0.0)	17	0.005
Liver dysfunction	2 (50)	2 (50)	0 (0.0)	4	0.405
Acute kidney injury	13 (48.1)	13 (48.1)	1 (3.7)	27	0.002
Sepsis	14 (45.2)	16 (51.6)	1 (3.2)	31	0.000
Total	26	20	3	49	

DISCUSSION

The most common complication observed at time of admission and during hospitalization was respiratory failure followed by sepsis as seen in many other studies.[19,20] In studies from China ARDS was found very frequently, as seen in our study.[16, 17] Mortality was also increased in patients who had ARDS at admission and also during hospital stay coinciding with the results of many studies.[16, 18, 19]

Patients with persistent fever, high total leucocyte count with predominant neutrophil counts, and deranged coagulation profile (Prothrombin time PT, activated partial thromboplastin time APTT) were labeled as having sepsis. Blood or urine culture was not positive in all patients because they were already on antibiotics. Although leading cause of sepsis is usually considered as bacterial infections, however viral infection can also cause sepsis syndrome. In a study done at Wuhan city, patients admitted with community acquired pneumonia due to viral infection, sepsis occurred in nearly 40% of subjects[21] while in our study 21% had at admission and 27.7% had during hospital stay but responsible for high mortality 42% and 51% respectively. Sepsis is a frequent complication seen in SARS-CoV-2 infection which might be directly caused by this virus, but further research is required to find out the pathogenesis of sepsis in COVID-19 illness.

High serum creatinine was noticed in patients at admission and during stay in HDU with high mortality - a finding consistent with multiple studies.[22-25]Kidney disease is a frequent complication in hospitalized COVID-19 patients. Many studies from China reported the occurrence of AKI from 0.5% to 29% in COVID-19 patients.[26-28] Data from New York City detected a 46% incidence of AKI among 3993 admitted patients with COVID-19.[29] However an immunologic risk factor has been identified for AKI and it is Soluble urokinase plasminogen activator receptor (suPAR).[30]

Acute cardiac injuries as compared to renal injury were found more frequently in a study, a finding not in accordance with our study.[16] Elevated cardiac enzymes (biomarkers and cut-offs) and/or electrocardiographic abnormalities and a high cardiac troponin I (cTnI) levels were taken as cardiac injury. In general the incidence of acute cardiac injury has been variable but roughly 12-30% of the positive cases are known to develop significant elevation of cTnI.[32] A Chinese study including only those patients who had a definite outcome (death or discharge from hospital) reported 17% incidence of cTnI elevation.[33] Acute cardiac injury has been associated with high mortality both at admission (50%) and during hospital stay (52.9%) in our study and it coincides with result of other studies.[31,33-35]

While damages of vital organ such as acute liver injury was not a common manifestation resembling with results of few studies.[16,18,36] For SARS-CoV-2-related multiorgan damage the underlying mechanisms is not clear. Angiotensin-converting enzyme 2 (ACE2) gene is predominantly present in vascular endothelial cells, lung alveolar cells, gastrointestinal tract, kidneys and heart.[37] The multi-organ damage was somewhat caused by direct attack of SARS COV- 2.

CONCLUSIONS

The findings of this study highlight the range of complications like ARDS, respiratory failure, acute cardiac injury, acute kidney injury, and sepsis either at admission or during hospitalization are associated with poor outcomes in COVID-19 severe disease like death. The determination of critical complications may help clinicians to identify and take early steps to prevent adverse outcomes.

REFERENCES

1. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395:565-74.
2. He L, Ding Y, Zhang Q, Che X, He Y, Shen H, et al. Expression of elevated levels of pro-inflammatory cytokines in SARS-CoV-infected ACE21 cells in SARS patients: relation to the acute lung injury and pathogenesis of SARS. J Pathol 2006;210:288-97.
3. Lam CW, Chan MH, Wong CK. Severe acute respiratory syndrome: clinical and laboratory manifestations. Clin Biochem Rev 2004;25:121-32.
4. Sheng WH, Chiang BL, Chang SC, Ho HN, Wang JT, Chen YC, et al. Clinical manifestations and inflammatory cytokine responses in patients with severe acute respiratory syndrome. J Formos Med Assoc 2005;104:715-23.
5. Zhu M. SARS immunity and vaccination. Cell Mol Immunol 2004;1:193-8.
6. World Health Organization. Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003. Available at: https://www.who.int/csr/sars/country/table2004_04_21/ en/
7. Covid-19 Coronavirus Pandemic. Available at: https://www.worldometers.info/coronavirus/
8. Government of Pakistan. COVID-19 dashboard. Available at: http://covid.gov.pk/stats/pakistan
9. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020;00:1–12.
10. Wu C, Chen X, Cai Y, Xia Ja, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China [published online ahead of print March 13, 2020]. JAMA Intern Med. https://doi.org/10.1001/jamainternmed.2020.0994.
11. Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol 2020;145(6):1-8.
12. Wu C, Chen X, Cai Y, Xia Ja, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China [published online ahead of print March 13, 2020]. JAMA Intern Med 2020;e200994.
13. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054-62.
14. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single centered, retrospective, observational study. Lancet Respir Med 2020;8(5):475-81.
15. Government of Pakistan. Available at https://www.nih.org.pk/ guidelines.
16. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J et al . Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
17. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine. 2020;382(18):1708-20.
18. Adhikari SP, Meng S, Wu YJ, Mao YP, Ye RX, Wang QZ, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infectious Diseases of Poverty. 2020;9(1):1-2.
19. Schuetz P, Birkhahn R, Sherwin R, Jones AE, Singer A, Kline JA, et al. Serial procalcitonin predicts mortality in severe sepsis patients: results from the multicenter procalcitonin MOnitoring SEpsis (MOSES) study. Critical care medicine. 2017;45(5):781.
20. Dennis JM, McGovern AP, Vollmer SJ, Mateen BA. Improving survival of critical care patients with coronavirus disease 2019 in England: a national cohort study, March to June 2020. Critical care medicine. 2021 ;49(2):209.
21. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The lancet. 2020 28;395(10229):1054-62.
22. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The lancet. 2020 15;395(10223):507-13.
23. Asghar MS, Kazmi SJ, Khan NA, Akram M, Khan SA, Rasheed U, Hassan M, et al. Clinical profiles, characteristics, and outcomes of the first 100 admitted COVID-19 patients in Pakistan: a single-center retrospective study in a tertiary care hospital of Karachi. Cureus. 2020 ;12(6).
24. Liu Y, Du X, Chen J, Jin Y, Peng L, Wang HH, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. Journal of Infection. 2020;81(1):e6-12.
25. Liu J, Li S, Liu J, Liang B, Wang X, Wang H, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. eBioMedicine. 2020;55:102763.
26. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. The Lancet. 2020;395(10229):1054-62.
27. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine. 2020;382(18):1708-20.
28. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney International. 2020;97(5):829-38.
29. Lili C, Kumardeep C, Aparna S, Kinsuk C, Akhil V, Shan Z. AKI in Hospitalized patients with COVID-19. JASN. 2020;31(9):2145-57.
30. Azam TU, Shadid HR, Blakely P, O'Hayer P, Berlin H, Pan M, et al. Soluble urokinase receptor (SuPAR) in COVID-19–related AKI. Journal of the American Society of Nephrology. 2020;31(11):2725-35.
31. Asghar MS, Kazmi SJ, Khan NA, Akram M, Khan SA, Rasheed U, et al. Clinical profiles, characteristics, and outcomes of the first 100 admitted COVID-19 patients in Pakistan: A single-

center retrospective study in a tertiary care hospital of Karachi. Cureus. 2020 ;12(6).
32. Lippi G, Plebani M. Laboratory abnormalities in patients with COVID-2019 infection. Clinical Chemistry and Laboratory Medicine (CCLM). 2020 1;58(7):1131-4.
33. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 2020 28;395(10229):1054-62.
34. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020 15;395(10223):497-506.
35. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus–infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.
36. Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chinese Medical Journal. 2020 5;133(9):1025.
37. Chen Z, wU D. GUO w. Li H and gerton JL: A genetic screen to discover pathways affecting cohesin function in *Schizosaccharomyces pombe* identifies chromatin effectors. g3 (Bethesda). 2012;2:1161-8.