International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Characteristic ARDS with COVID-19

Herani Mutia Riandini[1], Fajrinur Syarani[2], Syamsul Bihar[3], Putri C Eyanoer[4]

[1]Department of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Sumatera Utara, Universitas Sumatera Utara Hospital, Jl. DrMansyur No.66, Medan 20154, Indonesia

[2]Department of Public Health, Faculty of Medicine Universitas Sumatera Utara, Medan, Indonesia

[1]Corresponding author: *andienhmr[at]gmail.com*

Abstract: ***ARDS is a serious complication of COVID-19 disease that arises in approximately 10-29% of all cases of COVID-19. ARDS resulted from a cytokine storm event that occurred in the second week of the course of the disease. Few factors were related to increasing cytokine productions. This study aimed to describe the clinical characteristics of patients ARDS with COVID-19 in H. Adam Malik General Hospital as the center of COVID-19 in North Sumatera, Indonesia. This is a descriptive study with a retrospective cohort design. The samples of this study were secondary data from the medical record in patients with positive RT-PCR COVID-19 from November 2020 to April 2021. The inclusion criteria of this study were patients with moderate to the critical case of COVID-19 and confirmed by RT-PCR swab for SARS-COV2. Those subjects then followed up until discharged from the hospital to assess the ARDS episode confirmed by PaO2/FiO2 results in Arterial Blood Gases. Statistical analysis was performed using SPSS ver 26.0. A total of 91 subjects were enrolled in this study with the most participants being male, age > 40 years old. The smoker and comorbid factors such as COPD, kidney disease, cardiovascular disease, diabetes Mellitus were found to be more common in COVID-19 patients with ARDS. The clinical manifestations of COVID-19 were varied from mild disease including fever, cough, anosmia, ageusia, sore throat, myalgia, coryza until serious manifestations including shortness of breath and chest pain. All Chest X-rays showed bilateral infiltrations. ARDS-related COVID-19 was related to male gender with age > 40 years old and have a comorbid disease. Clinical manifestations were varied and few participants with moderate symptoms may progress to ARDS.***

Keywords: ARDS, COVID-19, D-DIMER

1. Introduction

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and has declared COVID-19 as a pandemic (1, 2) on March 11, 2020. SARS-COV-2 was mainly spread by droplet inhalations and arises various clinical manifestations from mild disease including fever, cough, coryza, sore throat to severe disease such as respiratory distress (Xu, 2021). The clinical course of COVID-19 was described in the previous study where ARDS will manifest in the second week in susceptible populations (Aguilar et al, 2020).

Cytokine storms will trigger a severe attack by the immune system, cause acute respiratory distress syndrome (ARDS) and multi-organ failure, and eventually lead to death in cases of severe SARS-CoV-2 infection, as is the case with SARS-CoV and MERS-CoV infections (3). Clinical data suggest severe COVID-19 was the most common category of COVID-19 disease that will progress to acute respiratory distress syndrome-induced viral pneumonia (ARDS) (4). ARDS was defined as acute onset hypoxemia with bilateral infiltrates on the frontal chest radiograph, without evidence of left atrial hypertension. COVID-19 can progress to ARDS in approximately 10-20% of cases, especially in elderly and comorbid patients (5). However, nowadays, the global experience of managing patients with COVID-19-associated acute respiratory distress syndrome (ARDS) is growing rapidly, along with an increasing number of reports on respiratory system mechanics and ventilator management (6).

In this study, we examined the characteristics of ARDS in patients with COVID-19, based on age, gender, clinical symptoms, comorbidities, laboratory results, chest X-ray results, therapy obtained, and treatment outcomes for COVID-19 patients at H. Adam Malik Hospital. Medan.

2. Methods

This is a descriptive study with a retrospective cohort design. The samples of this study were secondary data from medical records in patients with positive Reverse Transcriptase Polymerase Chain Reaction RT-PCR COVID-19 from November 2020 to April 2021 in the General Hospital of H. Adam Malik Medan as a center of COVID-19 in North Sumatera, Indonesia. The inclusion criteria of this study were patients with moderate to a critical case of COVID-19 and confirmed by RT-PCR swab for SARS-COV2. Those subjects then followed up until discharged from the hospital to assess the ARDS episode confirmed by PaO_2/FiO_2 results in Arterial Blood Gases. The exclusion criteria were incomplete medical records. This study was approved by the Ethics Committee of the Faculty of Medicine of Universitas Sumatera Utara. After collecting data and serving as categorical data in frequency distribution table by SPSS ver 26.0.

3. Results

Total 91 subjects enrolled in this study with most subjects were male as many as 58 (63.7%) and aged more than 40 years old (82.4%). Each patient has a variety of clinical symptoms, ranging from mild to severe complaints such as anosmia, ageusia, fever, nausea, myalgia, runny nose, diarrhea, chest pain, cough to shortness of breath. From all samples of this study, fever was the most common clinical symptom, which was 80 people (87.8%). Followed by

coughing 71 subjects (71%), shortness of breath 64 subjects (70.3%), myalgia 40 subjects (43.3%), anosmia 27 subjects (29.7%), diarrhea 17 subjects (18, 7%), nausea 15 subjects (16.6%), colds 15 subjects (16.5%), ageusia 8 subjects (8.8%), and chest pain 7 subjects (7.7%) in a row. As for smoking habits in the sample, 56 subjects (61.6%) were smokers, and the rest 35 subjects (38.5%) were nonsmokers. It was found that as many as 20 subjects (22%) have critical symptoms, then 30 people (33%) have severe symptoms and 41 subjects (45%) have moderate symptoms. In this study, there were no samples of COVID-19 without symptoms and COVID-19 with mild symptoms.

For laboratory results, the increase of d-dimer depicted with a value of more than 500 ng/mL was 53 people (58.2%). All subjects had bilateral infiltrates on chest X-ray. Furthermore, the comorbidities found in COVID-19 patients, it was found that 59 people (64.8%) had comorbidities and 32 people (35.2%) did not have comorbidities. The comorbities include COPD (10 subjects), kidney disease (5 subjects), cardiovascular disease (20 subjects), diabetes mellitus (27 subjects), pulmonary tuberculosis (3 subjects).

After following up until discharged hospital owing to death or home discharged, 51 subjects (56%) develop ARDS confirmed by a decrease of PaO2/FiO2 ratio (below 300 mmHg) and 40 people (44%) had a normal PaO2/FiO2 ratio. Further demographic characteristics were described in Table 1.

Table 1: Clinical characteristics of all subjects recruited in the study

No.	Characteristic	N	%
1	**Gender**		
	Man	58	63, 7
	Woman	33	36, 3
2	**Age**		
	≥40years	75	82, 4
	≤40years	16	17, 6
3	**Shortness of breath**		
	Yes	64	70, 3
	No	27	29, 7
4	**Cough**		
	Yes	71	78
	No	20	22
5	**Anosmia**		
	Yes	27	29, 7
	No	64	70, 3
6	**Ageusia**		
	Yes	8	8, 8
	No	83	91, 2
7	**Fever**		
	Yes	80	87, 8
	No	11	12, 1
8	**Nausea**		
	Yes	15	16, 6
	No	76	83, 5
9	**Myalgia**		
	Yes	40	43, 9
	No	51	56, 1
10	**Chest pain**		
	Yes	7	7, 7
	No	84	92, 3
11	**Rhinitis**		
	Yes	15	16, 5
	No	76	83, 5
12	**Diarrhea**		
	Yes	17	18, 7
	No	74	81, 3
13	**Smoke**		
	Smoke	56	61, 5
	No smoke	35	38, 5
14	**Severity of symptoms**		
	No symptom	0	0
	Mild	0	0
	Moderate	41	45
	Severe	30	33
	Critical	20	22
15	**Ratio PaO2/FiO2**		
	Normal	40	44
	Decrease	51	56
16	**D-dimer**		
	Normal	38	41, 8
	Increase	53	58, 2
17	**Comorbid**		
	With comorbid	59	64, 8
	No comorbid	32	35, 2
18	**Chest x-ray**		
	No Infiltrate	0	0
	Bilateral infiltrate	91	100
19	**Outcome**		
	No ARDS	51	56
	ARDS	40	44

4. Discussion

From this study, it was found that a total of 91 patients who met the inclusion and exclusion criteria for this COVID-19 patient related to the incidence of ARDS. In this study, male has a higher risk for developing ARDS than female. This could be due to the higher expression of angiotensin 2 (ACE2) enzyme in males compare with the female. ACE-2 enzyme is an integral part of the human renin-angiotensin-aldosterone system (RAAS), a functional receptor that allows SARS-CoV-2 to attack human alveolar epithelial cells (7, 8).

In this study, most subjects were in the age group >40 years. Therefore, older age is associated with the incidence of ARDS and the severity of COVID-19 due to decreased immune response as the consequence of higher age (9).

Each patient has a variety of clinical symptoms, ranging from mild to severe complaints such as anosmia, ageusia, fever, nausea, myalgia, runny nose, diarrhea, chest pain, cough to shortness of breath. From all samples of this study, fever was the most common clinical symptom, followed by cough, shortness of breath, muscle pain, loss of sense of smell, diarrhea, nausea, runny nose, loss of sense of taste, and chest pain, respectively. In line with research conducted by Wu, X. et al, that clinical manifestations such as shortness of breath, cough, loss of smell, loss of taste, fever, nausea, muscle aches, runny nose, and chest pain were associated with the development of ARDS (10).

As for smoking habits, a smoker tends to have a greater risk for ARDS compared with a nonsmoker. This is in line with WHO which shows that smoking is associated with an

increase in disease severity and a risk factor for the incidence of ARDS in hospitalized COVID-19 patients. Although likely to be related to severity, no evidence to measure the risk for smokers of hospitalization with COVID-19 or infection by SARS-CoV-2 was found in the literature (11). Further, hyper inflammation state in smoking habit was induced the hyper productions of cytokine that related to ARDS event during COVID19 (Gulsen, 2020).

Then the severity of symptoms in COVID-19 is needed to determine the patient's prognosis. Forty-five percent of subjects were having moderate symptoms, 33% of subjects were having severe symptoms, 32% subjects were in critical symptoms, yet no subjects were in mild and had no symptoms. This is due to samples of COVID-19 without symptoms and COVID-19 with mild symptoms are not an indication for hospitalization. This is in line with the research of Koichi et al. that showed ARDS was more common in patients admitted to the hospital with severe to critical symptoms (12).

Indicators of laboratory results also show varying results. Some of the indicators examined include D-dimer. In this study, higher D dimer in the first admission in the hospital tends to develop ARDS. This is in line with studies that showed subjects who had an increased d-dimer was related to the incidence of ARDS (D-dimer 0.5 mg/L, adjusted HR: 1.75, P = 0.015) and after adjustment for sex, age, comorbid, and other risk factors in the blood, d-dimer is an independent predictor of COVID-19 mortality (13, 14).

Imaging modalities are no less important in evaluating the clinical course and diagnosis of COVID-19 patients with the simplest and cheapest modality is chest X-Ray. In this study, all subjects had bilateral infiltrates (100%). This is because the indications for hospitalizations were the patients who were in moderate, severe, and critical symptoms who has infiltrated in their chest X-rays. The criteria for moderate, severe, and critical grades were based on the chest X-ray, it was found that there was bilateral pneumonia. Bilateral infiltrates and GGO, the patient must be isolated because it leads to COVID-19 (17). Unfortunately, there was no definite degree of infiltrating seen in the Chest X-Ray, so the researchers cannot categorize the severity of the Chest X-Ray.

The comorbidities most often associated with the severity of COVID-19 include obesity, heart disease, diabetes mellitus, kidney disease, malignancy, and other lung diseases. Of those conditions, there were continuous factors that induced a hyperinflammatory state. So, when there is an infection attack, the body's inflammatory response will be excessive and cause the secretion of large amounts of cytokines to lead to a cytokine storm. This cytokine storm will damage the epithelial and parenchymal tissue of the lung which interferes with the oxygen diffusion and perfusion process, resulting in ARDS (18).

5. Conclusion

COVID-19 patients with ARDS in this study showed that the majority of subjects were male over 40 years of age, with varying symptoms ranging from mild to severe complaints such as anosmia, ageusia, fever, nausea, myalgia, runny nose, diarrhea, chest pain, cough to shortness of breath. Smoking status and comorbid factors were also associated with the incidence of ARDS. The laboratory tests particularly d-dimer can be a predictor of ARDS.

References

[1] Susilo A, Rumende CM, Pitoyo CW, Santoso WD, Yulianti M, Herikurniawan H, et al. Coronavirus Disease 2019: Tinjauan Literatur Terkini. J Penyakit Dalam Indones [Internet].2020 Apr 1 [cited 2021 Jun 29]; 7 (1): 45. Available from: https: //www.ncbi. nlm. nih. gov/nuccore/

[2] Kementerian Kesehatan Republik Indonesia [Internet]. [cited 2021 Jun 29]. Available from: https: //www.kemkes. go. id/

[3] Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med [Internet].2020 Apr 1 [cited 2021 Jun 29]; 8 (4): 420–2. Available from: https: //doi. org/10.1016/

[4] Coronavirus disease (COVID-19) [Internet]. [cited 2021 Jun 29]. Available from: https: //www.who. int/emergencies/diseases/novel-coronavirus-2019?adgroupsurvey=%7Badgroupsurvey%7D&gclid=Cj0KCQjw5uWGBhCTARIsAL70sLLLZE1PTvX_lcguimZyPnYYfT4EGsfFOoBjvDJtQ5wmpg40_Nk2GGoaArOhEALw_wcB

[5] Li X, Ma X. Acute respiratory failure in COVID-19: Is it “typical” ARDS? [Internet]. Vol.24, Critical Care. BioMed Central Ltd.; 2020 [cited 2021 Jun 29]. p.1–5. Available from: https: //doi. org/10.1186/s13054-020-02911-9

[6] Soy M, Keser G, Atagündüz P, Tabak F, Atagündüz I, Kayhan S. Cytokine storm in COVID-19: pathogenesis and overview of anti-inflammatory agents used in treatment [Internet]. Vol.39, Clinical Rheumatology. Springer; 2020 [cited 2021 Jun 29]. p.2085–94. Available from: https: //pubmed. ncbi. nlm. nih. gov/32474885/

[7] Dumanski SM, Ahmed SB. Sex, Drugs, and Adverse Drug Reactions. Circ Cardiovasc Qual Outcomes [Internet].2020 [cited 2021 Jul 10]; 624–6. Available from: https: //www.ahajournals. org/doi/abs/10.1161/CIRCOUTCOMES.120.007045

[8] B L, S V. Macrophage activation syndrome: early diagnosis is key. Open Access Rheumatol Res Rev [Internet].2018 [cited 2021 Jul 10]; 10: 117–28. Available from: https: //pubmed. ncbi. nlm. nih. gov/30214327/

[9] Matthay MA, Zemans RL, Zimmerman GA, Arabi YM, Beitler JR, Mercat A, et al. Acute respiratory distress syndrome. Nat Rev Dis Prim [Internet].2019 [cited 2021 Jul 10]; 5 (1). Available from: https: //pubmed. ncbi. nlm. nih. gov/30872586/

[10] Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72314 Cases from the Chinese Center for Disease Control and Prevention [Internet]. Vol.323, JAMA-Journal of the American Medical Association. American Medical Association; 2020 [cited 2021 Jun

29]. p.1239–42. Available from: https: //jamanetwork. com/

[11] WHO supports people quitting tobacco to reduce their risk of severe COVID-19 [Internet]. [cited 2021 Jul 10]. Available from: https: //www.who. int/news/item/28-05-2021-who-supports-people-quitting-tobacco-to-reduce-their-risk-of-severe-covid-19

[12] Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clin Immunol [Internet].2020 Jun 1 [cited 2021 Jul 11]; 215: 108427. Available from: https: //www.ncbi. nlm. nih. gov/pmc/articles/PMC7169933/

[13] Bi Q, Wu Y, Mei S, Ye C, Zou X, Zhang Z, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. Lancet Infect Dis [Internet].2020 Aug 1 [cited 2021 Jun 29]; 20 (8): 911–9. Available from: www.thelancet. com/infection

[14] Ozen M, Yilmaz A, Cakmak V, Beyoglu R, Oskay A, Seyit M, et al. D-Dimer as a potential biomarker for disease severity in COVID-19. Am J Emerg Med [Internet].2021 Feb 1 [cited 2021 Jun 29]; 40: 55–9. Available from: https: //doi. org/10.1016/j. ajem.2020.12.023

[15] Pavlov I, Mcnicholas B, Perez Y, Tavernier E, Trump MW, Jackson JA, et al. Awake prone positioning in non-intubated patients with acute hypoxemic respiratory failure due to COVID-19: a systematic review and meta-analysis. [cited 2021 Jun 29]; Available from: https: //doi. org/10.21203/rs.3. rs-125426/v2

[16] Aboab J, Louis B, Jonson B, Brochard L. Relation between PaO2/FIO2 ratio and FIO2: A mathematical description. Intensive Care Med.2006 Oct; 32 (10): 1494–7. https: //pubmed. ncbi. nlm. nih. gov/16896846/

[17] Liu Y, Tang JW, Lam TTY. Transmission Dynamics of the COVID-19 Epidemics in England. Int J Infect Dis.2020; https: //www.ijidonline. com/article/S1201-9712 (20) 32579-0/fulltext

[18] Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, et al. Comorbidity and its Impact on Patients with COVID-19. Sn Compr Clin Med [Internet].2020 Aug [cited 2021 Jul 11]; 2 (8): 1. Available from: https: //pubmed. ncbi. nlm. nih. gov/32838147/