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Clinical and Radiological Characteristics of Pneumonia in COVID-19 Patients at First Admission to Dr. Soetomo General Academic Hospital, Surabaya, in June-August 2021

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ABSTRACT

Introduction: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) gave rise to the coronavirus disease (COVID-19) pandemic. Pneumonia in COVID-19 can cause acute respiratory distress syndrome (ARDS), which could lead to damage to end organs. This study aimed to describe the clinical and radiological profile of pneumonia in COVID-19 patients at first admission to the emergency department of Dr. Soetomo General Academic Hospital, Surabaya, in June-August 2021.

Methods: This was a single-center, descriptive study of COVID-19 patients with pneumonia (n=193) at their first admission to the emergency department of Dr. Soetomo General Academic Hospital, Surabaya, from June to August 2021. The demographic data, pre-existing comorbidities, clinical signs and symptoms, and radiological findings were collected from the electronic medical record and analysed using the International Business Machines Corporation (IBM) Statistical Package for Social Sciences (SPSS) version 26.

Results: Out of all the COVID-19 patients included in the study (n=193), most of them were 18-64 years old (86.0%), and the majority were males (50.8%). Of 193 patients, 51.3% had pre-existing comorbidities. Most patients (95.9%) experienced pulmonary symptoms, with shortness of breath being the most common. On chest radiograph, 60.1% patients showed consolidation with central and peripheral predominance (60.6%) and bilateral lung involvement (91.2%).

Conclusion: This study presented a description of the clinical and radiological findings in COVID-19 patients with pneumonia. The majority of patients displayed extensive lesions and dyspnea on the chest radiograph, potentially indicating late-stage and severe COVID-19 pneumonia. To confirm this suggestion, further research is needed.

Highlights:
1. This was the first study that described the radiological features of pneumonia in COVID-19 patients at first admission to Dr. Soetomo General Academic Hospital, Surabaya, during the Delta wave.
2. This study presented the gastrointestinal symptoms of COVID-19 patients with pneumonia.

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Introduction

COVID-19 (corona virus disease) is a highly infectious disease. The coronaviruses infect human's lower respiratory tract and causes mild to severe illness. A novel virus known as severe acute respiratory syndrome coronavirus-2 causes COVID-19 (SARS-CoV-2).[1] During June to August 2021, Indonesia experienced high number of confirm COVID-19 cases with an average of 30475 daily cases counting from 17 June to 22 August 2021.[2]

SARS-CoV-2 infection can either lead to pulmonary or extra-pulmonary manifestation. COVID-19 mostly affects the pulmonary system. The frequent clinical manifestations of COVID-19 include fever, cough and dyspnoea. Pneumonia is an infection in the lower respiratory tract.[3] Pneumonia is one of COVID-19 serious manifestations. Pneumonia can cause ARDS (acute respiratory distress Syndrome) which can lead to various organ failures.[1] Though pulmonary symptoms is common in COVID-19, isolated gastrointestinal symptoms, such as nausea and diarrhoea, can sometimes seems to appear before the pulmonary symptoms.[4] A study found that abdominal pain is associated with an increased risk of severe COVID-19.[5]

Being 65 years and older is one of the risk factors for developing pneumonia in COVID-19.[6] Age and comorbidities can increase the risk of COVID-19 mortality.[7] Men have a higher risk COVID-19 mortality compared to females.[8] Risk factors such as stated can affect COVID-19 infection.[6–8]

Accurate diagnosis of COVID-19 can help control the spread of the disease. Chest X-ray (CXR) is a simple, cheap, fast and safe modality for detecting pneumonia in COVID-19 especially on its intermediate and severe stage. Trough CXR, clinician can also determine COVID-19 severity.[9]

This descriptive study aims to describe the clinical and radiological findings of pneumonia in COVID-19 patients at first admission to the emergency departments of Dr. Soetomo General Academic Hospital during June – August 2021.[10]

Methods

This is a single-centered, descriptive study[10] of 193 COVID-19 patients on first admission to the emergency department of Dr. Soetomo General Academic Hospital from June to August 2021. This study include patients 18 years and older who showed pneumonia. The variables include demographic data, pulmonary and gastrointestinal symptoms, pre-existing comorbidities, and radiological findings which are collected from the electronic medical record and analysed using Statistical Package for the Social Science (SPSS) version 26.[11] This research had received ethical clearance from the ethics committee of Faculty of Medicine Universitas Airlangga and Dr. Soetomo General Hospital.

Results

From 193 COVID-19 patients with pneumonia included in this study, the majorities of the patients were around 18 – 64 years old (86.0%) and were male (50.8%) such as stated in Table 1.

Table 1. Demographic data of COVID-19 patients with pneumonia

Demographic Data	n=193 (100%)
Age	
18-64 years old	166 (86.0%)
≥65 years old	27 (14.0%)
Sex	
Male	98 (50.8%)
Female	95 (49.2%)

Source: Research data, processed

About 95.9% patients included in this study experienced pulmonary symptoms with dyspnoea (95.1%) reported as the most common pulmonary symptoms.

Table 2. Pulmonary symptoms in COVID-19 patients with pneumonia

Pulmonary Symptoms	n=193 (100%)
Total patients without pulmonary symptoms	8 (4.1%)
Total patients with pulmonary symptoms	185 (95.9%)
Dyspnea	176 (95.1%)
Cough	46 (24.9%)
Fever	35 (18.9%)
Fatigue	18 (9.7%)
Runny nose	4 (2.2%)

Source: Research data, processed

About 12.4% of the patients in this study reported to have gastrointestinal symptoms with nausea (58.3%) reported as the most common gastrointestinal symptoms.

Table 3. Gastrointestinal symptoms in COVID-19 patients with pneumonia

Gastrointestinal Symptoms	n=193 (100%)
Total patients without gastrointestinal symptoms	169 (87.6%)
Total patients with gastrointestinal symptoms	24 (12.4%)
Nausea	14 (58.3%)
Diarrhea	9 (37.5%)
Vomiting	8 (33.3%)
Melena	3 (12.5%)
Hematemesis	1 (4.2%)
Hematochezia	1 (4.2%)
Abdominal pain	1 (4.2%)

Source: Research data, processed

Consolidation is the most common radiological findings in this study (60.1%) with the most common location of the predominant lesion being in central and peripheral (60.6%) and involve bilateral lung (91.2%).

Table 4. Radiological findings in COVID-19 patients with pneumonia

Radiological Findings	n=193 (100%)
Consolidation	116 (60.1%)
Ground-glass opacity	71 (36.8%)
Other findings	
Infiltrate	6 (3.1%)
Fibrosis	4 (2.1%)
Lung collapse	2 (1.0%)
Cavitation	1 (0.5%)
Predominant Lesion	
Central and peripheral	117 (60.6%)
Peripheral	60 (31.1%)
Pericardial	13 (6.7%)
Perihilar	3 (1.6%)
Lung Involvement	
Bilateral	176 (91.2%)
Unilateral	17 (8.8%)

Source: Research data, processed

From 193 COVID-19 patients with pneumonia included in this study, 94 (48.7%) patients have no comorbidities. The other 99 (51.3%) patients have comorbidities such as stated in table 5.

Table 5. Radiological findings based on the comorbidities of COVID-19 patients with pneumonia

Comorbidities	Radiological Findings						Total Comorbidities n=99 (100%)
	Consolidation	GGO	Infiltrate	Fibrosis	Lung collapse	Cavitation	
Diabetes	32 (66.7%)	16 (33.3%)	0 (0.0%)	1 (2.1%)	0 (0.0%)	0 (0.0%)	48 (48.5%)
Obesities	22 (62.9%)	10 (28.6%)	3 (8.6%)	2 (5.7%)	1 (2.9%)	0 (0.0%)	35 (35.4%)
Hypertension	24 (72.7%)	9 (27.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	33 (33.3%)
CKD	7 (53.8%)	6 (46.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	13 (13.1%)
Pregnancy	2 (33.3%)	3 (50.0%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	1 (16.7%)	6 (6.1%)
Heart disease	5 (83.3%)	1 (16.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (6.1%)
SLE	1 (33.3%)	1 (33.3%)	1 (33.3%)	0 (0.0%)	1 (33.3%)	0 (0.0%)	3 (3.0%)
Asthma	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Cancer	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Mental health conditions	2 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (2.0%)
Tuberculosis	0 (0.0%)	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	1 (50.0%)	2 (2.0%)
HIV	1 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)

GGO: ground-glass opacity; CKD: chronic kidney disease; SLE: systemic lupus erythematosus; HIV: human immunodeficiency virus

Discussion

In this study, the patients are divided into two age groups, 18 – 64 and ≥ 65 years old. Natural immunity declines gradually in elderly thus making them more prone to infection. Despite the risk factor, this study shows that most patients are 18 – 64 years old. Other studies show similar result.[8,12] The high number of young individuals in this study is possibly because they tend to have higher mobility thus making them more prone to COVID-19 infection. Delta variant (the dominant COVID-19 variant during June – August 2021) could possibly infect the young individuals and worsen the COVID-19 infection. However, this study does not include the strain of COVID-19 that infected the patients.[2]

This study found that Male patients are the slight majority (50.8%). Other studies show same result.[8,13] Many factors play a role in the high number of male patients in this study. One of which is the sex-based immunological difference due to the X chromosome and certain sex hormones. This may explain why men are more prone to infection rather than female. Higher levels of ACE2 expression has also been reported in male, which may facilitate SARS-CoV-2 invasion.[8] Behaviours such as smoking and heavy drinking are usually found in males. In contrast, females tend to show more responsible attitudes toward the COVID-19 pandemic.[14]

The pulmonary symptoms appeared more often than gastrointestinal symptoms in this study. This is likely due to cell deaths and cytopathic effects induced by COVID-19 infection that occurs in the airway epithelial cells. Meanwhile, extensive tissue damage is not reported in the digestive system of COVID-19 patients. SARS-CoV-2 virus infection causes a difference in the immuno-inflammatory environment between the respiratory and gastrointestinal system. This results in different rate of SARS-CoV-2 replication and cell death between the respiratory and gastrointestinal system. However, further study needs to be conducted to know why gastrointestinal symptoms only appear in certain COVID-19 patients.[15]

Regarding the respiratory symptoms, most patients in this study has dyspnoea (95.1%). However, other studies report that the most common symptoms of COVID-19 is fever.[13,16] The high number of patients with dyspnoea in this study is likely related to "silent" or "happy hypoxia". Silent hypoxia revers to a condition where COVID-19 patient with

severe hypoxia does not experience dyspneu.[17] Silent hypoxia can be an early symptom of SARS-CoV-2 infection. Meanwhile, dyspnoea appears in moderate, severe, and critically ill COVID-19 patients.[18] In severely ill COVID-19 patients, dyspnoea appears after cardio-pulmonary damage. Based on this finding, it is suspected that the patients in this study are mostly moderately, severely, or critically ill.[18]

The most frequently reported gastrointestinal symptoms are nausea (58.3%), diarrhoea (37.5%), and vomiting (33.3%). These findings are similar to one study (n = 140) that reported nausea (17.3%), diarrhoea (12.9%), abdominal pain (5.8%), and vomiting (5%) as the most frequent symptoms.[19] Another study with 138 COVID-19 patients reports that diarrhoea (10.1%), nausea (10.1%), vomiting (3.6%), and abdominal pain (2.2%) are the gastrointestinal symptoms that appeared the most.[13]

The difference in the incidence of nausea and vomiting may be due to the subjective factor of patients. Nausea and vomiting are very subjective due to their dependence on memory and tolerance of individuals.[20] Diarrhoea that appears in patients in this study is possibly related to SARS-CoV-2 viroporin (E protein and Orf3a). The binding of E protein to PALS1 causes dysfunction of PALS1, leading to tight junctions and adherent junctions damage in the endothelial and intestinal epithelial cells. This may lead to leaky gut syndrome, systemic or local invasion of normal gut microbiota, and activation of the immune system.[15]

Abdominal pain is the least common gastrointestinal symptom in this study. This finding is similar to a study conducted by Zeng W., et. al. That study reported abdominal pain to be associated with greater COVID-19 severity than other symptoms which are diarrhoea, nausea, and vomiting). The precise mechanism of how patients with gastrointestinal symptoms develop severe pneumonia due to COVID-19 is still unclear. However, gut-lung axis might be one of its mechanisms. Changes in composition and function of the gut flora can affect the immune system regulation in the respiratory tract. Gut-lung axis is affected by viral load, gastrointestinal status, and immune function. The severity of COVID-19 is highly related to viral load. Based on the evidence, it is plausible to suspect that patients experiencing abdominal pain may have higher viral loads in their gastrointestinal tract compared to those with diarrhoea, nausea, and vomiting. The requirement of a sufficiently high viral load in the digestive system, may be the reason why only few COVID-19 patients in this study experienced abdominal pain.[5]

Typical findings of COVID-19 on CXR include reticular pattern, GGO (ground-glass opacity), and consolidations with bilateral lung involvement and peripheral lower zone predominant.[21] Regarding the radiological findings, most patients in this study show consolidation (60.1%) with central and peripheral predominant (60.6%) location, and bilateral lung involvement (91.2%). A study with 417 COVID-19 patients with abnormal CXR, found that GGO (92.6%) is more common than consolidation (22.8%), most lesions were peripheral predominant (69.5%), and most had bilateral lung involvement (74%).[22] Meanwhile, another study with 268 COVID-19 patients with abnormal CXR findings, found that consolidation (81.3%) is more common than GGO (32.5%), most lesions were peripheral predominance (58.2%), and most had bilateral lung involvement (67.5%).[23] The different frequency of GGO and consolidation between studies is likely related to the stage of COVID-19 pneumonia that the patients were in when they were examined. During the initial stage of COVID-19 pneumonia, the pattern in the CXR is dominated by reticular pattern. Later on, GGO will dominate the reticular pattern. On advanced stage, consolidation will be found more frequent.[21] The lesion's predominant location in this study is not in line with previous mentioned studies. According to the COVID-19 modified scoring system developed for Dr. Soetomo general hospital, a higher score is given to a larger area of infiltrate. The severity of the condition increases as the final score rises[9] Frequent finding of consolidation along with central and peripheral predominant lesion in this study may indicate that most patients are in the advanced stages of COVID-19 pneumonia. However, keep in mind that GGO pattern might be difficult to observe on CXR. This could contribute to the low number of GGO in this study.[21]

The possibility of secondary infections or co-infection in this study hasn't been ruled out. Secondary infections by bacteria, other viruses, fungi, or parasites can have an impact on the CXR findings. Consolidation can appear on bacterial infection. Fungi co-infection can also appear as peribronchial consolidation in COVID-19 patients. In co-infections with viruses, clinical symptoms and CXR findings can overlap with COVID-19, making it difficult to diagnose accurately. It is possible that the secondary infections or co-infections will influence the presence of consolidation or GGO in CXR of COVID-19 patients in this study. The possibility of secondary infection or co-infection could also explain why some patients show infiltrate, fibrosis, cavitation, and pneumothorax (lung collapse) in this study. This study includes "infiltrate", which is a nonspecific term and is prone to misinterpretation.[24]

Generally, individuals with comorbidities have lower immune system thus making them more prone to infection. They are also more prone to adverse drug effects because of their requirement to take multiple drugs for their comorbidities.[25] The most common comorbidities in this study include diabetes (48.5%), obesity (35.4%), and hypertension (33.3%). This is in line with a study of 172 COVID-19 pneumonia patients that found BMI of 25 kg/m^2 (52.3%) and higher, hypertension (48.3%), along with type II diabetes (19.2%) are the most common comorbidities.[16]

In patients with either diabetes or hypertension, the expression of ACE2 receptors in epithelial cells of the lung, intestine, kidney, and blood vessels are increased.[25] In patients with obesity, the expressions of ACE2 receptors in mature adipocyte cells are also increased.[26] Patients with diabetes, obesity, and hypertension also have a decrease regulation of microRNA-146a gene. MicroRNA-146a gene regulates the excessive inflammatory response to viral infections. Down regulation of the gene can result in lack of response to limit the inflammation due to COVID-19 infection.[27]

This study shows that consolidation is the most common radiological findings in diabetic patients. This result is similar to a study that found an increased bilateral airspace consolidation in diabetic COVID-19 patients. Diabetes causes damage in the microvascular system. This can disrupt the alveolar-capillary network in the lungs thus making the patient exhibit more signs of pulmonary damage.[28] Diabetes can induce oxidative stress, which plays a role in the development of pneumonia in COVID-19. The increased mitochondrial oxidative stress can induce alveolar epithelial cell apoptosis, which lead to alveolar membrane damage and fibroblast recruitment. This may explain the presence of fibrosis in diabetic COVID-19 patient in this study. Hyperglycaemia can increase virus replication. It can also damages innate immune components and triggers pathogen growth in the lung thus making patients with diabetes more susceptible to secondary bacterial infections.[29] In addition, there's no difference in COVID-19 severity between type 1 or type 2 diabetes.[30]

In this study, COVID-19 patients with obesity mostly show consolidation (62.9%) on CXR. It is assumed that these patients are in advanced stage of COVID-19. The chronic inflammatory state, immune system dysfunction, and metabolic disturbance in obesity affect the pathogenesis of COVID-19. SARS-CoV-2 infection can decrease CD4+ T cells, CD8+ T cells, B cells, and NK cells. Obesity impairs both T and B cell response. SARS-CoV-2 infection in obesity results in weakened immune system which could lead to higher viral load, rapid viral replication and spreading. This may also make the patient more vulnerable to secondary infection.[31]

Most of the patients with hypertension in this study show consolidation (72.7%) on CXR. Patients with high blood pressure are more vulnerable to COVID-19 due to increased inflammation, muscle contraction, and vasoconstriction caused by the renin-angiotensin system (RAS). These patients may take medications such as angiotensin receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) to control their blood pressure. These medications can increase ACE2 expression in the alveolar cells, which may facilitate SARS-CoV-2 invasion. Once SARS-CoV-2 infects alveolar cells, it reduces ACE2 expression, which can lead to increase aldosterone and decrease angiotensin II. However, stopping ARBs and ACEIs in COVID-19 patients with high blood pressure may do more harm than good, as these medications have protective effects on the cardiovascular and renal systems.[32]

The presence of underlying pulmonary disease is thought to worsen the COVID-19 infection. However, only few patients in this study are presented with asthma (2.0%) and tuberculosis (2.0%). Asthma is not an independent risk factor for increasing COVID-19 severity. The difference in phenotype and therapy may affect the level of susceptibility and severity of COVID-19 in patients with asthma. The use of inhaled corticosteroids for asthma therapy may have beneficial effects against COVID-19 because of its anti-inflammatory effect and it reduces the expression of ACE2 and TMPRSS2 on bronchial cells, which may reduce the likelihood of SARS-CoV-2 replication.[33] This is probably why only two asthma patients in this study present with pneumonia in COVID-19. Tuberculosis spreads through droplets from patients with active tuberculosis. The low number of COVID-19 patients with tuberculosis in this study is probably because COVID-19 prevention measures such as using masks also prevent the transmission of tuberculosis.[34]

Strengths and Limitations

The strength in this study is that the variables are measured precisely, using a software with a high level of trust. This study has some limitations which are the small sample size, variations in the radiological terminology used in the medical records, and the inability to differentiate pneumonia due to COVID-19 and pneumonia due to COVID-19 with secondary bacterial infection or co-infection.

Conclusion

Most patients included in this study are young male. In this study, pulmonary symptoms are more common than gastrointestinal symptoms with dyspnea as the most common pulmonary symptoms. On CXR most patients shows consolidation with central and peripheral predominance and bilateral lung involvements. Diabetes is the most common comorbidities. The presence of diabetes may play a role in the high number of consolidation found in this study. It is suggested that most patients in this study suffered from severe COVID-19 with pneumonia due to the presence of extensive lesions on CXR along with dyspnea. However, further study is needed to confirm this suggestion.

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Conflict of Interest

The authors declared there is no conflict of interest.

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Ethical Clearance

This study had received ethical clearance from the Ethics Committee Universitas Airlangga Faculty of Medicine and Dr. Soetomo General Hospital on 9-10- 2022 (No. 1077/LOE/301.4.2/X/2022).

Authors' Contributions

Concept and design: AASPP, HH, RS, WIE; data collection, analysis, and interpreting data: AASPP, HH, RS; drafting manuscript and revising: AASPP, HH, RS, WIE; supervision: HH, RS, WIE; All authors reviewed and approved the final version of the manuscript.

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