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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

Coronavirus disease (COVID-19) is a highly infectious disease. Coronaviruses infect the lower respiratory tract, causing mild to severe illness in humans. A novel virus, known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), causes COVID-19.[1] Between June and August 2021, Indonesia experienced a high number of confirmed COVID-19 cases, with an average of 3,475 daily cases from 17 June to 22 August 2021.[2]

Severe acute respiratory syndrome coronavirus-2 infection can lead to either pulmonary or extrapulmonary manifestations. Coronavirus disease primarily 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] It is one of the severe manifestations of COVID-19. It can cause acute respiratory distress syndrome (ARDS), which can lead to various organ failures.[1] Although pulmonary symptoms are common in COVID-19, isolated gastrointestinal symptoms, such as nausea and diarrhea, can sometimes appear before the pulmonary symptoms.[4] A study found that abdominal pain was associated with an increased risk of severe COVID-19.[5]

Being 65 years or older is one of the risk factors for developing pneumonia in COVID-19.[6] Age and comorbidities can increase the risk of mortality from COVID-19.[7] Males have a higher risk of COVID-19 mortality compared to females.[8] Risk factors, such as those mentioned, can increase the likelihood of contracting COVID-19.[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 in its intermediate and severe stages. Through CXR, clinicians can also assess the severity of COVID-19.[9]

This study aimed to describe the clinical and radiological findings 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 193 COVID-19 patients on first admission to the emergency department of Dr. Soetomo General Academic Hospital, Surabaya, from June to August 2021. This study includes patients aged 18 years and older who have been diagnosed with pneumonia. The variables include demographic data, pulmonary and gastrointestinal symptoms, pre-existing comorbidities, and radiological findings, which were collected from the electronic medical record and analyzed using the International Business Machines Corporation (IBM) Statistical Package for Social Sciences (SPSS) version 26.[10] This study had received ethical clearance from the Ethics Committee of the Faculty of Medicine, Universitas Airlangga, Surabaya (No.1077/LOE/301.4.2/X/2022).

Results

Of the 193 COVID-19 patients with pneumonia included in this study, the majority were between 18 and 64 years old (86.0%) and were males (50.8%), 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

Approximately 95.9% of patients included in this study experienced pulmonary symptoms, with dyspnea (95.1%) being the most common pulmonary symptom reported.

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

Approximately 12.4% of the patients in this study reported experiencing gastrointestinal symptoms, with nausea being the most common (58.3%).

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 was the most common radiological finding in this study (60.1%), with the predominant lesion most commonly located in the central and peripheral areas (60.6%) and involving both lungs (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

Of 193 COVID-19 patients with pneumonia included in this study, 94 (48.7%) patients had no comorbidities. The other 99 patients (51.3%) had comorbidities, as listed 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, patients were divided into two age groups: 18–64 years old and ≥65 years old. Natural immunity declines gradually in the elderly, making them more susceptible to infections. Despite the risk factor, this study revealed that most patients were between 18 and 64 years old. Other studies showed similar results.[8,11] The high number of young individuals in this study was likely due to their higher mobility, which makes them more susceptible to COVID-19 infection. The Delta variant (the dominant COVID-19 variant in June-August 2021) could infect young individuals and worsen the COVID-19 infection. However, this study did not include the strain of COVID-19 that infected the patients.[2]

This study found that males were the slight majority (50.8%). Other studies showed the same result.[8,12] Several factors contributed to the high number of male patients in this study. One of these was the sex-based immunological difference due to the X chromosome and certain sex hormones. This might explain why males are more prone to infection than females. Higher levels of angiotensin-converting enzyme 2 (ACE2) expression have also been reported in males, which may facilitate SARS-CoV-2 invasion.[8] Behaviors 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.[13]

The pulmonary symptoms appeared more often than gastrointestinal symptoms in this study. This was likely due to cell death and cytopathic effects induced by COVID-19 infection in the airway epithelial cells. Meanwhile, extensive tissue damage is not reported in the digestive system of COVID-19 patients. Severe acute respiratory syndrome coronavirus-2 virus infection causes a difference in the immunoinflammatory environment between the respiratory and gastrointestinal systems. This results in different rates of SARS-CoV-2 replication and cell death between the respiratory and gastrointestinal systems. However, further study is needed to determine why gastrointestinal symptoms only appear in certain patients with COVID-19.[14]

Most patients in this study had dyspnoea (95.1%). However, other studies reported that the most common symptom of COVID-19 was fever.[12,15] The high number of patients with dyspnoea in this study was likely related to "silent" or "happy hypoxia". Silent hypoxia refers to a

condition where a COVID-19 patient with severe hypoxia does not experience dyspnea.[16] It can be an early symptom of SARS-CoV-2 infection. Meanwhile, dyspnea appears in moderate, severe, and critically ill COVID-19 patients.[17] In severely ill COVID-19 patients, dyspnea appears after cardiopulmonary damage. Based on this finding, it is suspected that the patients in this study were mostly moderately, severely, or critically ill.[17]

The most frequently reported gastrointestinal symptoms were nausea (58.3%), diarrhea (37.5%), and vomiting (33.3%). These findings are similar to a study (n=140) that reported nausea (17.3%), diarrhea (12.9%), abdominal pain (5.8%), and vomiting (5.0%) as the most frequent symptoms.[18] Another study involving 138 COVID-19 patients reported that diarrhea (10.1%), nausea (10.1%), vomiting (3.6%), and abdominal pain (2.2%) were the gastrointestinal symptoms that appeared most frequently.[12]

The difference in the incidence of nausea and vomiting may be due to the subjective factors of patients. Nausea and vomiting are highly subjective due to their dependence on individual memory and tolerance.[19] The diarrhea observed in patients in this study was possibly related to SARS-CoV-2 viroporins (E protein and Open Reading Frames/ORF3a). The binding of E protein to protein associated with LIN7 1 (PALS1) causes dysfunction of PALS1, leading to damage to tight junctions and adherent junctions 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.[14]

Abdominal pain was the least common gastrointestinal symptom in this study. This is similar to a study conducted by Zeng, *et al*. (2022).[5] The study reported abdominal pain was associated with greater COVID-19 severity than other symptoms, which were diarrhoea, nausea, and vomiting.[5] The precise mechanism of how patients with gastrointestinal symptoms develop severe pneumonia due to COVID-19 is still unclear. However, the gut-lung axis might be one of its mechanisms. Changes in the composition and function of the gut flora can impact the regulation of the immune system in the respiratory tract. The 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 diarrhea, nausea, and vomiting. The requirement of a sufficiently high viral load in the digestive system may be the reason why only a few COVID-19 patients in this study experienced abdominal pain.[5]

Typical findings of COVID-19 on CXR include a reticular pattern, ground-glass opacity (GGO), and consolidations, with bilateral lung involvement and a predominant peripheral lower zone distribution.[20] Most patients in this study exhibited consolidation (60.1%), with a predominant central and peripheral location (60.6%), and bilateral lung involvement (91.2%). A study with 417 COVID-19 patients with abnormal CXR found that GGO (92.6%) was more common than consolidation (22.8%), most lesions were predominantly peripheral (69.5%), and most had bilateral lung involvement (74%).[21] Meanwhile, another study with 268 COVID-19 patients with abnormal CXR findings found that consolidation (81.3%) was more common than GGO (32.5%), most lesions were peripheral predominance (58.2%), and most had bilateral lung involvement (67.5%).[22] 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 a reticular pattern. Later on, GGO will dominate the reticular pattern. In the advanced stage, consolidation will be found more frequently.[20] The predominant location of the lesion in this study differs from that in previous studies. According to the COVID-19 modified scoring system developed for Dr. Soetomo General Academic Hospital, Surabaya, a higher score is assigned to a larger area of infiltrate.[9] The severity of the condition increases as the final score rises.[9] The frequent finding of consolidation, along with central and peripheral predominant lesions, in this study might indicate that most patients were in the advanced stages of COVID-19 pneumonia. However, it should be noted that the GGO pattern might be difficult to observe on CXR. This could contribute to the low number of GGO in this study.[20]

The possibility of secondary infections or co-infection in this study had not been ruled out. Secondary infections by bacteria, other viruses, fungi, or parasites can affect the CXR findings. Consolidation can appear in bacterial infection. Fungal co-infection can also occur 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. The secondary infections or co-infections may influence the presence of consolidation or GGO in the CXR of COVID-19 patients in this study. The possibility of secondary infection or co-infection could also explain why some patients showed infiltrate, fibrosis, cavitation, and pneumothorax (lung collapse) in this study. This study includes the term “infiltrate”, which is a nonspecific term prone to misinterpretation.[23]

Generally, individuals with comorbidities have a lower immune system, 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.[24] The most common comorbidities in this study include diabetes (48.5%), obesity (35.4%), and hypertension (33.3%). This aligns with a study of 172 COVID-19 pneumonia patients, which found that body mass index (BMI) of 25 kg/m² or higher (52.3%), hypertension (48.3%), and type II diabetes (19.2%) were the most common comorbidities.[15]

In patients with either diabetes or hypertension, the expression of ACE2 receptors in epithelial cells of the lungs, intestines, kidneys, and blood vessels is increased.[24] In patients with obesity, the expressions of ACE2 receptors in mature adipocyte cells are also increased.[25] Patients with diabetes, obesity, and hypertension also have a decreased regulation of the micro ribonucleic acid

(microRNA)-146a gene. The microRNA-146a gene regulates the excessive inflammatory response to viral infections. Downregulation of the gene can result in a reduced response to limit inflammation caused by a COVID-19 infection.[26]

This study shows that consolidation was the most common radiological finding in diabetic patients. This finding is similar to a study that reported increased bilateral airspace consolidation in diabetic patients with COVID-19.[27] Diabetes causes damage in the microvascular system. This can disrupt the alveolar-capillary network in the lungs, 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. Increased mitochondrial oxidative stress can induce apoptosis in alveolar epithelial cells, leading to damage of the alveolar membrane and subsequent recruitment of fibroblasts. This may explain the presence of fibrosis in diabetic COVID-19 patients in this study. Hyperglycaemia can increase virus replication. It can also damage innate immune components and trigger the growth of pathogens in the lungs, making patients with diabetes more susceptible to secondary bacterial infections.[29] Additionally, there is no difference in the severity of COVID-19 between individuals with type 1 and type 2 diabetes.[30]

In this study, COVID-19 patients with obesity mostly showed consolidation (62.9%) on CXR. It was assumed that these patients were in the advanced stage of COVID-19. The chronic inflammatory state, immune system dysfunction, and metabolic disturbances associated with obesity impact the pathogenesis of COVID-19. Severe acute respiratory syndrome coronavirus-2 infection can decrease the number of $CD4^+$ T cells, $CD8^+$ T cells, B cells, and natural killer (NK) cells. Obesity impairs both T- and B-cell responses. Severe acute respiratory syndrome coronavirus-2 infection in individuals with obesity can result in a weakened immune system, leading to a higher viral load, rapid viral replication, and increased spread. This may also increase the patient's vulnerability to secondary infection.[31]

Most of the patients with hypertension in this study showed 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 increased aldosterone production and decreased levels of 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 believed to exacerbate the severity of COVID-19 infection. However, only a few patients in this study presented with asthma (2.0%) and tuberculosis/TB (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 due to their anti-inflammatory properties, which reduce the expression of ACE2 and transmembrane protease serine 2 (TMPRSS2) on bronchial cells, potentially decreasing the likelihood of SARS-CoV-2 replication.[33] This is likely why only two asthma patients in this study presented with pneumonia in the context of COVID-19. Tuberculosis spreads through droplets from patients with active TB. The low number of COVID-19 patients with TB in this study was probably because COVID-19 prevention measures, such as using masks, also prevent the transmission of TB.[34]

Strengths and Limitations

The strength in this study was that the variables were measured precisely, using software with a high level of trust. This study had several limitations, including a small sample size, variations in radiological terminology used in the medical records, and the inability to differentiate between pneumonia caused by COVID-19 and pneumonia caused by COVID-19 with secondary bacterial infection or co-infection.

Conclusion

Most patients included in this study were young males. Pulmonary symptoms were more common than gastrointestinal symptoms, with dyspnea as the most common pulmonary symptom. On CXR, most patients exhibited consolidation with central and peripheral predominance, as well as bilateral lung involvement. Diabetes was the most common comorbidity. The presence of diabetes might play a role in the high number of consolidations 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 received ethical clearance from the Ethics Committee of the Faculty of Medicine, Universitas Airlangga, Surabaya (No.1077/LOE/301.4.2/X/2022) on 09-10-2022.

Authors' Contributions

Concept and design: AASPP, HH, RS, WIE. Data collection, analysis, and data interpretation: 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.

Data Availability

N/A.

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