Cross-sectional Study

Correlations between comorbidities, chest x-ray findings, and C-Reactive protein level in patients with COVID-19

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A B S T R A C T

Background: Patients with comorbidities have an increased risk for severe coronavirus disease (COVID-19) symptoms, including abnormal inflammation. Chest X-rays and C-reactive protein (CRP) level are frequently used to evaluate the severity of inflammation. The aim of this study was to investigate the correlation between comorbidities, chest X-ray findings, and CRP level in patients with COVID-19.
Materials and methods: This was a cross-sectional, analytic, observational study performed using a quantitative approach. The study population included in patients with confirmed COVID-19. Secondary data from the medical records of the patients were analysed to determine the correlations between comorbidities, chest X-rays, and CRP level.
Results: The data of 167 patients (87 [52.1%] females and 80 [47.9%] males) were evaluated. Regarding comorbidities, 86 (51.5%) patients had hypertension, 66 (39.5%) had diabetes mellitus, and 17 (10.2%) had dyspepsia. Chest X-rays showed that 144 (86.2%) patients had pneumonia, whereas 23 (13.8%) did not. A total of 143 (85.6%) patients showed increased CRP levels, whereas 24 (14.4%) did not show any increase. Patients who showed pneumonia on chest X-rays tended to have increased CRP levels. The results also showed that chest X-ray findings were correlated with CRP level. Diabetes mellitus and hypertension were significantly correlated with CRP level ($p = 0.05$), whereas dyspepsia did not show a significant relationship with CRP level ($p > 0.05$). Patients with hypertension had a 2.709-fold risk of having increased CRP level compared with patients without hypertension. Patients with pneumonia had a 2.953-fold increased risk for increased CRP level compared to those without pneumonia.
Conclusion: Hypertension and diabetes mellitus are significantly correlated with CRP level. Chest X-ray finding is also significantly correlated with CRP level.

1. Introduction

The coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first case of this viral pneumonia of unknown aetiology was reported on December 12, 2019, in Wuhan, China [1]. SARS-CoV-2 can be transmitted through contact and droplets, which spread during coughing or sneezing [2]. The incubation period for COVID-19 is about 3–14 days. In this phase, the patient is asymptomatic and leukocyte and lymphocyte counts are still within the normal threshold or are slightly decreased. In the next phase, the virus spreads through the bloodstream and mild symptoms generally start to appear. A second wave of

symptoms occurs 4–7 days after the initial symptoms appear. The patient has a fever and shows shortness of breath, lesions in the lungs worsen, and lymphocyte count decreases. Increased levels of inflammatory biomarkers and hypercoagulation are noted in this stage as well [3,4]. The hallmark of severe COVID-19 is the presence of a systemic inflammatory response, and most hospitalised patients with COVID-19 show abnormal inflammation [5]. Evaluation of the levels of inflammation markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), aids the management of patients with COVID-19 [6]. CRP, which is a protein produced by the liver, is as an early marker of inflammation and an important marker of severe COVID-19 [7,8].

A person with comorbid conditions has increased susceptibility to infection by SARS-CoV-2. Several studies have shown that regarding confirmed COVID-19, people with comorbidities, such as the elderly, have a higher risk of experiencing severe and fatal symptoms than those without comorbidities. The most common comorbidities recorded among patients with COVID-19 are hypertension, diabetes mellitus, heart disease, and chronic obstructive pulmonary disease [9,10].

Accurate diagnosis of COVID-19 is important and can control the spread of the disease. Screening and diagnosis of COVID-19 include laboratory and radiological examinations. Chest radiography is a common radiological examination modality. Pulmonary abnormalities caused by COVID-19 can be monitored on a chest radiograph [11]. According to Baj et al. the course of COVID-19 and the classification of its severity can be determined by imaging and evaluating each stage on chest radiographs [12]. Therefore, the aim of this study was to determine the relationship between comorbidities, chest X-ray findings, and CRP level values in hospitalised patients with confirmed COVID-19.

2. Materials and Methods

This study uses analytical observation and the research design used is cross sectional by taking secondary data from the medical records of inpatients with COVID-19. The study population included in patients with confirmed COVID-19 at the Jakarta Islamic Hospital, Sukapura, from August 2020 to August 2021. This study was performed according to the STROCSS criteria and has been registered at https://www.researchregistry.com [13]. This research was submitted to the ethics committee of the Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta, Jakarta, Indonesia (No. 185/PE/KE/FKK-UMJ/X/2021) for approval. Written informed consent was obtained from all participants.

3. Results

The baseline characteristics of the inpatients with confirmed COVID-19 at Jakarta Islamic Hospital, Sukapura are outlined in Table 1. A total of 167 patients, including 87 (52.1%) females and 80 (47.9%) males, were included in this study. Of these, 124 (74.3%) patients were aged <60 years old (youngest patient, 8 years old), whereas 43 (25.7%) were aged ≥60 years old (oldest patient, 90 years old). Regarding employment status, 93 (55.7%) patients were employed and 74 (44.3%) were unemployed.

Table 2 shows the comorbidities of the included inpatients. Hypertension was the common comorbidity (86 [51.5%] patients), followed by diabetes mellitus (66 [39.5%] patients) and dyspepsia (17 [10.2%] patients).

A total of 144 (86.2%) patients showed pneumonia on their chest X-rays, whereas 23 (13.8%) did not (Table 3). The patients without pneumonia showed other pulmonary anomalies, including tuberculosis, bronchitis, pleural effusion, pulmonary oedema, and pneumothorax.

Table 4 shows that of the 167 patients analysed, 143 (85.6%) showed an increase in CRP level, whereas 24 (14.4%) did not increase.

The results showed that diabetes mellitus and hypertension were significantly correlated with CRP level (p = 0.05). However, dyspepsia was not significantly correlated with CRP level (p > 0.05) (Table 5).

Among patients with pneumonia, 128 (76.6%) showed increased CRP levels, whereas 16 (9.6%) did not (Table 6). For patients without pneumonia, 15 (9.0%) showed increased CRP levels, whereas 8 (4.8%) did not. The results also showed that chest X-ray findings were significantly correlated with CRP level.

Multivariate logistic regression analysis showed that patients with hypertension had a 2.709-fold increased risk for elevated CRP level compared with patients without hypertension. Patients with pneumonia had a 2.953-fold increased risk for increased CRP level compared with patients without pneumonia (Table 7).

4. Discussion

The study was conducted to investigate the relationships between comorbidities, chest X-ray findings, and CRP level in hospitalised patients with confirmed COVID-19. The results showed that most of the patients were <60 years old, female, and employed. The findings regarding age and employment status are in line with that of a previous study conducted in Saudi Arabia, which showed that the average age of 99 patients treated for confirmed COVID-19 was 44 years, and that of a study conducted in the United Kingdom, which indicated that most patients with confirmed COVID-19 were employed [14,15]. However, the result regarding sex is not in line with that of a previous study conducted in India, which showed that COVID-19 mostly affects male patients, especially among Asian populations. This is suspected to be related to the fact the prevalence of smoking, which can increase the expression of ACE-2 receptors, is elevated in Asian populations. However, this is only a speculation and further study is needed to validate the theory [10,16].

The spread of COVID-19 has become a global pandemic, which has claimed the lives of more than one million people worldwide. Certain comorbidities are significant risk factors for COVID-19. In the present study, hypertension was the most common comorbid disease among the patients, followed by diabetes mellitus. Diabetes is a chronic inflammatory condition that leads to an increase in the levels of inflammatory markers, such as CRP. The results of the present study showed that diabetes mellitus is significantly correlated with CRP level. This is in accordance with the findings of the study by Koh et al. which revealed that CRP had a mediating proportion of 32.7% of the association of comorbid DM type 2 with severe COVID-19 outcome [17]. The results of

Table 1
Characteristics of hospitalised patients with confirmed COVID-19.

Characteristics	Total (n)	Percentage (%)
Age		
<60 years	124	74,3
≥60 years	43	25,7
Gender		
Male	80	47,9
Female	87	52,1
Employment status		
Employed	93	55,7
Unemployed	74	44,3

Table 2
Comorbidities of the inpatients with confirmed COVID-19.

Comorbidities	Total (n)	Percentage (%)
Diabetes Mellitus		
Present	66	39,5
Absent	101	60,5
Hypertension		
Present	86	51,5
Absent	81	48,5
Dyspepsia		
Present	17	10,2
Absent	150	89,8

Table 3
Thorax X-ray findings of hospitalised patients with confirmed COVID-19.

Thorax X-Ray	Total (n)	Percentage (%)
Pneumonia	144	86,2
No Pneumonia	23	13,8

Table 4
C-reactive protein levels of the hospitalised patients with confirmed COVID-19.

C-reactive protein level	Total (n)	Percentage (%)
Increased	143	85,6
Not increased	24	14,4

Table 5
Relationship between comorbidities and C-reactive protein level.

Comorbidities		C-reactive protein level		P value
		Increased	Not Increased	
Diabetes mellitus	Present	61	5	**0,043**
	Absent	82	19	
Hypertension	Present	79	7	**0,018**
	Absent	64	17	
Dyspepsia	Present	12	5	0,074
	Absent	131	19	

Table 6
Relationship between chest X-Ray findings and C-reactive protein level.

Thorax X-Ray	C-reactive protein level		P value
	Increased	Not Increased	
Pneumonia	128	16	0,007
No Pneumonia	15	8	

Table 7
Results of the multivariate logistic regression analysis.

Variable	Coefficient	P value	Odds ratio
Hypertension	0,997	0,045	2,709
Diabetes mellitus	1,006	0,065	2,736
Chest X-Ray	1,083	0,050	2,953

the present study also showed that hypertension is significantly correlated with CRP level. This is in line the findings a previous Brazilian study.

C-reactive protein is produced by adipocytes and the liver, regulated by IL-1, IL-6, and tumour necrosis factor, and can be measured routinely. Elevated CRP level is an independent risk factor for hypertension; thus, it is often detected in patients with hypertension. Hypertension can worsen if the levels of these inflammatory biomarkers increase because systemic and local inflammatory responses can damage vascular endothelial cells, resulting in a decrease in the levels of nitric oxide and prostaglandins. In addition, increased levels of biomarkers can lead to thickening of the vascular intima that affects the formation of atheroma, resulting in peripheral resistance and reduced vascular reactivity to vasodilators and blood flow velocity, which can exacerbate vascular sclerosis and increase blood pressure [18–26].

Dyspepsia is a relatively common gastrointestinal function disorder. Negative or unpleasant life events, stress, and anxiety are known to trigger and exacerbate irritable bowel syndrome (IBS) and functional dyspepsia (FD). Avoiding physical contact, staying at home, working from home, and reducing the frequency and size of gatherings, are some of the steps that can be taken to control the spread of COVID-19. However, some of these steps are likely to have an impact on mental health. A study conducted in the United Kingdom showed that physical distancing leads to increased anxiety and depression among the general population. A previous study showed that more than 20% of individuals with IBS and FD experienced worsening of symptoms, whereas a small percentage noted improvements during the ongoing COVID-19 pandemic; however, most did not show any change in symptoms. Factors that determine the worsening or improvement of symptoms during the COVID-19 pandemic include comorbid psychological illnesses and occupational problems [27].

In the present study, the number of patients with each comorbid disease was small; thus, it is possible that the relationships between the comorbidities and CRP level were not statistically significant. In addition, as this was retrospective study, some data were incomplete [28–35].

It has been reported that a 50% increase in chest X-ray abnormalities within 24–48 hours is considered an early warning indicator of an impending critical illness. CRP level is related to the level of inflammation. Patients with severe pneumonia show elevated CRP levels. It is an important index for the diagnosis and assessment of severe disease. It has been suggested that CRP level is closely related to lung lesions and disease severity. This may indicate that CRP level can reflect lung lesions and disease severity in the early stages of COVID-19. In the present study, chest X-ray finding was significantly correlated with CRP level. Similarly, another previous study showed that CRP, which is the laboratory parameter used for assessing acute inflammation, could be elevated in patients with positive chest X-rays and who have severe disease, associated lung damage, and poor prognosis [36–39].

The results of the multivariate analysis showed that hypertension and pneumonia had the most influence on CRP level. A previous study showed that CRP level can predict poor prognosis in patients with hypertension. Inflammation can cause aortic stiffness, leading to disruption of endothelial function. Endothelial dysfunction in older patients and/or patients with hypertension, diabetes, and obesity, combined with vascular damage caused by COVID-19, can lead to severe morbidity and mortality. It has been reported that some patients with COVID-19 who develop pneumonia show changes in chest X-ray images. In addition to older age (≥45 years), high CRP level (>5 mg/dL) and low absolute lymphocyte count (1500 cells/µL) are independent risk factors for the development of pneumonia. Several studies have shown that old age, underlying disease, elevated inflammatory parameters, such as CRP level, lactate dehydrogenase level, and low absolute lymphocyte count, are generally associated with poor prognosis in patients with COVID-19 [40–43]. In addition, there are two limitations of this study, namely: the number of confirmed inpatients of COVID-19 at Jakarta Islamic Hospital Sukapura who had comorbidities was only 167 and of each comorbid disease has a small number of patients. Therefore, I hope that the future research can be conduct in several hospitals that represent some areas with higher number of respondents. Furthermore, there are still incomplete data for the deepest analysis because the study was conducted in retrospective method. It was also the other limit of this study. Hence, I assure for the next research, the study should gather the data from primary source.

5. Conclusion

The study was conducted to evaluate the relationship between comorbidities, chest X-ray findings, and CRP level in hospitalised patients with confirmed COVID-19. The results showed that in patients with COVID-19, comorbidities, such as hypertension and diabetes, are correlated with CRP level. The results also showed that chest X-ray findings are significantly correlated with CRP level. Patients with hypertension and pneumonia on chest X-ray tend to have an increased risk for elevated CRP level.

Ethical approval

This research was submitted to the ethics committee of the Faculty of Medicine and Health, Universitas Muhammadiyah Jakarta, Jakarta, Indonesia (No. 185/PE/KE/FKK-UMJ/X/2021) to obtain approval for ethical studies. Written informed consent was obtained from all participants.

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Author contribution

M.F, M.H, and E.W. designed the study. M.F, M.H, and E.W. conducted the laboratory analyses. M.F., R.D., A.S., A.R.J., M.R.P, and R.A. reviewed the data, conducted the statistical analyses, and interpreted the results. M.F, M.H, E.W, R.A, R.D, A.S, A.F, and ARJ wrote the first draft of the paper, which all the authors critically reviewed. All the authors read and approved the final manuscript.

Trial registry number

1. Name of the registry: Research Registry
2. Unique Identifying number or registration ID: researchregistry7652
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://www.researchregistry.com/browse-the-registry#home/registrationdetails/620da1dc74e84d001e6b4ffa/

Guarantor

Prof. Mochammad Hatta, MD, PhD, Clin Microbiologist (Cons).

Patient consent

None.

Provenance and peer review

Not commissioned, externally peer reviewed.

Data availability

All data generated or analysed during this study are included in this published article.

Declaration of competing interest

The authors declare no conflict of interest, financial or otherwise.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103553.

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