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Original Research Article

C-reactive protein as the marker of COVID-19 severity at Sanjiwani general hospital, Gianyar, Bali in 2020

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ABSTRACT

Background: Coronavirus disease-2019 (COVID-19) is a novel coronavirus type infection disease that was first reported at Wuhan city, Hubei province, China in December 2019. Cases of COVID-19 in Indonesia were increasing, reaching up to 287,008 confirmed cases on 30th September 2020. Sanjiwani general hospital Gianyar, Bali, one of the COVID-19 referral hospital at Gianyar, Bali, has treated as many as 149 confirmed COVID-19 cases from August to October 2020. The most significant laboratory parameter associated with COVID-19 severity was C-reactive protein (CRP) and neutrophil to lymphocyte ratio (NLR).
Methods: This study is a descriptive cross-sectional study. Data were gathered through secondary data from the medical records using the total sampling method. Descriptive analyses were performed to describe the samples characteristics and to calculate the mean CRP level. Meanwhile, the chi-square test was done to investigate the association between CRP level and the severity level of COVID-19. The result is considered statistically significant if the p value is <0.05
Results: Most of the samples are >60 years old (24.4%), female (56.6%), and have diabetes mellitus as their comorbid (46,7%). The mean CRP level is 8.9 mg/L. CRP level >8.9 mg/l significantly affects COVID-19 patients' severity with the p value of 0.000 (p<0.005). The higher the initial CRP level of COVID-19 patients, the higher the severity level will be.
Conclusions: There is an association between the increased CRP level at the beginning of hospital admission and the severity of COVID-19 patients.

Keywords: COVID-19, CRP level, Severity, Cross-sectional

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is a novel coronavirus type infection disease that was first reported at Wuhan city, Hubei Province, China in December 2019. The source of infection has not been confirmed, the first case was associated with the seafood market at Wuhan. There was a rapid increase of cases from December 31st 2019 until January 3rd 2020, marked with the report of 44 cases. In less than a month, this disease has spread to other countries, including Thailand, Japan, and South Korea.[1]

Until September 30th, 2020 the number of confirmed COVID-19 cases reached 33.827.031. As many as 1.011.868 people passed away and 25.129.340 people have recovered. Indonesia reported its first two cases on March 2nd, 2020, allegedly from foreigners visiting Indonesia. Cases in Indonesia were also increasing, reaching 287.008 confirmed COVID-19 cases on September 30th, 2020 with 10.740 mortalities, and

219.947 recovered cases. Based on the data, Bali is one of the provinces in Indonesia with the second-highest COVID-19 confirmed cases with as many as 8.878 cases, 7.365 recovered cases (82.96%), and 275 people passed away (3.10%).[2-4]

Gianyar, Bali province has as many as 1.061 confirmed COVID-19 cases up to September 30th, 2020. From that number of cases, as many as 204 people underwent treatment. COVID-19 has a variety of clinical manifestations, from asymptomatic, mild symptoms, moderate symptoms, severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, to septic shock. It has been reported that approximately 80% of cases are mild-moderate, 13.8% of cases had severe symptoms, while 6.1% are critical.[1] Several factors that may increase the risk of becoming infected with COVID-19 are the history of close contact, male gender, smoking, the presence of comorbidities including hypertension, diabetes mellitus, cardiovascular disease, cancer, and chronic liver disease such as hepatitis B.[1,5]

Sanjiwani general hospital, which is one of COVID-19 referral hospital at Gianyar, Bali Province has treated 149 confirmed COVID-19 cases between August and October 2020. According to several studies, laboratory results also affect the COVID-19 severity, including the C-reactive protein (CRP), neutrophil lymphocyte ratio (NLR), D-dimer, IL-6, thrombocytopenia, and lymphocytopenia. COVID-19 mortality is also associated with the increase of bilirubin serum, urea, D-dimer, and ferritin. The most significant laboratory parameter related to COVID-19 severity are CRP and NLR.[6,7]

Based on the description above, we are interested to conduct a study regarding CRP marker as the predictor of COVID-19 severity at Sanjiwani general hospital, Gianyar, Bali from August to October 2020.

METHODS

This study was conducted at Sanjiwani general hospital from 30th December 2020 to 31st January 2021. This is a descriptive study with a cross-sectional design. Data was gathered through secondary data from the medical records of confirmed COVID-19 patients at Sanjiwani general hospital between August and October 2020. The samples were collected using the total sampling method, a method that includes all the study population as the study sample. In this study, the study population is all patients diagnosed with COVID-19 at Sanjiwani general hospital from August to October 2020.

A total of 149 COVID-19 patients were found at Sanjiwani general hospital from August to October 2020, in which as many as 59 samples were excluded due to incomplete data. Ninety (90) samples fulfilled the inclusion criteria and were analyzed using statistical package for service solution (SPSS) for windows version 21. Data was analysed using descriptive statistical analysis to describe the samples characteristics and to calculate the mean CRP level. The chi-square test was performed to analyse the association between CRP level and the severity level of COVID-19. The result was considered significant if the p value <0.005.

RESULTS

The characteristics of samples in this study, including age, sex, comorbid disease, case severity, and CRP value, were obtained from patient's medical records. Those characteristics are shown in Table 1.

Table 1: The distribution of samples (n=90).

Characteristic	F (%)
Age (years)	
25-29	13 (14.4)
30-34	4 (4.4)
35-39	8 (8.9)
40-44	9 (10.0)
45-49	11 (12.2)
50-54	7 (7.8)
55-60	16 (17.8)
>60	22 (24.4)
Sex	
Male	40 (44.4)
Female	50 (55.6)
Comorbid	
Without comorbid	32 (35.6)
Diabetes mellitus	42 (46.7)
Hypertension	8 (8.9)
Heart disease	1 (1.1)
Kidney failure	7 (7.8)
Case severity	
Moderate	17 (18.9)
Severe	73 (81.1)
CRP levels (mg/l)	
5.0-6.0	33 (36.7)
6.1-7.0	17 (18.9)
7.1-8.0	5 (5.6)
8.1-9.0	6 (6.7)
9.1-10.0	4 (4.4)
>10.0	25 (27.8)

Table 2: The characteristic of CRP levels based on the COVID-19 severity.

CRP levels (mg/l)	Case severity		Total	P value
	Moderate	Severe		
<8.9	17	39	56	0.000
>8.9	0	34	34	
Total	17	73	90	

Based on the characteristic features of the 90 samples in this study, most of the COVID-19 patients were female (55.6%) and aged >60 years old (24.4%). Based on the comorbid disease status, most COVID-19 patients have

diabetes mellitus (46.7%) as the comorbid and then followed by without comorbid (35.6%), hypertension (8.9%), heart disease (1.1%), and kidney failure (7.8%). Most of the COVID-19 patients in this study had severe cases (81.1%). Based on the distribution of CRP levels, most of the samples had CRP levels of 5.0-6.0 mg/l (36.7%) (Table 1).

The mean of CRP levels in this study was 8.9 mg/l. Seventy-three out of the total 90 samples in this study were severe COVID-19 patients, where 34 of them had CRP levels >8.9 mg/l. Therefore, the CRP levels >8.9 mg/L significantly associated with severe COVID-19 cases with p value 0.000 ($p<0.05$) (Table 2).

DISCUSSION

Coronavirus disease 2019 (COVID-19) is a viral infectious disease caused by severe acute respiratory Coronavirus 2 (SARS-Cov-2). The virus is an enveloped β-coronavirus with a genetic sequence very similar to SARS-CoV-1 and coronavirus RaTG13. The viral envelope is coated by spike (S) glycoprotein, envelope (E), and membrane (M) protein. Host cell binding and entry by the S protein. The S1 sub-unit of the S protein contains the receptor binding domain that binds to the peptidase domain of angiotensin-converting enzyme 2 (ACE-2).[8,9]

Based on the severity of the cases, COVID-19 is categorized into asymptomatic, mild, moderate, severe and critical cases. Asymptomatic cases of COVID-19 are patients who have no symptoms. Mild fever is the presence of atypical symptoms without evidence of pneumonia or without hypoxia. Moderate degrees were patients who had clinical signs of pneumonia (fever, cough, breathlessness) but no signs of severe pneumonia and SpO_2 ≥93% in room air. Meanwhile, severe cases are characterized by clinical signs of pneumonia (fever, cough, breathlessness) plus one of the following criteria, namely respiratory rate >30 times/minute, severe respiratory distress, or oxygen saturation (SpO_2) <93% in room air. Meanwhile, critical cases of COVID-19 are marked by the presence of acute respiratory distress syndrome (ARDS), sepsis, and septic shock. It is critical to identify COVID-19 patients who might become severely at the early stage.[10,11]

In this study 90 cases of COVID-19 were identified at Sanjiwani general hospital from August to October 2020, in which as many as 59 samples were excluded and 90 samples were analyzed. Based on the characteristics of the samples, most of patients diagnosed with COVID-19 were female (55.6%) while the others were male (44.4%) and aged >60 years old (24.4%). Diabetes mellitus (46.7%) was the comorbid disease found in most of the COVID-19 patients. Most of COVID-19 patients in this study were severe cases (81.8%) and had increased CRP levels in the early phase of infection.

All of the CRP levels data in this study were based on medical records. The CRP levels examined in this study were the result of the first laboratory examination when the patient was admitted to the hospital. It is difficult to obtain serial data on CRP levels based on the patients' medical records. Therefore, it is not possible to determine the pattern of increase or decrease of CRP levels of each patient after the acute onset of infection during the hospitalization.

Of the total 90 samples studied, 17 samples were diagnosed with moderate COVID-19 and 73 samples were diagnosed with severe COVID-19. All samples had different initial CRP levels. The initial CRP level is used as a parameter to predict the severity of COVID-19 cases. All of 17 moderate COVID-19 cases in this study had initial CRP levels <8.9 mg/l. There were 73 severe COVID-19 cases in this study, consisting of 39 samples with initial CRP levels <8.9 mg/l and 34 samples with initial CRP levels >8.9 mg/l. This proved that the higher the initial CRP level in a COVID-19 patient, the more severe the cases are.

CRP is a protein produced in the liver as a response to an increase in circulating proinflammatory cytokines, particularly the IL-6 and the tumor necrosis factor-alpha (TNF-α). The CRP levels will increase as a response to tissue damage, infection, and inflammation. CRP was highly correlated to the acute lung injury in COVID-19 patients. Therefore, the increased CRP levels can be used as a parameter to predict the severity of the patient's condition. The higher the IL-6 levels, the higher the stimulation of the liver to produce CRP.[12,13]

This is supported by the study conducted by Tan et al in 2020 shown there was a significant increase in CRP and ESR levels during the early stages of the disease and was associated with the disease progression in predicting the severity of COVID-19 patients.[14] Besides, Liu W et al also conducted a study on CRP levels in COVID-19 patients showed that a significant CRP level increase was associated with the disease progression and means a bad prognosis.[15] Another study conducted by Sun et al also found that a significant increase of CRP, serum ferritin, IL-6, and erythrocyte sedimentation rate (ESR) levels have occurred in severe and critical COVID-19 cases.[16] Study from Chen et al, 2020 shown the level of plasma CRP was positively correlated to the severity of COVID-19 and study from Ahnac et al found that the CRP level at administration represent a simple and independent factor that ca be useful for early detection of severity COVID-19.[17,18]

CONCLUSION

An increased in CRP levels was shown to be significantly associated with the severity of COVID-19 cases. Therefore, the CRP levels obtained in the early phase of COVID-19 cases could be used as a parameter to predict the severity of the COVID-19. So, the clinicians could

determine the prognosis of the COVID-19 cases as early as possible. These findings are expected to make it easier for clinicians to determine a progressive treatment in order to reduce the mortality rate in COVID-19 patients.

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REFERENCES

1. Adityo S, Martin CR, Ceva WP, Widayat DS, Mira Y, Herikurniawan et al. Coronavirus Disease 2019. Tinjauan Literatur Terkini. Jurnal Penyakit Dalam Indonesia. 2020;7:1.
2. Coronavirus Update. 2020. Available from: https://worldmeters.info/coronavirus/. Accessed on 12 Dec 2020.
3. Satuan Tugas Penanganan COVID-19. 2020. Available from: https://covid19.go.id. Accessed on 12 Dec 2020.
4. Info corona Bali. 2020. Available from: https://infocorona.baliprov.go.id/2020/10/03/update-penanggulangan-covid-19-rabu-30-september-2020/. Accessed on 12 Dec 2020.
5. Yuliana. 2020. Corona Virus Disease (COVID-19); Sebuah Tinjauan Literatur. Wellness and Healthy Magazine. 2020;2(1):187-92.
6. Yusra, Natasha P. Pemeriksaan Laboratorium pada Coronavirus Disease 2019 (COVID-19). Medica Hospitalia J Clin Med. 2020;7(1A):304-19.
7. Cheng B, Hu J, Zuo X, Chen J, Li X, Chen Y et al. Predictors of Progression from Moderate to Severe Coronavirus Disease 2019: A Retrospective Cohort. Clin Microbiol Infect, Elsevier. 2020;26:1400-5.
8. Cevik M, Kuppalli K, Kindrachuk J, Peiris M. Virology, Transmission, and Pathogenesis of SARS-CoV-2. BMJ. 2020;371:m3862.
9. Mason RJ. Pathogenesis of COVID-19 from a Cell Biology Perspctive. Eur Respir J. 2020;552000607.
10. Erlina B, Agus DS, Sally AN, Eka G, Ceva WP, Adityo S et al. Pedoman Tatalaksana COVID-19 Edisi Ke-3. pdpi. perki. papdi. perdatin. idai. Jakarta, 2020.
11. Mudatsir M, Jonny KF, Laksmi W, Gatot S, Muhammad I, Yeni P et al. Predictors of COVID-19 Severity: A Systemtic Review and Meta-Analysis. F1000 Research. 2020;9:1107.
12. Yuki K, Fujiogi M, Sophia K. Review Article: COVID-19 Pathophysiology. Clin Immunol. 2020;215:108427.
13. Tan C, Ying H, Fengxia S, Kui T, Qionghui M, Yong C et al. C-Reactive Protein Correlates with Computed Tomographic Findings and Predicts Severe COVID-19 Early. J Med Virol Wiley. 2020;1-7.
14. Liu W, Tao ZW, Wang L, Yuan M, Liu K, Zhou L et al. Analysis of Factors Associated with Disease Outcomes in Hospitalized Patients With 2019 Novel Coronavirus Disease. Chinese Med J. 2020;133:9.
15. Sun Y, Dong Y, Wang L, Xie H, Li B, Chang C et al. Characteristics and Prognostic Factors of Disease Severity in Patients with COVID-19: The Beijing Experience. J Autoimmunity. 2020;112:102473.
16. Chen W, Zheng K, Liu S, Yan Z, Xu C, Qiao Z. 2020. Plasma CRP Level is Positively Associated with the Severity of COVID-19. Ann Clin Microbiol Antimicrobials. 2020;19:18.
17. Ahnach M, Zbiri S, Nejjari S, Ousti F, Elkettani C. C-Reactive Protein as an Early Predictor of COVID-19 Severity. Original Paper. J Med Biochem. 2020;39(4):500-7.
18. Sang W, Dong J, Ren Y, Tian M, Li W, Hu J et al. The Value of Clinical Parameters in Predicting the Severity of COVID-19. J Med Virol Wiley. 2020;922:2188-92.

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