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OVERVIEW OF THE VALUE OF C-REACTIVE PROTEIN AGAINST THE INCIDENCE OF SARS-CoV-2 disease

Maghfira Darma Burhani
Piksi Ganesha Polytechnic, Bandung, Indonesia
*e-mail: maghfiradarmaburhani@gmail.com
*Correspondence: maghfiradarmaburhani@gmail.com

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Abstract: Coronavirus disease 2019 (COVID-19) is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 or SARS-CoV-2. Symptoms caused by the corona virus include mild to severe and serious respiratory tract infections. C-Reactive Protein is one of the acute phase proteins synthesized in the liver to monitor disease both non-specifically and systemically. C-Reactive protein examination can detect acute phase inflammation which can be used to predict the presence of inflammation in patients. The purpose of this study was to determine the results of the examination of C-Reactive Protein Levels of patients suspecting SARS-CoV-19.This research is a descriptive research with purposive sampling technique. The sample size in this study was 30 samples. This research was conducted at the Humana Peima Hospital from March to May 2022. The research data were analyzed descriptively. Based on the results of the research that has been carried out, it can be seen that the patients suspected of SARS-CoV-19 with positive CRP results were 24 patients with a percentage of 80% and negative CRP results as many as 6 patients with a percentage of 20%. .

Keywords: SARS-CoV-2, C-Reactive Protein, Inflammation.

INTRODUCTION

The SARS-CoV-2 virus or corona virus is an RNA (ribonucleic acid) virus that has a crown (corona) and can infect humans and animals. The symptoms caused by this virus are mild to severe and serious respiratory infections. Coronavirus disease 2019 (COVID-19) is a disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 or SARS- CoV-2.

Laboratory examinations take an important role in handling COVID-19 (Aryati, MS.2020). Starting from diagnosis, therapy monitoring, prognosis to surveillance. Abnormalities in laboratory results are strongly influenced by the clinical manifestations of a person infected by COVID-19 according to the established degree. (Rosdiana, etc al,2020). A literature analysis revealed that hematological abnormalities can predict mortality in COVID-19 patients (Am J Hematol. 2020).

C-Reactive Protein (CRP) is known to be the most sensitive inflammatory indicator. C-Reactive Protein (CRP) is one of the acute phase proteins synthesized in the liver to monitor the disease non-specifically or systemically. C-Reactive Protein (CRP) is a protein produced by the liver organ in response to inflammation in the body found in the blood. C-Reactive Protein (CRP) levels will increase in response to infection, trauma, bacteria, injury or inflammation. CRP is used as a prognostic marker for inflammation. Imflamation is the body's immune response to certain diseases. Increased CRP levels are associated with tobacco use, increased body mass index, age, hypertension, insulin resistance, diabetes, chronic kidney disease, decreased left ventricular function, and depression (Dewi, etc al. 2016).

The increase in C-Reactive Protein (CRP) levels in Covid-19 patients is caused by cytokine storms related to damage to body tissues. Increased levels of C-Reactive Protein (CRP) protein in COVID-19 patients can cause a decrease in oxygen saturation, venous thrombosis in pulmonary embolism, acute kidney injury, and death.

The purpose of this study was to determine the value of C-Ractive Protein against the Incidence of Sars-Cov-2 Disease.

Coronavirus is a single-strained, capsulated and non-segmented RNA virus. Coronavirus belongs to the order Nidovirales, family Coronaviridae. Coronavirus has a much higher potential for infectivity so that it spreads throughout the world quickly, causing a global pandemic (In Gennaro, 2020).

COVID-19 disease is caused by a new type of Coronavirus named SARS-CoV-2. The COVID-19 outbreak was first detected in Wuhan City, Hubei Province, China in December 2019. Patient zero who is suspected to be the mastermind of this pandemic is a 57-year-old woman selling shrimp at Huanan Seafood Wholesale Market, Wuhan named Wei Guixiang. Originally, on December 10, 2019, she felt feverish and unwell. He checked into the nearest clinic. However, after checking himself, he went back to selling. That's when SARS-CoV-2 spread. On January 30, 2020, the WHO (World Health Organization) declared a global health emergency caused by SARS-CoV-2. Because the progression of this disease is accelerating and the number of patients

exposed is increasing, since March 11, 2020, by WHO this global health emergency has been designated as a pandemic (Qin, etc al. 2020).

Coronavirus has capsules, particles of spherical or elliptical shape, often pleimorphic with a diameter of about 50-200m. The structure of coronavirus forms a cube-like structure with the S protein located on the surface of the virus This S protein plays a role in the attachment and entry of the virus into the host cell (Jin, et al. 2020).

Coronaviruses are sensitive to heat and can effectively be inactivated by chlorine-containing disinfectants, lipid solvents with a temperature of 56°C for 30 minutes, ethers, alcohols, perioxyacetic acid, non-ionic detergents, formalin, oxidizing agents andoform chlorine. (Wang, etc al. 2020). risk factors for COVID-19 include age, gender, history of disease, nosocomial infections from patients and hospital staff, history of smoking, use of personal protective equipment.

Coronavirus is called zoonotic virus, which is a virus that is transmitted from animals to humans (Huang, et al. 2020). Coronavirus in bats is the main source for the incidence of Severe Acute Respiratory Syndrome (SARS). In general, the flow of Coronavirus from animals to humans and from humans to humans through contact transmission, droplet transmission, fecal and oral routes (Wang, etc al. 2020). SARS-CoV-2 is transmitted primarily through respiratory, contact, and potentially fecal-oral droplets. The life cycle of the virus on its host occurs through 5 stages: attachment, penetration, biosynthesis, maturation and release. . Coronaviruses consist of four protein structures: Spike (S), membrane (M), envelope (E) and nucleocapsid (N) (Sohrabi, etc al. 2020).

The incubation period for COVID-19 is between 3-14 days. Characterized by a slightly decreased level of leukocytes and lymphocytes, the onset of tightness, decreased lymphocytes and worsening of lesions in the lungs. If this phase is not resolved, Acute Respiratory Distress Syndrome (ARSD) may occur (Gennaro, etc al. 2020). SARS- CoV-2 infection is characterized by rapid viral replication and late production of IFNs, mainly by dendritic cells, macrophages, and respiration epithelial cells followed by elevated levels of proinflammatory cytokines called cytokine storms. A cytokine storm is an event of excessive inflammatory reaction in which there is a rapid and large production of cytokines in response to an infection. This rapid pro-inflammatory triggers inflammatory infiltration by the lung tissue causing lung damage (Zhang, etc al. 2020).

C-Reactive protein is one of the acute phase proteins found in normal serum even in very small amounts (Kalma, 2018). CRP levels increase after the presence of trauma, bacterial infections, and inflammation. As a biomarker, CRP is considered an acute phase inflammatory response that is easy and inexpensive to measure compared to other inflammatory markers. CRP is also used as a prognostic marker for inflammation (Dewi, etc al. 2016). CRP is an alpha-globulin produced in hepar and its levels will increase greatly in inflammatory processes and tissue damage. CRP is a sensitive inflammatory indicator, which increases up to 1,000 times after inflammation and quickly drops when the

inflammation has subsided (Olson, 2014).

CRP is an acute phase protein Pentraxin, a calcium-binding protein with immunological defense properties. The CRP molecule consists of 5-6 identical non-glycocylic polypeptide subunits, consists of 206 amino acid residues, and binds to each other non-covalently, forming one disc-shaped molecule with a molecular weight of 110 – 140 kDa, each unit has a molecular weight of 23 kDa. W. Saunders (2003). Based on the theory of intra-arterial inflammation states that when inflammation occurs, cytokines are generated, one of which is Intraleukin-6 (IL-6). Intraleukin-6 stimulates hepatocytes to produce CRP (Agustin, 2016). The inflammatory response in the form of activation of macrophages and T lymphocytes releases pro-inflammatory mediators including TNF-α, IL-1 and IL-6 produced by macrophages in endothelial wounds. This cytokine will stimulate the formation of acute phase reactants, C-reactive protein (CRP) in the liver. the determinant of the concentration of CRP in the circulation is to calculate the synthesis of IL-6 thus describing directly the intensity of the pathological process that stimulates the production of CRP (Silalahi, 2013).

C-Reactive Protein is present in 2 forms, namely the pentamer form (pCRP) produced by hepatocyte cells as an acute phase reaction in response to infection, inflammation and tissue damage and the monomer (Mcrp) comes from the dissociated CRP pentamer and may also be produced by extrahepatic cells such as smooth muscle arterial walls, adipose tissue and macrophages (Silalahi, 2013).

The function and role of CRP is that it can bind C-polysaccharides (CPS) from various bacteria through precipitation/ag reactions, can increase the activity and motility of phagocyte cells such as granulocytes and monocytes/macrop, has selective binding power to T lymphocytes, can bind and detoxicate endogenous toxin materials formed as a result of tissue damage (Silalahi, 2013).

CRP normally circulates at low stinger concentrations, but in inflammatory processes, infections or injuries to tissues can lead to increased synthesis of CRP in the liver. So it is important to conduct a CRP examination (Agustin, 2016). In the CRP examination, several methods are used, including the Agglutination method, the Sandwich Elisa method, the c. High Sensitivity C-Reactive Protein (Hs-CRP) method, the colorymetry method, the Immunoturbidimetric method.

MATERIALS AND METHODS

The method used in this study is an analytical descriptive method using a crossectional study approach, which is a study conducted on a set of objects that aims to see a picture of a phenomenon (including health) that occurs in a certain population (Notoatmodjo, 2018) that uses dependent variables and independent variables. The dependent variable is the examination of C-reactive protein levels. Meanwhile, the independent variable is suspect Sars-Cov-2. The research was conducted at Humana Prima Hospital Bandung, from March to May 2022. The population of this sample is suspected SARS-CoV-2 prolanis patients at Humana

Prima Hospital Bandung. The sampling technique used is purposive sampling, which is a sampling technique using selected criteria. The type of data collected is by using primary data.

The research population is the entire object of study or object under study (Notoatmodjo, 2018). The sample population in this study was suspected SARS-CoV-2 patients at Humana Prima Hospital Bandung. The total population in this study was 43 people calculated from the average hospitalized patients suspected of SARS-CoV-2 who met the criteria for 3 months starting from March 2022 to May 2022.

The sample is a portion of the overall population studied and is considered representative of the population (Noor, 2017). The sample used in this study was a lender from the nose for rapid antigen and EDTA blood examination for the C-Reactive Protein examination of the research subjects carried out at Humana Prima Hospital Bandung. In order to obtain a representative sample of the population, every subject in the population is sought to have an equal chance of becoming a sample.

As for the formulation used to measure samples, the Slovin method is used in Husein Umar (2010: 146), namely the sample size which is a comparison of the population with the presentation of the looseness of inaccuracy. In this sampling, an error tolerance level of 10% was used and in determining the sample measurements (n) and population (N) that have been determined as follows:

N= Total Population

N= Number of Samples

e2= Error rate in selecting members of the sample that the population N = 43 people with the assumption of error rate (e) = 10%. Then the number of samples that should be used in this study is as many as

n = N/(1+N(e)^2)= 43/(1+43(0.1)^2) = 30.06 rounded to 30 samples.

So from the calculation results above, to find out the sample size with an error rate of 10% is 30 patients who are suspected of SARS-CoV-2 at Humana Prima Hospital Bandung. This study uses primary data as a data source and primary data form as a research instrument. The primary data used by the researchers is in the form of data on the results of the rapid antigen examination and the C-reactive Protein examination in COVID-19 patients at Humana Prima Hospital. The data analysis steps used are editing, coding, entering data, tabulation.

This study used the technique of Descriptive Statistical Analysis. Descriptive Statistical Analysis is statistics that discusses ways to summarize, present, and describe data with the aim of being easy to understand and have more meaning (Dahlan, 2015). The data obtained from the results of the CRP level examination will be recorded and encoded then made in the form of a table and calculated the frequency distribution in the form of % using the SPSS 23.0 program.

Tools and materials

Upperbio-tech tools, rapid test antigen sets, alcohol swabs, plasters, tourniquets, laboratory coats, detector buffers, blood collector capillaries, cassette tests, handscoons, micropipettes, stopwatches, tissues, syringes, EDTA tubes.

Principles of SARS- CoV-2 examination

The SARS-CoV-2 antigen rapid test is a lateral flow immunoassay based on the principle of the double antibody sandwich technique. SARS-CoV-2 nucleocapsid monoclonal antibody proteins conjugated with color microparticles were used as detectors and sprayed on conjugation pads. During testing, the SARS-CoV-2 antigen in the specimen interacts with SARS-CoV-2 antibodies conjugated with color microparticles creating a complex labeled antigen-antibody. This complex migrates on the membrane through capillary action up to the test line, where it will be captured by the precoated monoclonal antibodies of the SARS-CoV-2 nucleocapsid protein. The colored test line will not be visible in the results window if the SARS-CoV-2 antigen is present in the specimen. the absence of a T line indicates a negative result. control line C is used for procedural control, and should always appear if the test procedure is performed correctly.

Principle of examination of C-Reactive Protein

The test kit has the principle of colorimetry containing a membrane coated with anti-CRP specific monoclonal antibodies. when that sample is mixed with gold conjugate, the CRP molecule binds to the antibody-gold conjugate. After the dissolved sample is applied to the test device. CRP molecules are captured by immobile ants on the membrane, in the tpe sandwich reaction. Unbound conjugates are removed from the membrane with a washing solution. The paper layer under the membrane absorbs excess liquid. in the presence of a pathological lever CRP, the mebrane appears reddish with a color intensity proportional to the concentration of CRP. The q-pad reader measures the intensity of the colors.. The measured color intensity was measured quantitatively using Upperbio-tech with a normal value of less than 10mg/L.

RESULTS AND DISCUSSION

The following data from the study are described in the table as follows:

Table 1. Research Results

No.	Sample Code	Age	Rapid Antigen Test Results	CRP results (mg/L)
1.	A1	3 Yrs 1 Mo	Positive	101.1
2	A2	65 yrs 5 mo	Positive	26.5
3.	A3	35 yrs 1 mo	Positive	10.4
4.	A4	41 Yrs 1 Mo	Positive	23.5
5.	A5	64 yrs 6 mo	Positive	12.0
6.	A6	64 Yrs 5 Mo	Positive	14
7.	A7	64 Yrs 2 Mo	Positive	75
8.	A8	52 yrs 7 mo	Positive	26.4
9.	A9	7 Yrs 10 Mo	Positive	50
10.	A10	67 yrs 9 mo	Positive	40
11.	A11	46 yrs	Positive	25.4

		4 mo		
12.	A12	64 Yrs 5 Mo	Positive	23.1
13.	A13	0 Yrs 10 Mo	Positive	11.1
14.	A14	63 yrs 9 mo	Positive	3.1
15.	A15	52 Yrs 4 Mo	Positive	54.2
16.	A16	72 yrs 8 mo	Positive	43
17.	A17	33 Yrs 9 Mo	Positive	11
18.	A18	29 Yrs 11 Mo	Positive	13.2
19.	A19	58 Yrs 1 Mo	Positive	12
20.	A20	33 Yrs 6 Mo	Positive	29
21.	A21	18 Yrs 6 Mo	Positive	13
22.	A22	7 Yrs 6 Mo	Positive	25
23.	A23	69 yrs 6 mo	Positive	15
24.	A24	0 Yrs 0 Mo 19 Hr	Positive	18.5
25.	A25	59 Yrs 1 Mo	Positive	16.3
26.	A26	58 yrs 71 mo	Positive	1.2
27.	A27	0 Yrs 1 Mo	Positive	3.0
28.	A28	33 Yrs 9 Mo	Positive	1.00
29.	A29	5 Yrs	Positive	0.8
		5 Mo		
30.	A30	0 Yrs 10 Mo	Positive	0.80

Table 2. Normal Value of Examination

Probe Parameters	Normal Values
Rapid Test Antigen	Negative
CRP	< 10 mg/L

Table 3. Distribution of Proportion of CRP Results in Whole Blood of SARS-Cov-2 Confirmed Patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Negative	6	20	20	20
	Positive	24	80	80	100
	Total	30	100	100	

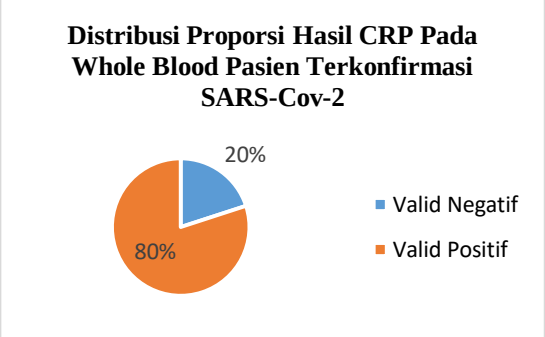
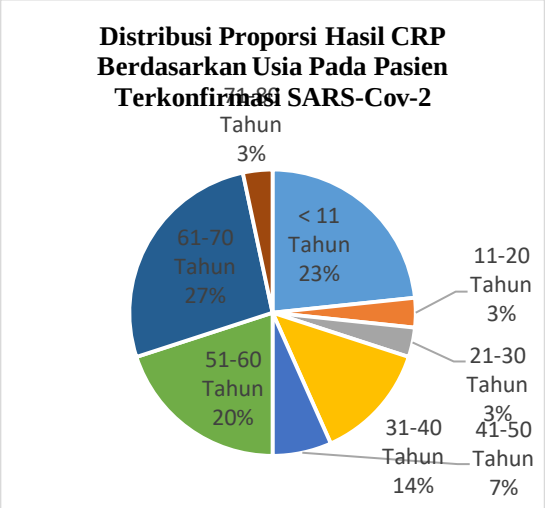


Table 4. Distribution of Proportion of CRP Results by Age in SARS-Cov-2 Confirmed Patients

	Frequency	Percent	Valid Perc	Cumulative Percen

				ent	t
Valid	< 11 Years	7	23.3	23.3	23.3
	11 - 20 Years	1	3.3	3.3	26.7
	21 - 30 Years	1	3.3	3.3	30.0
	31 - 40 Years	4	13.3	13.3	43.3
	41 - 50 Years	2	6.7	6.7	50.0
	51 - 60 Years	6	20.0	20.0	70.0
	61 - 70 Years	8	26.7	26.7	96.7
	71 - 80 Years	1	3.3	3.3	100
	Total	30	100	100	



Based on the results of a study conducted by researchers at the Humana Prima Hospital Laboratory Bandung on 30 confirmed SARS-CoV-2 patients from March to May 2022 with Positive CRP results of 24 patients with a percentage of 80% and Negative CRP results of 6 patients with a percentage of 20%. Most of the sample of patients aged 61-70 years was 8 patients with a percentage of 26.7%. In old age, there are physiological changes related to aging, subjugation of immune function and multimorbidity, namely having more serious diseases and complications, causing that age group to be more susceptible to infection and at risk of suffering from COVID-19 to the risk of death (WHO, 2020).

The SARS-CoV-2 virus in sars-CoV-2 confirmed patients is associated with increased inflammation in humans. C-Reactive Protein (CRP) is an inflammatory marker synthesized in the liver to non-specific local and systemic diseases. The

increase in CRP levels in patients with confirmed SARS-CoV-2 is caused by an inflammatory response arising from severe infection from the SARS-CoV-2 virus. The positive results in CRP are caused by enlarged adipocyte tissue and the body will produce a lot of protein in the body. When adipocytes produce a lot of protein here the body will experience inflammation or inflammation (Situmeang, 2018).

Basic changes or dysfunctions that occur in the endothelium of blood vessels, vascular smooth muscle cells and mesangial cells of the kidneys all cause changes in cell growth and survival, which will then lead to chronic inflammation. Elevated CRP levels in patients with complications found in the study subjects can have an effect on the results of the study. From the results of the study, it can be concluded that the positive CRP results in SARS-CoV-2 confirmed patients are more than the negative CRP results. This is because the patient experiences inflammation or inflammation that occurs in the body due to the SARS-CoV-2 virus. And negative results can be caused because the CRP level has decreased because the sufferer is doing drug therapy, a healthy lifestyle and it can also be due to factors that are less sensitive in detecting CRP.

CONCLUSIONS

Based on the research that has been carried out, it can be concluded that there are 24 confirmed SARS-CoV-2 patients with Positive CRP results with a percentage of 80% and 6 negative CRP results with a percentage of 20%. The positive CRP result is caused by the patient experiencing inflammation or inflammation in the body due to the SARS-CoV-2 virus. Negative CRP results are caused by patients doing drug therapy, a healthy lifestyle and can also be due to less sensitive tools in detecting CRP.

Based on the research above, the advice that can be conveyed in this study is that in sampling for the C-Reactive Protein examination, it must be considered correctly and clearly to determine the anticoagulants that are in accordance with the tools and reagents used, making the C-Reactive Protein examination one of the important examination items in the therapy of SARS-CoV-2 confirmed patients, not delaying the work of the C-Reactive Protein examination after obtaining a sample examination, and do not miss communication with the patient in order to obtain complete information about the patient's condition when undergoing the examination. It is necessary to carry out further examinations to find out the specifications of the inflammation that occurs, it is necessary to know the condition of the condition that can affect the results of the examination.

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