

## Description Of C-Reactive Protein (CRP) In Patients With Type 2 Diabetes Mellitus At Mulyorejo Health Center In Malang City

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### ABSTRACT

*Diabetes Mellitus Type 2 is a metabolic disorder condition characterized by hyperglycemia, due to decreased insulin secretion. Many cytokines play a role in the acute phase response, so that markers such as CRP increase in patients with type 2 DM. The type of research used in this study is descriptive research, which describes the results of CRP examination in patients with type 2 diabetes. Examination of respondents' serum C-Reactive Protein (CRP) levels was carried out qualitatively using the Latex Agglutination method and followed by a semi-quantitative method, namely dilution to determine the level of inflammation. The results of CRP examination on 30 serum samples that have been carried out on patients with Type 2 Diabetes Mellitus found that 29 (96.7%) were positive and 1 (3.3%) of respondents were negative. The group of CRP levels for titer 12 was 5 samples (16.7%), titer 24 was 17 samples (56.7%), titer 48 was 5 samples (16.7%), and titer 96 was 2 samples (6.7). The results of the four groups with the highest CRP levels, namely a titer of 24 mg/L as many as 17 samples (56.7%) showed that some of the CRP levels were higher than normal. Conclusion Almost all respondents with type 2 Diabetes Mellitus had positive C-Reactive Protein examination results and a small proportion of type 2 Diabetes Mellitus patients had negative C-Reactive Protein examination results.*

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### INTRODUCTION

Diabetes mellitus or diabetes or diabetes or diabetes is a disease characterized by higher than normal blood glucose levels due to absolute and relative insulin deficiency in the body (hyperglycemia) (Hasdianah, 2017). Increased glucose or blood sugar levels are caused by the body's inability to convert glucose or carbohydrates into energy. This occurs because the body stops producing enough insulin, stops producing insulin, or can no longer use the insulin produced, so that glucose is no longer taken up by cells and converted into energy, and eventually enters the blood. in. Increased concentration (Haryati, 2022).

The World Health Organization (WHO) estimates that the number of people with diabetes in Indonesia will increase from 8.4 million in 2000 to around 21.3 million in 2030. The International Diabetes Federation (IDF) predicts an increase in the number of people with diabetes. In Indonesia, it will increase from 9.1 million in 2014 to 14.1 million in 2035 (Decroli, 2019). More than 90% of all diabetics have type 2 diabetes, which is characterized by decreased insulin secretion due to progressive impairment of pancreatic beta cell function due to insulin resistance (Perkeni, 2018). According to Basic Health Research (RISKESDAS) data (2018) the prevalence of DM is the second largest cause of death in Indonesia at 2.0%, in East Java at 2.6% (Ministry of Health, 2019). According to data from the Malang City Health Office in 2020, the prevalence of type II DM in Malang was 20340

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people. DM is mostly suffered by people over 40 years old, and 1.8% of DM patients are women. (Veronika et al., 2021)

Type 2 diabetes is a characteristic metabolic disorder characterized by elevated blood glucose levels due to an inappropriate decrease in insulin secretion. This mismatch of insulin action in diabetes mellitus causes glucose to be unable to enter the tissue from the blood vessels. This situation causes most of the glucose to be in the bloodstream resulting in hyperglycemia (Widya Sari et al., 2020).

C-Reactive Protein (CRP) is an inflammatory marker and one of the acute phase proteins synthesized in the liver to non-specifically monitor local and systemic diseases. CRP levels increase after trauma, bacterial infection and inflammation. As a biomarker, CRP is considered an acute phase inflammatory response that is easy and cheap to measure compared to other inflammatory markers. CRP is also used as a prognostic marker for inflammation. Elevated 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, 2017).

Insulin resistance is a major risk factor for Type 2 Diabetes Mellitus. Insulin resistance can increase C-Reactive Protein levels in individuals with genetic and metabolic traits. The occurrence of increased C-Reactive Protein levels in patients with Type 2 Diabetes Mellitus is caused by an inflammatory response that arises due to complications from Diabetes Mellitus (Permatasari et al., 2020).

Based on research conducted by Kalma with the title Overview of C-Reactive Protein in Patients with Type 2 Diabetes Mellitus in the laboratory of Labuang Baji Makassar Hospital in 2018, out of 20 patients with type 2 Diabetes Mellitus, there were 16 positive samples (Agglutination) and 4 negative samples (No agglutination) and based on research conducted by Maria Monica Situmeang at the Hajj Adam Malik Medan Hospital Laboratory in 2018, out of 20 patients with type 2 Diabetes mellitus, there were 14 positive samples (Agglutination) and 6 negative samples (No agglutination). Then according to research by Mei Riska Br Ginting in 2019 with the title Overview of C-Reactive Protein in Patients with Type 2 Diabetes Mellitus at the Padang Bulan Health Center stated that in 16 serum samples of Type 2 Diabetes Mellitus patients obtained positive results (Agglutination) as many as 10 samples (62%) and obtained negative results (No agglutination) as many as 6 samples (38%).

Thus it can be concluded that there is an increase in CRP levels in patients with Type 2 Diabetes Mellitus as a sign of an inflammatory process. While research according to Dr. Efi Ramadhani (2018) with the title Hs-Crp Levels in Type 2 DM Patients With and Without Hypertension states that more than 50% of type-2 DM patients experience hypertension, hypertension contributes to the development of cardiovascular disease. hs-crp as an inflammatory marker is related to cardiovascular risk. The results obtained an average hs-CRP levels of type-2 DM patients with hypertension ( $4.03 \pm 2.49$ ) and without hypertension ( $1.98 \pm 1.93$ ). The similarities between the above research and the research that the researchers conducted lie in the research subjects, namely type 2 DM patients with CRP levels, while the difference with the research I conducted lies in the research location.

## **MATERIALS/METHOD**

This study used a qualitative descriptive method. This study was to determine the description of CRP levels in type 2 DM patients at the Mulyorejo Health Center in Malang City in August-September 2022 at the Mulyorejo Health Center in Malang City taken using purposive sampling technique. The number of research samples was 30 samples.

## RESULTS AND DISCUSSION

This study was conducted in August 2022 at Mulyorejo Health Center with the title "Overview of CRP (C-reactive Protein) levels in the serum of type 2 diabetes patients". The sample consisted of 30 patients with type 2 diabetes who had an examination at the Mulyorejo Health Center.

Table 1. Frequency distribution of patients with type 2 diabetes mellitus based on age at the Mulyorejo Community Health Center, Malang City, August 18-30, 2022.

Age Category	CRP Positive	CRP Negative	Number (%)
	Frequency (%)	Frequency (%)	
Late Adult (36-45 years)	2 (7%)	0 (0%)	2 (7%)
Early Elderly (46-55 years old)	6 (20%)	0 (0%)	6 (20%)
Late Elderly (56-65 years old)	12 (40%)	0 (0%)	12 (40%)
Elderly (65 years and above)	9 (30%)	1 (3%)	10 (33%)
	Number		30(100%)

Source: Primary Data, 2022

Based on the frequency table based on the age of the patients, it was revealed that there were 2 people (7%) in late adulthood (36-5 years) and 6 people in the early age group (6-55 years). the proportion (20%) in the elderly age group (56-65 years) occurred in 12 people (0%) in the elderly 9 people (30%).

Table 2. Frequency distribution of patients with type 2 diabetes mellitus based on gender at the Mulyorejo Community Health Center, Malang City, August 18-30, 2022.

Gender	F	%
Male	5	16,7

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Female	2	83,3
	5	
Total	3	100
	0	

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Source: Primary Data, 2022

Based on the patient frequency table according to gender, it is known that almost all respondents in this study were female, namely. 25 respondents ie. 83.3% And a small proportion were male, namely 5 respondents, ie. 16.7% Based on the frequency table of CRP levels, it was revealed that almost all participants in this study had positive CRP levels, namely 29 respondents or 96.7%. And a small proportion had negative CRP levels, namely 1 respondent or 3.3%.

Table 3. Results of C-Reactive Protein in Patients with Type 2 Diabetes Mellitus

No	Name	Glucose Level (mg/d L)	Qualitative CRP Test	Result Semiquantitative Test Result (Titer)
1	F1	130 GDP	Positive	12
2	F2	128 GDP	Positive	12
3	F3	350 GDS	Positive	96
4	F4	201 GDS	Positive	24
5	F5	140 GDP	Positive	24
6	F6	155 GDP	Positive	24
7	F7	200 GDP	Positive	24
8	F8	150GDP	Positive	24
9	F9	346 GDS	Positive	48
10	F10	148 GDS	Positive	24
11	F11	210 GDS	Positive	24
12	F12	175 GDP	Positive	24

<b>No</b>	<b>Na me</b>	<b>Glucos e Level (mg/d L)</b>	<b>Qualitat ive CRP Test</b>	<b>Result Semiquan titative Test Result (Titer)</b>
13	F13	367 GDP	Positive	96
14	F14	203GD P	Positive	24
15	F15	250 GDP	Positive	48
16	F16	115 GDP	Negative	-
17	F17	160 GDP	Positive	24
18	F18	201 GDP	Positive	24
19	F19	150 GDP	Positive	24
20	F20	140 GDP	Positive	24
21	F21	135 GDP	Positive	12
22	F22	160 GDS	Positive	24
23	F23	275 GDS	Positive	48
24	F24	155 GDP	Positive	24
25	F25	231 GDP	Positive	48
26	F26	277 GDP	Positive	48
27	F27	133 GDP	Positive	12
28	F28	160 GDP	Positive	24
29	F29	141 GDP	Positive	24
30	F30	127 GDP	Positive	12

Source: Primary Data, 2022

Table 4. Frequency distribution of CRP levels

CRP	f	%
Positive	29	96,7
Negative	1	3,3
<b>totally</b>	<b>30</b>	<b>100</b>

Based on a study of 30 serum samples from type 2 diabetes patients, latex agglutination was performed, where 29 (96.7%) samples were found positive and 1 (3.3%) negative. According to (Kalma, 2018), the results showed that the CRP titer in positive samples was  $>6$  mg/L and the CRP titer was negative, and 6 mg/L indicated the absence of sample agglutination. Latex-CRP is standardized to detect a serum CRP titer of 6 mh/L, which is considered clinically low. CRP titer monitoring is often used to assess disease activity and monitor therapy.

Based on research that has been conducted on 30 serum samples of patients with Type 2 Diabetes Mellitus, the latex agglutination test was carried out as an examination and the results of the C-Reactive Protein examination were found to be 29 (96.7%) positive samples and 1 (3.3%) negative sample. According to (Kalma, 2018) the examination results show that the positive CRP titer in the sample is  $> 6$  mg / L and the negative CRP titer  $< 6$  mg / L is indicated by the lack of agglutination in the sample. Latex CRP has been standardized to detect serum CRP titers  $\geq 6$  mh/L which is considered the lowest clinical. CRP titer monitoring is often used to assess disease activity and treatment monitoring.

The results of the examination that have been carried out based on table 5.4 obtained CRP level groups for titer 12 as many as 5 samples (16.7%), titer 24 as many as 17 samples (56.7%), titer 48 as many as 5 samples (16.7%), and titer 96 as many as 2 samples (6.7%). The results of the four groups of CRP levels were mostly titer 24 mg/L as many as 17 samples (56.7%), indicating that most of the results of CRP levels were higher than normal. This study found a significant difference between CRP levels and blood glucose levels of patients, that the higher the blood glucose levels of patients with type 2 diabetes mellitus, the higher the patient's CRP titer. This examination is in line with research conducted by Wulansari (2022) patients with severe symptoms have an average CRP concentration of 43.1 mg/L while patients with non-severe symptoms have an average concentration of 10 mg/L.

The average age of patients with Type 2 Diabetes Mellitus at the age of  $\geq 55$  years was found to be 21 positive respondents and the average age of patients with Type 2 Diabetes Mellitus at the age of  $\leq 55$  years was 8 positive respondents with CRP. This study is in line with the research of Kanmani, et al (2019) which states that the increase in C-Reactive Protein (CRP) in type 2 diabetes mellitus is higher at the age of 55-74 years. According to him there is a significant relationship between the risk of CRP and Type 2 diabetes mellitus only between older groups ( $\geq 50$  years) in both women and men. The low percentage in the younger age category of patients with Type 2 diabetes mellitus could be due to the small number of patients aged  $\leq 55$  years in this study who were examined for CRP.

With increasing age, the progressivity of atherosclerosis increases, thus increasing endothelial damage followed by increased levels of inflammatory markers, namely CRP. In patients with type 2 DM there is an increase in blood glucose levels which causes chronic hyperglycemia conditions. The occurrence of increased CRP levels in patients with type 2

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DM is caused by an inflammatory response that arises due to complications from Diabetes Mellitus (Kanmani et al, 2019).

Diabetes Mellitus is a state of hyperglycemia that will cause damage to all body tissues, especially to insulin-influenced tissues and will affect inflammatory responses such as CRP (Kalma, 2018). In patients with type 2 Diabetes Mellitus, the body's tissue cells and muscles are insensitive or have insulin resistance so that glucose cannot enter the cells and is eventually deposited in the blood circulation. Hyperglycemia in patients with type 2 Diabetes Mellitus is caused by cellular insensitivity to insulin. In addition, there is an insulin effect due to the inability of the pancreas to produce enough insulin to maintain normal plasma glucose.

C-reactive protein is an acute phase protein produced by the liver. Elevated CRP levels indicate that there is inflammation in the body, so CRP is often used as a marker of inflammation. There is a mild increase in CRP levels in chronic inflammatory conditions such as diabetes mellitus. Increased CRP levels in patients with Type 2 diabetes mellitus can cause oxidative stress which can trigger complications such as retinopathy, neuropathy, nephropathy, or cardiovascular disease, namely heart, blood pressure, uric acid, cholesterol and stroke. (Permatasari, 2020).

In general, mild inflammation and viral infections cause CRP levels to increase between 10 and 40 mg/L, while more severe inflammation and bacterial infections cause CRP levels to increase between 10 and 200 mg/L. According to research conducted by Dewi (2018), CRP levels in adults based on consensus are  $\geq 6$  mg/L. To obtain titer results in semi-quantitative examinations using the formula  $6 \times \text{titer}$  so that if you are looking for a titer of  $1/2$ , the CRP level is 12 mg/dl, if the titer is  $1/4$ , the CRP level is 24 mg/dl, titer  $1/8$  CRP level is 48 mg/dl, titer  $1/16$  CRP titer level is 96 mg/dl. The relationship between titers in Type 2 Diabetes and inflammatory markers such as CRP, tissue damage caused a lot so that the titer of CRP in the blood increases and the increasing titer of CRP, the inflammatory results that can exceed normal levels are  $\geq 6$  ml / L.

The progression of atherosclerosis is accelerated with age, leading to increased endothelial damage, followed by an increase in inflammatory markers, namely CRP. In patients with type 2 diabetes, blood sugar increases, leading to chronic hyperglycemia. The increase in CRP levels in patients with type 2 diabetes is due to the inflammatory response that occurs due to complications caused by diabetes (Kanmani et al, 2019).

Diabetes is a hyperglycemic condition that damages all body tissues, especially those affected by insulin, and affects inflammatory responses such as CRP (Kalma, 2018). In people with type 2 diabetes, the body's tissues and muscle cells are sensitive or experience insulin resistance, so glucose cannot enter the cells and eventually accumulates in the bloodstream. Hyperglycemia in type 2 diabetics is caused by cell sensitivity to insulin. In addition, insulin action occurs because the pancreas cannot produce enough insulin to maintain normal plasma glucose levels.

Hyperglycemia in diabetic patients is associated with increased inflammation in humans. C-Reactive Protein (CRP) is an inflammatory marker synthesized in the liver for non-specific monitoring of local and systemic diseases. A positive CRP result is caused by an increase in fat cells and the body producing a lot of protein in the body. When fat cells produce a lot of protein, the body experiences inflammation or inflammation (Situmeang, 2018).

Chronic hyperglycemia in diabetes predisposes to the development of chronic complications related to fundamental changes or dysfunctions that occur in the vascular system, especially in blood vessels and vascular smooth muscle cells. All these cause changes in cell growth, leading to diabetic vascular complications (Kalma, 2018).

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The development of diabetic complications causes endothelial dysfunction, disrupts and denatures several important proteins, and then increases the production of growth factors and pro-inflammatory factors in the blood, including IL-6 and TNF- $\alpha$ , which stimulate the liver to produce CRP.

The principle of CRP examination is the antibody antigen reaction between CRP in serum and latex which will cause agglutination reaction. If agglutination occurs, the result is positive, if no agglutination occurs, the result is negative. The examination of C-Reactive Protein (CRP) in this study used the Latex Agglutination Method. The principle of the latex agglutination CRP test is that particles are coated with antibodies to determine the presence of antigens in serum samples. In this assay, a suspension of latex particles coated with anti-human CRP antibodies is added to the serum sample being tested. The presence of visible agglutination indicates the presence of elevated CRP levels to clinically significant levels (CRP Latex Test Kit, 2018).

The C-reactive protein test in patients with type 2 diabetes gives positive results due to an increase in fat cells and the body producing a lot of protein in the body. When fat cells produce a lot of protein, inflammation or inflammation occurs in the body. C-reactive protein is a sensitive marker of systemic inflammation and is produced by the liver (Maria, 2018).

Another theory explains that negative CRP results in patients with type 2 diabetes are due to patients practicing a good lifestyle, such as vigorous physical activity, which can reduce CRP levels. In addition, negative results can also be caused because the tools used are less sensitive, so they cannot detect low CRP levels (Masfufah et al, 2019).

## CONCLUSIONS

Based on the results of CRP research covering 30 serum samples taken from type 2 diabetes patients, it can be concluded as follows:

1. Positive results were obtained in 29 samples (96.7%) with titers, namely titer 12 as many as 5 samples (16.7%), titer 24 as many as 17 samples (56.7%), titer 48 as many as 5 samples (16.7%), and titer 96 as many as 2 samples (6.7%)
2. Negative results were obtained in 1 sample (3.3%).
3. Almost all type 2 diabetes respondents have positive C-reactive protein test results, and a small proportion of type 2 diabetes patients have negative C-reactive protein test results.

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