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The Relationship between C-Reactive Protein (CRP) Levels and HbA1c Levels in Type II Diabetes Mellitus Patients

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Abstract
Background: Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia due to abnormalities in insulin secretion, insulin action, or both. Type II diabetes mellitus is caused by the pancreas gland being unable to meet the body's insulin needs. The HbA1c test reflects the average blood glucose level for 2-3 months or about 120 days before the test. C-reactive protein (CRP) is an inflammatory biomarker that is often used to assess the level of systemic inflammation. Elevated CRP levels have been associated with insulin resistance, endothelial dysfunction, and the development of atherosclerosis, all of which contribute to complications in diabetic patients. Therefore, further research is needed to evaluate the correlation between HbA1c and CRP levels, to better understand the relationship between glycemic control and systemic inflammation. *Objective*: This study aims to determine the relationship between C-reactive protein (CRP) levels and HbA1c levels in patients with Type II Diabetes Mellitus. *Materials and Methods*: This study used purposive sampling technique and analytic survey with cross-sectional approach. *Results*: Data analysis using the Chi-Square test obtained a p-value of 0.536, where if Sig> 0.05 then it shows there is no significant relationship. So, there is no relationship between C-reactive protein (CRP) levels and HbA1c levels in Type II Diabetes Mellitus patients.

Keywords
C-Recative Protein, Diabetes Mellitus Type II, HbA1c.

1. Introduction

A class of metabolic illnesses known as diabetes mellitus (DM) is typified by hyperglycemia brought on by either decreased insulin function or decreased insulin production, or both. Despite not being contagious, diabetes is becoming more and more common each year. Diabetes is not a communicable disease, yet the number of cases continues to increase every year. Non-communicable diseases are the leading cause of death in Indonesia, with the top five causes of death including stroke, hypertension, and cancer. Diabetes is also one of the leading causes of death and morbidity worldwide (Mentari et al., 2020).

Every year, 41 million people die from non-communicable diseases (NCDs), which is equivalent to

71% of total deaths in the world. More than 15 million of them are aged between 30 to 69 years, and 85% of them are from lower-middle-income countries. Diabetes Mellitus is one of the diseases that significantly contributes to NCD deaths, with 9.3 million people affected each year. There are two types of diabetes, Type I and Type II. Type I diabetes mellitus occurs when the pancreas destroys the cells that produce insulin, leaving the body unable to produce insulin and requiring insulin injections from outside. Meanwhile, Type II diabetes mellitus is caused by the pancreas being unable to fulfil the body's insulin needs. Type II diabetes mellitus is a serious threat to global health and economy, with about 1 in 11 adults in the world suffering from the disease. About 75% of people with diabetes live in developing countries, including Indonesia (Suputra et al., 2021).

Diabetes is a very serious disease and is often referred to as the 'Silent Killer.' The main risk factor for diabetes is being overweight, which is often caused by modern lifestyles that make people less active and more sedentary, as well as diets high in calories, sugar, and fat that can lead to significant weight gain (Pakaya et al., 2022).

One of the laboratory tests recommended to help diagnose Diabetes Mellitus is Haemoglobin A1c (HbA1c). The HbA1c test can be used to monitor the progression of Diabetes Mellitus as it provides more detailed information about the patient's condition. (Sartika & Hestiani, 2019). For patients who have reached their treatment targets and have stable glycaemic control, HbA1c testing should be done at least twice a year. However, HbA1c cannot be used as an evaluation tool in certain conditions, such as anaemia, haemoglobinopathy, a history of blood transfusion in the last 2-3 months, other conditions that affect the lifespan of red blood cells, and impaired renal function (Soelistijo et al, 2021).

One examination that can help diagnose and detect disorders in the body is CRP (C-Reactive Protein), which is used as a parameter to assess signs of inflammation (Bastian et al., 2022). CRP levels may be elevated in conditions such as hypertension, diabetes, dyslipidaemia, smoking, or a history of heart disease. CRP is also useful for diagnosing inflammation and infectious diseases (Pramonodjati et al., 2019). C-Reactive Protein (CRP) is an inflammatory marker and one of the acute phase proteins produced in the liver to non-specifically monitor local and systemic diseases. CRP levels increase after trauma, infection, or inflammation, and is also used as a prognostic marker for inflammatory conditions (Bastian et al., 2022). CRP is recognised as the most sensitive indicator of inflammation. This protein is found in the blood, and its production in the liver increases in response to infection, injury, or inflammation (Setyowatie et al., 2016).

Elevated blood concentrations of C-Reactive Protein (CRP) are often associated with impaired glucose tolerance and are used as a marker to identify the development of type 2 diabetes. As an indicator of acute systemic inflammation, CRP is produced by the liver and is often associated with various diseases, including diabetes problems. Diabetes mellitus is one of the risk factors that indicate the potential for metabolic syndrome. One of the ways in which metabolic syndrome

develops from diabetes mellitus is through an excessive inflammatory response, which in turn leads to an increase in CRP levels in the body (Mentari et al., 2020).

According to Khairinisa et al. (2022), there is a relationship between HbA1c and C-reactive protein in patients with uncontrolled type II diabetes mellitus ". There is a high hemoglobin A1c (HbA1c) relationship with increased CRP levels in patients with type 2 diabetes mellitus as an indicator of the inflammatory process that occurs due to chronic complications of diabetes mellitus. Therefore Based on the explanation above, the author is interested in conducting research to find out whether there is a relationship between C-Reactive Protein (CRP) levels and increased HbA1c levels in patients with Type II Diabetes Mellitus with different populations and places.

2. Materials and Methods

Study was conducted using Purposive sampling met inclusion criteria adult patients with a confirmed diagnosis of Type II Diabetes Mellitus. The population in this study consists of Type II Diabetes Mellitus patients who have elevated HbA1c levels, both male and female with ethics obtained from the East Kalimantan Ministry of Health Poltekkes with registration number DP.04.03/F.XLII.25/0420/2024 the Health Research Ethics Commission (KEPK). Their blood samples will be taken and centrifuged to obtain serum, then used to analyse the relationship between C-Reactive Protein (CRP) levels and elevated HbA1c levels. The tool used to use CRP Latex Agglutination Assay. Latex Agglutination Assay is a qualitative test (CRP fortess diagnostics, Product Code:LXCRP050/LXCRP100/LXCRP150, United Kingdom). Pipette 50 ul of serum, place on a black background test slide, add 1 drop of CRP latex reagent. The tool used to check HbA1C afinion'2 AS 100 Analyzer, No.Lot 10228990, America (Aboott) by inserting a whole blood sample of 1.5 µL into the sampling device into the cartidge and then inserted into the tray and waiting for results in 5 minutes. CRP data from patient serum with increasing HbA1c levels will be analysed using the SPSS (Statistical Program for Social Science) program and processed with Chi Square Test.

3. Results and Discussion

3.1. Results

This study was conducted at the Media Farma Samarinda Clinic. The specimens used were serum of Type II Diabetes Mellitus patients who underwent examination at the Laboratory Installation of the Samarinda Media Farma Clinic in April 2024, with a total of 30 samples. During the study, there were 30 Type II Diabetes Mellitus patients involved. The characteristics of respondents based on gender can be seen in Table 3.1.

Table 3.1 Research Subjects by Gender and by Age

No.	Gender	Total	Percentage (%)
1	Male	15	50
2	Female	15	50
Category		Total	Percentage (%)
Pre-elderly (45-59 years)		26	86
Elderly (60 years and over)		4	14

Based on Table 3.1, it can be seen that the subjects in this study consisted of 15 men (50%) and 15 female (50%). The patients examined were those who underwent CRP and HbA1c tests. Subjects were divided into the pre-elderly age group of 26 peoples and the elderly group of 4 peoples. Diabetes mellitus cases was increase in is influenced by various factors such as changes in lifestyle patterns, changes in age structure due to increased life expectancy, and cultural factors. In addition, several risk factors, including age above 45 years, also play a role in the incidence of diabetes mellitus (Komariah & Rahayu, 2020).

The following are C-Reactive Protein (CRP) levels with negative (<6 g/dl) and positive (≥6 g/dl) categories. The majority of research subjects had negative CRP levels, with 22 people, while 8 people had positive CRP levels. In the 30 samples studied, the majority of research subjects had high HbA1c levels, as many as 24 people or 80%, while 6 people or 20% had normal HbA1c levels. Patients with a history of Type II Diabetes Mellitus also provided information regarding their health historyHbA1c levels. Normal (<5.7%) High (>5.7%)

There were 17 people with high HbA1c values and normal CRP levels, representing 56.7%, and 7 peoples with high HbA1c values and high CRP levels, representing 23.3%. Data analysis in this study was carried out using the IBM SPSS Statistics Version 23 programs. The results of the SPSS test that have been carried out include data from 30 patients is shown in Table 3.2.

Table 3.2 Cross tabulation of HbA1c values with CRP levels

No	Description	Total	Percentage (%)
1.	HbA1c Normal-CRP Normal	5	16,7
2.	HbA1c Normal-CRP High	1	3,3
3.	CRP Normal-HbA1c High	17	56,7
4.	CRP High-HbA1c High	7	23,3

Patient history based on complications can be seen of Research Subjects Based on Complications. It can be seen that of the research subjects, 21 peoples had no complications, four people had hypertension complications, three people had heart complications, and 2 people had two types of

complications, namely hypertension-uric acid and hypertension-pulmonary. Patients with normal HbA1c values and negative CRP levels, there was one person who had heart complications. In patients with high HbA1c values and negative CRP levels, there were five people with hypertension complications, two people with heart complications, and one person with gout complications. In patients with high HbA1c values and positive CRP levels, one person with lung complications and 1 person with hypertension complications. There were no patients with normal HbA1c values and positive CRP levels who experienced complications.

Data on controlled and uncontrolled show Type II Diabetes Mellitus patients. From the data, there are 18 patients with controlled Type II Diabetes Mellitus, representing 93%, and 2 patients who are not controlled, representing 7%. It shows the length of diagnosis in Type II Diabetes Mellitus patients. From the data, there are 11 people with a history of diagnosis of diabetes mellitus for 1 year, 9 people with a history of diagnosis for two years, five people with a history of diagnosis for three years, three people with a history of diagnosis for four years, and two people with a history of diagnosis for five years. The Chi Square test results can be seen in Table 3.4.

Table 3.4 Chi Square Test

Chi-Square Tests	
	Asymptotic Significance (2-sided)
Pearson Chi-Square	0.536

In Table 3.4, the p value is 0.536, which indicates that the Sig value is > 0.05, which indicates that there is no significant relationship.

3.2 Discussion

The results of research with high HbA1c values and normal CRP levels with a percentage (56.7%), with high HbA1c values and high CRP levels with a percentage (23.3%). the results of table 3.1 show that the pre elderly case is 86% higher than the elderly risk.

According to the Indonesian Ministry of Health (2015) in Hanafi et al (2022), elderly or elderly is someone aged 60 years and over. The elderly are divided into presenilised elderly (45-59 years), elderly (60 years and over), and elderly at risk (70 years and over or 60 years and over with health problems). Gender is one of the factors that can affect the risk of developing type 2 diabetes mellitus. Women tend to have a higher risk than men, mainly because women tend to have higher cholesterol levels and differences in activities and lifestyles that affect the incidence of type 2 diabetes mellitus. The amount of body fat in men is around 15-20% of body weight, while in women it reaches 20-25%, so the increase in fat levels in women is higher than in men. Therefore, the risk of developing diabetes mellitus in women is 3-7 times higher than in men who have a 2-3 times higher risk (Gunawan & Rahmawati, 2021).

One of the factors associated with the incidence of type 2 diabetes mellitus is age. Masruroh's

research (2018) on the relationship between age and nutritional status with blood sugar levels in patients with type II diabetes mellitus at the Internal Medicine Clinic of RSUD dr. Iskak Tulungagung in 2017 showed a relationship between age and blood sugar levels in patients with type II diabetes mellitus, with a p value = 0.000, as well as a relationship between nutritional status and blood sugar levels in patients with type II diabetes mellitus (Gunawan & Rahmawati, 2021). Table 3.3 shows that of the Type II Diabetes Mellitus patients examined at the Samarinda Media Farma Clinic, most were from the age 20 the increase in diabetes mellitus cases is influenced by various factors such as changes in lifestyle patterns, changes in age structure due to increased life expectancy, and cultural factors. Other risk factors include age over 45 years, obesity, hypertension, fat metabolism disorders, hereditary history of diabetes, history of recurrent miscarriage, and giving birth to a child weighing more than 4 kg. Age is related to the physiology of aging, where as we age, body functions decline, including the work of the hormone insulin which cannot work optimally, causing high blood sugar levels (Komariah & Rahayu, 2020).

Several studies have shown that vascular abnormalities may result from mild chronic inflammation of the endothelium, characterised by an increase in chronic inflammatory markers such as CRP. This suggests that CRP is a sensitive marker for detecting subclinical inflammation associated with the development and progression of atherosclerosis. Elevated CRP levels are a significant indicator of cardiovascular disease risk. Early detection of this inflammatory marker in patients with type 2 diabetes mellitus allows for faster therapy to prevent chronic complications (Kalma, 2018).

The insignificant relationship between HbA1c and CRP levels in patients with type 2 diabetes mellitus can be caused by several factors. C-reactive protein is a parameter for acute inflammation, with CRP levels increasing during inflammation and decreasing within 18-20 hours after the stimuli that cause inflammation end. Diabetes mellitus is included in the category of chronic inflammatory diseases that increase CRP synthesis in plasma, although levels are not high (Permatasari et al., 2020).

This study used the Chi-Square test to evaluate the correlation between HbA1c and CRP levels in patients with type 2 diabetes mellitus. The Chi-Square test is a statistical tool commonly used to test hypotheses in the context of data that are not normally distributed (Wibowo, 2017).

The results of this study different from several previous studies. Research by Khairinisa et al. (2022) showed an association between HbA1c and CRP in patients with uncontrolled type 2 diabetes mellitus. In groups with low inflammatory risk factors, the relationship between CRP and HbA1c may not be so clear. Variability of Measurement Methods Several other factors, such as obesity, blood pressure, insulin resistance, or the use of certain medications, may influence the relationship between CRP and HbA1c. research design and sample size studies with more robust designs, such as longitudinal cohort studies or meta-analyses, may provide clearer results. Genetic factors may affect how a person responds to inflammation and blood glucose regulation. In

addition, environmental factors such as diet, physical activity and stress may also play a role in the relationship between CRP and HbA1c. CRP is a marker of acute inflammation that can change rapidly, while HbA1c reflects average blood glucose levels over the past 2-3 months. This difference in time dynamics may lead to an indirect or difficult-to-detect relationship in certain studies.

This suggests an association between high haemoglobin A1c (HbA1c) and increased CRP levels in patients with type 2 diabetes mellitus. In contrast, research by Puspita Sari & Sayekti (2023) found that there was no significant correlation between CRP and HbA1c levels in patients with type 2 diabetes mellitus. Which states that there is no significant correlation between C-Reactive Protein (CRP) levels and HbA1c levels in Type II Diabetes Mellitus Patients. According to the study, an increase in HbA1c levels was not followed by an increase in C-Reactive Protein (CRP) levels. It can be seen in the chi square test results that there is no relationship between C-Reactive Protein (CRP) levels and HbA1c levels in Type II Diabetes Mellitus patients.

4. Conclusions

In the study on 'The Relationship between C-Reactive Protein Levels and HbA1c Levels in Type II Diabetes Mellitus Patients,' the Chi-Square test results showed a p-value of 0.536. Because the Sig value > 0.05, this indicates that there is no significant relationship between C-Reactive Protein (CRP) levels and HbA1c levels in Type II Diabetes Mellitus patients.

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Author Contributions: SM: conceived the original idea. LOM and ZAS: provided suggestions. RA: reviewed the suggestions and evaluated the research results until the drafting of the manuscript.

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