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Analysis of C-reactive Protein as an Inflammation Biomarker in Type-2 Diabetes Mellitus Patients at Minahasa, North Sulawesi, Indonesia

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Abstract: C-reactive protein is a non-specific acute phase reactant produced by the liver and endothelial cells. Inflammation or acute infections cause a rise in C-reactive protein, which can be measured to determine the risk of cardiovascular disease. The hs-CRP test can detect CRP at lower concentrations because it is more sensitive, making it more effective than conventional CRP testing methods. This study aimed determine the relationship between hs-CRP levels and fasting blood glucose, and to examine whether there were differences in hs-CRP levels in patients with type-2 diabetes mellitus with or without hypertension, in Minahasa, North Sulawesi, Indonesia. A total of 123 diabetes mellitus patients were included in this cross-sectional study. Subjects were tested for blood pressure, body mass index, fasting blood glucose, and hs-CRP levels. The correlation between hs-CRP and fasting blood glucose had a correlation coefficient (r) 0.404 and *p*-value 0.000 (<0.05). The average hs-CRP level in type-2 diabetes mellitus patients with hypertension was 148.8 ± 24.9 mg/dL and 55.1 ± 54.0 mg/dL without hypertension. In conclusion, there was a significant relationship between hs-CRP and fasting blood glucose levels, and type-2 diabetes mellitus patients with hypertension also had greater hs-CRP levels than those without hypertension. This suggests that hs-CRP can be used to evaluate a diabetic patient's risk for cardiovascular disease.

Keywords: Diabetes Mellitus, Fasting Blood Glucose, hs-CRP

1. Introduction

Diabetes mellitus, a metabolic disorder characterized by hyperglycemia, continues to be a significant global health issue due to its high potential for morbidity and mortality. Since comorbid conditions affect more than 50% of diabetes patients, the prevalence of diabetic vascular consequences like retinopathy, renal disease, and other vascular dysfunction is also increasing. [1, 2] As a country that ranks seventh in the world in terms of the highest number of diabetics (after China, India, the United States, Pakistan, Brazil and Mexico), the incidence of type-2 diabetes mellitus in Indonesia is increasing every year and around 87.5% of patients do not achieve good and appropriate glycemic control. [3] According to data from Indonesia's Basic Health Study in 2018, out of Indonesia's 34 provinces, North Sulawesi ranks among the top 5 with the highest prevalence of diabetes, with an estimated 3% of the population. [4]

C-reactive protein, a nonspecific acute phase reactant produced by the liver and endothelial cells, is useful in the function of endothelial cells, vascular smooth muscle, monocyte/macrophage, and the coagulation system. C-reactive protein increases in response to acute infection or inflammation, and can be used to assess cardiovascular disease risk. [5] The hs-CRP test can detect CRP at lower concentrations because it is more sensitive, making it more effective than conventional CRP testing methods. [6] Analysis

of fasting blood glucose (FBG) in relation to hs-CRP in diabetics is considered limited Indonesia. Therefore, this study aimed to determine the association between hs-CRP and fasting blood glucose levels and to investigate whether there were differences in hs-CRP levels in patients with type-2 diabetes mellitus with or without hypertension, in Minahasa, North Sulawesi, Indonesia.

2. Material and Methods

2.1. Study Design and Patients

Sampling was carried out during six months at the Noongan Regional General Hospital, Minahasa Regency, North Sulawesi, Indonesia. The total sampling method was applied to all inpatients and outpatients with diabetes mellitus (fasting blood glucose ≥126 mg/dL and/or previous history of diabetes mellitus). The participants in this study were those who were assessed during the study period and met the inclusion and exclusion criteria. Exclusion criteria were liver disease, infection in the last two weeks, and obesity.

2.2. Clinical and Laboratory Data Collection

The participants' systolic and diastolic blood pressures were measured with an aneroid sphygmomanometer. Hypertension was defined as SBP ≥140 mmHg and/or DBP ≥90 mmHg. The patient's body mass index (BMI) value was calculated based on body weight (kg) and height (m^2). Venous blood was taken from all subjects after an overnight fasting, and serum samples were used for fasting blood glucose and hs-CRP examinations. Blood glucose levels were tested using a Sysmex BX-3010 chemistry analyzer, while Hipro analyzer was used to measure hs-CRP.

2.3. Statistical Analysis

Statistical analysis was performed using the SPSS version 26 software. The data was represented by number, mean values, and standard deviation (SD). An independent samples t-test was used to analyze continuous variables with a normal distribution, while a Mann-Whitney test was used to analyze data with an abnormal distribution. Spearman's correlation coefficient was used to identify the correlation between the fasting blood glucose and hs-CRP levels, as well as the direction. A *p*–value of <0.05 was considered significant.

3. Results

3.1. Demographic Data

One hundred and twenty-three blood specimens were collected from diabetes mellitus patients. The age of the subjects was between 26 and 92 years with an average age of 58.4 ± 12.4 years. Sixty two patients were females (50.4%), and of the 123 patients, 62 (50.4%) were found to have hypertension.

3.2. Correlation Between Fasting Blood Glucose and hs-CRP

The correlation between hs-CRP and fasting blood glucose had a correlation coefficient (r) 0.404 which can be categorized as moderate and directly proportional. The *p*-value was 0.000 (<0.05), meaning that there was a significant relationship between hs-CRP and fasting blood glucose levels (Figure 1).

3.3. Characteristics of Type-2 Diabetes Mellitus Patients with and Without Hypertension

Table 1 shows that while there were significant differences, including increases in systolic blood pressure, diastolic blood pressure, and hs-CRP in type-2 diabetes mellitus with hypertension compared to the group without hypertension, there were no significant differences in age, BMI, or fasting blood glucose, as expected. In type-2 diabetes mellitus individuals with hypertension, the average hs-CRP level was 148.8 24.9 mg/dL, compared to 55.1 54.0 mg/dL in those without hypertension.

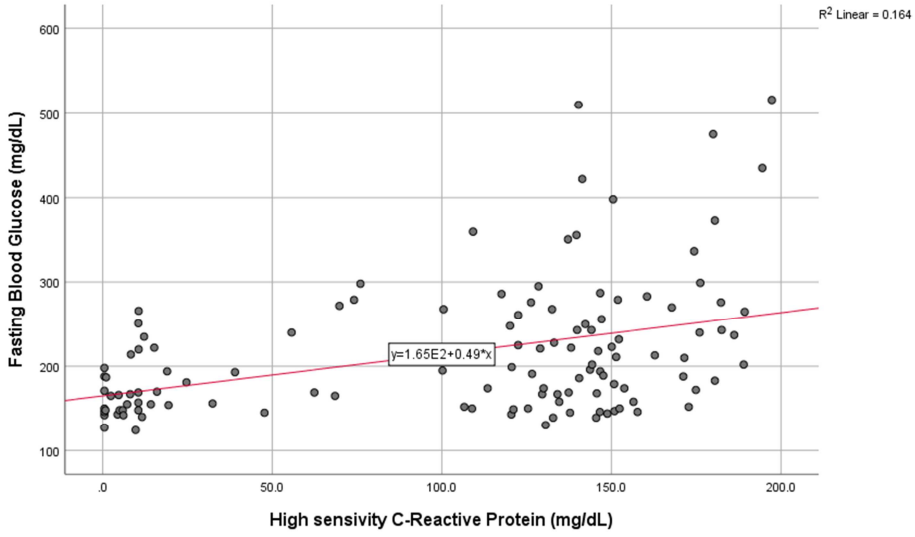

Figure 1. *Correlation between hs-CRP and fasting blood glucose.*

Table 1. *Characteristics of type-2 diabetes mellitus patients with and without hypertension.*

Characteristics	Total (n=123)	DM with HT (n=62)	DM without HT (n=61)	*p-value*
	mean ± SD	mean ± SD	mean ± SD	
Age (year)	58.4 ± 12.4	57.5 ± 11.5	59.3 ± 13.3	0.413
BMI (kg/m^2)	24.5 ± 2.9	24.5 ± 3.0	24.5 ± 2.8	0.962
SBP (mmHg)	130.3 ± 14.3	140.0 ± 12.8	120.8 ± 8.2	0.000*
DBP (mmHg)	81.7 ± 9.2	86.9 ± 7.6	76.3 ± 7.5	0.000*
FBG (mg/dL)	215 ± 78.9	222.6 ± 93.2	208.5 ± 61.1	0.903
hs-CRP (mg/dL)	102.3 ± 64.7	148.8 ± 24.9	55.1 ± 54.0	0.000*

Note: DM= diabetes mellitus, HT = hypertension, SBP = systolic blood pressure, DBP = diastolic blood pressure, BMI = Body Mass Index, FBG = fasting blood glucose, hs-CRP = high-sensitive C-reactive protein

4. Discussion

This study shows a moderate and directly proportional correlation between fasting blood glucose and hs-CRP. Our results were in accordance with the previous studies. Vinod *et al.,* in their retrospective study indicated that fasting, postprandial blood sugar, and HbA1c all show statistically significant positive correlations with hs-CRP, with correlation coefficients (r) of 0.873, 0.788, and 0.743, respectively. [7] Similarly, a cross-sectionally study conducted by Kawamoto *et al.,* in the Japanese population reported that hs-CRP levels increased with increasing fasting blood glucose and were independent on cardiovascular risk factors. [8]

People with type-2 diabetes mellitus have a higher chance of acquiring cardiovascular disease, according to previous research. There are several reasons for this increased risk. A higher risk of cardiovascular disease is due to hyperglycemia, which increases free fatty acid levels, insulin resistance, levels of oxidative stress, levels of advanced glycation end products, and disruption of the protein kinase cascade. Additionally, adipose tissue secretes cytokines that promote chronic inflammation and thrombosis in people with type-2 diabetes mellitus. Also, dyslipidemia, which frequently coexists with type-2 diabetes mellitus, can lead to atherosclerosis. [9, 10]

During the evolution of diabetes, functional endothelial activity impairment occurs prior to the emergence of morphological changes. The key factor contributing to the development of atherosclerosis and hypertension is inflammation. [11] Diabetes harms the kidneys by leaving scar tissue behind, increases water and salt retention, and raises blood pressure. Increased Renin Angiotensin Aldosterone System (RAAS) activity caused by high glucose will raise the risk of hypertension. AT-1 receptors are multiplied and the RAAS is activated by insulin. [12] Hypertension can cause stress oxidative and pro-inflammatory effects on the arterial wall. The presence of hypertension in type-2 diabetes mellitus is associated with an more active inflammatory state. [13] Studies have shown that the inflammatory marker hs-CRP is connected to metabolic profiles and is a good predictor of cardiovascular problems in type 2 diabetics without clinical atherosclerotic symptoms. [14, 15] Therefore, the hs-CRP levels can be seen in type-2 diabetes mellitus patients with hypertension is higher than people with type-2 diabetes mellitus without hypertension. [16]

5. Conclusion

This study concluded that fasting blood glucose levels and hs-CRP levels were significantly correlated, and type-2 diabetes mellitus patients with hypertension also had higher hs-CRP levels than those without hypertension. Therefore, hs-CRP is associated with an increased risk of cardiovascular disease as a complication of diabetes mellitus.

Conflicts of Interest Statement

Authors have no conflicts of interest to declare.

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