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ASSOCIATION BETWEEN FASTING BLOOD GLUCOSE AND C-REACTIVE PROTEIN LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS

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Abstract
Background: Diabetes mellitus (DM) is characterized by elevated blood glucose levels resulting from decreased insulin secretion by pancreatic beta cells. Fasting blood glucose (FBG) measurement is commonly used to monitor DM, requiring patients to fast for a minimum of eight hours. Insufficient insulin production impairs glucose uptake into body tissues, leading to hyperglycemia. Chronic hyperglycemia subsequently stimulates the production of inflammatory cytokines, which promotes the hepatic synthesis of C-reactive protein (CRP).
Objective: This study aims to determine the relation between FBG and CRP levels in patients with type 2 diabetes mellitus (T2DM) at Mangusada Hospital.
Method: An observational analytic study was conducted using purposive sampling, with a total sample of 25 T2DM patients.
Result: The lowest FBG level was 126 mg/dL, while the highest was 319 mg/dL. The lowest CRP level was 0.2 mg/L, whereas the highest was 23.7 mg/L. High FBG and CRP levels were observed in 44% of respondents, while high FBG with normal CRP levels were found in 56%. The highest FBG (319 mg/dL) also exhibited the highest CRP level (23.7 mg/L) The non-parametric Spearman's rank correlation revealed a significant association between FBG and CRP levels with p-value of 0.012 (<0.05) and r = 0.493 indicated a positive and moderate correlation.
Conclusion: There is a positive, moderate correlation between FBG and CRP levels in T2DM patients at Mangusada Hospital.

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INTRODUCTION

Diabetes mellitus (DM) remains a major public health problem worldwide, particularly in Indonesia, where the number of cases continues to increase (1). International Diabetes Federation (IDF) reported that in 2021, Indonesia had 19.5 million people living with diabetes, and by 2045, this number is projected to increase to 28.6 million (2). Bali is among the provinces in Indonesia with one of the highest prevalence rates of DM, recorded at 1.5 percent (3). Based on the profile of the Dinas Kesehatan Provinsi Bali 2021, the number of DM patients in 2020 was 14.353 and in 2021, that number increased significantly to 53.726 (4).

Diabetes mellitus (DM) is classified into four categories and specific types of DM caused by other conditions. Type 2 diabetes mellitus accounts for 90–95% of all diabetes cases (5). DM is characterized by elevated blood glucose levels caused by reduced insulin secretion by pancreatic beta cells. The management of DM focuses on monitoring blood glucose status, which is routinely checked. This monitoring is intended to anticipate possible complications or sudden death (6). A fasting blood glucose (FBG) level of ≥126 mg/dl or a random blood glucose (RBG) level of ≥200 mg/dl, accompanied by symptoms such as weight loss, polyphagia (excessive eating), polydipsia (excessive drinking), and polyuria (frequent urination), can confirm a diagnosis of DM. Proper blood glucose control can significantly reduce the risk of patients developing microvascular complications (7).

Fasting blood glucose (FBG) is one method used to monitor plasma glucose levels, in which the patient must fast for at least eight hours before the test. During this period, no food is consumed, so the body maintains plasma glucose levels through the liver, peripheral tissues, and hormones that can influence blood glucose levels (8).

Insulin dysfunction can occur when pancreatic beta cells that produce insulin are unable to produce it in sufficient amounts to meet the body's needs, resulting in glucose in the blood vessels being unable to enter the tissues, which is characterized by increased blood glucose levels in DM patients (9). This leads to hyperglycemia because most glucose continues to remain in the bloodstream for a long period (10). Chronic hyperglycemia stimulates the secretion of various inflammatory cytokines including Interleukin-6 (IL-6), Interleukin-1 (IL-1), and TNF-α, which in turn stimulate the liver to produce *C-reactive protein* (CRP). Prolonged exposure to hyperglycemia is currently recognized as a major causative factor in the pathogenesis of diabetic complications, including atherosclerosis in monocytes (11).

C-Reactive Protein (CRP) is one of the acute phase proteins of the liver that functions as a biomarker of acute inflammation. CRP can be produced by metabolic and inflammatory factors related to the progression of DM, such as increased blood glucose levels, obesity, and high levels of free fatty acids. In DM patients, elevated CRP levels are a fairly accurate indicator to predict the occurrence of vascular complications, the development of cardiovascular disease and can be considered a sensitive biomarker because CRP is an alpha-globulin produced in the liver with levels that increase significantly during inflammatory processes involving tissue damage and dysfunction of the vascular system, particularly in vascular endothelial cells. This condition contributes to the occurrence of vascular complications associated with the process of atherosclerosis, so that CRP can be used as a predictor of complications in DM patients (12,13).

High CRP levels are a strong indicator of cardiovascular disease risk resulting from the inflammatory response in DM patients. Early detection of this inflammatory biomarker allows for the provision of appropriate therapy to be given promptly, thereby preventing the occurrence of chronic complications (11).

Previous research has indicated a significant association between C-reactive protein (CRP) levels and Type 2 Diabetes Mellitus (DM). The previous research found an increase in CRP levels among DM patients, with the highest titer reaching 96 in 6.7% of samples, while 56.7% of samples had a titer of 24 (14). This suggests a correlation between elevated CRP and diabetic conditions. Similarly, previous research reported that 20% of the samples demonstrated elevated CRP levels accompanied by high fasting blood glucose. (>120 mg/dL) in 66% of cases at Rumah Sakit Umum Prof. Dr. W. Z. Johannes Kupang (15). Another study reported that 80% of examined DM patients showed positive CRP results, especially among those with high fasting blood glucose levels (12).

Given these findings, the authors are interested in exploring the relationship between fasting blood glucose levels and CRP levels in DM patients. The study will utilize a chemistry analyzer employing the hexokinase method for FBG and the latex method for CRP, both of which are regarded as the gold standard in laboratory diagnostics. This research is motivated by the rising number of DM patients at Rumah Sakit Daerah Mangusada in 2024. Understanding this relationship could help in early detection and management of chronic complications in DM, potentially guiding effective therapeutic interventions.

MATERIALS AND METHODS

Study design

This was an observational analytic study with a cross-sectional design, providing a snapshot of the association between fasting blood glucose (FBG) and C-reactive protein (CRP) levels. This research was conducted in Clinical Pathology Laboratory of Rumah Sakit Daerah Mangusada, Badung Regency, Bali. Ethical approval for all procedures involving human was granted by the Ethics Committee of Rumah Sakit Daerah Mangusada (No. 000.9/2969/RSDM/2025). The samples used in this study were utilized 25 patients with confirmed T2DM. All participants were informed about the study procedures and provided written informed consent prior to participation.

Sample collection and processing

Venous blood samples were collected under standardized conditions. Personnel involved in sampling adhered to biosafety protocols and wore appropriate personal protective equipment (PPE), including gloves, masks, and laboratory coats. Blood samples were centrifuged at 3,000 rpm for 10 minutes to separate serum, which was subsequently transferred to sample tubes for analysis.

Serum analyses were conducted in the Clinical Pathology Laboratory of Rumah Sakit Daerah Mangusada using a chemistry analyzer. Fasting blood glucose (FBG) was measured by the hexokinase method, and C-reactive protein (CRP) was determined by the latex agglutination method. All assays were performed in accordance with the manufacturer's instructions and IFCC guidelines, with a wavelength setting of 340 nm where applicable. Results generated by the analyzer were recorded in the laboratory information system (LIS)

and validated by a clinical pathologist. In the event of critical values, repeat testing and clinical correlation were performed prior to result validation.

Statistical analysis

Data analysis was conducted to evaluate the relationship between FBG and CRP levels. Normality of data was assessed using the Shapiro–Wilk test. Spearman's rank correlation coefficient was used to assess the association between FBG and CRP. A two-sided p-value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

As presented in Table 1, the largest proportion of respondents with diabetes mellitus (DM) were classified as elderly (60–74 years), representing 60% (n = 15) of the study sample. Meanwhile, the smallest proportion was observed among adults aged 26–44 years, accounting for only 8% (n = 2).

Table 1. Distribution of Respondents According to Age

Age (years)	Frequency (N)	Percentage (%)
Adult (26 - 44)	2	8
Middle age (45- 59)	8	32
Elderly (60 - 74)	15	60
Total	25	100

Based on Table 1, the largest proportion of respondents with diabetes mellitus (DM) was in the elderly category (60–74 years), accounting for 60% (15 individuals), while the smallest proportion was in the adult age group (26–44 years), accounting for only 8% (2 individuals). This finding is consistent with survey data of Riskesdas 2019 (18), which reported that the prevalence of DM in Indonesia is highest among individuals aged ≥55 years. Older adults tend to have greater difficulty controlling blood glucose levels compared to younger individuals. Poor glycemic control in the elderly is mainly attributed to degenerative factors, namely the progressive decline in body functions that affect multiple systems, particularly the endocrine system, resulting in insulin resistance (16). The physiological decline is related to reduced insulin secretion, which limits the body's capacity to regulate blood glucose levels. These changes begin at the cellular level, then extend to tissues, eventually impairing organ function and disrupting homeostatic balance. Consequently, pancreatic beta-cell activity in producing insulin decreases alongside diminished cellular sensitivity, particularly in the ability of beta cells to secrete insulin (17).

Table 2. Distribution of Respondents by Gender

Gender	Frequency (N)	Percentage (%)
Male	12	48
Female	13	52
Total	25	100

As presented in Table 2, the majority of DM respondents were female, accounting for 52% (13 individuals). Females are more likely than men to develop DM. Physiologically, hormonal changes that occur after menopause contribute to increased fat accumulation. A decline in estrogen and progesterone levels can further impair glucose regulation, thereby elevating the risk of DM in women. The reduction of estrogen during menopause is particularly associated with abdominal fat accumulation, which triggers an increased

release of free fatty acids, leading to insulin resistance. In addition, poor glycemic control in women may also be influenced by excessive carbohydrate intake and psychological stress (18).

Table 3. Test Results of C-reactive protein (CRP) Levels

CRP level	Percentage (%)
High (>5 mg/L)	44
Normal (≤ 5 mg/L)	56
Total	100

Table 4. Minimum and Maximum Medical Test Results of Fasting Blood Glucose (FBG) and C-reactive protein (CRP) Levels

Hematologic Test	Minimum Result	Maximum Result	Mean	Standard Deviation
FBG (mg/dL)	126	319	172.96	51.78
CRP (mg/L)	0.2	23.7	5.276	5.02

Based on the data in Table 3, the lowest fasting blood glucose (FBG) level was 126 mg/dL, while the highest reached 319 mg/dL. For C-reactive protein (CRP), the lowest value was 0.2 mg/L, and the highest reached 23.7 mg/L.

Excessive carbohydrate consumption leads to increased blood glucose levels as carbohydrates are broken down into monosaccharides, which subsequently raise glucose concentrations in the blood. This condition stimulates insulin production, but when insulin secretion is insufficient, insulin resistance develops. This resistance impedes glucose distribution to peripheral tissues, resulting in hyperglycemia (18).

Stress exacerbates this condition by activating the sympathetic nervous system, which alters gluconeogenesis and promotes glycogen breakdown into glucose, thereby elevating blood glucose levels (19). Stress also increases cortisol production, which interferes with insulin action and contributes to hyperglycemia (18).

In this study, the lowest fasting blood glucose (FBG) level was 126 mg/dL, while the highest was 319 mg/dL. The lowest CRP level was 0.2 mg/L, whereas the highest was 23.7 mg/L, with standard deviations of 51.78 for FBG and 5.02 for CRP (Table 4). Based on Table 3, High FBG and high CRP levels were observed in 44% of respondents (11 individuals), while high FBG with normal CRP levels were found in 56% (14 individuals). The respondent with the highest FBG value (319 mg/dL) also exhibited the highest CRP level (23.7 mg/L), both of which exceeded normal ranges. Hypothesis testing using the non-parametric Spearman's rank correlation revealed a significant association between FBG and CRP levels among DM patients at Rumah Sakit Daerah Mangusada, with a significance value (2-tailed) of 0.012 (<0.05). The correlation coefficient of 0.493 indicated a positive and moderate correlation. This suggests that higher FBG levels in DM patients tend to be accompanied by increased CRP levels. These findings highlight that hyperglycemia in DM is associated with systemic inflammatory processes measurable through CRP levels.

Based on statistical analyses, the significance value (2-tailed) was 0.012, which is less than 0.05, indicating a significant relationship between fasting blood glucose (FBG) levels and C-reactive protein (CRP) levels. The correlation coefficient was 0.493, suggesting a positive relationship with a moderate level of correlation.

The results of this study are consistent with previous research showing that among 30 DM patients with high FBG levels, 29 (96.7%) also exhibited elevated CRP levels (14).

Similarly, previous research reported that DM patients are at risk of increased CRP, with 80% (8 out of 10 patients) demonstrating positive CRP results at high FBG levels (12). In DM, blood glucose is unable to effectively enter tissues due to insulin resistance or beta-cell dysfunction, leading to persistent hyperglycemia as glucose accumulates in circulation. Chronic hyperglycemia stimulates the release of pro-inflammatory cytokines, including interleukin-6 (IL-6), interleukin-1 (IL-1), and tumor necrosis factor-α (TNF-α) from adipose tissue and immune cells. These cytokines, in turn, stimulate the liver to synthesize and release CRP as part of the systemic inflammatory response to metabolic stress (11).

C-reactive protein (CRP) is a well-established acute-phase marker of inflammation associated with tissue damage. This indicates that chronic hyperglycemia has the potential to cause widespread tissue injury, particularly in insulin-dependent tissues, while also triggering a chronic inflammatory response, such as elevated CRP levels (11). The increase in CRP is associated with oxidative stress and the accumulation of reactive oxygen species (ROS), which are free radicals generated when oxygen molecules capture unpaired electrons. Excess ROS can damage both large and small blood vessels through inflammatory processes, leading to vascular injury and endothelial dysfunction (20). These conditions contribute to vascular complications related to atherosclerosis and coronary heart disease. Therefore, CRP may serve as a predictor of complications in patients with DM (12).

CLINICAL IMPLICATION

The demonstrated positive and moderate correlation between fasting blood glucose and C-reactive protein levels highlights the importance of incorporating inflammatory biomarkers into routine monitoring of patients with type 2 diabetes mellitus. Elevated CRP in individuals with poor glycemic control suggests ongoing systemic inflammation, which may precede or accompany vascular complications. Integrating CRP testing with standard glucose monitoring could therefore support earlier identification of high-risk patients, guide timely therapeutic interventions, and improve long-term management strategies aimed at reducing the burden of diabetes-related cardiovascular and inflammatory complications.

LIMITATIONS

This study is limited by its relatively small sample size, which may restrict the generalizability of the findings to the broader diabetic population. Additionally, participants were recruited from a single clinical center, thereby limiting the representation of demographic and clinical heterogeneity across different regions. Several potential confounders influencing CRP levels, including BMI, obesity, medication use, and acute or chronic inflammatory conditions, were not systematically measured. Future investigations incorporating larger, more diverse cohorts and longitudinal designs are warranted to strengthen the evidence supporting this association.

CONCLUSIONS

The findings demonstrate a positive and moderate correlation between fasting blood glucose (FBG) levels and C-reactive protein (CRP) levels in patients with diabetes mellitus at Rumah Sakit Daerah Mangusada. Therefore indicates that elevations in FBG among diabetic patients are generally accompanied by increased CRP concentrations. These results

support the concept that hyperglycaemia in diabetes mellitus is associated with systemic inflammatory activity, as reflected by measurable increases in CRP levels.

CONFLICT OF INTEREST

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

AUTHOR CONTRIBUTIONS

K.A.A.G.D conceived the original idea. K.A.A.G.D planning and carried out the experiment. C.E.S contributed to the interpretation of the results. K.A.A.G.D wrote the manuscript with support from C.E.S and L.A.W.K. L.A.W.K supervised the project. All authors provided critical feedback and helped shape the research, analysis and manuscript.

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DECLARATION OF ARTIFICIAL INTELLIGENCE USE

No artificial intelligence (AI) tools were used in the preparation of this manuscript.

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