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Research Article

Evaluation of Procalcitonin in Type-2 Diabetes Mellitus Patients in Minahasa, North Sulawesi, Indonesia

Diana Shintawati Purwanto[1, 2, *], Sylvia Ritta Marunduh[3], Stefana Helena Margaretha Kaligis[1]

[1]Department of Biochemistry, Faculty of Medicine, Sam Ratulangi University, Manado, Indonesia
[2]Department of Clinical Laboratory, R. D Kandou Central General Hospital, Manado, Indonesia
[3]Department of Physiology, Faculty of Medicine, Sam Ratulangi University, Manado, Indonesia

Abstract

Diabetes mellitus (DM) remains a significant global health challenge, contributing to high morbidity and mortality rates. In Indonesia, type 2 diabetes is increasing, with a substantial percentage of patients experiencing poor glycemic control. This study aims to explore the relationship between serum procalcitonin levels and fasting blood glucose (FBG) in patients with type 2 diabetes, assessing procalcitonin's potential as a biomarker for diabetes complications. A total of 122 patients with confirmed type 2 diabetes were included, excluding those with infection or recent trauma. Clinical parameters, including blood pressures, body mass index (BMI), and blood samples for FBG and procalcitonin levels, were collected. Statistical analysis was performed using SPSS version 26.0. The mean age of participants was 56.7 years, with 43.4% diagnosed with hypertension. A significant correlation was found between procalcitonin and FBG (p = 0.024, r = 0.205), indicating a weak positive relationship. No significant differences in procalcitonin levels were observed between hypertensive and non-hypertensive patients. The findings suggest that procalcitonin may serve as a useful biomarker in managing complications associated with type 2 diabetes. While the correlation with FBG was weak, the role of inflammation in diabetes progression highlights the need for further investigation. Integrating procalcitonin testing into clinical practice could enhance patient management, and future research should explore the mechanisms linking procalcitonin levels to diabetes complications, as well as establish reference values for procalcitonin in diabetic populations.

Keywords

Diabetes Mellitus, Fasting Blood Glucose, Procalcitonin

1. Introduction

Diabetes mellitus is still a major worldwide health concern because of its propensity to result in high rates of morbidity and mortality. High blood glucose levels, or hyperglycemia, are an indicator of diabetes mellitus (DM), a metabolic illness. This disorder is caused by problems affecting insulin function or secretion, or both, which impact the way insulin functions in target tissues. [1] Individuals with type 2 diabetes have an increased risk of problems due to high

*Corresponding author: dianashintapurwanto@unsrat.ac.id (Diana Shintawati Purwanto)

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blood pressure (BP), obesity, smoking, physical inactivity, and hyperlipidemia. [2]

In Indonesia, the number of people with type 2 diabetes is increasing annually, and 87.5% of patients do not have appropriate glycemic control. [3] With about 10.7 million affected people, Indonesia is ranked seventh out of the top ten countries with the largest number of diabetes cases. [4] The overall health of the public is adversely affected by diabetes mellitus and its consequences, which increase the health burden on families and communities. According to doctor diagnoses among the Indonesian population across various provinces, North Sulawesi ranks fourth out of 34 provinces in Indonesia for the highest prevalence of DM, at approximately 3%. Additionally, DM is one of the top ten diseases in Minahasa Regency, contributing to 1.6% of the total prevalence. [5] The complex and chronic progression of DM leads to various vascular complications, both macrovascular and microvascular. These vascular complications, including nephropathy and retinopathy, are associated with type 2 diabetes and can result in decreased quality of life and life expectancy. [6]

Many current studies are investigating procalcitonin (PCT) as a specific and effective biomarker for bacterial infections, aiming to replace traditional markers. PCT is a polypeptide made up of 116 amino acids and serves as the prohormone for calcitonin. It is produced by parafollicular cells, as well as in the lungs and pancreas. Normally, its levels in the bloodstream are very low or undetectable, but they rise significantly during bacterial infections, while only experiencing slight increases in cases of viral infections and non-infectious inflammatory diseases. [7]

Research in this area has shown that there is still limited analysis of FBG in diabetes patients related to procalcitonin and diabetes complications. While procalcitonin testing is more commonly used for infectious diseases, it can also be valuable in assessing the risk of complications in diabetes patients and may serve as a non-invasive indicator of atherosclerotic vascular disease. [8] As the demand for procalcitonin testing in hospitals increases, it is crucial to determine whether serum procalcitonin levels can be utilized in monitoring complications in diabetes patients. Therefore, the aim of this study is to investigate the relationship between procalcitonin levels and FBG in patients with type 2 diabetes.

2. Material and Methods

2.1. Study Design

Four months of sampling were conducted at the Noongan Regional General Hospital and the Awaloei Hospital in the Minahasa Regency of North Sulawesi, Indonesia. All patients with diabetes mellitus (fasting blood glucose ≥126 mg/dL and/or a history of the disease) who were inpatients or outpatients were subjected to the complete sampling procedure. Individuals who fulfilled the inclusion and exclusion criteria and were evaluated during the study period. Patients with infection/sepsis and who underwent surgery/trauma were excluded as research subjects. This research received approval from the Medical Research Ethics Committee at R. D. Kandou General Hospital (No. 169/EC/KEPK-KANDOU/VIII/2024).

2.2. Measurements of Clinical and Laboratory Data

The systolic and diastolic blood pressures of the participants were assessed using an aneroid sphygmomanometer, with hypertension classified as a systolic blood pressure (SBP) of 140 mmHg or higher and/or a diastolic blood pressure (DBP) of 90 mmHg or higher. Additionally, the body mass index (BMI) was calculated for each participant as body weight (kg) divided by height (m) squared. Following an overnight fast, venous blood samples were collected from all subjects for further analysis. These serum samples were utilized to measure fasting blood glucose levels and procalcitonin concentrations. Blood glucose levels were analyzed with a Cobas C111 chemistry analyzer, while procalcitonin levels were measured using a Hipro analyzer.

2.3. Statistical Analysis

SPSS version 26.0 was used to process the statistical analysis. Standard deviation (SD), mean values, and numbers were used to represent the data. Differences in continuous variables were compared by the Mann–Whitney test. The correlation between procalcitonin levels and fasting blood glucose were performed by Spearman's correlation test. A *p*-value of less than 0.05 was considered statistically significant.

3. Results

3.1. Demographic Data

A total of 122 blood samples were collected from individuals diagnosed with type 2 diabetes mellitus. The subjects ranged in age from 23 to 82 years old, with an average age of 56,7 ± 10,6 years. Out of the 122 patients, 52 (43.4%) had hypertension, and eighty-two patients (67.2%) were female.

3.2. Association between Procalcitonin and Fasting Blood Glucose

There was a significant correlation between procalcitonin and fasting blood glucose levels, as indicated by the p-value of 0.024 (<0.05). With a correlation value (r) of 0.205, procalcitonin and fasting blood glucose have a weak and directly proportional relationship (Figure 1).

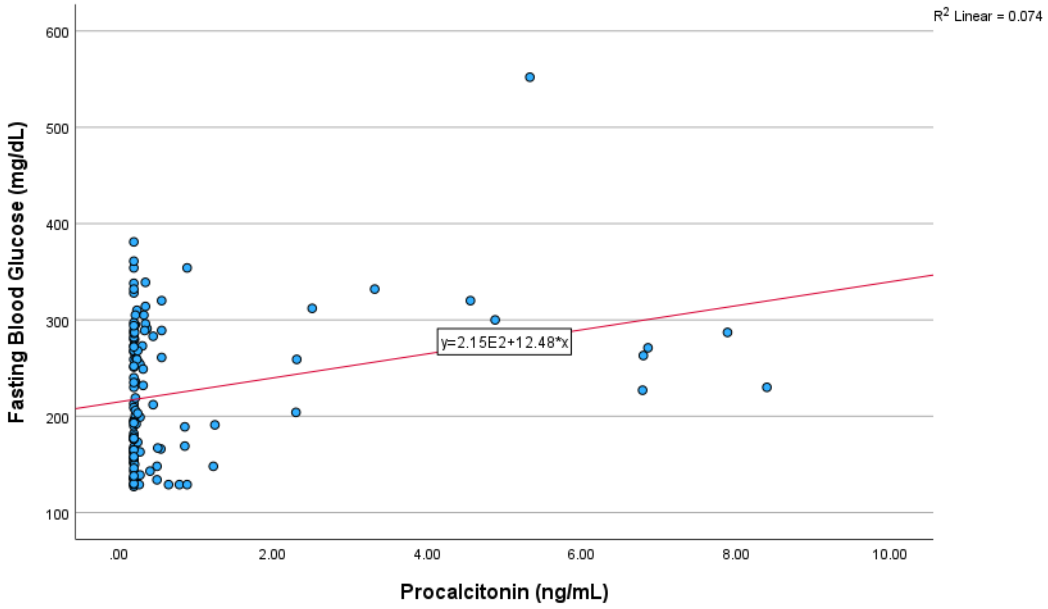

Figure 1. *Correlation between procalcitonin and fasting blood glucose.*

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

As shown in Table 1, there were no significant differences in terms of age, BMI, fasting blood glucose, or procalcitonin, but there were significant differences in terms of increases in systolic and diastolic blood pressure in type-2 diabetes mellitus with hypertension compared to the group without hypertension. The average procalcitonin level was 0.7 ± 1.6 ng/mL in people with type-2 diabetes mellitus who also had hypertension, as opposed to 0.8 ± 1.6 ng/mL in people without hypertension.

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

Characteristics	Total (n=122)	Diabetes Mellitus with Hypertension (n=53)	Diabetes Mellitus without Hypertension (n=69)	*p-value*
	mean ± SD	mean ± SD	mean ± SD	
Age (year)	56.7 ± 10.6	57.6 ± 8.8	56.0 ± 11.7	0.181
Body Mass Index (kg/m^2)	25.1 ± 2.7	25.1 ± 3.0	25.1 ± 2.8	0.361
Systolic blood pressure (mmHg)	134.5 ± 22.8	155.3 ± 14.5	118.6 ±12.9	<0.001*
Diastolic blood pressure (mmHg)	75.7 ± 15.4	82.6 ± 15.5	70.8 ± 13.3	<0.001*
Fasting blood glucose (mg/dL)	224 ± 74.0	228.4 ± 61.6	221.6 ± 82.6	0.372
Procalcitonin (ng/mL)	0.8 ± 1.6	0.7 ± 1.6	0.8 ± 1.6	0.217

*Statistically significant

4. Discussion

The findings of this study indicate a significant correlation between procalcitonin levels and FBG in patients with type 2 diabetes mellitus, highlighting the potential role of procalcitonin as a biomarker in managing diabetes complications. The weak positive correlation (r = 0.205) suggests that while procalcitonin levels may rise with increased FBG, other factors likely influence this relationship,

necessitating further exploration. This aligns with existing literature that emphasizes the multifaceted nature of diabetes management, where inflammation plays a critical role in the progression of vascular complications. Asirvatham *et al.,* in their prospective study evaluates procalcitonin as a reliable prognostic marker for predicting clinical outcomes in acute diabetic foot infection (DFI), finding it more effective than traditional markers such as white blood cell count, erythrocyte sedimentation rate, and C-reactive protein (CRP). [9].

Research has shown that individuals with type 2 diabetes mellitus are at an elevated risk for developing cardiovascular disease, and this heightened vulnerability can be attributed to several factors. One significant contributor is hyperglycemia, which leads to increased levels of free fatty acids, insulin resistance, oxidative stress, and advanced glycation end products, alongside disruptions in the protein kinase cascade. Furthermore, adipose tissue in these patients releases cytokines that trigger chronic inflammation and promote thrombosis. Dyslipidemia, commonly associated with type 2 diabetes, also plays a role in the progression of atherosclerosis. Importantly, functional impairments in endothelial activity occur early in diabetes development, often preceding visible morphological changes, with inflammation serving as a central factor in the onset of both atherosclerosis and hypertension. [10-12].

Moreover, the lack of significant differences in procalcitonin levels between hypertensive and non-hypertensive diabetes patients raises intriguing questions about the underlying mechanisms linking these conditions. It suggests that while hypertension is a known risk factor for diabetes-related complications, the inflammatory response—as measured by procalcitonin—may not be uniformly elevated across all individuals. These results could prompt clinicians to consider additional inflammatory markers in conjunction with procalcitonin to obtain a more comprehensive understanding of each patient's risk profile. A study carried out by Ahmed *et al* assesses procalcitonin and CRP as prognostic markers for cardiovascular complications in type 2 diabetic patients, finding that elevated procalcitonin levels are particularly indicative of such complications. [13] Our previous research found a significant correlation between high-sensitivity C-reactive protein (hs-CRP) levels and fasting blood glucose in type 2 diabetes mellitus patients, with higher hs-CRP levels observed in those with hypertension, indicating hs-CRP's potential utility in assessing cardiovascular disease risk in diabetic patients. [14].

The weaknesses of this study may stem from the inclusion of diabetic patients treated with insulin, as several studies suggest that insulin can have an anti-inflammatory effect independent of its glycemic control. Insulin has been shown to reduce inflammation through various mechanisms, including enhancing endothelial nitric oxide release and decreasing the expression of pro-inflammatory cytokines and immune mediators, such as nuclear factor kappa B (NF-kB), intercellular adhesion molecule-1, monocyte chemoattractant protein-1 (MCP-1), and several toll-like receptors (TLRs). [15].

Given the increasing prevalence of type 2 diabetes in Indonesia and concerning statistics regarding glycemic control, our study underscores the urgent need for more robust monitoring strategies; integrating procalcitonin assessments into routine clinical practice may help healthcare providers better identify patients at risk for complications and ultimately improve management outcomes. Future research should not only explore the causal pathways linking procalcitonin and fasting blood glucose, establish reference values for procalcitonin in diabetic populations, and incorporate factors such as age, duration of diabetes, and comorbid conditions, but also investigate the interactions between these inflammatory markers and various metabolic parameters, potentially leading to tailored therapeutic strategies that address the unique needs of diabetic patients, particularly those with concurrent hypertension.

5. Conclusions

In conclusion, this study highlights the significant correlation between procalcitonin levels and fasting blood glucose in patients with type 2 diabetes mellitus, suggesting the potential of procalcitonin as a valuable biomarker for monitoring diabetes-related complications. While the observed weak positive correlation indicates that additional factors may influence this relationship, it reinforces the necessity for integrated approaches in managing diabetes, particularly in regions like Indonesia where the prevalence of this condition is rising. The findings advocate for the incorporation of procalcitonin assessments into clinical practice, alongside traditional monitoring methods, to enhance patient care and risk stratification. Future research should aim to clarify the mechanisms underlying this relationship, establish reference values for procalcitonin in diabetic populations, and explore the interplay between various inflammatory markers and metabolic parameters. By doing so, healthcare providers can develop more tailored therapeutic strategies that effectively address the multifaceted needs of diabetic patients, especially those with complicated conditions such as hypertension.

Abbreviations

DM	Diabetes Mellitus
BP	Blood Pressure
FBG	Fasting Blood Glucose
BMI	Body Mass Index
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
SD	Standard Deviation
DFI	Diabetic Foot Infection
CRP	C-Reactive Protein

hs-CRP	High Sensitivity C-Reactive Protein
NF-kB	Nuclear Factor Kappa B
MCP-1	Monocyte Chemoattractant Protein-1
TLRs	Toll-Like Receptors

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Author Contributions

Diana Shintawati Purwanto: Conceptualization, Methodology, Investigation, Funding acquisition, Formal Analysis, Writing – Original Draft

Sylvia Ritta Marunduh: Conceptualization, Methodology, Investigation, Writing – Review & Editing

Stefana Helena Margaretha Kaligis: Conceptualization, Methodology, Data Curation

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Data Availability Statement

The data supporting the outcome of this research work has been reported in this manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

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Biography

Diana Shintawati Purwanto is an associate professor at Sam Ratulangi University, Biochemistry Department. She completed her Master of Laboratory Medicine from The School of Health and Biomedical Sciences at Royal Melbourne Institute of Technology, Australia in 2009, and her Clinical Pathologist Specialization Doctor from Universitas Indonesia in 2018. Apart from being a lecturer, she also works in several hospitals including Department of Clinical Laboratory, R. D Kandou Central General Hospital, Awaloei Hospital, and Budi Mulia Bitung Hospital, North Sulawesi Indonesia, as a clinical pathology specialist. So far, she has been involved in studies related to communicable and non-communicable diseases in North Sulawesi, Indonesia. She also has participated in multiple international research collaboration projects in recent years, especially with Indonesia National Research and Innovation Agency.

Research Fields

Diana Shintawati Purwanto: Hematology, Clinical Chemistry, Infectious Disease, Biomolecular, Entomology.

Sylvia Ritta Marunduh: Hematology, Imunology, Reproductive physiology, Marine nutraceutical, Physiology.

Stefana Helena Margaretha Kaligis: Medical biochemistry, Endocrinology, Metabolic disease, Molecular biology, Hematology.