

Differences in Interleukin-6 Levels in Controlled and Uncontrolled Type 2 Diabetes Mellitus Patients at Dr. M. Hatta Brain Hospital Bukittinggi

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Abstract

Diabetes Mellitus is an epidemic disease worldwide. Type 2 diabetes mellitus (T2DM) is characterized by hyperglycemia which results in inflammation. The inflammatory process will stimulate a non-specific immune response, macrophages will be activated to produce and secrete inflammatory cytokines so that there is an increase in cytokine levels, one of which is Interleukin-6 (IL-6). High levels of Interleukin-6 (IL-6) in T2DM patients cause insulin resistance and β -cell function failure. The role of Interleukin-6 (IL-6) in the pathogenesis of T2DM is considered an independent risk factor in the development of T2DM. This study aims to compare Interleukin-6 (IL-6) levels in Controlled and Uncontrolled T2DM patients. The study design was cross-sectional. Sample: Inpatients and outpatients at the Dr. M. Hatta Bukittinggi Brain Hospital with a diagnosis of T2DM. The diagnosis of T2DM was confirmed by examining blood sugar levels. Samples that met the inclusion and exclusion criteria consisted of 32 people with controlled T2DM and 32 people with uncontrolled T2DM. The total sample was 64 people. Interleukin-6 (IL-6) levels were examined using the ELISA (Enzyme Linked Immunosorbent Assay) method. Data normality was tested using the Shapiro-Wilk test. Data analysis used the Mann Whitney test. IL-6 levels in controlled T2DM patients were 69.86 pg/ml (57.95 – 114.32pg/ml). IL-6 levels in uncontrolled T2DM patients were 77.80 pg/ml (58.04 – 135.51 pg/ml). IL-6 levels in uncontrolled T2DM patients were higher than those in controlled T2DM patients. Interleukin-6 levels in uncontrolled T2DM patients were higher than those in controlled T2DM patients. There was a significant and statistically significant difference.

Keywords

Interleukin-6, Type 2 Diabetes Mellitus (T2DM), Controlled and Uncontrolled

Introduction

Diabetes mellitus is a major global health concern with rapidly increasing prevalence. Lifestyle changes and rising obesity rates have significantly contributed to the growing global prevalence of diabetes mellitus.¹ According to the International Diabetes Federation (IDF), in 2019, 463 million people (9.3% of the global

population) were living with diabetes. This number is projected to increase to 578 million by 2030 and 700 million by 2045. The World Health Organization (WHO) reported that in 2022, there were 422 million people with diabetes globally. This number is expected to rise to 643 million by 2030 and 783 million by 2045.² The number of people with diabetes in Indonesia is projected to increase two- to three-fold by 2030 compared to the year 2000.³

Diabetes mellitus is a metabolic disorder marked by elevated blood glucose levels due to impaired insulin production or action, which disrupts glucose homeostasis.⁴ As diabetes mellitus is closely linked to lifestyle, maintaining a balance in daily activities such as eating, sleeping, and physical activity is crucial. Dietary regulation is fundamental in diabetes management, requiring careful attention to caloric intake, nutrient composition, and consistent meal timing.⁵ Diabetes mellitus is generally classified into type 1 and type 2, with type 2 diabetes being the most prevalent form worldwide. It is often associated with physical inactivity and an unhealthy diet.⁶

Glycated Hemoglobin (HbA1c) testing is considered the gold standard for monitoring glycemic control in T2DM patients. HbA1c reflects the average blood glucose level over the previous 2–3 months. T2DM patients with HbA1c levels $\geq 6.5\%$ are at greater risk of developing complications compared to those with levels below 6.5%. Among inflammatory markers, Interleukin-6 (IL-6) has shown significant correlation with T2DM. IL-6 is considered an independent risk factor and a marker of insulin resistance and T2DM progression, as elevated circulating IL-6 levels are frequently observed in T2DM patients.⁷ According to a study by Angga (2024), IL-6 levels are significantly higher in uncontrolled T2DM patients compared to those with controlled T2DM. In light of the above, this study aims to investigate "Differences in Interleukin-6 Levels in Controlled and Uncontrolled Type 2 Diabetes Mellitus (T2DM) Patients at Dr. M. Hatta Bukittinggi Brain Hospital.

Material and Methods

The study design was cross-sectional by comparing Interleukin-6 Levels in Controlled and Uncontrolled Type 2 Diabetes Mellitus (T2DM) Patients. The research location was at the Dr. M. Hatta Bukittinggi Brain Hospital. The study duration was 4 months and Interleukin-6 (IL-6) examination was conducted at the Biomedical Laboratory of the Faculty of Medicine, Andalas University, Padang. The population was inpatients and outpatients at the Dr. M. Hatta Bukittinggi Brain Hospital with T2DM. Inclusion criteria: Inpatients and outpatients with T2DM, patients who routinely take medication (routine check-ups at T2DM was diagnosed based on blood glucose levels. Participants were selected based on inclusion and exclusion criteria. Leukocyte count $>10,000/\mu\text{L}$; presence of infectious comorbidities.

Patients have comorbidities accompanied by infectious diseases. The sample size uses the hypothesis test formula on the average of two independent sample populations. The minimum number of samples required is 32 people with Controlled T2DM and 32 people with Uncontrolled DMT2. Total sample 64 people. Independent variable: DMT2 patients with HbA1C $\geq 6.5\%$ (uncontrolled) and HbA1C $< 6.5\%$ (controlled). Dependent variable: Interleukin - 6 (IL-6). Serum samples were used for IL-6 analysis. Data were manually processed and tested for normality using the Shapiro-Wilk test. Bivariate analysis to compare IL-6 levels between controlled DMT2 patients and uncontrolled DMT2 patients used the Mann Whitney Test. IL-6 examination used the ELISA (Enzyme-Linked Immunosorbent Assay). IL-6 levels used the "Human IL-6 (Interleukin 6) Kit ELISA" (BT LAB Bioassay Technology Optimize Your Research). Catalog No.: E-0090Hu; Assay range: 2–600 ng/L; Sensitivity: 1.03 ng/L; 96-wells.

Ethical statement

The study protocol had been reviewed and granted ethical approval by Research Ethics Committee at the Dr. M. Hatta Brain Hospital Bukittinggi No: 002501/KEP.RSOMH BUKITTINGGI/2024.

Results

This study was conducted for 4 months at the Dr. M. Hatta Brain Hospital Bukittinggi and IL-6 examination at the Biomedical Laboratory of the Faculty of Medicine, Andalas University, Padang. This study was conducted on 32 people with Controlled T2DM and 32 people with Uncontrolled T2DM. The total sample was 64 people.

Table 1: Characteristics of Research Subjects

Respondent characteristics	Mean±SD (years)	n	Percentage
Gender Male (person)	-	25	39.1%
Female (person)	-	39	60.9%
Age (Mean±SD)	61±10	-	-

Table1 shows the distribution of research samples based on gender of the research subjects, in the female gender group there were 39 more people (60.9%) than males 25 people (39.1%) with an average age of 61±10 years.

Table 2: IL-6 Levels in Controlled and Uncontrolled T2DM Patients

Variable	IL-6 levels (pg/ml) Median (min-max)
Controlled T2DM	69.86 (57.95 – 114.32)
Uncontrolled T2DM	77.80 (58.04 – 135.51)

Table2 shows that the Median (min-max) IL-6 Levels in Uncontrolled T2DM Patients were higher at 77.80 pg/ml (58.04 – 135.51 pg/ml) compared to the IL-6 Levels in Controlled T2DM Patients at 69.86 pg/ml (57.95 – 114.32 pg/ml).

Table 3: Differences in IL-6 Levels in Controlled and Uncontrolled T2DM Patients

Variable	Distribution of IL-6 Levels (pg/ml) Mean ± SD	p*
Controlled T2DM	74,63 ±15,19	0,043
Uncontrolled T2DM	81,08 ±17,26	

*Mann – Whitney Test.

Table.3 shows the difference in IL-6 levels in controlled T2DM patients 74.63 pg/ml with a standard deviation of 15.19 with uncontrolled T2DM 81.08 pg/ml with a standard deviation of 17.26 from the results of the Mann-Whitney Test statistical test, the IL-6 levels in uncontrolled T2DM patients were higher than the IL-6 levels in controlled T2DM patients with a p value of 0.043, meaning that at 5% alpha, there was a significant difference in the average IL-6 levels between controlled and uncontrolled DM patients.

Discussion

Based on gender, more T2DM cases were observed in women (60.9%) than in men (39.1%), as shown in Table 1. This finding is consistent with Effendi et al. (2014), who reported a higher prevalence of DM among women compared to men.⁸ Similarly, Angga (2024) found that 61% of the respondents were female and 39% male.⁹ Popko K. (2010) also reported that diabetes was more prevalent among women.¹⁰ However, Moonika T. (2023) found a higher number of T2DM cases among men than women.¹¹ Women are at greater risk of developing diabetes due to a higher likelihood of increased body mass index (BMI). Hormonal changes during premenstrual syndrome and post-menopause promote fat accumulation, increasing the risk of T2DM in women.¹² Estrogen helps regulate blood glucose levels and supports fat storage, while progesterone helps normalize blood sugar and promote fat utilization.¹³

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels due to insufficient insulin production or action. A high-fat, high-cholesterol diet may impair insulin sensitivity, reducing its effectiveness in regulating blood glucose.¹⁴ Based on age, most T2DM patients fall within the 50–72 year age range.

Table 2 shows that the median IL-6 level in controlled T2DM patients was lower. T2DM patients with poor glycemic control (uncontrolled T2DM) tend to have higher IL-6 levels. High IL-6 levels increase the risk of complications in uncontrolled T2DM patients. T2DM is characterized by hyperglycemia, which promotes inflammation. Elevated IL-6 levels in T2DM patients worsen insulin resistance and may accelerate the onset of diabetes-related complications.

Table 3 shows that the mean IL-6 level in controlled T2DM patients was 74.63 pg/ml, while in uncontrolled T2DM patients it was 81.08 pg/ml. Verify values; if accurate than in controlled T2DM (4.37 pg/ml); however, this value appears inconsistent with previous data. According to Chanchira et al. (2017), elevated IL-6 levels were associated.

Conclusion and Recommendations

Based on this study, it can be concluded that Interleukin-6 Levels in Uncontrolled Type 2 Diabetes Mellitus (T2DM) Patients are higher compared to Controlled Type 2 Diabetes Mellitus (T2DM) Patients, there is a significant and statistically significant difference.

Further research is needed on other factors related to T2DM and other inflammatory mediators. For people with diabetes mellitus, they must control their blood sugar well, so that complications that may occur can be prevented.

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Conflict of Interest Disclosure

None to declare.

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