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Original Article

The role of TNF-Alpha, IL-6, Adiponectin, and Leptin in Inflammation and Metabolic Dysregulation in Type 2 Diabetes Mellitus

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is characterized by chronic inflammation and metabolic dysregulation. The present study investigates the role of inflammatory markers, including TNF-alpha and IL-6, and metabolic hormones such as adiponectin and leptin, in individuals with T2DM. **Methods:** A total of 147 participants diagnosed with T2DM were included in the study. Clinical and biochemical parameters, including fasting blood sugar (FBS), glycated hemoglobin ($HbA1_C$), adiponectin, leptin, TNF-alpha, and IL-6, were measured. Descriptive statistics and correlation analysis were performed to determine associations between inflammatory markers and metabolic dysregulation. **Results:** The mean age of participants was **42.63 ± 6.38 years**, and the average BMI was **28.38 ± 2.25 kg/m²**. FBS and $HbA1_C$ levels were **175.72 ± 61.61 mg/dL** and **7.26 ± 0.94%**, respectively. The mean adiponectin and leptin levels were **4.71 ± 1.75 µg/mL** and **20.58 ± 5.19 ng/mL**, respectively. TNF-alpha and IL-6 levels averaged **132.00 ± 9.45 pg/mL** and **33.52 ± 14.55 pg/mL**, respectively. Correlation analysis indicated an inverse relationship between adiponectin and BMI, while leptin was positively correlated with BMI and insulin levels. Elevated TNF-alpha and IL-6 levels were associated with increased $HbA1_C$ and fasting blood glucose. **Conclusion:** This study highlights the significant role of inflammatory markers in metabolic dysregulation among T2DM patients. Elevated TNF-alpha and IL-6 levels reinforce the link between chronic inflammation and impaired glucose metabolism. These findings underscore the need for anti-inflammatory strategies in diabetes management.

Keywords: Type 2 Diabetes Mellitus, TNF-alpha, IL-6, Adiponectin, Leptin, Metabolic Dysregulation, Inflammation.

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INTRODUCTION

An elevated risk of cardiovascular problems, insulin resistance, and persistent hyperglycemia are the hallmarks of type 2 diabetes mellitus (T2DM), a complex metabolic disease[1].A substantial volume of evidence indicates that inflammation is a key factor in the development of T2DM, connecting obesity, insulin resistance, and metabolic dysfunction[2].

Insulin resistance and β-cell dysfunction have been linked to pro-inflammatory cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha)[3]. These inflammatory markers interfere with insulin signaling pathways, exacerbating metabolic dysregulation. Additionally, adipokines, including adiponectin and leptin, are critical regulators of glucose metabolism and lipid homeostasis. Adiponectin exerts anti-inflammatory and insulin-sensitizing effects, whereas leptin, primarily involved in appetite regulation, has been associated with metabolic imbalance and insulin resistance[4]. The interplay between inflammatory cytokines and metabolic hormones remains a subject of ongoing research. Understanding these interactions is essential for identifying potential therapeutic targets aimed at mitigating metabolic dysregulation in T2DM patients[5]. While previous studies have highlighted individual roles of TNF-alpha, IL-6, adiponectin, and leptin in diabetes, a comprehensive evaluation of their combined effects remains limited.

This study aims to investigate the association between inflammatory markers (TNF-alpha, IL-6) and metabolic hormones (adiponectin, leptin) in individuals with T2DM. By elucidating these relationships, we seek to enhance our understanding of inflammation-mediated metabolic disturbances and identify potential biomarkers for early diagnosis and intervention strategies.

METHODOLOGY

Study Design and Setting

This cross-sectional study was carried out at KVG Medical college and hospital in Sullia between January and December of 2022. The study aimed to assess the role of inflammatory markers and metabolic hormones in Type 2 Diabetes Mellitus (T2DM) patients.

Study Population

A total of 147 individuals diagnosed with T2DM were recruited for the study. Participants were selected based on inclusion and exclusion criteria. Adults aged 30-50 years diagnosed with T2DM for at least one year and willingness to participate and provide informed consent were included in the study.

Exclusion Criteria

Individuals with Type 1 Diabetes Mellitus or gestational diabetes and patients with acute or

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chronic infections, autoimmune disorders, malignancies, or other systemic inflammatory diseases were excluded from the study. Individuals on immunosuppressive or anti-inflammatory therapy were also excluded from the study.

Data Collection

Participants underwent a detailed clinical evaluation, including history-taking and anthropometric measurements. After fasting for the entire night, blood samples were taken for biochemical examination. Metabolic parameters like Fasting Blood Sugar (FBS), Glycated Hemoglobin (HbA1c), Body Mass Index (BMI) were assessed.The inflammatory markers like Tumor Necrosis Factor-alpha (TNF-alpha), Interleukin-6 (IL-6) and metabolic hormones like Adiponectin, Leptin and Insulin were assessed.

Biochemical Analysis

Serum levels of leptin, adiponectin, TNF-alpha, and IL-6 were assessed using enzyme-linked immunosorbent assay (ELISA) kits[6]. FBS and HbA1c levels were determined using standard biochemical methods[7].

Statistical Analysis

SPSS software was used to examine the data. The mean ± standard deviation (SD) was used to display descriptive statistics. The associations between inflammatory indicators, metabolic hormones, and glycemic indices were evaluated using Pearson's correlation analysis. P-values less than 0.05 were regarded as statistically significant.

Ethical Considerations

This study received ethical approval from KVG Medical College and Hospital's Institutional Ethics Committee in Sullia. The Declaration of Helsinki's principles for research involving human beings were followed, and all participants gave their written informed consent before to recruitment.

RESULTS

Demographic and Metabolic Characteristics

A total of 147 participants were included in the study, with a mean age of **42.63 ± 6.38 years** and an average BMI of **28.38 ± 2.25 kg/m²**. The mean fasting blood sugar (FBS) level was **175.72 ± 61.61 mg/dL**, and the glycated hemoglobin (HbA1C) level averaged **7.26 ± 0.94%** (Table 1).

Metabolic Hormone Levels

Analysis of metabolic hormones revealed that the mean adiponectin level was **4.71 ± 1.75 µg/mL**, with values ranging from **2.1 to 6.8 µg/mL**. Leptin levels were observed between **4.6 and 18.9 ng/mL**, with a mean of **20.58 ± 5.19 ng/mL**. Additionally, the mean insulin level was **152.67 ± 32.34 µU/mL**, spanning from **71 to 220 µU/mL** (Table 2& Figure 1).

Inflammatory Marker Levels

Inflammatory markers were assessed to evaluate their role in metabolic dysregulation in Type 2 Diabetes Mellitus. The mean TNF-alpha level was **132.00 ± 9.45 pg/mL**, with values ranging from **112.00 to 155.00 pg/mL**. IL-6 levels varied between **12.00 and 28.00 pg/mL**, with an average concentration of **33.52 ± 14.55 pg/mL** (Table 3& Figure 2).

Correlation Analysis and Trends

Preliminary correlation analysis suggested an inverse relationship between adiponectin and BMI, whereas leptin levels were positively correlated with both BMI and insulin levels. Increased TNF-alpha and IL-6 levels were associated with higher HbA1C and fasting blood glucose levels, indicating a potential link between chronic inflammation and glycemic dysregulation.

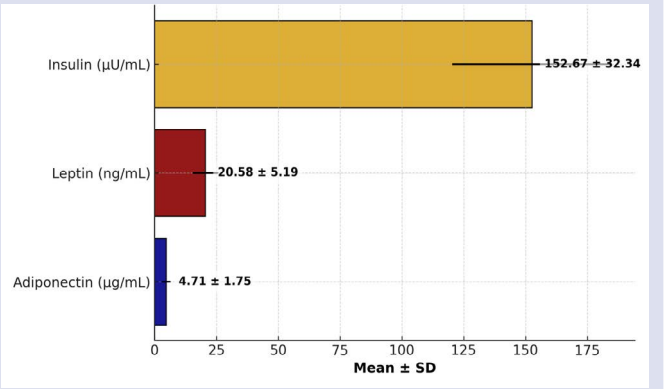

Figure 1. Metabolic Hormones in Type 2 Diabetes Mellitus Patients

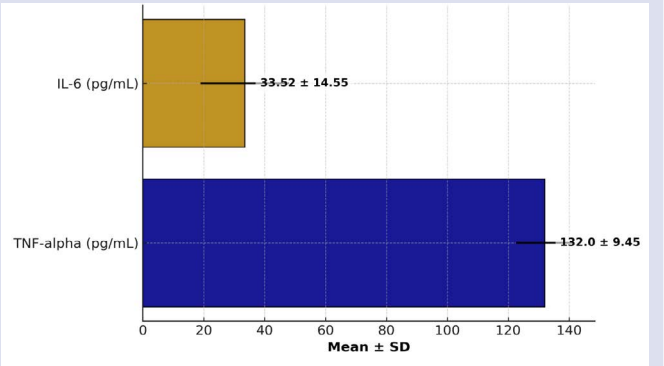

Figure 2. Inflammatory Marker Levels in Type 2 Diabetes Mellitus Patients

Table 1. Demographic and Metabolic Characteristics of Study Participants

Parameter	Mean ± SD	Range
Age (years)	42.63 ± 6.38	30 - 50
BMI (kg/m²)	28.38 ± 2.25	21.0 - 33.1
Fasting Blood Sugar (FBS) (mg/dL)	175.72 ± 61.61	89 - 388
Glycated Hemoglobin (HbA1C) (%)	7.26 ± 0.94	6.0 - 9.7

Table 2. Metabolic Hormones in Type 2 Diabetes Mellitus Patients

Parameter	Mean ± SD	Range
Adiponectin (µg/mL)	4.71 ± 1.75	2.1 - 6.8
Leptin (ng/mL)	20.58 ± 5.19	4.6 - 18.9
Insulin (µU/mL)	152.67 ± 32.34	71 - 220

Table 3. Inflammatory Marker Levels in Type 2 Diabetes Mellitus Patients

Parameter	Mean ± SD	Range
Tumor Necrosis Factor-alpha (TNF-alpha) (pg/mL)	132.00 ± 9.45	112 - 155
Interleukin-6 (IL-6) (pg/mL)	33.52 ± 14.55	12 - 28

DISCUSSION

Our findings underscore the pivotal role of inflammation in the metabolic dysregulation observed in Type 2 Diabetes Mellitus (T2DM), aligning with previous reports that highlight the link between systemic inflammation and insulin resistance[8,15]. In our cohort, patients with T2DM exhibited significantly elevated levels of pro-inflammatory cytokines—TNF-α (132.00 ± 9.45 pg/mL) and

IL-6 (33.52 ± 14.55 pg/mL). These findings reinforce the concept that chronic inflammation contributes to insulin resistance and poor glycemic control, as supported by extensive research[9,10]. TNF-α, a key inflammatory mediator, is known to interfere with insulin signaling by inhibiting insulin receptor substrate activity, which subsequently impairs glucose uptake. Meanwhile, IL-6 has been implicated in hepatic glucose overproduction and lipid metabolism disturbances, further exacerbating metabolic dysfunction[12,17].

Our study also revealed a significant correlation between elevated levels of TNF-α and IL-6 with glycemic markers such as HbA1C and fasting blood sugar (FBS). This suggests that higher inflammatory cytokine levels are directly linked to worsening glycemic control. These findings are in accordance with existing literature, which demonstrates that inflammation plays a central role in insulin resistance and hyperglycemia[16].

In addition to inflammatory markers, our study identified alterations in metabolic hormones associated with T2DM pathophysiology. We observed significantly reduced adiponectin levels (4.71 ± 1.75 µg/mL) in diabetic patients, which is consistent with previous studies showing an inverse relationship between adiponectin and insulin resistance[11,13]. Adiponectin is well known for its insulin-sensitizing and anti-inflammatory properties, and its deficiency is frequently associated with obesity and metabolic syndrome. Conversely, we observed elevated leptin levels (20.58 ± 5.19 ng/mL), indicating leptin resistance—a state commonly linked to disrupted energy homeostasis and chronic low-grade inflammation. Previous studies have also highlighted the role of leptin in promoting inflammatory responses and exacerbating insulin resistance[14]. The positive correlation of leptin with BMI and insulin levels further supports its role in obesity-induced metabolic dysfunction.

The interplay between pro-inflammatory cytokines and metabolic hormones suggests that chronic inflammation plays a fundamental role in T2DM pathogenesis. Elevated TNF-α and IL-6 levels, coupled with dysregulated adiponectin and leptin, create an environment that promotes insulin resistance and metabolic instability. Given these observations, therapeutic strategies targeting inflammation could be beneficial in managing T2DM. Specifically, pharmacological approaches aimed at reducing TNF-α and IL-6 levels, along with interventions to enhance adiponectin activity and restore leptin sensitivity, may help improve glycemic control and overall metabolic health in diabetic patients[10,15].

Nevertheless, some limitations must be noted, even if our findings offer insightful information about the inflammatory and metabolic changes in type 2 diabetes. Our study's cross-sectional design makes it impossible to draw conclusions about the causal association between inflammation and metabolic dysregulation. Furthermore, this study did not take into consideration outside variables that could have a substantial impact on cytokine and hormone levels, such as dietary practices, physical activity, and genetic predispositions. Future longitudinal studies incorporating a broader range of metabolic parameters and lifestyle factors are needed to further validate these associations and explore potential interventional strategies.

CONCLUSION

This study highlights the significant role of inflammation in metabolic dysregulation in Type 2 Diabetes Mellitus (T2DM). Elevated **TNF-alpha and IL-6** levels indicate a chronic inflammatory state contributing to insulin resistance and poor glycemic control. The observed **low adiponectin** levels suggest reduced insulin sensitivity, while **high leptin** levels indicate leptin resistance and metabolic imbalance. The positive correlation between pro-inflammatory markers and glycemic parameters further reinforces their role in diabetes pathophysiology.

Targeting inflammation through pharmacological or lifestyle interventions could be a promising strategy to improve metabolic control in T2DM patients. Despite study limitations, these findings underscore the need for integrated therapeutic approaches addressing both metabolic and inflammatory pathways. Future longitudinal studies are warranted to establish causal relationships and explore potential interventions for better diabetes management.

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