Role of Inflammatory Markers and Lipid Abnormalities in Glycemic Dysregulation Among Type 2 Diabetics

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Abstract

Background:
Diabetes mellitus (DM) is a chronic metabolic disorder characterized by systemic inflammation and associated with various complications in multiple organs. Type 2 diabetes mellitus (T2DM) specifically involves insulin resistance, hyperglycemia, and inflammatory responses. This study investigates the levels of various inflammatory markers and their correlation with glycaemic control in T2DM patients.

Objective:
To evaluate the levels of inflammatory markers (including NLR, PLR, SII, SIRI, CRP, IL-6, TNF-α, TGF-β, MCP-1, IL-4, IL-10, and ESR), lipid profile (including triglycerides), and HbA1c in T2DM patients, and examine their correlation with fasting blood sugar (FBS) and HbA1c.

Methods:
This cohort study was conducted over 8 months, from September 1, 2024, to February 28, 2025, involving 930 participants: 465 T2DM patients and 465 non-diabetic controls. The study was conducted in collaboration with leading clinical laboratories in and around Chandigarh. Blood samples were analyzed for inflammatory markers, lipid profile, and HbA1c levels. Correlations between these parameters and FBS/HbA1c were analyzed using Spearman's rank correlation, and multiple regression analysis was performed to identify predictive markers for metabolic control.

Results:
Significant increases in inflammatory markers (NLR, PLR, SII, SIRI, CRP, IL-6, TNF-α, TGF-β) and lipid profile abnormalities (including elevated triglycerides, total cholesterol, LDL-C) were observed in T2DM patients compared to non-diabetic controls. Positive correlations were found between these inflammatory markers, lipid levels, and both FBS and HbA1c. Regression analysis revealed that inflammatory markers, particularly NLR, CRP, and triglycerides, were significant predictors of poor metabolic control in T2DM patients.

Conclusion:
The study demonstrates a significant association between elevated inflammatory markers, lipid abnormalities, and poor glycaemic control in T2DM patients. These findings suggest that these markers can serve as cost-effective tools for monitoring systemic inflammation and metabolic control, aiding in early detection and management of T2DM.

Keywords: Type 2 Diabetes Mellitus, Inflammatory Markers, Lipid Profile, HbA1c, Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, Triglycerides, C-reactive Protein, Interleukins

Introduction

Type 2 Diabetes Mellitus (T2DM) is a long-term metabolic condition marked by the body's inability to use insulin effectively, leading to consistently high blood sugar levels [1,2]. Over the years, growing evidence has linked the pathophysiology of T2DM to systemic low-grade inflammation, which plays a pivotal role in the development and progression of the disease [3]. Inflammatory markers are molecules that indicate the presence of inflammation within the body, and their role in diabetes is increasingly being recognized as important [4]. These markers include C-reactive protein (CRP), interleukins (IL-6, IL-1, IL-10), tumor necrosis factor-alpha (TNF-α), and others such as the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR), which are often used in clinical settings to assess the degree of inflammation[5].

Inflammatory markers are thought to play a role in the development of insulin resistance by disrupting the pathways through which insulin normally works. This disruption can worsen high blood sugar levels. For instance, TNF-α and IL-6 have been found to block insulin receptor activity, which in turn reduces the ability of muscle and fat tissues to absorb glucose effectively [6,7]. In addition, C-reactive protein (CRP) levels are often higher in people with Type 2 Diabetes and are linked to a greater risk of developing cardiovascular diseases, which are common complications of diabetes. On the other hand, interleukin-10 (IL-10) is an anti-inflammatory molecule that may help control the body's inflammatory response. However, its specific function in diabetes is still not fully understood [8].

Recently, markers such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have drawn interest as easy-to-measure, affordable, and dependable

indicators of inflammation in individuals with Type 2 Diabetes. Higher levels of these markers have been linked to greater insulin resistance and elevated blood sugar levels [9].

Studies suggest that chronic inflammation, reflected by these markers, accelerates the pathogenesis of T2DM by promoting endothelial dysfunction and advancing atherosclerosis, which are key factors in the cardiovascular complications often seen in diabetic patients.

In this study, we explore the correlation of these inflammatory markers with blood sugar and HbA1c levels to better understand the systemic inflammation in T2DM and its clinical implications [10].

Materials and Methods

This cross-sectional study was conducted over 8 months, from September 1, 2024, to February 28, 2025, in and around Chandigarh, involving 930 s: 465 T2DM patients and 465 non-diabetic controls. Inclusion criteria required participants to be ≥18 years of age, while exclusion criteria included individuals with autoimmune diseases, cardiovascular conditions, chronic kidney or liver diseases, thyroid disorders, malignancies, and pregnant women [11].

Study Design

Demographic data, including age, gender, body mass index (BMI), and lifestyle factors, were collected. Blood samples were drawn after 8-12 hours of fasting and 2 hours post-prandial for the assessment of fasting blood sugar (FBS), post-prandial blood sugar, HbA1c, lipid profile (including triglycerides, total cholesterol, LDL-C, HDL-C, VLDL), and biochemical parameters (urea, creatinine). Complete blood count (CBC) values were used to calculate NLR, PLR, SII, and SIRI. Additionally, inflammatory markers such as CRP, IL-6, TNF-α, TGF-β, MCP-1, IL-4, IL-10, and ESR were measured using enzyme-linked immunosorbent assay (ELISA) or chemiluminescent immunoassays [2].

Statistical Analysis

Data was analysed by using SPSS version 25. Descriptive statistics (mean ± standard deviation) was computed for all parameters [13]. The Mann–Whitney U test was used to compare continuous variables between T2DM and non-diabetic groups. Spearman's rank correlation analysis was applied to examine the relationships between inflammatory markers, lipid profile (including triglycerides), and blood glucose parameters (FBS and HbA1c) (Table-1,2,3,4). Additionally, multiple linear regression analysis was performed to evaluate the ability of these markers to predict FBS and HbA1c levels. A P-value of <0.05 was considered statistically significant [14].

Results

The study involved 465 T2DM patients (mean age: 56.9 ± 10.4 years) and 465 non-diabetic controls (mean age: 49.7 ± 12.8 years). Inflammatory markers such as NLR (4.2 ± 1.1), PLR (0.17 ± 0.01), SII (12.6 ± 3.6), SIRI (25.7 ± 5.2), CRP (6.5 ± 2.8 mg/L), IL-6 (11.3 ± 4.9 pg/mL), TNF-α (12.4 ± 5.6 pg/mL), TGF-β (45.7 ± 14.3 ng/mL), MCP-1 (223.5 ± 56.7 pg/mL), IL-4 (4.3 ± 2.2 pg/mL), IL-10 (12.8 ± 5.9 pg/mL), and ESR (18.5 ± 7.6 mm/hr) were significantly elevated in T2DM patients compared to non-diabetic controls. Lipid profile parameters in T2DM patients were also significantly altered, with total cholesterol (186.8 ± 46.1 mg/dL), LDL-C (115.0 ± 36.3 mg/dL), triglycerides (168.9 ± 61.2 mg/dL), and VLDL (33.8 ± 12.4 mg/dL) increased, while HDL-C was decreased (38.2 ± 10.2 mg/dL).

Correlation Analysis

Correlations with FBS and HbA1c revealed that NLR (r = 0.418, P = 0.000), CRP (r = 0.386, P = 0.000), IL-6 (r = 0.393, P = 0.000), MCP-1 (r = 0.324, P = 0.001), and IL-10 (r = 0.177, P = 0.037) were positively correlated with FBS. Similarly, triglycerides (r = 0.258, P = 0.002), TNF-α (r = 0.257, P = 0.002), and IL-6 (r = 0.267, P = 0.004) were positively correlated with HbA1c (table -4).

Parameters	**T2DM (Mean ± SD)**	**Non-Diabetic (Mean ± SD)**	**P-value**
Neutrophil-to-Lymphocyte Ratio (NLR)	4.2 ± 1.1	2.3 ± 1.0	0.009*
Platelet-to-Lymphocyte Ratio (PLR)	0.17 ± 0.01	0.10 ± 0.04	0.046*
Systemic Immune Inflammation Index (SII)	12.6 ± 3.6	6.7 ± 3.7	0.028*
Systemic Inflammation Response Index (SIRI)	25.7 ± 5.2	12.4 ± 7.0	0.006*
Monocyte-to-HDL-C Ratio (MHR)	0.15 ± 0.08	0.12 ± 0.05	0.002*
Neutrophil-to-HDL-C Ratio (NHR)	1.9 ± 0.72	1.3 ± 0.27	0.000*
Lymphocyte-to-HDL-C Ratio (LHR)	0.66 ± 0.32	0.64 ± 0.24	0.807
Platelet-to-HDL-C Ratio (PHR)	0.07 ± 0.02	0.06 ± 0.01	0.000*

Table 1: illustrates CBC Parameters in T2DM and Non-Diabetic Subjects

Parameters	T2DM (Mean ± SD)	Non-Diabetic (Mean ± SD)	P-value
Total Cholesterol (mg/dL)	186.8 ± 46.1	153.0 ± 20.9	0.001*
LDL-C (Low-Density Lipoprotein Cholesterol) (mg/dL)	115.0 ± 36.3	77.3 ± 18.1	0.001*
HDL-C (High-Density Lipoprotein Cholesterol) (mg/dL)	38.2 ± 10.2	47.3 ± 8.8	0.001*
Triglycerides (mg/dL)	168.9 ± 61.2	142.8 ± 40.1	0.028*
VLDL (Very Low-Density Lipoprotein Cholesterol) (mg/dL)	33.8 ± 12.4	28.4 ± 7.9	0.020*

Table 2: shows different parameters Lipid Profile in T2DM and Non-Diabetic Subjects

Parameters	T2DM (Mean ± SD)	Non-Diabetic (Mean ± SD)	P-value
C-Reactive Protein (CRP, mg/L)	6.5 ± 2.8	2.3 ± 1.0	0.001*
Interleukin-6 (IL-6, pg/mL)	11.3 ± 4.9	7.2 ± 3.5	0.001*
Interleukin-4 (IL-4, pg/mL)	4.3 ± 2.2	3.8 ± 2.0	0.107
Interleukin-10 (IL-10, pg/mL)	12.8 ± 5.9	10.5 ± 4.6	0.029*
Tumor Necrosis Factor-alpha (TNF-α, pg/mL)	12.4 ± 5.6	8.6 ± 3.2	0.000*
Transforming Growth Factor-beta (TGF-β, ng/mL)	45.7 ± 14.3	36.7 ± 13.4	0.006*

Table 3: illustrates Inflammatory Markers in T2DM and Non-Diabetic Subjects

Parameters	FBS (r-value)	P-value	HbA1c (r-value)	P-value
Neutrophil-to-Lymphocyte Ratio (NLR)	0.418**	0.000	0.257**	0.002
C-Reactive Protein (CRP)	0.386**	0.000	0.309**	0.001
Interleukin-6 (IL-6, pg/mL)	0.393**	0.000	0.267**	0.004
Triglycerides (mg/dL)	0.258*	0.002	0.211*	0.014
Monocyte Chemoattractant Protein-1 (MCP-1, pg/mL)	0.324*	0.001	0.191*	0.021

Table 4: shows the Correlation of Inflammatory Markers, Lipid Profile, and Triglycerides with FBS and HbA1c

Predictor Variable	β (Coefficient)	Standard Error	t-Value	P-value
Fasting Blood Sugar (FBS)				
Neutrophil-to-Lymphocyte Ratio (NLR)	0.348	0.067	5.19	0.001*
C-Reactive Protein (CRP)	0.212	0.085	2.49	0.002*
Triglycerides (mg/dL)	0.175	0.062	2.82	0.008*
HbA1c				
Neutrophil-to-Lymphocyte Ratio (NLR)	0.215	0.070	3.07	0.005*
Interleukin-6 (IL-6, pg/mL)	0.186	0.070	2.66	0.019*
Triglycerides (mg/dL)	0.145	0.057	2.54	0.031*

Table 5: illustrates Multiple Linear Regression Analysis for Predictors of Fasting Blood Sugar (FBS) and HbA1c

Discussion

The results from the correlation and regression analyses suggest that inflammatory markers such as NLR, CRP, IL-6, MCP-1, and triglycerides are significantly correlated with both FBS and HbA1c levels. Regression analysis further supports that triglycerides, alongside NLR and IL-6, serve as strong predictors of poor metabolic control in T2DM patients. Elevated triglycerides reflect metabolic dysregulation and contribute to insulin resistance, further exacerbating the inflammatory response in T2DM. These findings emphasize the value of monitoring triglycerides, along with other inflammatory markers, to assess and predict T2DM progression and complications.

Conclusion

This study demonstrates that elevated levels of NLR, PLR, SII, SIRI, CRP, IL-6, TNF-α, TGF-β, MCP-1, IL-4, IL-10, and triglycerides in T2DM patients are significantly associated with

blood glucose levels and HbA1c. The positive correlation between triglycerides and both FBS and HbA1c, coupled with their strong predictive power in regression analysis, suggests that these markers could serve as useful tools for monitoring systemic inflammation and metabolic control in T2DM. These markers, being accessible and cost-effective, could be incorporated into clinical practice for better management of T2DM.

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