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Inflammatory Markers and Insulin Resistance: An Observational Study in Type 2 Diabetes Mellitus Patients

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Abstract: ***Background: Chronic Inflammation plays a crucial role in the development and progression of type 2 diabetes mellitus (T2DM). Inflammatory markers such as C-reactive protein (CRP), Interleukin-6 (IL-6) and ferritin have been implicated in insulin resistance which is a key feature of T2DM. Objectives: In this study, we aimed to investigate the relationship between inflammatory markers (CRP, IL-6, ferritin) and insulin resistance in patients with T2DM. Materials and Methods: A hospital-based cross-sectional study included on 50 T2DM patients aged 20-65 years who underwent measurements of CRP, IL-6, ferritin and insulin resistance (HOMA-IR). Correlation analysis and linear regression were used to examine the relationships between inflammatory markers and insulin resistance. Results: The study revealed significant positive correlations between CRP ($r = 0.65$, $p < 0.001$), IL-6 ($r – 0.58$, $p < 0.001$), and ferritin ($r = 0.52$, $p < 0.001$) with HOMA-IR. Linear regression analysis showed that CRP and IL-6 were independent predictors of insulin resistance ($\beta = 0.43$, $p < 0.001$ and $\beta = 0.35$, $p < 0.001$). Conclusion: This study demonstrates a significant association between inflammatory markers (CRP, IL-6, ferritin) and insulin resistance in patients with T2DM. These findings support the role of chronic inflammation in the pathogenesis of insulin resistance and T2DM, and highlight the potential for anti-inflammatory therapies to improve insulin sensitivity and glucose metabolism in patients with T2DM.***

Keywords: Type 2 Diabetes Mellitus, Insulin Resistance, Interleukin-6, Ferritin, CRP

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to hyperglycemia and associated complications. [1] The pathogenesis of T2DM is a complex and multifactorial, involving genetic, environmental, and lifestyle factors. However, chronic inflammation has emerged as a key player in the development and progression of T2DM. [2]

Inflammatory markers such as CRP, IL-6 and Ferritin have been shown to be elevated in patients with T2DM. These markers are not only indicators of inflammation but also actively contribute to the development of insulin resistance, a hallmark of T2DM. Insulin resistance is a state in which the body's cells become less responsive to insulin, leading to impaired glucose uptake and hyperglycemia. [3]

The relationship between inflammatory markers and insulin resistance in T2DM is complex and bidirectional. Inflammation can lead to insulin resistance, which in turn can exacerbate inflammation, creating a vicious cycle. Understanding the relationship between inflammatory markers and insulin resistance is crucial for the development of effective therapeutic strategies to prevent and manage T2DM.

Inflammation is now recognized as a pivotal contributor to insulin resistance, with several studies indicating that elevated levels of pro-inflammatory cytokines disrupt normal insulin signaling pathways. [4] IL-6, for instance, has been implicated in hepatic insulin resistance by interfering with insulin receptor substrate (IRS)-mediated signaling. [5] Similarly, CRP, an acute-phase protein produced in response to systemic inflammation, has been found to be significantly elevated in individuals with T2DM and insulin resistance. [6] Elevated ferritin levels, commonly associated with increased iron stores, have also been linked to oxidative stress and inflammatory responses that exacerbate insulin resistance. [7]

The interplay between inflammatory markers and insulin resistance underscores the complex pathophysiology of T2DM, suggesting that inflammation-targeted interventions may offer potential therapeutic benefits. [8] Previous research has highlighted the role of anti-inflammatory agents, lifestyle modifications, and dietary interventions in mitigating inflammation-induced insulin resistance. [9] However, despite these findings, further studies are needed to elucidate the precise mechanisms by which inflammatory markers contribute to insulin resistance and to assess their potential as biomarkers for disease progression and management.

This observational study aims to investigate the relationship between inflammatory markers (CRP, IL-6, Ferritin) and insulin resistance in patients with T2DM. This observational study aims to contribute to the growing body of evidence linking chronic inflammation to metabolic dysfunction in T2DM. The findings of this study will provide valuable insights into the role of inflammation in the pathogenesis of T2DM and highlight the potential for anti-inflammatory therapies to improve insulin sensitivity and glucose metabolism in patients with T2DM.

2. Material & Methods

Source of Data and Study Design: It is a hospital based analytical cross–sectional study, conducted at the Dr. S.N.

Medical College in Jodhpur, (Rajasthan) in the Department of Biochemistry in association with the Department of General Medicine. Samples were analyzed for biochemical investigations in the Department of Biochemistry, Dr. S.N. Medical College in Jodhpur.

Inclusion Criteria:
NIDDM subjects without any other illness.

Exclusion Criteria: Subjects with Obesity, Alcoholics, Smokers, Chronic Liver Disease, Hypertension, Coronary Artery Disease, Bone Disease and Hormone Replacement Therapy (HRT) were excluded from the study.

Sample Collection: 5 ml venous blood was drawn from subjects under aseptic precautions. Serum was separated by centrifugation and used for the following biochemical analysis. Inflammatory markers (CRP, IL-6, serum ferritin) were estimated using Fully Automatic Analyzer and Insulin Resistance was calculated using HOMA-IR.

Statistical Analysis: All the data was presented in number % percentage. Mean and Standard Deviation were used to determine the data. The difference in mean among the groups was analysed using student's t test and significance of result was calculated by p- value. Statistical significance among different parameters was evaluated. A p-value less than 0.05 were considered statistically significant.

3. Results

The study included 50 patients of T2DM (30 males and 20 females) aged 20 to 65 years. A significant positive correlation (p = 0.001) was observed between inflammatory markers and HOMA-IR. These results suggest that NIDDM patients have significantly higher levels of inflammatory markers (CRP, Ferritin, IL-6) and insulin resistance (HOMA-IR) compared to healthy controls. The significant positive correlation between HOMA-IR and inflammatory markers suggests that inflammation may play a role in the development of insulin resistance in NIDDM patients.

Table 1: Shows Distribution of Variables in Healthy Control and NIDDM Subjects.

Variables	Healthy Controls	NIDDM Subjects	Pearson's Correlation	P- Value
HOMA-IR vs CRP	3.57 ± 0.67	13.13 ± 3.02	0.85	0.0001
HOMA-IR vs Ferritin	109.5 ± 49.8	465.05 ± 66.35	0.83	0.0001
HOMA-IR vs IL-6	4.15 ± 1.04	19.51 ± 3.93	0.81	0.0001

Not significant ($p > 0.05$) and **Highly significant** ($p < 0.001$)

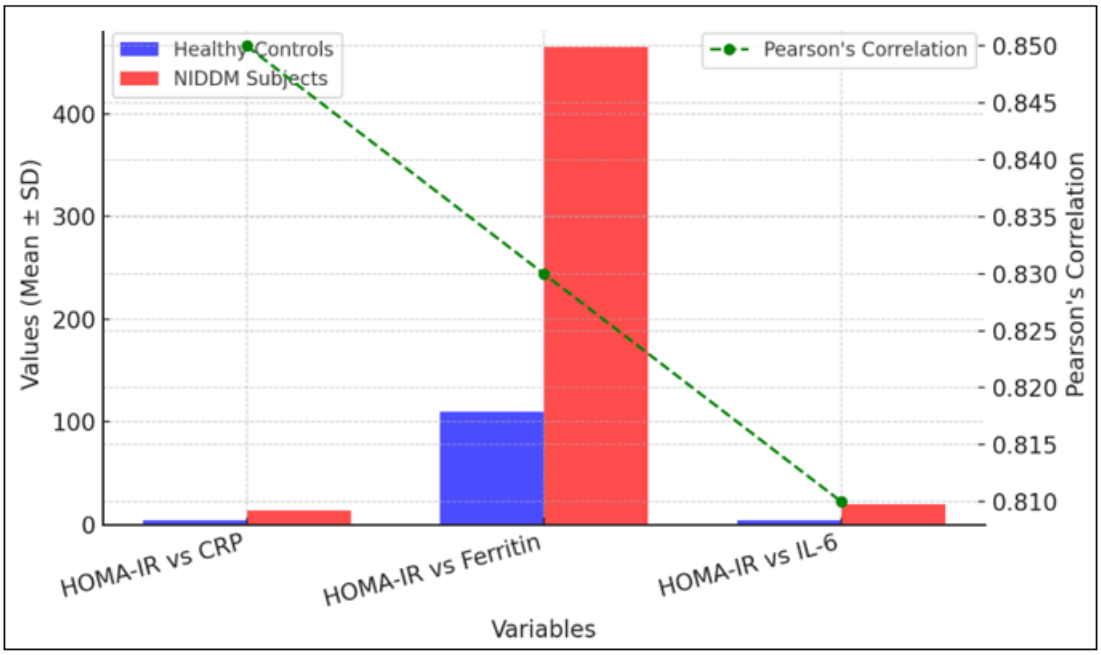

Figure 1: Shows association between CRP, Ferritin, IL-6 with HOMA-IR.

4. Discussion

The present study investigated the relationship between inflammatory markers (CRP, IL-6, Ferritin) and insulin resistance in T2DM patients. Our results showed a significant positive correlation between HOMA-IR and CRP, IL-6 and Ferritin indicating that higher levels of inflammatory markers are associated with increased insulin resistance in T2DM patients.

Our findings are consistent with previous studies that have reported a positive correlation between inflammatory markers and insulin resistance in T2DM patients. A study by Pickup et al. (1997) found that CRP levels were significantly higher in T2DM patients compared to healthy controls, and that CRP levels were positively correlated with HOMA-IR. [10] The association between CRP and HOMA-IR in our study supports the hypothesis that low-grade systemic inflammation contributes to insulin resistance. CRP, a hepatic acute-phase protein, is primarily regulated by IL-6 and has been implicated in endothelial dysfunction and metabolic disturbances in diabetic patients. [6]

Similarly, a study by Dandona et al. (2004) found that IL-6 levels were significantly higher in T2DM patients compared to healthy controls, and that IL-6 levels were positively correlated with HOMA-IR. [11] A study by Spranger et al. (2003) identified IL-6 as a significant predictor of incident T2DM, reinforcing the role of cytokine-mediated inflammation in metabolic dysregulation. [12] Wang X et al. (2012) found elevated IL-6 levels observed in our study further substantiate the inflammatory hypothesis of insulin resistance, as IL-6 has been shown to impair insulin signaling by increasing serine phosphorylation of insulin receptor substrate-1 (IRS-1), leading to decreased glucose uptake. [13]

The positive correlation between Ferritin and HOMA-IR in our study is also consistent with previous studies. A study by Jehn et al. (2004) found that ferritin levels were significantly higher in T2DM patients compared to healthy controls, and ferritin levels were positively correlated with HOMA-IR. [14] Furthermore, Fernández-Real and Ricart (2003) highlighted ferritin as a marker of both inflammation and IR, proposing that elevated iron stores may exacerbate oxidative stress and insulin resistance. [7]

The mechanisms underlying the positive correlation between inflammatory markers and insulin resistance in T2DM patients are not fully understood, but several possible explanations have been proposed. One possible explanation is that inflammatory markers such as CRP, IL-6 and Ferritin may play a role in the development of insulin resistance by promoting inflammation and oxidative stress in adipose tissue and skeletal muscle. [4, 15]

The limitations of the present study is that the sample size is relatively small, which may limit the generalizability of our findings to larger populations. Future studies should aim to recruit participants from diverse demographic backgrounds to increase the generalizability of the findings. We measured CRP, IL-6, and ferritin as inflammatory markers, but there may be other inflammatory markers that are more closely linked to insulin resistance. Future studies should consider measuring a more comprehensive range of inflammatory markers.

5. Conclusion

This observational study provides evidence of a positive correlation between inflammatory markers (CRP, IL-6, and ferritin) and insulin resistance (HOMA-IR) in patients with type 2 diabetes mellitus. These findings support the hypothesis that chronic inflammation plays a key role in the development and progression of insulin resistance in type 2 diabetes.

The positive correlations observed between HOMA-IR and CRP, IL-6, and ferritin suggest that these inflammatory markers may be useful biomarkers for identifying patients with type 2 diabetes who are at increased risk of developing insulin resistance and related complications.

The study's findings also highlight the importance of addressing chronic inflammation as a therapeutic target in the management of type 2 diabetes. Interventions aimed at reducing inflammation, such as lifestyle modifications (e.g., diet, exercise) and pharmacological therapies (e.g., anti-inflammatory medications), may help to improve insulin sensitivity and reduce the risk of complications in patients with type 2 diabetes.

Overall, this study contributes to our understanding of the complex relationships between inflammation, insulin resistance, and type 2 diabetes, and highlights the need for further research into the development of effective therapeutic strategies for managing chronic inflammation and insulin resistance in patients with type 2 diabetes.

Conflicts of Interest: None

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