Review Article

Study of Serum TNF-α and Leptin Levels in Association with Insulin Resistance Among Type 2 Diabetes Mellitus Patients

Sarguru Datchanamurthi[1,2], Dr V.S.Kalaiselvi [3]

1. Assistant Professor, Department of Biochemistry, Sri Lalithambigai Medical College & Hospital, Maduravoyal, Chennai, Tamilnadu, India.
2. Ph.D Scholar, Department of Biochemistry, Bharath Institute of Higher Education & Research, Chennai, Tamilnadu, India.
3. Professor, Department of Biochemistry, Shree Balaji Medical College & Hospital, Chrompet, Chennai, Tamilnadu, India.

***Corresponding author's E-mail:** sarguru2@gmail.com

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ABSTRACT

Background: Leptin is one of the important adipokines released from adipocytes, and its level increases with increasing body mass index (BMI). Tumor necrosis factor alpha (TNF-α) is a cytokine that is released by adipocytes and inflammatory cells in response to chronic inflammation, Type 2 diabetes mellitus (T2DM) is believed to be associated with low-grade chronic inflammation.

Aim and Objective: To investigate the involvement of leptin and TNF-α in T2DM associated with obesity.

Materials and Methods:

- It is a retrospective – cross sectional study.
- Sample size - 200 (100- DM patients and 100 -Non Diabetic age matched controls)
- Medical records of and laboratory reports of 100 patients and 100 controls were retrieved and parameters were retrospectively viewed for clinical findings

Inclusion: Patients with type II DM Patients were included

Exclusion: The subjects with another metabolic syndrome (Were excluded)

Collection of Blood Samples:

- 5ml of blood samples were collected into a labeled heparinized bottles
- Centrifuged and plasma was separated
- Blood samples were used for the analysis

Results and Discussion: Our study shows a significantly higher level of TNF-α in T2DM patients compared to controls In obese diabetic patients, the serum level of TNF-α showed ssignificantly increased in comparison with non-obese diabetic patients and obese non diabetic group. TNF-α was Ccorrelated positively with HbA1c.

Conclusion: TNF-α is associated with concurrent obesity and T2DM and it was correlated with HbA1c. & it may suggest that TNF-α needs further investigation to explore if it has a role in monitoring the effectiveness of management in individuals with obesity and T2DM.

Keywords: TNF-α - Tumor Necrosis Factor alpha, T2DM - Type II Diabetes Mellitus, Leptin.

INTRODUCTION

Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycemia and metabolic disturbances of various metabolisms of Carbohydrates and majorly caused by the Dysfunction of Beta cells in the pancreas. It is increasing concern in which person will have hyperglycemia, because the body does not produce enough insulin or because the cells in the body do not respond to the insulin that is produced, majorly, diabetes have been classified into three types.

Type I DM results from inability or failure of our body to produce insulin, which increase Blood glucose levels rapidly and whereas in type II DM the person requires to inject the insulin or wear an insulin pump has emerged as a pandemic health problem in the world right now and the prevalence is increasing rapidly and the type II DM which accounts for about 20% to 50% cases of new-onset of diabetes in the young people, it is a common endocrine disorder.

Adipose tissue is a metabolically active organ which in obese individuals can be the source of low-grade chronic inflammation. inflammatory process plays an important role in pathogenesis of T2DM, and chronic inflammation precedes the onset of the disease.[1]

Leptin is one of the important adipokines released from adipocytes, and its level increases with increasing body mass index (BMI). Tumor necrosis factor alpha (TNF-α) is a cytokine that is released by adipocytes and inflammatory cells in response to chronic inflammation[2] Type 2 diabetes mellitus (T2DM) is believed to be associated with low-grade chronic inflammation.

In obese T2DM patients, the TNF-α plasma level is related to the amount of visceral fat and is not instantly affected in

poorly controlled diabetic patients by acute lowering of blood glucose level. In this study, we aim to look into the correlation between TNF-*α, insulin* resistance, and HbA1c level in addition

to the association between TNF-*α* obesity, and diabetes. Specifically, we will investigate the effect of obesity and diabetes separately on the level of TNF-*α* in type II DM

Aim and Objective:

To investigate the involvement of Leptin and TNF-*α* levels in T2DM patients in association with obesity.

MATERIALS AND METHODS

- It is a cross-sectional study.
- Sample size - 200 (100- DM patients and 100 -non-diabetic age matched controls).
- Medical records of and laboratory reports of 100 patients and 100 controls were retrieved, and parameters were retrospectively viewed for clinical findings.

Inclusion:

- Patients with type II DM Patients with thyroid dysfunction were included.

Exclusion:

- The subjects with other metabolic syndromes (Were excluded)

Collection of Blood Samples

- 5 ml of blood samples were collected into a labeled heparinized bottle.
- Centrifuged and plasma was separated
- Blood samples were used for the analysis

Biochemical Parameters

Fasting venous blood samples were collected and analyzed the parameters of fasting blood glucose, glycosylated hemoglobin (HbA1c), serum insulin, and TNF-*α* levels were measured. Insulin, leptin, and TNF-*α* immunoassays were performed by the quantitative standard sandwich ELISA technique using monoclonal antibody specific for these parameters with kits, indices of basal insulin resistance and beta-cell function were assessed using the homeostasis model assessment (HOMA-IR in which

HOMA-IR (mmol/L × *μ*IU/mL) fasting glucose (mmol/ L) × fasting insulin (*μ*IU/mL)/22.5)

Anthropometric clinical and biochemical measurements

- Age
- BMI
- Sex was noted
- Estimation of Blood glucose was done by using (GOD-POD method) using semi-auto analyzer
- HbA1c will be measured by the affinity column method
- Estimation of Insulin, and TNF-α and Leptin immunoassays were analyzed by using the ELISA technique.
- Insulin resistance and beta-cell function were assessed using the homeostasis model assessment (HOMA-IR)

RESULTS

Table 1: The anthropometric and biochemical measurements

Parameters	Diabetes (100)	Controls (100)	P* Value
BMI	31.4 ± 5.7	28.9 ± 4.2	<0.05
Age (years)	47.2 ± 7.7	49.5 ± 10.2	<0.790
HbA1C	8.8±1.9	4.5± 0.4	<0.05
FBS	186± 12	108±13	<0.05
Basal insulin (*μ*IU/ml)	8.5 ± 6.2	9.5± 0.4	<0.02
HOMA-IR	2.9±2.2	1.5±0.3	>0.05
TNF-*α* (pg/ml)	8.1±1.2	6.8±1.6	<0.05
Leptin (ng/ml)	35.2±16.29	29.9±14.09	>0.05

Table 1 shows Clinical and demographic characteristics were compared between controls and T2DM patients.

Age ranges for controls were 40–55 years (mean: 47.2 ± 7.7) and 39–55 years for diabetic patients (49.5 ± 10.2).

BMI body mass index was significantly higher in patients with T2DM compared to controls (31.4 ± 5.7 and 28.9 ± 4.2, respectively; P*< 0.05). Patients with T2DM have a higher waist to hip ratio when compared to healthy controls (1.03 ± 0.08 and 0.97 ± 0.07, respectively; P* <0.05.

TNF-*α* level was significantly higher in T2DM patients than in controls (8.1±1.2 and ,6.8±1.6 respectively; P* <0.05), while the difference was not significant for leptin (35.2 ± 16 .2 and 29.9 ± 14.09, respectively; P * >0.05)

DISCUSSION

Our study demonstrated that the serum TNF-*α* level was significantly higher in T2DM patients compared to healthy subjects while the difference between the two groups was not significant for leptin, the level of TNF-*α* has a strong

positive correlation with HbA1c and was positively associated with insulin resistance.

These findings suggest that TNF-*α* plays an important role in the pathogenesis of T2DM via mechanisms related to insulin peripheral action independent of leptin.

Our patients have higher insulin resistance indices and a lower beta-cell function than control subjects. The catabolic effect of TNF-*α* on adipose tissue and increased peripheral glucose uptake after neutralizing TNF- *α* in obese indicate its important role in development of insulin resistance and diabetes as a consequence of obesity[3.]

Previous studies reported that TNF-*α* contributes to insulin resistance and T2DM that is associated with obesity [4-6] however, Miyazaki et al. did not confirm this association[14]. In our study, we found a significantly higher TNFα levels in obese diabetic patients compared to non-obese diabetic patients.

Additionally, we reported a higher TNFα level in obese diabetic patients in comparison with obese nondiabetic healthy subjects.[9]

The majority of diabetic patients in the current study have BMI above 30, and their elevated TNF-*α* levels showed a significant positive correlation with insulin resistance. On the other hand, leptin level was not higher in our patients than in control subjects and its correlation with insulin resistance is weak.

linear regression test for BMI and leptin to find the threshold of BMI at which serum leptin level starts increasing, and there is an increase in leptin levels, which indicates that some metabolic changes occur before reaching obesity levels.

We found that in patients with T2DM, the higher the level of TNF-*α* [1,] the higher their HbA1c value, which means that TNF-*α* level can be used to predict glycemic control in obese diabetic patients. Mirza et al [15] showed that diabetes was strongly associated with elevated levels of TNF-*α*, which was most significantly elevated in the group of patients with HbA1c values higher than 6.5% [14]. In our study, the average value for HbA1c in patients with T2DM was 7.3% and it was positively associated with TNF-*α* level.

Since HbA1c is not a direct measure of glycemia there is a chance that its level might change due to factors unrelated to blood glucose levels such as rate of glycation and turnover of erythrocytes [16]. Recently, studies indicated that elevated levels of inflammatory cytokines, including TNF-*α*, were strongly associated with increased risk to occurrence of T2DM [6]

Moreover, the finding that TNF-*α* level decreases with good glycemic control would confirm this hypothesis, Interestingly, a previous study showed a significant reduction in TNF-*α* serum level in obese T2DM patients following 4 weeks of treatment with diet and exercise.

Tsukui et al [9] reported a correlation between the drop in serum TNF-*α* level and HbA1c value after regular exercise in healthy women. Theoretically, this association between TNF-*α* and HbA1c might be useful clinically to follow up the level of glycemic control in patients with T2DM after medical treatment or changed lifestyle or in cases where HbA1c cannot be trusted due to defect in glycation or severe anemia [8].

Our study shows a significant higher level of TNF-*α* in T2DM patients compared to controls In obese diabetic patients, the serum level of TNF-*α* will be ssignificantly higher in comparison with non-obese diabetic patients and obese nondiabetic group, TNF-*α* will be Ccorrelated positively with HbA1c.

CONCLUSION

TNF-*α* is associated with concurrent obesity and T2DM and it was correlated with HbA1c. It suggests that TNF-*α* needs further investigation to explore if it has a role in monitoring the effectiveness of management in individuals with obesity and T2DM.

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