

# Assessment of Inflammatory Markers IL- 6 and TNF- Alpha in Newly Diagnosed Type II Diabetics without Hypertension in Comparison with Non-Diabetic Normotensive Subjects

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## Abstract

**Background:** The present study was conducted to assess inflammatory markers IL- 6 and TNF- alpha in newly diagnosed type II diabetics without hypertension. **Subjects and Methods:** 68 types of II diabetes mellitus patients and equal numbers of normotensive non-diabetic subjects were also recruited. Glycated hemoglobin (HbA1c) levels, TNF- alpha and IL- 6 were determined. **Results:** The mean IL- 6 level in group I was 17.4 pg/ml and in group II was 4.2 pg/ml. TNF- alpha level in group I was 35.8 pg/ml and in group II was 12.5 pg/ml. The difference was significant ( $P < 0.05$ ). **Conclusion:** TNF- alpha and IL- 6 level was higher among diabetic patients as compared to healthy normotensive non-diabetic subjects.

**Keywords:** Diabetic, Normotensive, TNF- alpha

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## Introduction

Type II diabetes mellitus (T2DM) is a non-communicable, chronic disorder and progresses slowly because of multifactorial etiology. T2DM is a leading cause of premature deaths worldwide, and its exceptional upsurge poses a severe threat and imposes a huge economic burden worldwide (825 billion dollars per year).<sup>[1]</sup> According to a recent estimation of the World Health Organization (WHO), 422 million people globally are affected by diabetes with a prevalence rate of 8.5% and 46.3% still remains undiagnosed and the number is projected to rise to 552 million in 2030.<sup>[2]</sup> Clinical findings revealed the role of IL-6 and TNF- $\alpha$  in glucose homeostasis and metabolism and also the indirectly possible action on the pancreatic  $\beta$ -cell. Furthermore, the presence of these cytokines leads to inflammatory responses with elevated CRP. IL-6 and TNF- $\alpha$  were suggested as possible markers for T2DM prediction. However, non-statistically significant results have also been reported. The biological role of these cytokines on T2DM development may still be uncertain.<sup>[3]</sup> Few studies reported that it has an association with the pathogenesis of T2DM. On the other hand, many studies suggest that IL-6 has a dual role of anti-inflammatory and improves glucose metabolism in T2DM

patients.<sup>[4]</sup> IL-6 has a great impact on glucose homeostasis and metabolism by acting indirectly on the  $\beta$ -cells of the pancreas and on adipocytes.<sup>[5]</sup> However, its role as an early biomarker for T2DM is still doubted and more such studies are needed in different populations.<sup>[6]</sup> The present study was conducted to assess inflammatory markers IL- 6 and TNF- alpha in newly diagnosed type II diabetics without hypertension.

## Subjects and Methods

The present study was conducted in the department of internal medicine among 68 type II diabetes mellitus patients of both genders. Equal numbers of normotensive non-diabetic subjects were also recruited. Ethical approval was obtained beforehand. All involved patients were informed regarding the study and their consent was obtained. Data such as name, age, gender, etc. were recorded. 5 ml of venous blood was collected from all enrolled subjects. Glycated hemoglobin (HbA1c) levels, TNF-alpha and IL- 6 were determined. Results were statistically analyzed for correct inference. A P-value of less than 0.05 was considered significant.

**Results**

**Table 1: Distribution of patients**

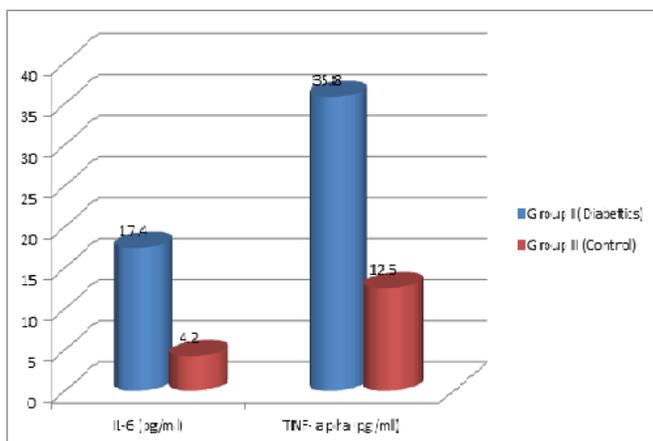
| Groups | Group I (Diabetics) | Group II (Control) |
|--------|---------------------|--------------------|
| M: F   | 40:28               | 38:30              |

[Table I], shows that there were 40 males and 20 females in group I and 38 males and 30 females in group II.

**Table 2: Assessment of parameters**

| Parameters         | Group I (Diabetics) | Group II (Control) | P-value |
|--------------------|---------------------|--------------------|---------|
| IL-6 (pg/ml)       | 17.4                | 4.2                | 0.001   |
| TNF- alpha (pg/ml) | 35.8                | 12.5               | 0.001   |

[Table II], the graph I show that the mean IL- 6 level in group I was 17.4 pg/ml and in group II was 4.2 pg/ml. TNF- alpha level in group I was 35.8 pg/ml and in group II was 12.5 pg/ml. The difference was significant (P< 0.05).



**Figure 1: The graph I Assessment of parameters**

**Discussion**

Fasting Blood glucose (FBG), 2-hour postprandial blood glucose (2hr-PP) and glycated hemoglobin (HbA1c) levels are most widely used as glycemic control markers which indicates the progression of the disease and development of its complications.<sup>[7]</sup> T2DM is reported to be linked with lipid and lipoprotein irregularities, including reduced HDL cholesterol and raised triglycerides.<sup>[8]</sup> Trend of T2DM is changed from metabolic disorder to inflammation as effects of the pro and anti-inflammatory cytokines like tumor necrosis factor-alpha

(TNF- $\alpha$ ), interleukin-6 (IL-6) and C-reactive protein (CRP) has been reported in insulin signaling pathways, cross-linking and ultimately developing insulin resistance in  $\beta$ -cells of the pancreas which further risks to T2DM.<sup>[9]</sup> The present study was conducted to assess inflammatory markers IL- 6 and TNF- alpha in newly diagnosed type II diabetics without hypertension. In the present study, there were 40 males and 20 females in group I and 38 males and 30 females in group II. Darko et al,<sup>[10]</sup> examined the associations of IL-6 and TNF- $\alpha$  with anthropometric measurement and the effect of co-morbidity with hypertension using rural and urban dwellers in participants aged 25–70 years consisting of 77 T2DM  $\pm$  hypertension patients and 112 controls were selected from a larger study on Research on Obesity and Diabetes among African Migrants (RODAM). Anthropometric measurements, blood pressure and body fat percentage were measured. Fasting blood samples were analyzed for glucose, IL-6 and TNF- $\alpha$  level. The median level of IL-6 was significantly higher ( $p < 0.0001$ ) among rural dwellers compared to urban dwellers. Inversely, urban dwellers had a significantly higher ( $p = 0.0424$ ) median level of TNF- $\alpha$  compared to rural cases. No significant differences were observed in IL-6 ( $p = 0.3571$ ) and TNF- $\alpha$  ( $p = 0.2581$ ) among T2DM patients compared with T2DM  $\pm$  hypertension patients. A weak negative correlation was found between IL-6 and BMI in urban T2DM. The average level of IL-6 was higher in rural T2DM participants compared with those in an urban setting. However, higher levels of TNF- $\alpha$  were observed among the study participants with T2DM in urban settings compared to those of rural. In this study, we observed that the co-morbidity of hypertension had no significant effect on the levels of IL-6 and TNF- $\alpha$ . We found that the mean IL- 6 level in group I was 17.4 pg/ml and in group II was 4.2 pg/ml. TNF- alpha level in group I was 35.8 pg/ml and in group II was 12.5 pg/ml. Lainampetch et al,<sup>[11]</sup> evaluated the association of baseline inflammatory marker levels and variation with the incidence of T2DM. After the 2-year follow-up, 18.6% of the total subjects had developed T2DM. The risk of developing T2DM was significantly increased in subjects with a high level of baseline CRP and a stronger impact was found with the combination of high CRP and IL-6 levels. One-year inflammatory marker variation analysis also revealed the significant association of elevated TNF- $\alpha$  and the risk of developing T2DM. Findings suggested that IL-6 outstandingly plays a contributing role in T2DM progression and elevated TNF- $\alpha$  level over time could be a potential predictor of T2DM.

Bashir et al,<sup>[12]</sup> a total of 340 subjects were selected in this study among them 160 were T2DM cases and 180 were healthy controls. Serum expression of inflammatory mediators (TNF- $\alpha$  and IL-6) were quantified by the ELISA technique. The expressions of candidate cytokines (TNF- $\alpha$ , IL-6, CRP, and WBC) were highly significant ( $p < 0.001$ ) in T2DM. Among inflammatory mediators, TNF- $\alpha$  shows a positive correlation

( $p < 0.001$ ) with glycemic profile and insulin sensitivity in T2DM cases in comparison with healthy normal. Biochemical (fasting sugar, HbA1c, insulin resistance, lipid profile) and anthropometric (BMI) parameters were highly significant ( $p < 0.001$ ) in T2DM cases as compared to non-diabetic normal. The shortcoming of the study was the small sample size.

## Conclusion

Authors found that TNF- alpha and IL- 6 level was higher among diabetic patients as compared to healthy normotensive non-diabetic subjects.

## References

1. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. *Nat Rev Immunol*. 2011;11(2):98–107. Available from: <https://dx.doi.org/10.1038/nri2925>.
2. Krakoff J, Funahashi T, Stehouwer CDA, Schalkwijk CG, Tanaka S, Matsuzawa Y, et al. Inflammatory Markers, Adiponectin, and Risk of Type 2 Diabetes in the Pima Indian. *Diabetes Care*. 2003;26(6):1745–1751. Available from: <https://dx.doi.org/10.2337/diacare.26.6.1745>.
3. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. *JAMA*. 2001;286(3):327–334. Available from: <https://doi.org/10.1001/jama.286.3.327>.
4. Salomaa V, Havulinna A, Saarela O, Zeller T, Jousilahti P, Jula A, et al. Thirty-One Novel Biomarkers as Predictors for Clinically Incident Diabetes. *PLoS One*. 2010;5(4):e10100–e10100. Available from: <https://dx.doi.org/10.1371/journal.pone.0010100>.
5. Nadeem A, Naveed AK, Hussain MM, Raza SI. Correlation of inflammatory markers with type 2 Diabetes Mellitus in Pakistani patients. *J Postgrad Med Inst*. 2013;27(03):267–273.
6. Bertoni AG, Burke GL, Owusu JA, Carnethon MR, Vaidya D, Barr RG, et al. Inflammation and the Incidence of Type 2 Diabetes: The Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes Care*. 2010;33(4):804–810. Available from: <https://dx.doi.org/10.2337/dc09-1679>.
7. Singhai M, Faizy A, Goyal R, Siddiqui S. Evaluation of TNF- $\alpha$  and IL-6 levels in obese and non-obese diabetics: Pre- and postinsulin effects. *N Am J Med Sci*. 2012;4(4):180–180. Available from: <https://dx.doi.org/10.4103/1947-2714.94944>.
8. Al-Shukaili A, AL-Ghafri S, Al-Marhoobi S, Al-Abri S, Al-Lawati J, Al-Maskari M. Analysis of Inflammatory Mediators in Type 2 Diabetes Patients. *Int J Endocrinol*. 2013;2013:1–7. Available from: <https://dx.doi.org/10.1155/2013/976810>.
9. Agyemang C, Beune E, Meeks K, Owusu-Dabo E, Agyei-Baffour P, de Graft Aikins A, et al. Rationale and cross-sectional study design of the Research on Obesity and type 2 Diabetes among African Migrants: the RODAM study. *BMJ Open*. 2015;4(3):e004877–e004877. Available from: <https://dx.doi.org/10.1136/bmjopen-2014-004877>.
10. Darko SN, Yar DD, Owusu-Dabo E, Awuah AAA, Dapaah W, Addofoh N. Variations in levels of IL-6 and TNF- $\alpha$  in type 2 diabetes mellitus between rural and urban Ashanti Region of Ghana; 2015. Available from: <https://dx.doi.org/10.1186/s12902-015-0047-9>.
11. Lainampetch J, Panprathip P, Phosat C, Chumpathat N, Prangthip P, Soonthornworasiri N, et al. Association of Tumor Necrosis Factor Alpha, Interleukin 6, and C-Reactive Protein with the Risk of Developing Type 2 Diabetes: A Retrospective Cohort Study of Rural Thais. *J Diabetes Res*. 2019;2019:1–9. Available from: <https://dx.doi.org/10.1155/2019/9051929>.
12. Bashir H, Bhat SA, Majid S, Hamid R, Koul RK, Rehman MU, et al. Role of inflammatory mediators (TNF- $\alpha$ , IL-6, CRP), biochemical and hematological parameters in type 2 diabetes mellitus patients of Kashmir. *Med J Islam Repub Iran*. 2020;34:5–5. Available from: <https://doi.org/10.34171/mjiri.34.5>.

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