ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 17, Issue 5, 2024

Online - 2455-3891
Print - 0974-2441

Research Article

TO EVALUATE THE INFLAMMATORY MARKERS IN TYPE 2 DIABETES MELLITUS AND COMPARED IT WITH NORMAL HEALTHY CONTROLS

JASWANT KAUR[1], SHWETA[2], MOHIT SHARMA[3], SEEMA[4], MOHAMMED NADEEM SHAIKH[1]

[1]Department of Biochemistry, Dr. S.S. Tantia Medical College, Hospital and Research Centre, Sriganganagar, Rajasthan, India. [2]Department of Physiology, NC Medical College and Hospital, Israna, Panipat, India. [3]Medical Officer, 7th Battalion Punjab Armed Police, Jalandhar Cantonment, Punjab, India. [4]Department of Physiology, Dr. S.S. Tantia Medical College, Hospital & Research Centre, Sriganganagar, Rajasthan, India.

*Corresponding author: Dr. Mohammed Nadeem Shaikh; Email: coolnadeem7@gmail.com

Received: 21 December 2023, Revised and Accepted: 04 February 2024

ABSTRACT

Objective: The study aimed to evaluate the serum levels of Interleukin-6, Tissue Necrosis factor-α, C-reactive Protein (IL-6, TNF-α, CRP) in type 2 diabetes mellitus (T2DM) in North Population.

Methods: A total of 200 participants were recruited, 100 were recruited as Cases with T2DM and 100 were healthy controls. The parameters were estimated by fully autoanalyzer. Serum levels ofTNF-α CRP and IL-6 were estimated by ELISA. The $p<0.05$ is taken as statistically significant.

Results: We observed that serum levels of candidate cytokines, TNF-α, IL-6, and CRP were highly significant ($p<0.001$) in T2DM as compared to healthy control. Blood sugar, HbA1c and lipid profile parameters were recorded significant ($p<0.001$) in T2DM compared to normal healthy controls.

Conclusion: Inflammatory cytokines play a significant role in the pathogenesis of T2DM. These cytokines can be acting as early prediction biomarkers; it may be helpful in the reduction of mortality rate of T2DM.

Keywords: Cytokines, Type 2 diabetes mellitus, Inflammation, BMI, IL-6, TNF-α, CRP.

 DOI: http://dx.doi.org/10.22159/ajpcr.2024v17i5.50194. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Diabetes is one of the most common chronic illnesses in both developed and developing countries. The number of people with diabetes mellitus (DM) has increased by four folds in the past three decades as a result of urbanization and associated lifestyle change [1]. Numbers of risk factors such as age, obesity, and family history are involved in the development of Type 2 DM (T2DM) [2]. Chronic inflammation associated with T2DM. These markers are important for the detection of T2DM and associated morbidities [3]. Tumor necrosis factor-α (TNF-α) and Interleukin-6 (IL-6) are twoinflammatory markers, acting primarily as autocrine or paracrine factors. TNF-α produced by several types of cells such as macrophages, monocytes, neutrophils, and T-cells. Several studies revealed that increased TNF-α expression induces insulin resistance. TNF-α plays a direct pathogenic role in glucose metabolism. Impaired insulin sensitivity in skeletal muscle is a feature of Type-2 diabetes [4]. These pro-inflammatory cytokines, IL-6 have a strongest correlation with insulin resistance and Type-2 diabetes [5]. The circulating IL-6 is produced from the adipose tissue [6]. Hence, through impairment and destruction of beta cells and progression to T2DM [7], numerous mechanisms have demonstrated by which IL-6 produces the insulin resistance status patients with obesity. Insulin plays a key role in glucose metabolism, its effects that increasing glucose uptake by the skeletal muscle and adipose tissue, promoting hepatic glycogen synthesis, inactivate gluconeogenesis by the liver and kidney.IL-6 reduces the activity of insulin signaling [8]. CRP is an acute-phase reactant produced in the liver and a sensitive marker of low-grade inflammation. Studies completed on prospective studies found a significant association between CRP and risk of T2DM [9]. We try to determine the association between IL-6, CRP, and TNF- α in T2DM patients and compare with normal healthy controls.

METHODS

A case-control study was done in the Department of Biochemistry, Govt. Medical College, Sri Amritsar. Among 100 subjects, 50 T2DM patients in the age group 30–70 years as case in the study, diagnosed as per standard of the American Diabetes Association criteria, and 50 healthy individuals (age-sex matched) were taken as controls. The patients suffering from thyroiditis, cancer, and pregnant women were excluded from the study. Participants gave written informed consent. Ethics Committee approved this study.

5 mL of blood was taken by venipuncture from T2DM patients and healthy control for the biochemical analysis. The following investigations were estimated, that is, blood glucose, HbA1c, by fully automated analyzer.IL-6, CRP, and TNF- α were estimated by Elisa Reader. Statistical analysis was performed using SPSS 16.0 software. $p<0.005$ was considered as statistically significant.

RESULTS AND DISCUSSION

One hundred study participants were selected for the study and categorized into two groups, Group I as healthy control and Group II as T2DM cases. Mean and standard deviation for the age distribution are 57.93±8.31 years for Group 1 and 29.83±7.62 years for Group 2. It seems that most of the patients lies in the age 50–60 years. The current study shows in Group I (control) 62% of males and 38% of females. In Group II (cases), 35% of males and 65% of females. Women exhibit a higher prevalence of T2DM (65%) compared to males (35%) shown in Table 1.

Table 2 illustrates the biochemical parameters such as HbA1C, FBS, and lipid profile levels of Group I and Group II. Blood sugar was significantly higher in diabetic patients compared to controls (166.09±30.30 vs.

Table 1: Gender distribution in Group I and Group II

Gender	Group I (Control) %	Group II (Cases) %
Male	62	35
Female	38	65

Table 2: Status of biochemical parameters of Group I (Healthy control) subjects and Group II (T2DM Cases)

Parameter	Group I (control) Mean±SD	Group II (T2DM cases) Mean±SD	p<0.001
FBS (mg/dL)	75.05±10.47	166.09±30.30	0.001
HbA1C (%)	00.29±00.03	00.78±00.13	0.001
TC (mg/dL)	168.52±22.47	258.96±53.69	0.001
HDL-C (mg/dL)	47.39±08.27	30.43±03.44	0.001
TG (mg/dL)	125.0±18.04	267.48±86.48	0.001
LDL-c (mg/dL)	91.31±25.57	158.28±42.07	0.001
VLDL-c (mg/dL)	25.62±04.53	55.52±17.93	0.001

FBS: Fasting blood glucose, HbA1c: Glycated hemoglobin, TC: Total cholesterol, TG: Triglycerides, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein

Table 3: Inflammatory parameters of Group I (Healthy control) subjects and Group II (T2DM Cases)

Parameter	Group I control (mean±SD)	Group II T2DM (mean±SD)	p<value
IL 6	9.1±1.52	26.91±8.28	0.001
TNF -α	1.52±0.1.46	27.40±10.32	0.001
CRP	1.5±0.5	4.5±0.5	0.001

IL-6: Interleukin, TNF-α: Tissue necrosis factor-α, CRP: C-reactive protein

75.05±10.47), and HbA1c observed elevated in T2DM patients due to disturbance in glucose metabolism. In lipid profile parameters, only HDL decreases in diabetic group (30.43±03.44 vs. 47.39±08.27). total Cholesterol, TG, and LDL levels significantly differed in both the groups (258.96±53.69 vs. 168.52±22.47 mg/dL), (267.48±86.48 vs. 125.0±18.04 mg/dL) and (158.28±42.04 vs. 91.31±25.57 mg/dL), respectively.

In Group II, serum levels of parameters were higher than Group I. P-value was highly significant (p<0.001) in Group II compared to Group I. In Table 3, we observed that serum levels of inflammatory markers such as IL-6, CRP, and TNF- α levels increased in diabetic group than our control subjects. Serum CRP levels of patients in Group II in Indian population to be with mean±S.D. 4.5±0.5 mg/dL of as compared to 1.5±0.5 mg/l in Group I.

Our study revealed that DM is a group of metabolic disease, interlinked with disturbances of various mechanisms. In this context, we evaluated the association between inflammatory markers and T2DM. It affirms the association between inflammatory markers and T2DM. Women are more prevalent in T2DM and then men. Similar study was done by Insha *et al.* [10]. Data revealed that lipid profile, HbA1c, and blood glucose levels are increased in T2DM compared to control. Multiple studies also supported our study [11-14]. Shows in Table 3, IL-6 levels are elevated in case T2DM patients and found significant as compared to controls. Studies were documented the correlation of IL-6 with T2DM [15,16]. Cytokines have to enhance insulin resistance of T2DM, Samuel *et al.* [17]. CRP actin the pathogenesis of T2DM and synthesis triggered by cytokines and regulated by the pro-inflammatory cytokine IL-6, which is produced and released into the bloodstream by macrophages and adipocytes [18]. The results also ensured a positive correlation between CRP and T2DM. It was observed that increased levels in biochemical parameters (FBS, lipid profile, and HbA1c) and inflammatory markers (IL-6, TNF-α, and CRP) in T2DM patients than controls in the North Indian population. Many inflammatory cytokines have implicated in the development of chronic inflammation IL-6, TNF-α, and CRP at the higher end of the normal range.

CONCLUSION

Our study concluded that inflammatory markers CRP, IL-6, and TNF-α are higher in T2DM cases in the North Indian population. These inflammatory markers may contribute to the development of Type 2 diabetes. Hence, it can act as early prediction marker in this population. Hence, early detection of inflammatory markers may be helpful in T2DM and its complications.

ACKNOWLEDGMENT

We would like to thank all those who participated in the preparing of this manuscript.

AUTHORS CONTRIBUTIONS

The paper write-up was done by Dr. Jaswant Kaur, Dr. Seema. The data analysis were done by Dr. Jaswant Kaurand Dr. Shweta. The research was reviewed and edited by Dr. Mohit Sharma, Dr. Seema and statistical analysis was done by Dr. Mohammed Nadeem Shaikh. The manuscript was finalized by Dr. Seema, Dr. Mohammed Nadeem Shaikh, and Dr. Shweta and submitted for publication by Dr. Jaswant Kaur.

CONFLICTS OF INTEREST

The authors affirm no conflicts of interest.

AUTHORS FUNDING

None.

REFERENCES

1. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, *et al*. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes Res Clin Pract. 2019;157:107843. doi: 10.1016/j.diabres.2019.107843, PMID 31518657
2. Khan RM, Chua ZJ, Tan JC, Yang Y, Liao Z, Zhao Y. From pre-diabetes to diabetes: Diagnosis, treatments and translational research. Med (Kaunas Lith). 2019;55(9):546. doi: 10.3390/medicina55090546, PMID 31470636
3. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nat Rev Immunol. 2011;11(2):98-107. doi: 10.1038/nri2925, PMID 21233852
4. Smitka K, Marešová D. Adipose tissue as an endocrine organ: An update on pro-inflammatory and anti-inflammatory microenvironment. Prague Med Rep. 2015;116(2):87-111. doi: 10.14712/23362936.2015.49, PMID 26093665
5. Pradhan AD, Cook NR, Buring JE, Manson JE, Ridker PM. CRP is independently associated with fasting insulin in nondiabetic women. Atheroscler Thromb Vasc Biol. 2003;23(4):650-5. doi: 10.1161/01.ATV.0000065636.15310.9C
6. Ali M. Adipose tissue as an endocrine and paracrine organ. Int J Obes Relat Metab Disord. 1998;22:1145-58.
7. Rehman K, Akash MS, Liaqat A, Kamal S, Qadir MI, Rasul A. Role of interleukin-6 in the development of insulin resistance and type 2 diabetes mellitus. Crit Rev Eukaryot Gene Expr. 2017;27(3):229-36.doi:10.1615/CritRevEukaryotGeneExpr.2017019712, PMID 29199608
8. Rotter V, Nagaev I, Smith U. IL-6 induces insulin resistance in 3T3-L, adipocytes and is like IL-8, TNF-α, over-expressed in human fat cells from insulin resistant subjects. J Biol Chem. 2021;278:457777-84.
9. Wang X, Bao W, Liu J, Ouyang YY, Wang D, Rong S, *et al*. Inflammatory markers and risk of type 2 diabetes: A systematic review and meta-analysis. Diabetes Care. 2013;36(1):166-75. doi: 10.2337/dc12-0702, PMID 23264288
10. Inshah D, Sabhiya M, Fouzia R, Rabia F, Jasiya Q, Rouf M, *et al*. Combinatorial effect of leptin, tumor necrosis factor-α-alpha, and

vitamin D intype 2 diabetes in Kashmiri population. Asian J Pharm Clin Res. 2018;10(11):477-82.
11. Bhat MA, Bhat SA, Ahmad SB, Qureshi W, Majid S, Ali A. Biochemical profile and genetic polymorphism of MTHFRC677T in risk of type 2 diabetes mellitus. Int J Diabetes Endocrinol. 2017;2(2):19-25.
12. Ali A, Ayaz A, Dar MA, Singh N, Bhat SA. A key role of insulin in diabetes mellitus. Int J Sci Res Sci. 2017;3(6):80-5.
13. Singh PS, Sharma H, Zafar KS, Singh PK, Yadav SK, Gautam RK, *et al*. Prevalence of type 2 diabetes mellitus in rural population of India- a study from Western Uttar Pradesh. Int J Res Med Sci. 2017;5(4):1363-7. doi: 10.18203/2320-6012.ijrms20171227
14. VinodMahato R, Gyawali P, Raut PP, Regmi P. Association between glycemic control and serum lipid profile in type 2 diabetic patients: Glycated hemoglobin as a dual biomarker. Biomed Res. 2011;22(3):375-80.
15. Singh U. Prevalence of diabetes and other health-related problems across India and worldwide: An overview. J Nat Appl Sci. 2016;8(1):500-5. doi: 10.31018/jans.v8i1.825
16. 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):804-10. doi: 10.2337/dc09-1679, PMID 20097779
17. Samuel ND, Denis DY, Ellis OD, Dark SN, Yar D, Owasu D, *et al*. Variations in levels of IL-6 and TNF-α in type 2 diabetes mellitus between rural and urban Ashanti Region of Ghana. BMC Endocrinol Disord. 2015;15:50.
18. Phosat C, Panprathip P, Chumpathat N, Prangthip P, Chantratita N, Soonthornworasiri N, *et al*. Elevated C-reactive protein, interleukin 6, tumor necrosis factor - alpha and glycemic load associated with type 2 diabetes mellitus in rural Thais: A cross-sectional study. BMC Endocr Disord. 2017;17(1):44. doi: 10.1186/s12902-017-0189-z, PMID 28716139