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Evaluation of interleukin -17a levels in Iraqi patients with type 2 diabetes mellitus

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Abstract---Type 2 Diabetes mellitus (T2DM) is one of the major non-communicable diseases worldwide. Interleukin-17 (IL-17, also known as IL-17A) is a key cytokine that links T cell activation to neutrophil mobilization and activation. In the cytokine storm, up-regulation of T-helper 17 cell cytokine IL-17A, and maybe also IL-17F, is primarily responsible for the immunopathology. This study aims to assess the Interleukin-17 A levels among the susceptibility of T2DM Iraqi diabetic patients as well as to determine the Interleukin-17 A levels among those patients and controls. A total of 70 participants 50 confirmed type 2 diabetic patients and 20 apparently healthy individuals as controls were selected using a convenient sampling method. Evaluation of serum levels of IL-17A were performed using by enzyme-linked immunosorbent assay technique (ELISA) using a Human- IL-17A kit. (Elabscience Company /china). The results of the current study indicated that the levels of this interleukin were higher in the sera of patients with type 2 diabetes compared to healthy controls, although there were no significant differences, in patients (243.7233 ± 38.45944), vs. controls (148.8930 ± 11.79280), $P = 0.135$. We conclude that there may be a correlation between high levels of IL-17A and T2DM.

Keywords---IL-17A, T2DM , ELISA

Introduction

Type 2 Diabetes mellitus (T2DM) is one of the major non-communicable diseases worldwide (Knowler et al.,2002). T2DM accounts for around 90% of all cases of diabetes. The development of T2DM is caused by a combination of lifestyle and genetic factors(Pedersen et al.,2016). Around 1.4 million Iraqis have diabetes. Reported T2DM prevalence in Iraq ranges from 8.5% to 13.9% (World Health

Organization,2019).

Interleukin-17 (IL-17, also known as IL-17A) is a key cytokine that links T cell activation to neutrophil mobilization and activation. As such, IL-17 can mediate protective innate immunity to pathogens or contribute to the pathogenesis of inflammatory diseases, such as psoriasis and rheumatoid arthritis (Hu et al.,2019). Studies have shown that increased IL-17 levels were detected in STZ-induced diabetic animal models and non-obese diabetic (NOD) mice from insulinitis to diabetes (Aggarwals and Gurney,2002; Fossiez et al.,1996). However, to date, there is little published data evaluating the role of IL-17A. This study aims to investigate to measure the levels of IL-17 A in sera from patients with T2DM, in addition apparently healthy individuals. Enzyme-linked immunosorbent assay (ELISA).

Method

Materials and Methods

This study included (50 confirmed type 2 diabetic patients and 20 controls), their age range between 40–85 years. They were selected from the local community of Wasit province – Iraq. All patients were diagnosed according to the criteria of the American Diabetes Association (ADA).

Five milliliters of blood were collected from all participants and placed in a tube without anticoagulant and placed in a centrifuge at a speed of 2000 rpm for 10 minutes. After that, the serum was withdrawn into an Eppendorf tube 2ml and preserved after being labeled with deep freezing until further processed.

Interleukin-17A concentrations in sera from patients and controls were measured by enzyme-linked immunosorbent assay technique (ELISA) using Human-IL-17A (Bioassay Technology Laboratory, China) according to the manufacturer's instructions.

Results

Serum levels of IL-17A/IL-17A in patients with T2DM and controls

Determination of interleukin-17A in sera of patients with T2DM and control was done using Enzyme-linked immunosorbent assay (ELISA). The results of is shown in Table (3-1). The results reveal that although there were no significant differences, the IL-17A levels in the diabetic patients were clearly higher than the controls (24.37233 ± 3.845944), controls (14.88930 ± 1.179280), $P = 0.135$

Table (3-1)
Serum IL-17A levels in patients with T2DM and controls

Parameters	Pg\ml
Groups	Mean $\pm$ SD
Control	14.8893 $\pm$ 1.179280
T2DM patients	24.37233 $\pm$ 3.845944
P-value	0.135
LSD	24
Statistical significance	NS

NS :Non-significant $P > 0.05$

SD: Standard deviation

Discussion

IL-17a is one of the cytokines that have been studied for its relationship with the development of diabetes. The results of the current study indicated that the levels of this interleukin were higher in the sera of patients with type 2 diabetes compared to healthy controls, although there were no significant differences, which are often due to variations in the studied sample. These findings are consistent with the study of (Parhi *et al.*,2019) and who studied the level of interleukin-17 in Indian populations with T2DM .The results also are in agreement with (Chen *et al.*,2016) which showed increase in level of IL-17A in newly diagnosed diabetes than the healthy controls. Based on the results of the current study and previous studies, interleukin 17 may have a role in the inflammatory process of type 2 diabetes, and therefore it also has a significant impact on its pathogenesis. The exact role of IL-17A in the pathogenesis type 2 DM has not been explored. IL-17A is capable of inducing the expression of pro-inflammatory cytokines such as TNF- α , IL-1 β , IL-6, chemokines and adhesion molecules, which mediate tissue infiltration and tissue destruction. In addition to stimulating the secretion of other pro-inflammatory cytokines, IL-17 is involved in the induction of potentially harmful mediators of inflammation, such as free radical nitric oxide (Miljkovic and Trajkovic,2004). Recent studies have described an ongoing process of β cell destruction by apoptosis in animal models of type 2 diabetes and in human T2DM (Naureen *et al.*,2017).A study reported that the plasma level of IL-17 is increased in obese women (umarac-Dumanovic *et al.*,2009). Obesity is considered the main environmental cause for the development of insulin resistance and type 2 DM. Obesity is defined as BMI>25 kg/m² in Asian .And prior evidence suggests all of these characteristics are associated with higher Th17 cell or IL-17A signaling activity. Patients with diabetes may also have altered Th17 activity. Higher levels of Th17 cell activity are observed in individuals with type-I and type II diabetes compared with controls (Ryba-Stanisławowska *et al.*,2013; Abdel-Moneim *et al.*,2018) and evidence suggests that this increase may be a result of signaling via miRs such as miR-

146a. miR-146a negatively regulates the expression of proinflammatory cytokines such as IL-1R-associated kinase 1 (IRAK1), TNF receptor-associated factor 6 (TRAF6), IL-21, and IL-6 (Balasubramanyam et al., 2011).

Conclusion

Serum levels of IL-17A are increased in patients with T2DM. Our results suggested IL-17A might promote the inflammatory state of patients, and participate in the pathogenesis of T2DM.

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