EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

ASSESSMENT OF INTERLEUKIN_23 SERUM LEVELS T1DM PATIENTS IN DIYALA GOVERNORATE

Zainab A. Fadhil*

Department of Biology, College of Education for Pure Science, University of Diyala, Diyala, Iraq.

*Corresponding Author: Zainab A. Fadhil

Department of Biology, College of Education for Pure Science, University of Diyala, Diyala, Iraq.

ABSTRACT

It is understood that T1DM is an autoimmune, inflammatory illness. This study's objective was to evaluate certain Iraqi diabetes mellitus patients' immunological conditions. The patients in the current study were divided into groups. At Baquba Teaching Hospital and Al-Batoul Hospital Education Feminine & Pediatric in the Diyala Governorate, blood samples were gathered from patients with diabetes mellitus. Which was conducted between December 2022 and April 2023. Between the ages of 10 and 13 to serve as a control group for this study, They were between the ages of (19_63). There are 23 men and 27 women in the Type 1 Diabetes Group. They were between the ages of (17- 75). The study investigated how the ELISA method and immunological detection of IL-23 cellular motility interacted. The results of the current investigation showed that the number of males with type 1 diabetes was 23, with a rate of (46%), while the number of infected females was 27, with an infection rate of (54%). It was found that the incidence of females is higher than that of males. revealed as compared to the control group (5.86 1.04) pg / ml and the Type 1 Diabetes group (9.36 ± 1.93) pg / ml no significant in serum IL_23 level was observe.

KEYWORDS: Hyperglycemia, T1DM, IL-23.

INTRODUCTION

Persistent hyperglycemia is a pathologic condition brought on by diabetes mellitus (DM), a metabolic illness that may also result in irregularities in insulin secretion and action. (Kim HG, 2019; Yedjou et al, 2023). According to its origin and clinical signs, diabetes mellitus is divided into different categories. The four varieties or classifications of diabetes mellitus are T1DM, T2DM, gestational diabetes, and other specific variants. (Sicree et al., 2006; Piero et al., 2015). The auto immune condition T1 diabetes mellitus is characterized by a complete insulin deficiency, high blood sugar levels, auto-reactive T-cell-induced beta-cell malfunction and death. (DiMeglio, 2018; Pang, 2020). The insulin hormone's function is to regulate blood glucose levels. Diabetes mellitus is brought on by insulin insufficiency as a result of poor control or regular use, which affects the blood glucose level and over time causes serious complications that affect the body's functions and tissues. (2015, WHO). Acute complications are the signs and symptoms that result from inadequate management or uncontrolled hyperglycemia. When these warning signs and symptoms are disregarded or delayed, they increase the risk of developing long-term consequences such hypertension, stroke, blindness, erectile dysfunction, and renal disease (Adinortey et al., 2019). Recent estimates place the number of persons with diabetes at 463 million

9.3% worldwide; by 2030, that number is expected to rise to 578 million 10.2% (Abdel-Moneim et al., 2020).The two components of interleukin (IL)-23, p19 and p40, are members of the cytokine family IL-12.7 The main sources of IL-23 production are Dendritic cells and macrophages. Through its interaction with the IL-23 receptor (IL-23R), which is made up of the IL-12R1 unit and the distinct IL-23R unit, IL-23 plays a key role in inflammation, including the activation of Th17 cells (Al-Saffar OB, Ad'hiah, 2020). Numerous environmental variables that contribute to the pathophysiology of T1D explain the infiltration of lymphocytes in the pancreatic islet tissues, which causes insulitis and ultimately leads to the death of β-cells. The pro-inflammatory cytokines produced by the invading immune cells intensify the T cell infiltration and β cell death. T cells, dendritic cells, macrophages, and other immune cells are often implicated in the killing of β-cells (Fatima etal., 2016). In a mouse model, It is well known that administering IL-23 damages pancreatic beta-cells, which results in hyperglycemia. (Mensah-Brown et al., 2006).

MATERIALS AND METHODS
Subjects
The research was conducted Baquba Teaching Hospital in Diyala governorate from December 2022 to April 2023. the current study comprised 73 samples of

males and females, 50 of which were type 1 diabetes blood samples.27 female and 23 males, Whose ages ranged between (17_75) years. A control group of 23 healthy individuals who appeared to be in control was also included in the research. 10 female and 13 males, whose ages ranged between (19-63) years. samples were taken from hospitalized patients, Following the diagnosis through laboratory testing The specialist physician evaluated the HbA1c and C-peptide levels.

Collection of Blood Samples
Venous blood was drawn, and 3 mL of blood was extracted using disposable plastic medical syringes. Gel

test tubes were used to collect the blood, which was then kept at room temperature for 30 minutes. Minutes pass during coagulation. The serums were divided into equal quantities of 100 microliters and placed in tiny tubes expender, where they were maintained at - 20 oC until use.

Assay procedure
The test was conducted in accordance with the assay protocol. Human Immunoglobulin E ELISA kit mentioned in China. Shangha.
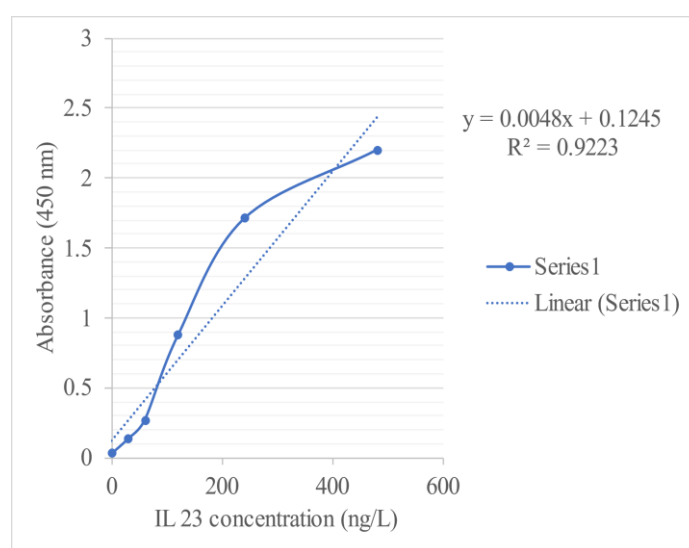

Figure 1-1: Standard curved for lL-23.

Statistical analysis
The statistical analysis of the data was performed using version 27 of the IBM SPSS software.Mean and standard error were calculated for the study variables, and probability value was calculated at the level of 0.05 and 0.001 using the independent t-test and ANOVA table (Duncan test) to indicate the statistical differences between the study variables. Percentages for non-parametric data were calculated, and the chi-square test was used to indicate significant differences.

RESULTS AND DISCUSSION
The current study included 73 individuals, including 50 patients with type 1 diabetes. Males made up 23, at a rate of (46%), while females made up 27, at a rate of (54%). The control group, which included 23 people, was made up of 13, or 56.5% of the male population, and 10, or 43.5 percent of the female population.

Table 1-1: Type 1 diabetes patients gender with gender controls groups.

Gender	Patients group No. (%)	Control group No. (%)	Probability
Males	23 (46.0)	13 (56.5)	
Females	27 (54.0)	10 (43.5)	
Total	50 (100.0)	23 (100.0)	

The results of the current study showed that the number of males with T1DM was 23, with a rate of (46%), while the number of infected females was 27, with an infection rate of (54%). It was found that the incidence of females

is higher than that of males, and this difference is significant, as P = Value = p = 0.001 as shown in Table (1-1)
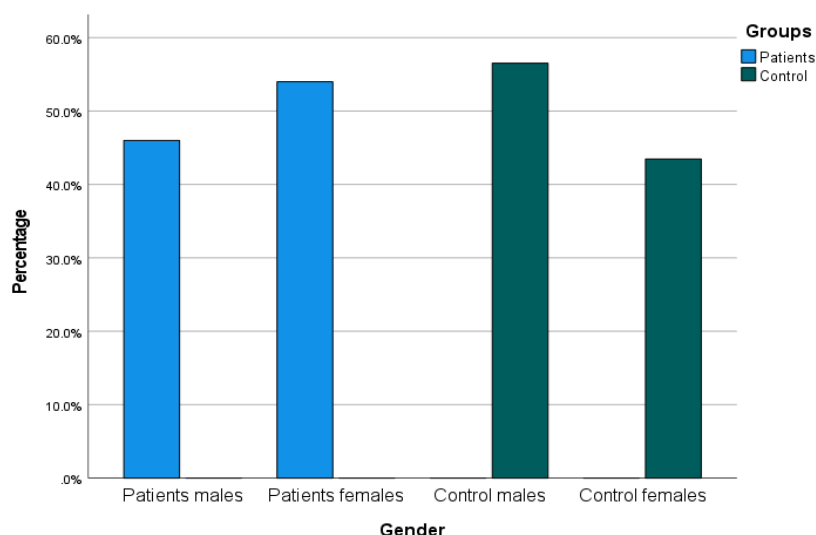
Shape (1-1): Distribution of the study groups according to the percentage of gender

The findings of the present investigation concurred with those of (Roohi et al., 2014) which indicated that the number of females with type 1 diabetes is more than that of males. While the results of the present study and the previous's findings did not coincide (Ali et al., 2023). which revealed that the incidence of type 1 diabetes in males is higher than the incidence in females. There is also a study that did not agree with the current study, as males had a higher percentage than females, but there was no significant difference (Khalil etal., 2021, Khalaf et al., 2022). Type 1 diabetes is associated with higher weight in women than men due to unhealthy food intake and lack of movement, which provides an opportunity for chronic diseases that weaken the efficiency of the immune system, in addition to the presence of other factors that have a significant impact on the weakening of the efficiency of the immune system, such as aging and family history. For type 1 diabetes (Samuel et al., 2018). The disruption of sex hormones is related to the incidence of type 1 diabetes in females, as the hormones estrogen and proclatin have receptors on T and B cells that stimulate the formation of Th1 and activate the immune response (Maboudi et al., 2019). This could be due to the hormonal effect in the case of type 1 diabetes for women, which is more than that of men, and it is due to the female sexual hormonal differences to Menstrual, Menopause, Endocrinopathy, Hormonal Contraceptive. It is also believed that the sex hormone receptors have an effect on the functions of immune and inflammatory cells (Fatima et al. al., 2017). Both sexes are affected by type 1 diabetes, and the disease can occur as a result of an endocrine (pituitary gland) disorder in both sexes (Gopta et al., 2017). It has been observed that there is an interaction between endogenous sex hormones and the occurrence of inflammation, with an increased risk of developing type 1 diabetes (Shen et al., 2018).

Measurement of IL-23 level

The results in Table 3_1 showed no significant reduction in serum IL_23 levels when compared to the control group (5.86 ± 1.04) pg/ml and the Type 1 Diabetes group (9.36 ± 1.93) pg/ml.

Table 2-1: Serum IL-23 levels in the T1DM group and the control group.

Gender	IL-23 mean ± SE (pg/ml)		Probability
	Patients group	**Control group**	
Males	11.17 ± 2.87	6.25 ± 1.47	$P > 0.05$
Females	7.01 ± 2.36	5.56 ± 1.49	$P > 0.05$
Total	9.36 ± 1.93	5.86 ± 1.04	$P > 0.05$
Probability	$P > 0.05$	$P > 0.05$	

The study of the present was not supported by the study of (Abbasi, et al., 2011). The current study agreed with a study conducted in Tehran that there was no significant difference between the level of cytokine lL_23 in patients compared to healthy subjects (Roohi etal., 2014). Despite the fact that the findings of the current study did not match those of a study carried out in Egypt (Rehab G. Khalil et al., 2021). It revealed that the concentration of lL_23 was higher in the serum of diabetes patients than it was in the serum of the healthy group. A research including 70 youngsters with type 1 diabetes made this claim. The role of IL-23 in the development of Th-17 cells and the indirect effects this has on autoimmune inflammatory illnesses are examined. This role has been researched. (Mus et al., 2010). Antigens in chronic infections activate macrophages, dendritic cells, and the creation of IL-23, which in turn drives the synthesis of IL-17. Furthermore, in the autocrine/paracrine pathway, IL-23 raises the synthesis of IL-6, IL-1, and tumor necrosing factor (TNF)-

α.(Maboudi etal., 2019). When NOD mice are given a neutralizing antibody against the IL-12 and IL-23 p40 subunit, insulitis is suppressed and diabetes is avoided. Th1 and Th17 cell formation are connected because similar heterodimeric cytokines (IL-12 and IL-23, respectively) that share the IL-12 p40 subunit regulate their differentiation. Therefore, p40 blockage ought to reduce Th1, Th17, and Th17.1 cell differentiation. In the islets of people with T1D, there is an upregulation of IL-23 and associated cytokine pathways (Marwaha etal., 2022). Being essential for the development and differentiation of Th17 cells, which release IL-17F, IL-21, IL-22, and IFN-γ, IL-23 plays a pivotal role in intestinal inflammation (Harrison etal., 2023).

CONCLUSIONS
The results of showed that the number of males with type 1 diabetes was 23, with a rate of (46%), while the number of infected females was 27, with an infection rate of (54%).It was found that the incidence of females is higher than that of males. There were no statistically significant differenes between the serum IL-23 Ievel concentration in Type 1 Diabetes patients (9.36 ± 1.93) pg / ml and healthy controls (5.86 ± 1.04) pg/ml.

REFERENCES
1. Al-Saffar OB, Ad'hiah AH. Genetic variants in IL4RA, IL6, and IL12B genes and susceptibility to hepatitis B and C virus infections among Iraqi patients. J Med Virol, 2020; 92(12): 3448-3458.
2. Abbasi, F., Amiri, P., Sayahpour, F. A., Pirmoradi, S., Abolhalaj, M., Larijani, B., … Amoli, M. M. *TGF-β and IL-23 gene expression in unstimulated PBMCs of patients with diabetes. Endocrine,* 2011; *41(3): 430–434.*
3. Abdel-Moneim, Adel; Abd El-Twab, Sanaa M.; Nabil, Ahmed; El Kazafy, Salma A. *Effect of antidiabetic therapy on TNF-α±, IL-18, IL-23 and IL-35 levels in T2DM patients with coincidental <i>Helicobacter pylori</i> infection. Journal of Taibah University for Science,* 2020; *14(1): 1377–1385.*
4. Adinortey, M. B., Agbeko, R., Boison, D., Ekloh, W., Kuatsienu, L. E., Biney, E. E., … Nyarko, A. K. *Phytomedicines Used for Diabetes Mellitus in Ghana: A Systematic Search and Review of Preclinical and Clinical Evidence. Evidence-Based Complementary and Alternative Medicine, 2019; 1–23.*
5. Ali, R.Z., Hassan, I. B., Abbas, A. H., & Saihood, Y.D. Association Between RETN Gene Polymorphism and Serum Resistin Levels in Type 1 and Type 2 Diabetes Patients. Journal of Population Therapeutics and Clinical Pharmacology, 2023; 30(9): 239–247.
6. DiMeglio LA, Evans-Molina C, Oram RA. Type 1 diabetes. Lancet, 2018; 391(10138): 2449–62.
7. Fatima, N., Faisal, S. M., Zubair, S., Siddiqui, S. S., Moin, S., & Owais, M. Emerging role of Interleukins IL-23/IL-17 axis and biochemical markers in the pathogenesis of Type 2 Diabetes: Association with age and gender in human subjects. International journal of biological macromolecules, 2017; 105: 1279-1288.
8. <u>Fatima, N., Faisal, S. M., Zubair, S., Ajmal, M., Siddiqui, S. S., Moin, S., & Owais, M. Role of Pro-Inflammatory Cytokines and Biochemical Markers in the Pathogenesis of Type 1 Diabetes: Correlation with Age and Glycemic Condition in Diabetic Human Subjects. PLOS ONE, 2016; 11(8): e0161548.</u>
9. Gupta, S., Maratha, A., Siednienko, J., Natarajan, A., Gajanayake, T., Hoashi, S., & Miggin, S. Analysis of inflammatory cytokine and TLR expression levels in Type 2 Diabetes with complications. Scientific reports, 2017; 7(1): 1-10.
10. Harrison, L. C., Bandala-Sanchez, E., Oakey, H., Colman, P. G., Watson, K., Kim, K. W., ... & Yau, C. (2023). A surge in serum mucosal cytokines associated with seroconversion in children at risk for type 1 diabetes. *Journal of Diabetes Investigation.*
11. Khalil, R. G., Abdel-Moneim, A., Yousef, A. I., Abdel-Rahman, H., Zanaty, M. I., & El-Sayed, A. (2021). Association of interleukin-2, interleukin-21 and interleukin-23 with hyperlipidemia in pediatric type 1 diabetes. Molecular Biology Reports. doi:10.1007/s11033-021-06545-0
12. Kim HG. Cognitive dysfunctions in individuals with diabetes mellitus. Yeungnam Univ J Med., Sep. 2019; 36(3): 183-191.
13. Maboudi, A., Eghbalian, A., Seifi, H., Bahar, A., Heidari, M., & Mohammadpour, R A. Serum levels of interleukin-23 and 35 in patients with and without type 2 diabetes mellitus and chronic periodontitis. Caspian J Intern Med., 2019; 10(3): 295-302.
14. Maboudi, A., Eghbalian-Nouzanizadeh, A., Seifi, H., Bahar, A., Mohadese, M., Mohammadpour, R. A., ... & Sepehrimanesh, M. Serum levels of interleukin-23 and 35 in patients with and without type 2 diabetes mellitus and chronic periodontitis. Caspian Journal of Internal Medicine, 2019; 10(3): 295.
15. Marwaha, A. K., Chow, S., Pesenacker, A. M., Cook, L., Sun, A., Long, S. A., ... & Dutz, J. P. A phase 1b open-label dose-finding study of ustekinumab in young adults with type 1 diabetes. *Immunotherapy Advances*, 2022; *2*(1): ltab022.
16. Mensah-Brown EP, Shahin A, Al-Shamsi M, Lukic ML New members of the interleukin-12 family of cytokines: IL23andIL-27modulate autoimmune diabetes. Ann NY Acad Sci., 2006; 1079: 157–160.
17. Mus, A. M. C., Cornelissen, F., Asmawidjaja, P. S., van Hamburg, J. P., Boon, L., Hendriks, R. W., & Lubberts, E. *Interleukin-23 promotes Th17 differentiation by inhibiting T-bet and FoxP3 and is required for elevation of interleukin-22, but not interleukin-21, in autoimmune experimental arthritis. Arthritis & Rheumatism,* 2010; *62(4): 1043–1050.* doi:10.1002/art.27336

18. Khalaf, A., AL-Tameemi, H. K., & Jasem Abdullah, Y. Detection of Genes ermB, mecA, bla Z and msrA in Uropathogenic Staphylococcus aureus Isolates between the Gram-Positive Bacteria that Cause Urinary Tract Infections. Iranian Journal of War and Public Health, 2022; 14(1): 99-104.

19. Pang, H., Luo, S., Huang, G., Xia, Y., Xie, Z., & Zhou, Z. Advances in knowledge of candidate genes acting at the beta-cell level in the pathogenesis of T1DM. Frontiers in Endocrinology, 2020; 11: 119.

20. Piero, M. N., G. M. Nzaro, and J. M. Njagi. Diabetes mellitus-a devastating metabolic disorder.Asian journal of biomedical and pharmaceutical sciences, 2015; 5.40: 1.

21. Roohi, A., Tabrizi, M., Abbasi, F., Ataie-Jafari, A., Nikbin, B., Larijani, B., … Maleki, A. Serum IL-17, IL-23, and TGF-βLevels in Type 1 and Type 2 Diabetic Patients and Age-Matched Healthy Controls. BioMed Research International, 2014; 1–7.

22. Samuel, T. R., Tejaswi, N., Kumar, P., Prudhvi, K., Sravani, N. S., Govardhini, B., ... & Rajagopalan, B. Clinical significance of screening for anaemia in diabetic patients. Artic Int J Pharm Sci Rev Res., 2018; 48(2): 20-24.

23. Shen, J., Fang, Y., Zhu, H., & Ge, W. Plasma interleukin-22 levels are associated with prediabetes and type 2 diabetes in the Han Chinese population. Journal of diabetes investigation, 2018; 9(1): 33-38.

24. Sicree R, Shaw J & Zimmet P. The Global Burden. Diabetes and Impaired Glucose Tolerance. Prevalence and Projections. In: Gan, D. ed. Diabetes Atlas, 3rd edn. Brussels: International Diabetes Federation, 2006; 16–103.

25. World Health Organization, Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. World Hearth Org, 2015.

26. Yedjou, Clement G., Jameka Grigsby, Ariane Mbemi, Daryllynn Nelson, Bryan Mildort, Lekan Latinwo, and Paul B. Tchounwou. "The Management of Diabetes Mellitus Using Medicinal Plants and Vitamins" *International Journal of Molecular Sciences,* 2023; 24(10): 9085.