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Estimation the Serum Levels of IL-8 and IL-12 in Iraqi Children with Rheumatoid Arthritis

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ABSTRACT

Rheumatoid Arthritis (RA) is a chronic autoimmune disease. Many etiological agents are proposed to play a role in its pathogenicity, cytokines play an important role in the immune-pathogenesis of RA. This study aims to measure the levels of cytokines (IL-8 and IL-12) in untreated children patients with RA. The present study involved 50 patients with RA (17 males and 33 females) whom their ages are between (5-10) years, besides 25 apparently healthy children (10 males and 15 females) in the same ages involved as control group. The data demonstrates that there was a significant increase in the mean level of IL-8 in the peripheral blood of patients group in comparison with control group, the mean levels in RA patients was 42.7 ± 0.4 pg/ml, while the mean levels in control was 10.3 ± 0.2 pg/ml. Besides a significant increase in the mean level of IL-12 in peripheral blood of RA patients 75.3 ± 0.6 pg/ml in comparison with control 26.3 ± 0.1 pg/ml. Based on our results, the high levels of IL-8 and IL-12 in children with RA may be used as a marker of disease or may participate in the severity of RA.

Keywords: Rheumatoid arthritis, IL-8, IL-12, ELISA.

1. INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, inflammatory autoimmune disease characterized by inflammation of the synovial joints and progressive destruction of cartilage and bone [1]. The RA pathogenesis is activation of the innate immune response, which includes the activation of dendritic cells and other leukocytes in the synovial fluid result in increased production of cytokines and chemokines [2,3]. Cytokines involvement in the development of cellular and humoral immune responses, consequently, pro-inflammatory and anti-inflammatory cytokines are highly produced in RA patients, especially in those with active RA [4]. Cytokines mediate communication between cells, resulting in the attraction of inflammatory and immune cells into the joints and the activation of cells to release products that lead to tissue destruction [5]. Consequently, many cytokines are detected at the synovium in patients with RA, where they have a role in inflammation with RA. Cytokine can be used to diagnose, measure the progress of diseases, and to predict the effects of treatment [6].

Chemokines, a subgroup of small cytokines, play a central role in inflammatory processes by regulating leukocyte migration into sites of tissue damage. Chemokines in autoimmune diseases may be used for prediction and evaluation of the diseases. In the rheumatoid synovium, chemokines are derived primarily from macrophages and fibroblasts. One of The major chemokines in RA is IL-8, which is an important chemo attractant for neutrophils, monocytes, and T cells into the rheumatoid synovium [4]. IL-8 is responsible for the increased number of neutrophils in RA joints, and therefore for the clinical manifestation of joint as well as pain [7].

IL-12 is a pro-inflammatory cytokine produced by different antigen presenting cells. It also promotes a Th1 phenotype thus initiating cell mediated immune response, therefore it is involved in the pathogenesis of rheumatic diseases [8]. IL-12 has been implicated in the pathogenesis of autoimmune disease like type 1 diabetes [9]. There are only a few reports about the

cytokine profiling in children with RA in Iraq, therefore the aim of this study is to investigate the serum levels of IL-8 and IL-12 in a group of Iraqi children patients with RA compared with healthy controls.

2. MATERIALS AND METHODS

2.1. Patients

Fifty children aged between 5-10 years with RA (17 males and 33 females) were enrolled in the study. They were referred to the Central Pediatric Hospital, and Al Elwea Hospital. The diagnosis was done by the consultant medical staff at the hospital. According to the medical history of the children, clinical examination and the results of laboratory tests. The patients with RA have a significant increase in the Erythrocyte Sedimentation (ESR) and C - reactive protein (CRP). 25 healthy children (10 males and 15 females) and between (5-10 years) were included as a control sample.

2.2. Sample Collection

Blood samples were collected from the children. Then, the sera were separated after centrifugation at 3000 rpm for 5 minutes. Which in turn was distributed into tightly closed eppendorf tubes, and stored at −20∘C until analysis.

2.3. Measurement of Cytokine Serum Levels

Sera of RA patients and controls were assessed for level of IL-8 and IL-12 using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Immunotech-France), which was designed for the quantitative measurement of cytokine in human sera. According to the manufactures protocol, the assay were performed.

2.4. Statistical Analysis

Serum level of cytokines was statistically analyzed using the computer programme statistical package of social sciences (SPSS). Data were analyzed using Analysis of variance test (ANOVA) for differences between means, followed by Duncan multiple range test.

3. RESULTS AND DISCUSSION

3.1. Serum Level of IL-8

The present results showed that serum level of IL-8 were significantly higher in RA patients than in healthy controls (P<0.01). According to gender, the level of IL-8 was significantly higher in male patients (43.1 ± 0.4 pg/ml) as compared to control (10.8 ± 0.1). Furthermore, serum level of IL-8 in female patients also showed significant differences between patients (40.9 ± 0.3 pg/ml) and control (9.7 ± 0.6 pg/ml) (Table. 1).

3.2. Serum Level of IL-12

Patients with RA had higher serum level of IL-12 in comparison to the healthy control group (P<0.01). Male and female RA patients showed high mean IL-12 (76.1 ± 0.5 and 72.9 ± 0.3 pg/ml), when compared with male and female control group (25.7 ± 0.6 and 28.2 ± 0.2 pg/ml) (Table. 2).

Table 1. Serum level of IL-8 in RA patients and controls.

Groups	IL-8 serum level Mean ± S.E. (pg/ml)		Probability P ≤
	Patients No. = 50	Controls No. = 25	
Male	43.1 ± 0.4	10.8 ± 0.1	0.01
Female	40.9 ± 0.3	9.7 ± 0.6	0.01
Total	42.7 ± 0.4	10.3 ± 0.2	0.01

Table 2. Serum level of IL-12 in RA patients and controls.

Groups	IL-12 serum level Mean ± S.E. (pg/ml)		Probability P ≤
	Patients No. = 50	Controls No. = 25	
Male	76.1 ± 0.5	25.7 ± 0.6	0.01
Female	40.9 ± 0.3	28.2 ± 0.2	0.01
Total	72.9 ± 0.3	26.3 ± 0.1	0.01

In RA, the inflammation gets out of control, and the immunity system becomes more active, thus increases the concentration of the factors that induce the secretion of cytokines [4]. The T cells, B cells and the orchestrated interaction of pro-inflammatory cytokines play key roles in the pathophysiology of RA. The release of cytokines causes synovial inflammation. In addition to their articular effects, pro-inflammatory cytokines promote the development of systemic effects resulting in fatigue and depression [2,7].

In this study the serum levels of IL-8 and IL-12 were substantially higher in RA as compared with that of healthy control. These results have similarly to other studies were conducted to confirmed the role of IL-8 and IL-12 are involved in the pathogenesis of RA, and elevated in serum of RA, and may provide clinically useful markers for the diagnosis of disease activity [10]. In the study of Al-Hassan *et al*., (2013) confirmed further the significant role of IL-8 in the pathogenesis and inflammatory processes of RA, and may be used as an indicators of disease activity [11].

Additionally, the study of Al-Hassan, (2010) observed the high levels of cytokines in RA disease and IL-8, IL-12 is one of them, and also confirmed about the role of IL-8 in inflammatory processes of RA, which provides a clinically useful marker for the diagnosis of disease activity [7].

Ebrahimi *et al*., (2009) observed that the serum level of IL-12 was significantly increased in RA Iranian patient when compared to healthy control, and also confirmed about the role of IL-12 as predictive factor in RA [12]. The effect of age and gender on cytokines production was observed in this results, therefore several reports discussed the differences in cytokine production associated with age, and demonstrated that chronic, low grade inflammation is linked with the age. The cytokine production in pediatric and adult patients identified multiple differences in terms of pro-inflammatory and anti-inflammatory cytokines between the two groups. Therefore, the age of onset in RA patients is to be taken into consideration as it may reflect the cytokine production profile [6].

Gender also influences the way that the immune system responds. Females demonstrate better B cell-mediated immunity than males, and also influences T cell immunity, females having greater resistance to induced tolerance, and higher levels of IL-1, IL-4, and IFN-gamma in contrast to males who produce more IL-2, IL-4 and IL-13. Differences in cytokine production profile have also been suggested to play an important role in the gender bias with regards to the ratio of autoimmune disease [6].

4. CONCLUSION

This study has provided the analysis of IL-8 and IL-12 in Iraqi children with RA, and confirmed the role of these cytokine in inflammatory process, through the highly serum levels of IL-8 and IL-12 in children with RA compared with healthy children.

5. REFERENCES

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