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Serum levels of interleukine-12 in women with toxoplasmosis in Diyala province

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Abstract:

Toxoplasma gondii (*T. gondii*) is a major cause of chronic parasitic infection in the world. Primary infection with *T. gondii* stimulates production of high levels of interleukine -12 (IL-12) and interferon (IFN- γ) by cells of innate immune system. The aim of the study to determine the levels of IL-12 in sera of women with serologically confirmed toxoplasmosis. The results revealed a statistically significant increase in IL-12 levels ($p<0.05$) in women infected with *T. gondii* as compared to control group in Diyala province.Women with *T. gondii* infection exhibit high levels of IL-12.

Keywords: *T. gondii*, serum , IL-12

مستويات انترلوكين -١٢ في مصل النساء المصابات بمرض داء القطفي محافظة ديالى

يعد طفيلي(*Toxoplasma gondii* (*T. gondii* المسبب الرئيسي لاحد الامراض الطفيلية المزمنة في العالم ان الاصابة الاولية بالطفيلي تحفز انتاج IL-12 و انترفيرون كاما (IFN- γ) بواسطة خلايا الجهاز المناعي.ان الغرض من الدراسة الحالية تحديد مستوى IL-12 في مصل النساء المصابات بداء القطط . وقد اظهرت النتائج ظهور ارتفاع معنوي في مستوى IL-12 في النساء المصابات مقارنة بغير المصابات في محافظة ديالى مما يدل على ان المرض قديسبب ارتفاع في مستوى IL-12 .

كلمات مفتاحية : مرض داء القطط، مصل ، IL-12

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Introduction:

Toxoplasmosis is a disease caused by worldwide obligatory intracellular parasite *Toxoplasma gondii*. Although the disease is generally asymptomatic, it may result in important clinical manifestations in some patients were suffer from immunodeficiency or under immunosuppressive therapy. The disease may be acquired congenitally or at any time in life by oral route (WHO,1979). Many factors may influence the outcome of the disease , such as duration and frequency of exposure, route of infection, parasite and load immunological factors and unidentified factors (Bahra-Oliveira, 2009). The clinical manifestations of toxoplasmosis results from direct tissue destruction by the parasites, but inflammatory cytokines mediated immunopathological changes may also contribute to disease progression (Oktenli *et al.*, 2004). Several studies had been shown that *T.gondii* infection induce a strong cell-mediated immune response especially , Th1(Hodi and Soiffer, 2002).

It is well established that pathogens such as viruses, bacteria, protozoans and helminthes stimulates immune response involving the development of T helper cells characteristic Th1 and Th2 depending on the type of organisms. Induction of a Th1 response characterized by production of pro-inflammatory mediators such as interleukine-12 (IL-12), interferon γ (IFN- γ) and nitric oxide (Jankovic *et al.*,2001). While the Th2 response characterizes by production of IL-4, IL-5 and IL-10 (Miller *et al.*,2009). Arguably, the quintessential Th1 inducing pathogen is *T. gondii*. So, the aim of this study was to determine the levels of IL-12 in sera of women infected with *T. gondii* to understand the developing immune response in these patients.

Materials and methods:

Blood samples were collected from 40 individuals (25 patients and 15 controls). The samples were collected during April and May 2011.sera were stored at -80 C° until used. Both anti- *T. gondii* IgG and IgM antibodies were detected by enzyme-linked immunosorbant assay (ELISA) accordinf to manufacturer instruction. The levels of IL-12(p70)was determined by RayBio® ELISA kit for the quantitative measurement of human IL-12 in sera. Statistical analyses were done to determine the significant difference among study groups using SPSS computer program. Descriptive statistic are shown as arithmetic mean ± SD. The differences between groups were investigated by using t-test for equality of means, while the Levene's test was used for equality of variance. $p\leq$ was considered statistically significant.

Results:

Toxoplasmosis was confirmed by the presence of anti- *T. gondii* IgG and IgM antibodies by ELISA. The mean levels of IL-12 (p70) in patients group was significantly higher than that of the control group ($p<0.05$), table (1).

Table (1): Mean levels ± SD of IL-12in study groups

Study group	No. tested	IL-12 levels (pg/mL) (mean ± SD)	P value
Control	15	7.2 ± 2.9	<0.05
Patient	25	30.8 ± 9.8	

Discussion:

The result of the present study revealed that the levels of IL-12 (p70) in patients with toxoplasmosis were significantly higher than in controls (30.8 ± 9.8 pg/mL and 7.2 ± 2.9 pg/mL, respectively).for the best of our knowledge there were no previous Iraqi studies on this cytokine among patients with toxoplasmosis. However , there were some Iraqi studiescdocumented a high CD4+T lymphocyte and CD8+B lymphocyte counts in women infected with *T. gondii* (Abass, 2005), and high concentration of INF- γ in women infected with this parasite(AL-Sorchee, 2005).

Cell mediate immunity involving INF- γ activated macrophage effecter cells is critical in host resistant to infection with obligatory intracellular protozoan *T. gondii* (Khan *et al.*,1994; James, 1995). In *T. gondii* infection , the source of INF- γ may not include the stimulated CD4 and CD8 T lymphocytes only but it may also elaborated from natural killer (NK) cells (Gazzinelli et al., 1992). These NK cells produced INF- γ, which in turn activates macrophages in a microbicidal state. The IL-12 molecule is a heterodimer of 70 KDa consisting of two disulphide – bonded subunits , IL 12 p40 and p70 , which must be expressed in the same cell to generate bioactive IL-12 . IL-12 ,which is major cytokine produce by the macrophage and the dendritic cells during antigen stimulation appears to play amajor anti –*Toxoplasma* role during the acute phase of the infection (Waree, 2008).The mechanism by which IL-12 increase host production against *T. gondii* infection appears to be induction of NK cells which produced INF-γ that enhancing the microbicidal activity of microphages(Khan *et al.*,1994). This mechanism may be a suitable explanation for the significant increase in IL-12 levels obtained in this study .This contention may be supported by evidences accumulated through studies on mice infected with *T. gondii* which affirmed an increase INF-γ levels as well as NK, CD4 T lymphocytes and B lymphocytes (Khan *et al.*,1994; Hunter *et al.*, 1995; Abass, 2005; Al-Sorchee, 2005). Of note , IL-12 production is enhanced by INF- , γ B lymphocytes act as source of IL-12 (Hodi and Soiffer, 2002).

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