Changes in Interleukins and Follicle Stimulating Hormone in Toxoplasmosis Male Patients

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Abstract

In several countries there are endemic of parasitic diseases, specifically in developing countries, several studies investigated that toxoplasmosis is related with sterility of male. Aims of study are assessment of anti-*Toxoplasma* IgG antibodies in patient's serum and their relation with interleukins and FSH hormone. IL-6 stimulates antibody production and extend effect of proinflammatory by stimulating the production of acute phase proteins. IL-10 and IL-12 control the immune response type. Cytokine synthesis is inhibits by the former and by blocking the IL-6 and TNF-α production, the response with involvement of Th2 and activation of B cells has an advantage. Detection for the toxoplasmosis which is based on toxo IgG , interleukins and FSH used the classic ELISA technique that based on immunoassay system using fluorescence technology and antigen antibody interaction. They were found in 1 (3.03%) of azoospermic patients and 4(12.12%) of oligozoospermic patients, while the negative results found in 32(96.97%) of azoospermic patients and 29(87.88%) of oligozoospermic patients. The control group had 34(100%) negative results in toxoplasmosis. The mean serum levels of IL-6 and IL-17 (pg / ml) increased significantly in patients with Toxoplasma gondii compared to the control group (237.97±9.09 pg / ml 285.52±12.45and pg / ml, respectively; $p<0.0001$) . In this study, it has been concluded that infection with *T. gondii* can effect on the level of the interleukins and FSH in infertile couples.

Keyword: *Toxoplama gondii, Interluekin, FSH hormone , Cytokine , Immune Response*

Introduction

Toxoplasmosis is caused by parasite *Toxoplasma gondii*, then might be cause impaired folliculogenesis , endometritis, uterine and ovarian atrophy, vasculitis ,adrenal hypertrophy and decrease in semen quality, concentration, and motility in male [(1)]. Through ingestion of parasite cysts present in infected foods, undercooked or through swallowing oocysts contained in polluted water and vegetables it is highly transmitted. So, human infections from T. Gondii are normal but are minimally symptomatic or asymptomatic in most cases of immunocompetent humans and their effects may remain unnoticed [(2)] . It was confirmed that in this case, T. Gondii infection is slightly higher in infertile couples relative to fertile couples. Another researchs found that the amount of anti-sperm antibody in toxoplasma infected pairs was higher than in non-infected pairs [(3)] .

For most cases of adults infection with T. Gondii doesn't cause severe illness, but during pregnancy may have implications for the deformities of developing fetus [(4)] . It was later reported that after the T. gondii infection there was a reduced fertility in the rats. along with lower epididdymis weight, and increased irregular morphology of the sperm. In addition, the association between increased apoptosis of sperm and toxoplasmosis, especially of diploid spermatozoa [(5)] .

Cytokines are significant mediators during the whole pregnancy in the bidirectional association between the reproductive system and the maternal immune system [(6)] . IL-17 is a pro-inflammatory cytokine created by several tissues induced by several factors, inclusive viruses and different cytokines, whose effect is directed cellular targets either to myeloid or non-myeloid [(7)] . Various cytokines (IL-4, IL-5, IL-6, IL-10, IL-13, and IL-14)

synthesize by Th2 lymphocytes, which play an important part in pathogenesis of parasites. IL-6 stimulates the synthesis of antibodies and extend proinflammatory action by stimulating acute phase protein development [8] . Both IL-10 and IL-12 regulate the form of immune response. Cytokine synthesis is inhibits by the former and by blocking the IL-6 and TNF-α production, the response with involvement of Th2 and activation of B cells has an advantage, reaction with Th2 involvement and B cell activation has an advantage [9] .

Materials and Methods

This study was conducted on 130 samples (100 Patients , and 30 control group) their age ranged from (19-55years). Blood samples were collected from High institute of infertility diagnosis during the period from December to March 2020. About 5 ml fasting venous blood specimens were gathered from both patients and control groups , and transferred into anticoagulant gel tube for centrifugation. After that, serum was separated which then used for assess biochemical parameters. Follicle-stimulating hormone (FSH) was evaluated by (I-chromaTM FSH), and IgG was assessed from serum samples by enzyme-linked immunosorbent assay (ELISA) using Human IgG anti Toxoplasma gondii ELISA Kit (Human company).

The levels of interleukins were assessed in blood serum using ELISA method for IL-6, and IL-17 by (MyBioSource, USA, Cat No. MBS261259 , and Cat No MBS764076) respectively.

Results

Table (1) show the presence of anti-*toxoplasma gondii* IgG antibodies (ELISA test) in 100 men. They were found in 1 (3.03%) of azoospermic patients and 4(12.12%) of oligozoospermic patients, while the negative results found in 32(96.97%) of azoospermic patients and 29(87.88%) of oligozoospermic patients. The control group had 34(100%) negative results in toxoplasmosis.

Table (1). Distribution of samples study according to presence of anti- toxoplasma IgG antibodies with difference groups.

The Groups	Positive No. (%)	Negative No. (%)	P-value
Azoospermia (No. = 33)	1 (3.03%)	32 (96.97%)	0.0001 **
Oligozoospermia (No. = 33)	4 (12.12%)	29 (87.88%)	0.0001 **
Normozoospermia (No. = 34)	0 (0.00%)	34 (100%)	0.0001 **
P-value	0.00965 **	0.00965 **	---
**** (P<0.01).**			

When study the hormonal change of toxoplasmosis infected patients can observe low testosterone level in 1 (3.03%) of azoospermic patient and oligozoospermic patient, while there were decreased in FSH and LH hormones in 2 (6.06%) of oligozoospermic patients as it clear in table (2).

Table (2): The hormonal study of toxoplasmosis infected patients.

The Groups	FSH (mIU/ml)
(n=33) Azoospermia	0(0.00%)
(n=33) Oligozoospermia	2(6.06%)

The mean serum levels of IL-6 and IL-17 (pg / ml) increased significantly in patients with Toxoplasma gondii compared to the control group (237.97±9.09 pg / ml 285.52±12.45and pg / ml, respectively; p<0.0001) as shown in Table 3.

Table (3). Laboratory results of patients and controls.

Variable	Sample	No.	Mean	Standard Error of Mean	P-value
IL-6(pg/ml)	Control	30	85.32	11.26	0.0001
	Patients	100	237.97	9.09	
IL-17(pg/ml)	control	30	41.94	3.22	0.0001
	patient	100	285.52	12.45	

Discussion

The one of most usual disease consider to have adverse effect on the human reproduction is toxoplasmosis; previous studies of parasite infections in the male genital tract proved the possibility of *T. gondii* infection increase the defects of testicular during secondary hypogonadism via hypothalamic-hypophyseal axis changes and found that toxoplasmosis can change all spermatic parameters include concentration, morphology and motility that lead to the production of significantly decreased sperm cells but without sterility [10] .

This study proved that the infection with *T. gondii* in infertile male is intensity higher than fertile male, four patients of oligozoospermic patients and one patient of azoospermic patients have toxoplasmosis infection.

The patients of *T. Gondii* had significantly higher the IL-6 and IL-17 levels compared to the control group, which indicate an inflammatory condition. The key role of IL-6 is immune response involvement by lymphocyte intervention B. It is a mediator in charge of the development of acute phase protein and the cytotoxic activity of NK cells will be increased, though unspecific, inflammatory marker which states this study agreement with Matowicka's study found *T. Gondii* patients had double the IL-6 levels compared with control group [11] .

The study conducted by Satti showed the mean serum level of IL-17 in patients a highly significant increase when compared with control group [12] this agreement with our study .In the present study, the early increase in IL-17 serum level matches the results of different researchers [13], investigated that an early rise in IL-17 was identified in the early stages of infection. IL-17 was also presented to be included in the early recruitment and development of neutrophils, which are necessary for parasite clearance during initial stages of infection [14] .

Previous studies correlated the decrease in the concentration of sperms with toxoplasmosis infection that *Toxoplasma* parasites lead to elevate the level of cell apoptosis that is stimulated by a decreased in

gonadotropin level. As well as, decrease in the levels of LH, FSH and testosterone and these results effect the spermatogenesis process that lead to decrease proliferation of sperms and spermatocytes which predict to be the most sensitive stage [15] . Marathe's research showed that, in addition to testosterone and FSH, selective immunoneutralization of LH triggers the apoptotic cell death of meiotic and post-meiotic germ cells in testes that have been shown to regulate the survival of germ cells, the cellular apoptosis in the testis result from exposure to decrease of hormones which related with the lower numbers of sperms in toxoplasmosis infected patients. Also more previous findings indicated that Toxoplasma has the effect on the efficiency of immune system and induction of IL-1b which triggered the modification of hypothalamic GnRH release and may be manufacture is interposed by increased release of the dopamine and norepinephrine from neurons in the brain stem as well as, hypothalamus that are suppressor to gonadotropin releasing hormone [16] . Another studies indicated that cytokines have more effects in deficiency the release of anterior pituitary hormones. Also, cytokines are show to depress the HPG axis, directly or indirectly via increased corticotrophin-releasing hormone (CRH) and/or cortisol. indicating it or not changed CRH and/or cortisol participate in part to HPG axis selectively suppress serum FSH concentrations [17] .

Conclusion

Toxoplasmosis infection leads to decrease in sperm concentration. As well as, significantly increased the levels of interleukin in contrast, decrease in the level of FSH of infected patients affect the spermatogenesis process that lead to decrease proliferation of sperms and spermatocytes in toxoplasmosis patients.

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