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Original Article

Effects of *Toxoplasma gondii* Infection in Level of Serum Testosterone in Males with Chronic Toxoplasmosis

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Abstract

Background: *Toxoplasma gondii* is an intracellular protozoan parasite that infects human and animals. *Toxoplasma* parasites are isolated from different parts of animals even from semen but there are little information about the effect of toxoplasmosis on fertility in animals and humans. In present study, the effect of chronic toxoplasmosis on serum levels of testosterone in men was studied.

Methods: In this case-control study, 1026 men referred to Arak Post Marriage Center were selected. Three ml of blood samples were collected and sera separated by centrifugation at room temperature. These sera were analyzed for detection of anti-*T. gondii* IgG antibody. Next 365 positive sera were selected as cases and also the same number of negative sera (365) as controls. Finally the level of testosterone was analyzed for the cases and controls samples.

Result: Serological tests on the sera of 1,026 men in Arak City showed that 365 of them had anti-*Toxoplasma* antibody. Comparison of testosterone concentration in case and control groups showed that testosterone concentration in case group was less than control group and this difference was statistically significant ($P<0.05$).

Conclusion: The chronic toxoplasmosis could affect reproductive parameters in men.

Introduction

Toxoplasma gondii is an intracellular protozoan parasite that infects human and animals. Infection *by T. gondii* is widely prevalent in human and animals throughout the world, and of both veterinary and medical importance, because it may cause abortion, fetal death, and stillbirths in its intermediate hosts (1). Apart from children

with congenital infection and in immunocompromised patients, normally the infection is asymptomatic (1).

Mice with chronic toxoplasmosis suffer from secondary hypogonadism induced by dysfunction of hypothalamos (2-4). In addition, a male patient was previously reported with transient hypogonadotrophic hypogonadism owing to *Toxoplasma* infection (5). Children with congenital toxoplasmosis have a high frequency of precocious puberty (5). Although previous reports suggest that toxoplasmosis may cause transient hypogonadotrophic hypogonadism, but no detailed analysis has been conducted in humans. *Toxoplasma* parasites are isolated from different parts of animals even from semen but there is practically no risk of venereal transmission (1).

There are little information about the effect of toxoplasmosis on fertility in animals and humans. Therefore, in the present study, the effect of chronic toxoplasmosis on serum levels of testosterone in men was evaluated.

Materials and Methods

In this case-control study, 1026 men referred to Arak Post Marriage Center, central Iran were selected. Firstly, written consent and the demographic questionnaire were completed. Then, 3 ml of blood samples were collected and sera separated by centrifugation at room temperature. These sera were analyzed for detection of anti-*Toxoplasma* IgG antibody. Next 365 positive sera were selected as cases and also the same number of negative sera (365) was selected as controls. Finally the level of testosterone was analyzed in the cases and controls samples.

Antibody assay

ELISA method was used for determination of anti-*Toxoplasma* IgG . The ELISA kits were provided by Pishtaz Teb CO. LTD., Iran. The procedure was performed according to the manufacturer's instructions.

Testosterone determination

Testosterone assay was performed by DRG Testosteron ELISA kit (EIA-1559) as mentioned by manufacturer instruction. All standards, samples, and controls were performed as duplicate. Finally, a standard curve was constructed and testosterone concentrations were calculated in samples.

Statistical analysis

Statistical analyses were carried out using the SPSS software version 16. This quantitative data were presented as mean ± standard deviation. Comparison of quantitative variants between two groups was assessed by student *t*-test. Differences with *P* values less than 0.05 were considered significant.

Results

Serological tests on the sera of 1,026 men in Arak City showed that 365 of them had anti-*Toxoplasma* antibody. In other words, the prevalence of this infection among was 35.57%. These 365 positive samples were selected as cases and same number of negative sera as controls. Demographic characteristics in case and control group are shown in Table 1.

Table 1: Demographic characteristics in case and control group

Variable	Case group N (%)	Control group N (%)
Age (yr)		
15-19	4(1)	9(2.4)
20-29	279(76.4)	297(81)
30-39	60(16.4)	47(12.8)
40-49	13(3.5)	7(1.9)
50-59	2(0.5)	2(0.5)
>60	6(1.6)	2(0.5)
Missed	1(0.25)	1(0.25)
Habitat		
Urban	281(77)	296(81)
Rural	84(23)	69(19)
Keeping cat		
Yes	4(1)	7(1.8)
No	356(97.75)	354(97.2)
Missed	5(1.25)	4(1)

The mean of anti-toxoplasma IgG concentration in case and control groups are shown in Table 2. The mean of testosterone concentration and anti-toxoplasma IgG concentration in case and control groups are shown in Table 3.

Comparison of testosterone concentration in two groups showed that testosterone concentration in case group was less than control group and this difference was statistically significant ($P<0.05$).

Table 2: Anti-*Toxoplasma* IgG concentration in case and control groups

Variable	IgG concentration mean in case group(IU/ml)	IgG concentration mean in control group (IU/ml)
Age (yr)		
15-19	37	3.1
20-29	83.54	2.7
30-39	68.74	3.22
40-49	68.6	3.62
50-59	20.7	3.25
>60	42.28	5.35
Habitat		
Urban	76.28	2.84
Rural	88.35	2.92
Keeping cat		
Yes	87.82	4.7
No	79.23	2.82

Comparison of testosterone in two groups according to age showed that testosterone level differences in 20-29 and 40-49 age in case group was statistically significant($P<0.05$). (Table 4).

Comparison of testosterone in two groups according to habitat showed that testosterone level differences in urban habitant in case group was statistically significant ($P<0.05$) (Table 5).

Table 3: Comparison of testosterone and anti-toxoplasma IgG concentration in case and control groups

Group	Number	Testosterone concentration mean (ng/ml)	SD	*P* value
Case	365	5.081	2.518	0.022 *
Control	365	6.214	3.876	
Group	Number	IgG concentration mean(IU/ml)	SD	*P* value
Case	365	79.06	56.571	0.001 *
Control	365	2.863	1.745	

* *P* value<0.05 is significant

Discussion

The purpose of this study was to evaluate and comparison of testosterone concentration in males with chronic toxoplasmosis (case group) and non-toxoplasmosis males (control group). The results showed that the mean of testosterone concentration in case group was less than control group ($P = 0.022$). But it should be noted that serum testosterone concentrations in cases and controls was in normal range.

Table 4: Comparison of testosterone concentration in case and control groups according to age

Age groups (yr)	Testosterone concentration mean in case group(ng/ml)	Testosterone concentration mean in control group(ng/ml)	*P* value
15-19	5.925	6.511	0.733
20-29	4.941	6.025	0.001
30-39	5.575	5.957	0.472
40-49	4.630	8.74	0.030
50-59	5.9	8.15	0.593
>60	6.433	6.4	0.994

Table 5: Comparison of testosterone concentration in case and control groups according to habitat

Habitat	Testosterone concentration mean in case group(ng/ml)	Testosterone concentration mean in control group(ng/ml)	*P* value
Urban habitant	4.981	6.12	0.043
Rural habitant	5.411	6.614	0.276

Also comparison of testosterone levels showed that testosterone concentration in urban habitants and 20-29 and 40-49 yr age groups, in case and control was statistically significant. In normal condition the average of testosterone level declines with age in men but in current study testosterone level in 40-49 yr age group in controls increased. Perhaps this result is due to the small sample size in this age group. This study was designed based on toxoplasmosis infection in men and then the samples were divided into age groups so some groups included fewer samples.

The studies that have been conducted by some researchers indicate that there is a relation between chronic toxoplasmosis and disturbance of the reproductive parameters in male animals (1, 6-8).

Terpsidis et al. studied the influence of toxoplasmosis on male reproductive parameters. Their results showed marked increasing of sperm abnormalities in infected mice. In this study, toxoplasmosis could affect main reproductive parameters in male rats, which are the most predictive of their fertilizing capacity (1).

Arantes et al. studied the presence of *T. gondii* in semen, testicle and epididymis of dogs experimentally infected. The parasite was present in these tissues. Artificial insemination of female dogs with *T. gondii* -positive seminal samples induced the serologic conversion. These results suggest that *T. gondii* can be sexually transmitted in domestic dogs (6). Lopes et al. (2009) conducted a similar study on the rams that had similar results (7).

Kanˇkova et al. studied changes in the testosterone levels in the latent phase of toxoplasmosis in laboratory mice artificially infected with cystogenic but relatively virulent strain T38 of *T. gondii*. Testosterone levels in both female and male mice with latent toxoplasmosis were decreased in comparison to uninfected controls (8). Whereas previous studies (9-11) could not determine whether *Toxoplasma* infection induces changes in testosterone concentration or whether low- and high-testosterone subjects differ in the probability of acquiring *Toxoplasma* infection. The former hypothesis is correct and toxoplasmosis influences the level of testosterone. Increased concentrations of testosterone to have immunosuppressive effects, according to this the decrease of testosterone concentration could be an adaptive response of infected mice to *Toxoplasma*-induced immunosupp-ression (8). Some researchers believe that the direct and indirect evidences in human infected to toxoplasmosis, concentration of testosterone was increased. For example infected males are taller, have a lower

left hand 2D:4D ratio (9, 10), and are perceived as more dominant and masculine (11). Infected females have a (nonsignificantly) lower left hand 2D:4D ratio and are more likely to give birth to a boy than a girl (12); the latter is also true for laboratory infected mice (13). Also the results of his study showed that males had a (non-significantly) higher and, surprisingly, *Toxoplasma*-infected females had a lower concentration of testosterone than *Toxoplasma*-free controls.

The opposite direction of the testosterone shift in men compared to women can explain the observed gender specificity of behavioral shifts in *Toxoplasma*-infected subjects (14).

Oktenli and colleagues announced the transient hypogonadotrophic hypogonadism in men is not rare in toxoplasmosis (5). His results were consistent with the results of experimental studies in animals (2-4).

Mice with chronic toxoplasmosis suffer from secondary hypogonadism induced by dysfunction of hypothalamus.

Conclusion

The result of current study showed that the chronic toxoplasmosis could affect reproductive parameters in men.

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