

Original article

Effects of *Toxoplasma gondii* infection on plasma testosterone and cortisol level and stress index on patients referred to Sina hospital, Tehran

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Abstract

Introduction and objective: *Toxoplasma gondii* is an intra cellular protozoan parasite which infects 30 to 60% of the world population. A wide range of toxoplasmosis conditions has been studied, but there are still unknown damages which must be explored. In the present research, the effect of this parasite on testosterone and cortisol changes in the infected men and women was examined.

Materials and methods: A total of 180 patients (73 females and 107 males), were examined for IgG anti-*Toxoplasma* antibody, cortisol and testosterone in their plasma. In addition, the patients also filled in personality questionnaire DASS21 (depression, anxiety, and stress).

Results: Results showed that 24(%13/33) females and 39(%20) males were positive with IgG anti-*Toxoplasma* antibody, respectively. A statistically significant correlation between *Toxoplasma* infection and testosterone and cortisol increase in women and men were observed. Stress and anxiety index also increased in men and women whereas depression index increased only in men.

Conclusion: The results show a direct relation between raise *Toxoplasma* infection and cortisol, and testosterone increase in bout men and women and high DASS21 test score in *Toxoplasma* infected group.

Significance and impact of the study: Our results may indicate that following *Toxoplasma* infection, the probability of stressful condition is high.

Keywords: *Toxoplasma*; *Toxoplasma gondii*; Testosterone; Cortisol; Stress

Introduction

Toxoplasma gondii is an intra-cellular protozoan parasite which causes infection in many warm-blood vertebrates such as cats, pigs, and 30-60% of the world population; 27% in Denmark [1] 40% in south Italy [2], 84% in Paris [3], 20% of pregnant women in Finland [4] are infected. Human usually get infected after swallowing *Toxoplasma* cysts excreted by cats or raw/not well-cooked meat.

This parasite has been reported to cause four types of disease. The most dangerous is congenital toxoplasmosis, which often results in serious damages to fetus and development of various symptoms like micro-cephalic, hydro-cephalic and mental problems in infants [5]. The Second form is acute postnatally acquired toxoplasmosis. This form recognized by the presence of tachyzoite in blood and other tissues. A wide range of clinical symptoms like cervical lymphadenopathy, fever, headache, and psychiatric and neurological complications can be found in immunocompetent patients. But symptoms of acute toxoplasmosis are usually mild and harmless. Accordingly, toxoplasmosis is usually misdiagnosed with bacterial or viral diseases [5]. Inconsistence in testosterone levels among infected and uninfected people result in behavioural differences [6].

Lower cellular immunity which is associated with high levels of steroid hormones contributes to the survival of the parasite in the body. Such these people, cause of steroid hormones increase with weak immune system, contribute to this parasite survive in body [7]. Other reports indicate that *Toxoplasma* can increase the number of son [8], height in infected men and change personality factors in men and women [5]. It is likely that sexual hormone changes can play an important certain role in relation with *Toxoplasma* and aforementioned phenomena. Patients suffer

from chronic toxoplasmosis are taller than uninfected ones, and sexual hormones concentration, testosterone, is higher than uninfected people, and also sexual maturity age of infected men is lower that uninfected men [9].

Regarding, the above report, it seems that there is a relationship between infected individuals by toxoplasmosis and stress hormones increase. It must be noted that stress hormones increase can lead to behavioural challenges in individuals. The aim of this survey was effect of chronic *Toxoplasma* infection on testosterone and cortisol changes also behavioural changes include: depression, anxiety, stress, in the infected men and women

Materials and methods

This study was done on patients referred to Sina hospital in the form of case-control (Double blind trial). 180 individuals were examined in this study. After referring to this centre, patients - if desired- fill DASS21 questionnaire (*Depression Anxiety Stress*) personality [10,11]. Blood samples were taken at the same time, and the conditions met aseptic considerations and then centrifuged at 2000rpm for 10mins. ELISA test was run on all of the samples using IgG Kit (Pishtaz Teb Co., Iran) and final results were recorded by ELISA reader (optical absorbance, OD=450). Using this kit, samples less than 0.9unit/ml, 0.9-1.1unit/ml and more than 1.1unit/ml were considered as negative, suspicious and positive, respectively.

Out of 180 people, IgG (anti-*Toxoplasma* antibody) positive samples were regarded as the case group (24 females and 39 males) and the others as the control group (12 females and 19 males). Control group was identical with the test group in terms of age, sex, and job. Then, both groups were examined by ELISA method for testosterone (Diaplus Inc. kit, America)

and cortisol (Diaplus Inc. kit, America) level. Final results were recorded by ELISA reader and in the form of optic absorbance (OD=450). Quantitative examination of the samples was done by drawing standard curve and through optic absorbance of positive and negative controls and determined consistencies.

Results

In women suffering from *Toxoplasma*, serum level of testosterone ($p=0.002$, $t=2.491$) is shown in figure 1 and cortisol ($t=5.774$, $P<0.0001$) (Fig. 2) were higher than control group. Considering DASS21 form spread among individuals, a significant relation was found between *Toxoplasma* and stress ($t=7.514$, $P<0.0001$) as shown in (Fig. 3), and anxiety ($t=2.53$, $p=0.04$) (Fig. 4). But, no significant difference was found between *Toxoplasma* and depression ($P=0.1$) (Fig. 5). Also, in the infected women, the amount of face hairiness ($P=0.001$) (Table 1), and hair reduction ($P=0.002$) (Table 2) was higher than control group. This is because of the fact that 75% of the patients were positive to hairiness, but 83.3% of control group negatively responded to it. Besides, 66.7% of the infected women positively responded to hair fall.

In comparison with control group, the infected women were taller ($t=4.13$, $P<0.0001$). But, there was not any significant difference between weight reduction and *Toxoplasma* among the patients ($t=-1.27$, $P=0.2$). Also, there was

not any significant relation between the infected and uninfected ones ($P=0.8$). The amount of testosterone ($t=6.03$, $P<0.0001$) as shown in figure. 1 and cortisol ($t=7.93$, $P<0.0001$) (Fig. 2), serum, and - using DASS21 - stress ($t=8.125$, $P<0.0001$) (Fig. 3), anxiety ($t=3.187$, $P=0.001$) (Fig. 4), and depression ($t=2.93$, $P=0.001$) (Fig. 5) were higher than the control group.

There was a significant relation between height increase and *Toxoplasma* in the patients ($t=3.87$, $P<0.0001$). Most of the infected men had a less hair reduction, compared with control group ($P<0.002$) (Table 2). There was not a significant relation between age ($P=0.5$) and weight reduction ($P=0.1$, $t=-1$), comparing with control group. Also, this study examined the relation between *Toxoplasma* antibody titer and testosterone and cortisol level increase of which the results are as follow.

There was a significant correlation between antibody titer increase and testosterone increase ($P<0.0001$), where antibody titer was higher, cortisol serum level was also higher ($P<0.0001$). In the infected men and women, there was a significant correlation between anti-*Toxoplasma* antibody increase and stress ($P<0.0001$), anxiety ($P=0.01$), and depression ($P=0.005$) increase.

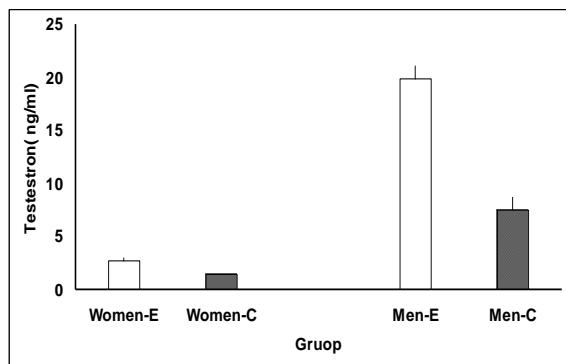


Fig. 1: Testosterone level concentration blood serum between two groups case-control; E: group experimental, C: group control

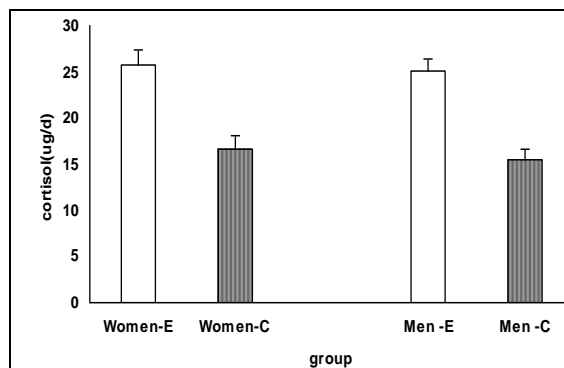


Fig. 2: Cortisol concentration blood serum between two groups case and control; E: experimental group, C: control group

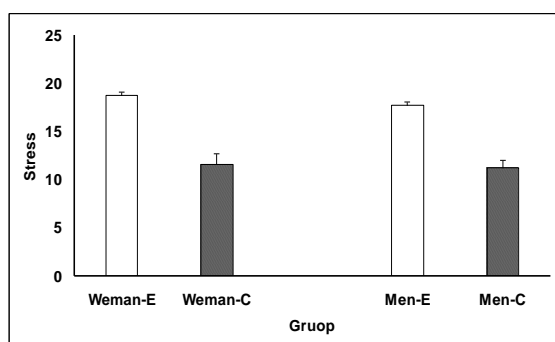


Fig. 3: Rate stress between men and women, case and control; E: experimental group, C: control group

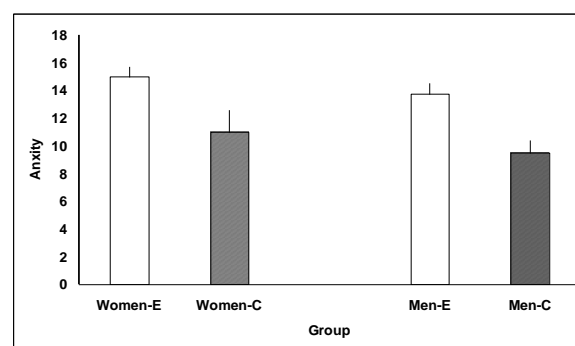


Fig. 4: Rate anxious between men and women, case and control group; E: experimental group, C: control group

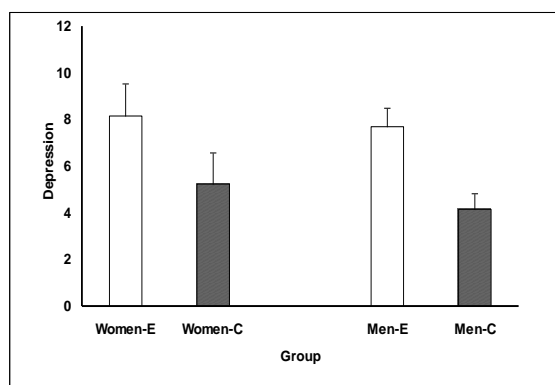


Fig. 5: Rate depression between men and women, case and control; E: experimental group, C: control group

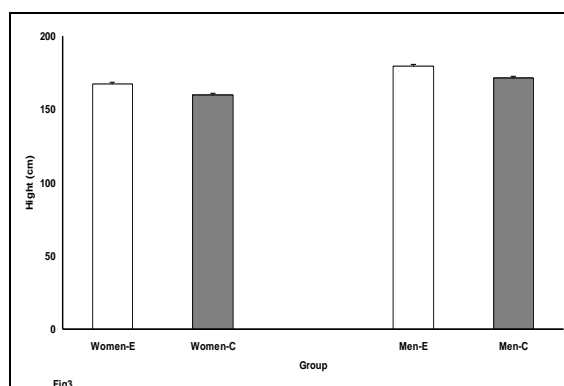


Fig. 6: Tall comparison between infected and non infected women and men; E: experimental group, C: control group

Discussion

The present study is conducted for exploring the relation between *Toxoplasma* infection and stress changes and stress hormones, on one hand, and testosterone changes, on the other. Our study demonstrated that there is a significant correlation between these hormones levels and their complication (excessive stress resulted from high cortisol levels), and hair reduction and hairiness cause high blood testosterone and *Toxoplasma* infection. *Toxoplasma* is one of the almost widespread parasite diseases common between human and warm-blood animals, which is widely distributed around the world. In Iran also, its prevalence is different in various areas; 55.7% in Gilan and Mazandaran [12], 44% in Kerman [13]. Positive serological outbreak is different in different areas; the infection in warm weather and lowlands is more widespread than mountains.

Table 1: Relative frequency rate hairy in women

Women response to hairy	Yes	No	Total	
Infected women	No	18	6	24
	%	75.0	25.0	100
Non infected women	No	2	10	12
	%	16.7	83.3	100
Total	No	20	16	36
	%	55.6	44.4	100

Table 2: Loss hair relative frequency

Response to hair loss	Yes	No	Total	
Infected women	No	16	8	24
	%	66.7	33.3	100
Non infected women	No	2	10	12
	%	16.7	83.3	100
Infected men	No	9	30	39
	%	23.1	76.9	100
Non infected men	No	8	11	19

Of the main ways of parasite and *Toxoplasma* infection transmission is

consuming raw or semi cooked meat infected with *T. gondii* [14-16], or infected cat feces, and also congenital through placenta to fetus [17,18], drinking unpasteurized milk and even blood transfusion, transplantation and semen reception [19]. *T. gondii* is a famous protozoan which can result in behavioural changes in its host and has been studied in mice models [20,21]. Our research results indicated that there is a direct relation between *Toxoplasma* infection and testosterone increase in blood plasma.

Previous studies demonstrated that the infection is a result of dopamine increase in brain [21], following *Toxoplasma* infection and adrenal glands sensibility and secretion of hormones from hypothalamus hypophysis adrenal axis. On the other hand, note that this axis plays a critical role in regulating stress hormones secretion. We hypothesized that it might firstly induced by testosterone increase among women and stress stimulating hormones (cortisol) irritation when they got infected by *Toxoplasma*.

The second reason of this study was; it seems that this hormone is not a good criterion for *Toxoplasma* infection diagnosis in men. So, in the present research cortisol titer changes and also psychological tests related to stress stimulation are considered as other index for *Toxoplasma* infection. Results indicated that cortisol titer in the infected individuals is severely higher in both infected men and women than uninfected ones. Cortisol increase is a symptom of significant stress in a person, and in case it lasts for a while, it will lead to stress-induced behaviours and anxiety. On the other hand, this hormone titer increase can damage different parts of nervous system. However, cortisol titer was not measured in different times (three months, six months, one year), but the study proved

that cortisol increase in these people lasted for a long time after the infection.

This research showed that *Toxoplasma* infection does not end in problems resulted from testosterone increase and more serious implication are induced in the infected individual like stress increase and the like (depending on the sex) which can be the origin of anti-social behaviours. Nevertheless, researchers' reports show that stress and high cortisol levels are directly related with serious diseases like cardiovascular diseases, diabetes, addiction and anti-social behaviours [22-26], and also stress and anxiety.

On the other hand, in the case of stressful condition in pregnant women, it will result in deformations of fetus and infant [26]. Accordingly, researchers suggest that women, before pregnancy, have a *Toxoplasma* test and become certain of the absence of this parasite. Regarding the direct relation found between *Toxoplasma* infection and severe stress behaviour and high blood cortisol. It suggested that; since cortisol titer is not high in usual circumstances, stressful behaviour result from cortisol increase which can be considered as acceptable factor than testosterone increase.

Based on the present research findings, no significant relation was observed between this parasite infection and depression in women patients. But, it was observed in the infected men. Since anxiety and stress are consequences of being stressful, further researches must be conducted on the relation between *Toxoplasma* infection and stress in women population.

Conclusion

It is concluded that *Toxoplasma* infection are likely considered as an important factor in stress induction. Besides, since it is probable that parasite presence in the body

leads to blood cortisol increase, it is suggested that its accuracy be explored in the next researches.

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Conflict of interest statement: All authors declare that they have no conflict of interest.

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References

- 1) Lebech M, Larsen SO, Petersen E. Prevalence, incidence and geographical distribution of *Toxoplasma gondii* antibodies in pregnant women in Denmark. *Scand J Infect Dis.* 1993; 25: 751-6.
- 2) Buffolano W, Gilbert RE, Holland FJ, Fratta D, Palumbo F, Ades AE. Risk factors for recent *Toxoplasma* infection in pregnant women in Naples. *Epidemiol Infect.* 1996; 116: 347-51.
- 3) Desmonts G, Couvreur J. Congenital toxoplasmosis. A prospective study of 378 pregnancies. *N Engl J Med.* 1974; 290: 1110-16.
- 4) Lappalainen M, Koskela P, Hedman K, *et al.* Incidence of primary *Toxoplasma* infections during pregnancy in Southern Finland, A prospective cohort study. *Scand J Infect Dis.* 1992; 24: 97-104.
- 5) Flegr J, Hrdá Š, Kodym P. Influence of latent 'asymptomatic' toxoplasmosis on body weight of pregnant women. *Folia Parasitol.* 2005; 52: 199-204.
- 6) Flegr J. Effects of *Toxoplasma* on Human Behavior. *Schizophrenia Bulletin.* 2007; 33: 757-60.
- 7) Flegr J, Zitkova S, Kodyn P, Frynta D. Induction of changes in human behavior by the parasitic protozoan *Toxoplasma gondii*. *Parasitology.* 1996; 113: 49-54.
- 1) Kankova S, Sule J, Nouzova K, Fajfrlik K, Frynta D, Flegr J. Women infected with

- parasite *Toxoplasma* have more sons. *Naturwissenschaften*. 2007: 94: 122-7.
- 2) Hodkov H, Kolbekov P, Skallov A, Lindov J, Flegr J. Higher perceived dominance in *Toxoplasma* infected men, a new evidence for role of increased level of testosterone in toxoplasmosis associated changes in human behavior. *Neuro Endocrinol Lett*. 2007: 28: 110-4.
 - 3) Lovibond SH, Lovibond PF. Manual for the Depression Anxiety Stress Scales. 2nd ed. Sydney. Psychology Foundation. 1995: 520-6.
 - 4) Lovibond PF, Lovibond SH. The structure of negative emotional states. Comparison of the depression anxiety stress scales (dass) with the beck depression and anxiety inventories. *Behav Res Ther*. 1995: 33: 335-43
 - 5) Ghorbani M, Edrissian GW, Afshar A. Serological survey of north west and sought west part of Iran. *Med Hygn*. 1981; 75: 38-40.
 - 6) Noorbakhsh S, Mamishi S, Rimaz S, MR Monavari. Toxoplasmosis in primiparus pregnant women and their neonates. *Iranian J Publ Health*. 2002: 31: 51-4.
 - 7) Raquel Coelho AL, Kobayashi M, Carvalho LB Jr. Prevalence of IgG antibodies specific to *Toxoplasma gondii* among blood donors in Recife. Northeast Brazil. *Revista do Instituto de Medicina Tropical de Sao Paulo*. 2003: 45: 229-34.
 - 8) Saebi E. Parasite diseases in Iran. 6th ed, Tehran, Cultural Institute. 1998: 251-41.
 - 9) Jones JL, Ogunmodede F, Schftel J, Kirkland E. Toxoplasmosis-related knowledge and practices among pregnant women in the United States. *Infect Dis Obstet Gynecol*. 2003: 11: 139-45.
 - 10) Mandell GL, Bennet JE, Dolin R. Bennett's principles and practice of infectious disease. 5th ed. Philadelphia, Churchill Livingstone, 2000: 2858-81.
 - 11) Segundo GR, Silva DA Mineo JR, Ferreira MS. Congenital toxoplasmosis in Uberlandia, MG, Brazil. *J Trop Pediatr*. 2004: 50: 50-5.
 - 12) Haj Ghany H, Abasalan A, Parto F, Mohammadi H, Ravagh M, Hosseini Shami F. The prevalence of serum anti-*Toxoplasma* IgG antibodies among the female students of Kerman University of Medical Sciences in 2005-2004. *J Infect Dis Trop*. 2008: 41: 39-43.
 - 13) Skallova A, Frynta D, Kodym P, Flegr J. The role of dopamine in *Toxoplasma*-induced behavioural alterations in mice. An ethological and ethopharmacological study. *Parasitology*. 2006: 133: 525-35.
 - 14) Otte C, Marmar C, Pipkin S, Moos R, Browner W, Whooley M. Depression and 24-hour urinary cortisol in medical outpatients with coronary heart disease. *Biol Psychiatry*. 2004: 56: 241-7.
 - 15) Roy M, Roy A, Brown S. Increased urinary-free cortisol outputs in diabetic patients. *J Diabetes Complication*. 1998: 12: 24-7.
 - 16) Chiodini I, Adda G, Scillitani A, et al. Cortisol secretion in patients with type 2 diabetes relationship with chronic complications. *Diabetes Care*. 2006: 30: 183-8.
 - 17) Lovallo WR. Cortisol secretion patterns in addiction and addiction risk. *Int J Psychophysiol*. 2006: 59: 195-202.
 - 18) Vescovi PP, Coiro V, Volpi R, Passer M. Diurnal variations in plasma ACTH, cortisol and beta-endorphin levels in cocaine addicts. *Horm Res*. 1992: 37: 221-4.
 - 19) O'Keane V, Marsh MS. Depression during pregnancy. *BMJ*. 2007; 334: 1003-5.

