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Study of Latent *Toxoplasma gondii* Role in Level of Testosterone, DHEA, Cortisol and Prolactin Hormones of Young Persons

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ABSTRACT

Toxoplasmosis influences the behavior and personality of infected persons. Possible mechanisms for these psychic disorders include its effect on dopamine and on hormone levels. In the present research, the effect of latent toxoplasmosis on testosterone, DHEA, cortisol and prolactin hormones in the infected and noninfected individuals was examined. A total of 215 plasma sample were examined for IgG and IgM anti-*Toxoplasma* antibody, testosterone, DHEA, cortisol and prolactin levels. In addition the prevalence of hirsutism, acne and alopecia also evaluated in individuals. Serological analysis confirmed that 61 men (28.37%) and 58 women (26.97%) were sero-positive. A statistically significant correlation between toxoplasmosis and testosterone and cortisol increase were observed but there were no significant differences between infected and noninfected individuals in level of prolactin and DHEA. There were significant differences in frequency of allopoy, acne and hirsutism between two groups. Because of these hormones have though helps in management of stress and human behavior and personality so the direct correlation between toxoplasmosis and psychological disorders is suggested due to effect of *Toxoplasma* on host's hormone levels.

Key words: *Toxoplasma gondii*, hormone level, hirsutism

INTRODUCTION

The causative agent of toxoplasmosis is an obligate intracellular protozoan, *Toxoplasma gondii*, which is widely prevalent in humans, warm blooded animals and birds throughout the world. It is estimated that 1/3 of the world population is infected with toxoplasmosis (Tenter *et al.*, 2000). Humans become infected by the oral route through the consumption of undercooked meat contaminated with cysts, food products or water contaminated with oocysts (De Moura *et al.*, 2006; Galvan-Ramirez *et al.*, 2010). Other routes of transmission are organ transplantation (Schaffner, 2001), blood transfusion (Siegel *et al.*, 1971) and congenital transmission (Vanni *et al.*, 2008).

Although human toxoplasmosis in healthy adults is usually asymptomatic, a serious disease can occur in the case of a congenital infection and immunocompromised individuals such as AIDS

patients and transplant recipients (Rostami *et al.*, 2006; Siteo *et al.*, 2010). After a short phase of acute toxoplasmosis, the infection proceeds to its latent stage when tissue cysts with bradyzoites are formed and these survive for the rest of the host's life mainly in neural and muscular tissues (Vanni *et al.*, 2008).

One of the dramatic characteristics of *T. gondii* is its ability to change the behavior of its host (Webster *et al.*, 2006). Infected mice and rats have been shown to suffer from impaired motor performance and coordination (Hutchinson *et al.*, 1980), learning deficits (Witting, 1979) and reduced avoidance of open spaces and predators (Skalova *et al.*, 2006). These traits are believed to be an evolutionary mechanism to increase the chance of hosts being eaten by felines (Moore, 2002). Current results suggest that changed concentrations of testosterone and dopamine probably play an important role in the differences in the personality and behavior between *Toxoplasma* infected and *Toxoplasma* free subjects (Skalova *et al.*, 2006; Kankova *et al.*, 2011). Testosterone is a hormone that is responsible for the growth of secondary male sexual characteristics. Change testosterone levels, one might experience physical symptoms like dermal reactions-include irritation, erythema, hirsutism and acne-abnormal growth of the muscles, kidney failure and psychological side effects like mood swings, depression and anxiety. Dehydroepiandrosterone (DHEA) is an important endogenous steroid hormone which is the most abundant circulating steroid in humans. It is produced in adrenal gland. The DHEA serves as precursor to estrogens and testosterone (Cox and John-Alder, 2005; Tuck and Francis, 2009).

Prolactin a hormone released from the anterior pituitary (under the inhibitory control of dopamine) plays a major role in the lactation, regulation of reproductive functions, growth (Benedetto and Auriault, 2001). Prolactin has been considered as a cytokine able to modulate immune response (Benedetto *et al.*, 1995).

On the other hand, a hypothesis of endocrine-immune interaction is based on the fact that sex hormones, as example testosterone, prolactin, cortizole influence the immune system. The localization of sex hormones receptors in immune cells, including lymphocytes, macrophages, granulocytes and mast cells illustrates that there are direct connections between the endocrine and immune systems and that endocrine factors can directly modulate the expression of target genes in immune cells (Klein, 2000). Thus, the aim of this study was evaluating effect of latent toxoplasmosis on testosterone, cortisol, prolactin and DHEA changes of young persons in Ahvaz city.

MATERIALS AND METHODS

Specimen collection: This study performed on 215 blood sample collected from persons referred to hospitals of medicine university of Ahvaz. Sera were separated by centrifuging the blood samples at 2000 rpm for 10 min then they kept at -20°C until examination.

ELISA test for toxoplasmosis and hormone levels: In order to determine anti-IgG and anti-IgM *Toxoplasma* antibodies ELISA test was run. The measurements were performed by IgG and IgM ELISA kit (Trinity Biotech Captia™, USA). According to the manufacturer's protocol, the IgG anti-*Toxoplasma*, levels lower than 1 UI mL⁻¹ was reported negative and the level >1 UI mL⁻¹ was reported positive. In regard to IgM levels lower than 1 UI mL⁻¹ was reported negative and levels equal or higher than 1 UI mL⁻¹ was reported positive. Also, ELISA method performed for determination of testosterone, dehydroepiandrosterone (DHEA), cortisol and prolactin (Monobinde USA) concentration. 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. The prevalence of hirsutism, acne and alopecia also evaluated in individuals.

Statistics analysis: Data was analyzed using multiple univariate analyses of variance (ANOVA), Chi-square test. The probability level of 0.05 was accepted as statistically significant. Statistical analyses were carried using SPSS version 16.

RESULTS

Frequency of toxoplasmosis in samples: About 215 blood samples (age 18-35 years), were collected. Serological analyses confirmed that 61 men (28.37%) and 58 women (26.97%) were sero-positive and 47 men (21.86%) and 49 women (22.79%) were sero-negative for toxoplasma antibodies. Frequencies of the participants’ demographic features are listed in Table 1.

Correlation between toxoplasmosis and hormone levels: Levels of testosterone, DHEA, hirsutism, acne and alopecia hormones in infected and non-infected subjects were compared using multiple univariate ANOVA (Table 2).

There were differences between infected and non-infected subjects in level of testosterone (F = 13.88, p = 0.00) and cortisol (F = 5.36, p = 0.02) because they were significantly higher in IgG positive group than IgG negative group. There were no significant differences between two groups in level of prolactin and DHEA. A comparison of all 4 hormones is shown in Fig. 1.

Table 1: Frequency of the participant’s demographic features

Demographic variables	Total	
	N	%
Sex		
Women	106	49.30
Men	107	46.76
Marital status		
Single	157	73.02
Married	58	26.97
Divorced/widowed	0	
Employed		
Yes	136	63.25
No	79	36.74
Level of education		
Diploma	25	11.62
Associate degree	33	15.34
Bachelor	129	60.00
Graduate	28	13.02
Ethnicity		
Fars	78	36.27
Arab	58	26.97
Lor	40	18.60
Kord	16	7.44
Turk	11	5.11
Other	12	5.58

Table 2: Comparison of levels of testosterone, DHEA, cortisol and prolactin hormones in infected and non-infected subjects

Levels of hormones	IgG-negative subjects		IgG-positive subjects		F _{1,125}	p-value
	Mean	SD	Mean	SD		
Testosterone	3.38	3.92	5.83	5.39	13.88	0.00
DHEA	1.31	1.31	1.69	1.67	3.23	0.07
Cortizol	12.64	5.82	14.00	6.41	3.23	0.02
Prolactin	5.06	3.70	5.7	4.22	1.37	0.24

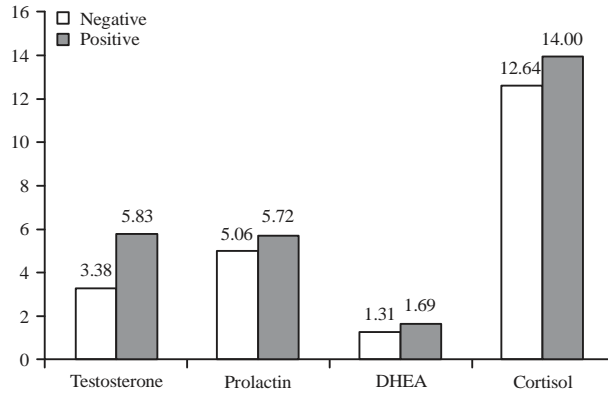


Fig. 1: Comparison of levels of testosterone, DHEA, cortisol and prolactin hormones in infected and non-infected subject

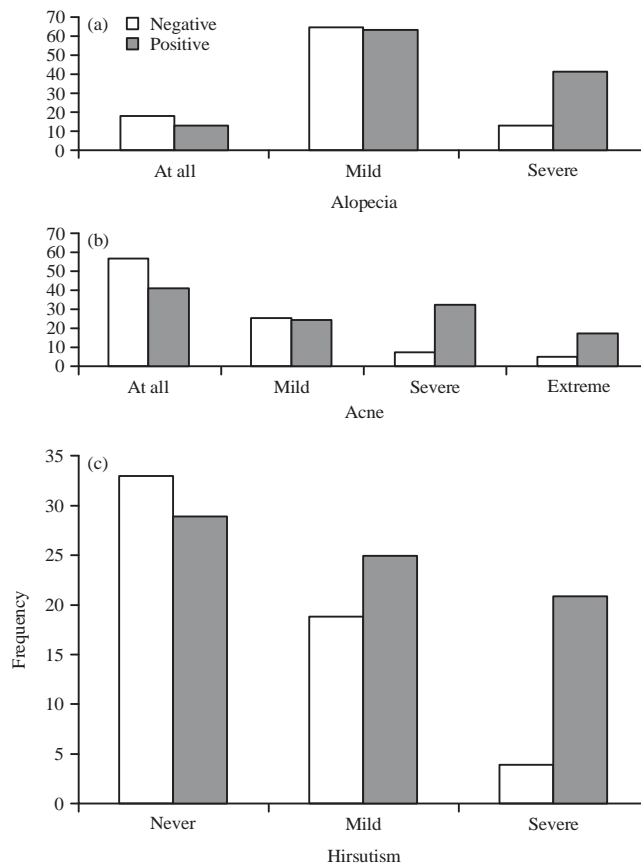


Fig. 2(a-c): Frequency of (a) Alopecia, (b) Acne and (c) Hirsutism in infected and non-infected women

Correlation between toxoplasmosis and alopecia, acne and hirsutism: Frequency of alopecia and acne in infected and non-infected subjects was compared using Chi-square test. The results have been shown in Table 3-4 and Fig. 2. As shown in Table 3 and 4, there were significant differences between infected and non-infected men in alopecia ($p < 0.001$) and acne ($p = 0.001$).

Table 3: Comparison between infected and non-infected subjects in alopecia

	At all		Mild		Severe	
	N	%	N	%	N	%
IgG-positive	13	10.92	64	53.78	42	35.29
IgG-negative	18	18.75	65	67.70	13	13.54

Table 4: Comparison between infected and non-infected subjects in acne

	At all		Mild		Severe		Extreme	
	N	%	N	%	N	%	N	%
IgG-positive	42	35.50	25	21.18	33	27.96	18	18.75
IgG-negative	58	60.41	26	27.08	7	7.29	5	5.20

Table 5: Comparison between infected and non-infected women in hirsutism

	Never		Mild		Severe	
	N	%	N	%	N	%
IgG-positive	29	38.66	25	33.33	21	28.00
IgG-negative	33	58.92	19	33.92	4	7.14

This is because of the fact that 35.29 and 18.75% of the patients were positive to severe alopecia and acne, respectively but in sero-negative group 13.54 and 5.20% of individuals were positive to alopecia and acne, respectively.

Frequency of hirsutism in infected and non-infected women was compared using Chi-square test. There was difference in hirsutism between infected and non-infected women (Table 5). In comparison with sero-negative group 28% of the patients were positive to severe hirsutism but 4% of control group responded to it positively.

DISCUSSION

Present study demonstrated that the concentration of testosterone and cortisol changed in relation to latent toxoplasmosis and they were significantly higher in IgG positive individuals. On the other hand, according to our finding there is a significant correlation between these hormone levels and their complication such as alopecia, acne and hirsutism.

In addition to the generally mild physical health effects of *Toxoplasma gondii*, there is an increasing amount of evidence that infected humans also experience a variety of personality changes. For instance, infection has been associated with neuroticism and schizophrenia, but also more commonly with slightly less serious characteristics such as reduced intelligence and novelty-seeking and increased apprehension (Flegr, 2007; Yolken *et al.*, 2009). Studies comparing individuals with anti-*Toxoplasma* antibodies to an uninfected control group show that latent toxoplasmosis tends to increase guilt, vigilance and distrust, at least among men (Lindova *et al.*, 2006; Flegr, 2007). Infection is linked to reduced conscientiousness, morality and rule-conscious behavior among males (Flegr and Hrdy, 1994; Webster *et al.*, 2006). The underlying mechanism for these behavioral effects are usually thought to be changes in neurotransmitter functions and more specifically increased dopamine levels (Webster, 2001; Skallova *et al.*, 2006). In addition, there are indications that increased testosterone levels play a role (Kankova *et al.*, 2007). For example, infected male university students have increased concentrations of testosterone and their faces are more masculine (Flegr *et al.*, 2008). In contrast, infected female students have decreased levels of testosterone which corresponds to decreased levels of testosterone in infected male and female mice (Kankova *et al.*, 2011). Infected male students are 3 cm taller than non-infected male students and

both male and female students have a lower index finger to ring finger ratio which is considered as an indication of being exposed to higher concentrations of testosterone during pregnancy (Manning, 2002; Flegr *et al.*, 2005). The increased concentration of testosterone was also recently reported in *Toxoplasma* infected men, women and rats (Shirbazou *et al.*, 2011; Vyas, 2013).

Results in current study indicated that there is relation between toxoplasmosis and testosterone and cortisol increase in anti-IgG *Toxoplasma* antibody positive patients. There were no significant differences in prolactin and DHEA level in these individuals. An explanation for the observed increase in the level of testosterone in latent toxoplasmosis is that individuals with high testosterone levels are more susceptible to any infection including toxoplasmosis (James, 2010). Hirsutism, acne, alopecia are clinical expressions of testosterone in women of reproductive age (Karrer-Voegeli *et al.*, 2009). This study showed that frequency of these disorders in *Toxoplasma* infected patients are significantly higher from sero-negative individuals.

These results indicated that cortisol level in the infected persons is higher than uninfected ones. High level of cortisol in the blood disrupts the normal functioning of the immune system and people with elevated cortisol levels may become more prone to infection such as toxoplasmosis. Excessive production of cortisol can also hinder the functioning of the thyroid gland and cause high blood pressure and hyperglycemia.

Increase testosterone and cortisol levels in patients may cause harmful psychological side effects. Excessive levels of testosterone (social hormone) can lead to depression and anxiety. Individuals with increased level of cortisol (stress hormone) may suffer from emotional disorders like depression, paranoia and anxiety (Cox and John-Alder, 2005; Karrer-Voegeli *et al.*, 2009). Based on the present research findings *Toxoplasma* infection can induce elevation of testosterone and cortisol level in infected patients and by this manner this protozoan parasite probably effects on human behavior, personality and phenotypic traits.

CONCLUSION

Toxoplasma infection has very serious impacts on human health and socio-economic burdens throughout the world. This study results indicated that in latent toxoplasmosis cortisol and testosterone level in patient's increased. Because of these hormones have though helps in management of stress and human behavior and personality so it is suggested that the direct correlation between toxoplasmosis and psychological disorders especially in human models be explored in the next researches.

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