

ORIGINAL ARTICLE

Latent Toxoplasmosis and Testosterone level affect second to fourth digit ratio in Human

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ABSTRACT

Toxoplasmosis infections vary from an asymptomatic, self-limiting infection to a fatal disease, as in patients with congenital infections. Anti- Toxoplasma gondii specific immunoglobulin (IgG) antibodies in serum samples from 185 apparently healthy males and 130 females were detected by enzyme-linked immunosorbent assay (ELISA). 2D:4D digit ratio was measured and quantitative determination of testosterone total concentration in human sera by microplate Enzyme Immunoassay was done for latent toxoplasmosis infections. Results showed that toxoplasmosis infected males and females had significant differences in circulating level of testosterone from toxoplasmosis free subjects. Also Toxoplasmosis infected males and females to have significantly lower left hand 2D:4D digit ratio than right hand from healthy subjects. These results suggested that subjects with clinically asymptomatic latent toxoplasmosis differ from those who are Toxoplasma free in some morphological parameters like 2D:4D digit ratio, which may be associated with postnatal testosterone level.

Key words: latent toxoplasmosis, testosterone, 2D:4D digit ratio, Toxoplasma gondii.

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INTRODUCTION

The protozoan parasite *Toxoplasma gondii* infects 20–60 % of the population in most countries, depending on climate, hygienic standards and cooking habits [1]. Postnatal acquired toxoplasmosis in immunocompetent subjects causes usually only mild disease, acute toxoplasmosis, which turns spontaneously into lifelong latent toxoplasmosis. Latent toxoplasmosis is characterized by the presence of the dormant cyst stage of the parasite mainly in the neural and muscular tissues [2]. Latent toxoplasmosis in humans is considered as clinically asymptomatic [3].

Toxoplasmosis disease can be severe in the immune suppressed patients [4]. In addition, the ability of sex and pregnancy associated hormones to influence the severity of *T. gondii* infection is of particular public health interest due to the ability of this parasite to cause congenital disease if infection occurs during pregnancy [5].

Most cases of non-congenitally acquired toxoplasmosis are asymptomatic in healthy humans, but lymphadenopathy is a possible clinical symptom. Lower cellular immunity which is associated with high levels of steroid hormones contributes to the survival of the parasite in the body [6]. Some reports indicate that *Toxoplasma* can increase the ratio of son birth, the height in infected men and change personality factors in men and women [7, 8].

Sex differences in infected people are mediated, in part, by the effect of androgens as example, testosterone, C19 steroid hormone that is the predominant circulating in blood stream and is producing from Leyding cells in testicles. They play an important role in the normal development of male characteristics and demonstrate the male.

Latent toxoplasmosis is known to influence the morphology of infected persons and also increases the probability of the birth of male offspring in both humans and mice. All these traits can be related to the observed differences in the concentration of testosterone between *Toxoplasma*-infected and *Toxoplasma* free subjects [9].

A number of studies have shown a correlation between the 2D:4D digit ratio and various physical and behavioral traits. Males and females in many species [10] including humans [11] differ in second to fourth digit ratio (2D:4D ratio). It has been suggested by some scientists that the ratio of two digits in particular, the 2nd (index finger) and 4th (ring finger), is affected by exposure to androgens e.g. testosterone, while in the uterus. The 2D:4D ratio can be considered as a crude measure for prenatal androgen exposure. The lower 2D:4D ratio values are pointing to higher androgen exposure [12]. The 2D:4D digit ratio is sexually dimorphic: in males, the second digit tends to be shorter than the fourth, and in females the second digit tends to be the same size or slightly longer than the fourth [13].

In this study we tested the possibility of finding any association between *Toxoplasma* infected and free males and female as well as their postnatal testosterone hormone concentration with the change in their 2D:4D digit ratio of left and right hand.

MATERIALS AND METHODS

Samples collection

Five ml of venous blood were drawn from apparently healthy 135 males and 180 women subjects attending the Central Health Laboratory in Baghdad during the period from April 2012 to December 2012, their age between (20 - 50) years. Serum was aspirated from each subject, and stored at -20°C until used for serological and hormonal tests.

Serological tests

Measurements of anti-*Toxoplasma* IgG antibodies were performed and interpreted according to the direction of the manufacturer of bio Check *Toxoplasma* IgG ELISA (BC-1085) kit.

Measurement of serum testosterone hormone concentration

Quantitative determination of testosterone total concentration in human sera by microplate Enzyme Immunoassay was done according to the manufacturer's instructions using Monobind Testosterone Enzyme Immunoassay (3725-300- USA) Test kit.

Anthropometric measurement

The length of the second and fourth finger on the ventral surface of the hand from the basal crease of the digit to the tip were measured for the right and left hands using a vernier caliper with a resolution of 0.1 mm.

A longer index finger will result in 2D:4D digit ratio higher than 1, while a longer ring finger will result in a digit ratio of less than 1.

Statistical analysis

The Statistical Analysis System [14] was used to effect of treatments in study parameters. T-test was used to compare between means and percentages in this study.

RESULTS AND DISCUSSION

Ages of subjects used in this study range from 20 - 50 year. Among 135 male, there were 42 (31.11%) infected with *Toxoplasma*, and from 180 female, there were 67 (37.22%) also infected with *Toxoplasma* using IgG- ELISA test, there were significant differences between infected and non-infected males and females (table 1,2), whereas, there was no significant difference between infected males and females (table 3).

The mean concentration of testosterone hormone for *Toxoplasma*- infected males was 12.136 ng/ml, while it was 8.312 ng/ml for *Toxoplasma*- free males. The difference between them was significant (table 1).

On the other hand the mean concentration of testosterone hormone for *Toxoplasma*-infected females was 0.76 ng/ml, while it was 2.48 ng/ml for *Toxoplasma*- free females. Also, the difference between them was significant (table 2).

For right and left hands 2D:4D digit ratio, *Toxoplasma*- infected males recorded 1.07 and 0.98 respectively. There was significant difference between them, while, there was no significant between them in free males (table 1).

In *Toxoplasma*- infected females' right and left hands the average of 2D:4D digit ratio was 1.06 and 0.97 respectively. There was significant difference between them, while there was no difference between them in free females (table 2).

The present study showed some factors such as gender, postnatal testosterone concentration, and *Toxoplasma* infection may correlate with 2D:4D ratio. The relationship between 2D:4D ratio and *Toxoplasma* infection is particularly significant for the left hand. This mention that right hand 2D:4D ratio should be favorite used to quantify prenatal testosterone levels.

This study searched for such morphological differences between *Toxoplasma*-infected and *Toxoplasma*-free subjects that could be influenced by the parasite, or could rather correlate with their natural resistance to parasitic infection. We found *Toxoplasma*-infected males and females to have lower left hand 2D: 4D digit ratios. The lower 2D:4D digit ratio in infected males and females, suggest that sex steroid hormones like testosterone could play a role in these shifts.

These results agreed with a case control study done by [15] that showed that *Toxoplasma*-infected males had a non-significantly higher and, *Toxoplasma*-infected female had a lower concentration of testosterone than *Toxoplasma*-free controls.

Table 1. Correlation between latent toxoplasmosis, digit ratio & testosterone level in male.

Subject	Latent toxoplasmosis	Digit ratio 2D: 4D Right	Digit ratio 2D: 4D Left	T-test	Testosterone (ng/ml)	Total
Toxoplasmosis infected	42 (31.11%)	1.07	0.98	0.10*	12.136	135
Toxoplasmosis free	93 (68.88%)	0.99	0.97	0.142 NS	8.312	
T-test	9.551 *	0.08 *	0.144 NS	---	2.664 *	---

* (P<0.05), NS: Non-significant.

Table 2. Correlation between latent toxoplasmosis, digit ratio & testosterone level in female.

Subject	Latent toxoplasmosis	Digit ratio 2D: 4D Right	Digit ratio 2D: 4D Left	T-test	Testosterone (ng/ml)	Total
Toxoplasmosis infected	67 (37.22%)	1.06	0.97	0.05 *	0.76	180
Toxoplasmosis free	113 (62.77%)	0.98	0.99	0.150 NS	2.48	
T-test	9.682 *	0.06*	0.118 NS	---	0.972 *	---

* (P<0.05), NS: Non-significant.

Table 3. Latent toxoplasmosis, digit ratio & testosterone level in male & female (infected group)

Subject	Latent toxoplasmosis	Digit ratio 2D: 4D Right	Digit ratio 2D: 4D Left	Testosterone (ng/ml)
Toxoplasmosis infected male	42 (31.11%)	1.07	0.98*	12.136
Toxoplasmosis infected female	67 (37.22%)	1.06	0.97*	0.76
T-test	8.552 NS	0.202 NS	0.250 NS	4.195 *

* (P<0.05), NS: Non-significant.

Table 4. Latent toxoplasmosis, digit ratio & testosterone level in male & female (free group)

Subject	Latent toxoplasmosis	Digit ratio 2D: 4D Right	Digit ratio 2D: 4D Left	Testosterone (ng/ml)
Toxoplasmosis free male	93 (68.88%)	0.99	0.97	8.312
Toxoplasmosis free female	113 (62.77%)	0.98	0.99	2.48
T-test	8.701 NS	0.202 NS	0.247 NS	3.037 *

* (P<0.05), NS: Non-significant.

2D:4D ratio varies during postnatal life and therefore, at least theoretically, could be influenced by toxoplasmosis induced increased testosterone levels [16, 17]. It might indicate that perceived dominance, as well as several other psychological traits is related to the 2D:4D ratio for the right hand, while

toxoplasmosis is associated with a lower left hand 2D:4D ratio [18, 19]. The possible explanation of this sample, could be that the right hand 2D:4D ratio reflects more the prenatal testosterone levels, while the left hand 2D:4D ratio is rather linked to postnatal testosterone levels and thus is more apt to be influenced by environmental factors, including *Toxoplasma* infection.

Both *Toxoplasma* infected males and females showed lower digit ratio for the left hand than the right hand (table 3), while *Toxoplasma*- free males and females showed no significant difference between right and left hand digit ratio (table 4).

Toxoplasma infection has a significant association with left than right hand 2D:4D digit ratio in both genders. This could explain the stronger relationship between different physiological and psychological traits and 2D:4D ratio for the right hand that is usually found [11]. A higher age stability of right hand 2D:4D ratio was observed by [17].

The higher influence of the left hand 2D:4D ratio to environmental factors such as *Toxoplasma* infection is also supported by the results of a twin study, which showed higher heritability of right hand than left hand 2D:4D ratio [20].

The mechanism for the association between lower 2D:4D ratio and toxoplasmosis is not understood. *Toxoplasma* infection showed associated with a significantly lower left hand 2D:4D ratio in males and a non-significantly lower left hand 2D:4D ratio in females [21]. *Toxoplasma* infection was also shown to be associated with higher testosterone levels in males and lower testosterone levels in females by [7].

Some previous studies recorded no relationship between postnatal testosterone concentration and the 2D:4D ratio [11, 22]. The problem with the estimation of postnatal levels of steroid hormones, and testosterone in particular, is that they vary widely with, time of day, season and in response to various external alarms [23]. This makes it difficult to estimate long-period concentrations of testosterone based on one measurement [24].

The probability of infection with this intracellular parasite is expected to correlate negatively with the activity of the cellular arm of the immune system, which is known to be inhibited by a high concentration of steroid hormones [25]. However, *Toxoplasma* is also known to induce behavioral and neuro-physiological changes in infected human or animal hosts. Increased dopamine and testosterone levels are suspected to play an important role in the observed changes [26].

In conclusion the statistical association between low 2D:4D ratio and *Toxoplasma* infection inform us that subjects with low 2D:4D ratios have a higher probability of *Toxoplasma* infection and change of testosterone hormone level in infected hosts.

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