



Original Article

Is *Toxoplasma gondii* IgG seropositivity a predisposing factor for infertility?

Haytham Ahmed Zakai^{1*} and Mazen Abid Bisharah²

¹Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences, King Abdulaziz University, P.O. Box-80324, Jeddah-21589, Kingdom of Saudi Arabia.

²Department of Obstetrics and Gynecology, King Faisal Specialist Hospital & Research Center, Jeddah, Saudi Arabia.

Abstract: Toxoplasmosis is a disease caused by an obligate intracellular protozoan parasite *Toxoplasma gondii*. Approximately one-third of the world population is infected with this parasite. Several studies have examined the causes of human infertility in the Middle East. A high proportion of secondary infertility and a great contribution of the female factor was the major finding in most of these studies. In this study, we aim to explore the relationship between *Toxoplasma gondii* seropositivity and female infertile patients. Serum samples from 83 female patients visiting the infertility clinic and 57 normal prim gravid females attending the ANC clinic were collected during the year 2014. Serum samples were analyzed for anti-*Toxoplasma* IgG by chemiluminescent microparticle immunoassay (CMIA) technology. Patients visiting the infertility clinic, aged from 18-40 years ($\chi=29.7$) while normal prim gravid females attending the ANC clinic aged from 18-38 ($\chi=26.1$). Of the 83 samples collected from patients visiting the infertility clinic, 15 samples were positive for anti-*Toxoplasma* IgG while only 2 samples (out of 57) collected from normal prim gravid females attending the ANC clinic were positive. There was a statistically significant correlation between positive anti-*Toxoplasma* IgG and infertility ($p<0.01$). We suggest considering the presence of anti-*Toxoplasma* antibodies in serum of young females as an indicator for possible future infertility.

Keywords: *Toxoplasma gondii*, infertility, anti-*Toxoplasma*, IgG.

1. Introduction

Toxoplasmosis is a disease caused by an obligate intracellular protozoan parasite *Toxoplasma gondii* [1,2]. Approximately one-third of the world population is infected with this parasite [3]. Infection with *Toxoplasma gondii* is very common. Postnatally acquired toxoplasmosis is usually asymptomatic. However, clinical disease is greatly confined to risk groups, including infants and immunocompromised individuals. Congenital toxoplasmosis is seen in cases of the mother acquiring the infection for the first time during pregnancy. The incident of prenatal toxoplasmosis is estimated to vary from 1 to 100 per 10,000 births. Toxoplasmic encephalitis and disseminated toxoplasmosis have been reported in immunocompromised patients [2].

Level of seroprevalence for toxoplasmosis ranged from 8-77% worldwide. High seroprevalence for toxoplasmosis has been reported among pregnant

women and women of childbearing age from different parts of the world, including the Middle East [2,3]. The prevalence of infection in Saudi Arabia showed wide variations as revealed by previous studies. The highest positivity rate was reported in Jeddah 61.4% [4], Al Hassa of 51.4% [5,6], 41% in Aseer [9], 38% in Riyadh [8], and 35.6% in Makkah [7]. Moreover, studies showed a relation between positivity for toxoplasmosis and female sterility. Furthermore, visual impairment, hearing loss, and malignant neoplasms were major coincidental diseases in *Toxoplasma gondii* seropositive cases [10-13].

Several studies have examined the causes of infertility in the Middle East. A high proportion of secondary infertility and a great contribution of the female factor was the major finding in most of these studies [14-19]. Review of the literature since 1995 did not reveal any data regarding the relation between female infertility and infections.

*Corresponding author:

E-mail: hzakai@kau.edu.sa; Telephone: +966 0554334116; Fax: +966 12 6404065.

In this study, we aim to explore the relationship between *Toxoplasma gondii* seropositivity and female infertility patients.

2. Materials and Methods

Serum samples from 83 female patients visiting the infertility clinic at King Faisal Specialist Hospital & Research Center in Jeddah, Saudi Arabia were collected during the year 2014. Inclusion criteria included female, aged 18-40, married for more than one year, with no children, and unable to conceive. Fifty-seven control samples were collected from normal prim gravid females attending the ANC clinic with no history of infertility. Patient demographics including age, nationality, medical history, height, and weight were also collected. Serum samples were analyzed for anti-*Toxoplasma* IgG by chemiluminescent microparticle immunoassay (CMIA) technology in ARCHITECT i2000 System using commercial kits (Abbott Diagnostics) with appropriate positive and negative controls provided by the manufacturer. Data were analyzed using SPSS (Ver. 16). The research was approved by the research ethics committee at the Faculty of Applied Medical Sciences, King Abdulaziz University.

3. Results

One hundred and forty serum samples were collected from female patients visiting the infertility clinic and normal prim gravid females attending the ANC clinic as described above. Patients visiting the infertility clinic, aged from 18-40 years ($x=29.7$) while normal prim gravid females attending the ANC clinic aged from 18-38 ($x=26.1$). Of the 83 serum samples collected from patients visiting the infertility clinic, 15 samples were positive for anti-*Toxoplasma* IgG while only 2 serum samples (out of 57) collected from normal prim gravid females attending the ANC clinic were positive.

Statistical analysis revealed a statistically significant correlation between having a positive anti-*Toxoplasma* IgG antibody in serum and infertility ($p<0.01$). There was no statistically significant correlation between infertility and other demographic data.

4. Discussion

Toxoplasmosis has gained tremendous interest among researchers since the emergence of AIDS. However, many aspects of this parasitic infection are still unveiled to date. Several studies discussed the role of *Toxoplasma gondii*, as a causative agent of congenital disease. There is a controversy about the issue of recurrent abortion being caused by toxoplasmosis [20]. However, congenital toxoplasmosis is considered a severe disease that can result in abortion and/or severe handicap [2,21]. Latent toxoplasmosis in

immunocompetent individuals is usually overlooked from the health point of view. Nowadays, several studies have explored the effect of toxoplasmosis on personality profile. It has been shown that latent toxoplasmosis can affect the personality profile in a negative manner [22-24]. Furthermore, changes in hormones have been known to also affect the personality profile [25].

In this study, we investigate the relation between seroprevalence to toxoplasmosis and infertility. There was a significant positive correlation between the presence of IgG antibodies to *Toxoplasma gondii* and having problems in conceiving a child normally. However, the mechanism and how this effect takes place is still open to wide speculations. This is in agreement with other findings which investigated the effect of toxoplasmosis on infertility/sterility in animals and humans [10]. Dvorakova-Hortova [13] found low levels of luteinizing hormone in urine of mice infected with toxoplasmosis. Moreover, infected mice had also lower sperm count compared to non-infected mice [13]. Although the host-parasite relationship in the case of toxoplasmosis has been substantially researched, we still lack valuable information about the effect of such relationship on many health aspects. We speculate that toxoplasmosis may affect the level of different hormones in the body. This may have a secondary effect resulting in infertility. We suggest considering the presence of anti-*Toxoplasma* antibodies in serum of young females as an indicator for possible future infertility. Furthermore, more research should be conducted to deeply study the mechanism that controls this relation between positive anti-*Toxoplasma* antibodies and infertility and to investigate the role of personality and its effect on hormones in this matter. The Results of this study call for the urge in setting virtuous applicable control programs to control toxoplasmosis.

References

- [1]. Dubey, J.P. (2008). The History of *Toxoplasma gondii*—The First 100 Years. *Journal of Eukaryotic Microbiology*, 55(6): 467-475.
- [2]. Tenter, A.M., Heckeroth, A.R., Weiss, L.M. (2000). *Toxoplasma gondii*: from animals to humans. *International Journal for Parasitology*, 30 (12-13): 1217-1258.
- [3]. Pappas, G., Roussos, N. & Falagas, M.E. (2009). Toxoplasmosis snapshots: Global status of *Toxoplasma gondii* seroprevalence and implications for pregnancy and congenital toxoplasmosis. *International Journal for Parasitology*, 39(12): 1385-1394.
- [4]. Tonkal, A.M. (2008). PCR versus ELISA in diagnosis of human toxoplasmosis in Jeddah, Saudi Arabia. *Journal of the Egyptian Society of Parasitology*, 38(3): 707-714.
- [5]. Al-Mohammad, H.I., Amin, T.T., Balaha, M.H., Al-Moghannum, M.S. (2010). Toxoplasmosis

- among the pregnant women attending a Saudi maternity hospital: seroprevalence and possible risk factors. *Annals of Tropical Medicine and Parasitology*, 104(6): 493-504.
- [6]. Al-Qurashi, A.R., Ghandour, A.M., Obied, O.E., Al-Mulhim, A. and Makki, S.M. (2001). Seroepidemiological study of *Toxoplasma gondii* infection in the human population in the Eastern Region. *Saudi Medical Journal*, 22(1): 13-18.
 - [7]. Bin Dajem, S.M., Almushait, M.A. (2012). Detection of *Toxoplasma gondii* DNA by PCR in blood samples collected from pregnant Saudi women from the Aseer region, Saudi Arabia. *Annals of Saudi Medicine*, 32(5): 507-512.
 - [8]. Almogren, A. (2011). Antenatal screening for *Toxoplasma gondii* infection at a tertiary care hospital in Riyadh, Saudi Arabia. *Annals of Saudi Medicine*, 31(6): 569-572.
 - [9]. Al-Harthi, S.A., Jamjoom, M.B. & Ghazi, H.O. (2006). Seroprevalence of *Toxoplasma Gondii* among pregnant women in Makkah, Saudi Arabia. *Umm Al-Qura University Journal of Science, Medicine and Engineering*, 18: 217 -227.
 - [10]. Li, S, Cui, L., Zhao, J., Dai, P., Zong, S., Zuo, W., Chen, C., Jin, H., Gao, H. and Liu, Q. (2011). Seroprevalence of *Toxoplasma gondii* Infection in Female Sterility Patients in China. *Journal of Parasitology*, 97: 529-530.
 - [11]. Noorbakhsh, S., Farhadi, M., Tabatabaei, A., Mohamadi, S. and Jomeh, M. (2008). Infection in childhood sensory hearing loss. *Saudi Medical Journal*, 29(10): 1470-1474.
 - [12]. Alvarado-Esquivel, C., Liesenfeld, O., Torres-Castorena, A., Estrada-Martínez, S., Urbina-Alvarez, J.D., Ramos-de la Rocha, M., Márquez-Conde, J.A., Dubey, J.P. (2010). Seroepidemiology of *Toxoplasma gondii* infection in patients with vision and hearing impairments, cancer, HIV, or undergoing hemodialysis in Durango, Mexico. *Journal of Parasitology*, 96(3): 505-508.
 - [13]. Dvorakova-Hortova, K., Sidlova, A., Ded, L., Hladovcova, D., Vieweg, M., Weidner, W., Steger, K., Stopka, P., Paradowska-Dogan, A. (2014). *Toxoplasma gondii* decreases the reproductive fitness in mice. *PLoS ONE*, 9(6):e96770, doi: 10.1371/journal.pone.0096770.
 - [14]. Shin, D.W., Cha, D.Y., Hua, Q.J., Cha, G.H. and Lee, Y.H. (2009). Seroprevalence of *Toxoplasma gondii* infection and characteristics of seropositive patients in general hospitals in Daejeon, Korea. *Korean Journal of Parasitology*, 47: 125-130.
 - [15]. Elusseini, E.A., Magid, Y.M., Omer, M.M. and Adam, I. (2008). Clinical patterns and major causes of infertility among Sudanese couples. *Tropical Doctor*, 38: 243-244.
 - [16]. Igietseme, J.U., Omosun, Y., Partin, J., Goldstein, J., He, Q., Joseph, K., Ellerson, D., Ansari, U., Eko, F.O., Bandea, C., Zhong, G., Black, C.M. (2013). Prevention of Chlamydia-induced infertility by inhibition of local caspase activity. *Journal of Infectious Diseases*, 207(7): 1095-1104.
 - [17]. Zayed, A., Nabil, H., State, O. and Badawy, A. (2012). Subfertility in women with familial Mediterranean fever. *The Journal of Obstetrics and Gynaecology Research*, 38: 1240-1244.
 - [18]. Caserta, D., Bordi, G., Ciardo, F., Marci, R., La Rocca, C., Tait, S., Bergamasco, B., Stecca, L., Mantovani, A., Guerranti, C., Fanella, E.L., Perra, G., Borghini, F., Focardi, S.E., Moscarini, M., (2013). The influence of endocrine disruptors in a selected population of infertile women. *Gynecological Endocrinology*, 29(5): 444-447.
 - [19]. van Oostrum, N., De Sutter, P., Meys, J. and Verstraelen, H. (2013). Risks associated with bacterial vaginosis in infertility patients: a systematic review and meta-analysis. *Human Reproduction*, 28(7): 1809–1815.
 - [20]. Ebadi, P., Solhjoo, K., Bagheri, K. and Eftekhari, F. (2011). Seroprevalence of toxoplasmosis among the women with recurrent spontaneous abortion in comparison with the women with uncomplicated delivery. *Journal of Jahrom University of Medical Sciences*, 9(1):32-36.
 - [21]. Fernandes, M.A, Batista, G.I., Carlos Jda, C., Gomes, I.M., Azevedo, K.M., Setúbal, S., Oliveira, S.A., Velarde, L.G., Cardoso, C.A. (2012). *Toxoplasma gondii* antibody profile in HIV-1-infected and uninfected pregnant women and the impact on congenital toxoplasmosis diagnosis in Rio de Janeiro, Brazil. *The Brazilian Journal of Infectious Diseases*, 16(2):170-174.
 - [22]. Flegr, J., Kodym, P. and Tolarova, V. (2000). Correlation of duration of latent *Toxoplasma gondii* infection with personality changes in women. *Biological Psychology*, 53: 57–68.
 - [23]. Yolken, R.H. and Torrey, E.F. (2008). Are some cases of psychosis caused by microbial agents? A review of the evidence. *Molecular Psychiatry*, 13: 470–479.
 - [24]. Khademvatan, S., Khajeddin, N., Saki, J. and Izadi-Mazidi, S. (2013). Effect of toxoplasmosis on personality profiles of Iranian men and women. *South African Journal of Science*, 109: 1-4.
 - [25]. Evardone, M., Alexander, G.M. and Morey, L.C. (2008). Hormones and Borderline Personality Features. *Personality and Individual Differences*, 44(1): 278–287.