



Journal homepage: www.microbial.sciencearchives.org



Original Research Article

Study of the relationship between toxoplasmosis and its effect on the level of the hormones prolactin and progesterone and the level of interleukin 27 among aborted women in the city of Tikrit

Zainab Karem Mohammed Al-Taei, Maysoun Mustapha Jasim

College of Education for Pure Sciences, Tikrit University, Tikrit, Iraq

*Corresponding author: zainab@st.tu.edu.iq

Abstract

This study included 100 women, 75 women with recurrent miscarriages (one or more miscarriages) and 25 women without previous miscarriages and without any infection (control group). The study included a number of immunological tests, and these tests included estimation of the levels of immunoglobulins (immunoglobulin G and immunoglobulin M) for *Toxoplasma gondii*, and measuring the level of the hormones prolactin and progesterone, as well as measuring some cytokines (interleukin 27). The study showed that the prevalence of infection with *Toxoplasma gondii* parasite was the highest within the age groups (25-34 years), and it was found through the study that there was a significant increase in the concentration of IgG and IgM, as well as a significant difference in the level of prolactin hormone between infected and control women. The results of the statistical analysis at the 0.01 probability level showed that there were significant differences, as it was found that there was a decrease in the hormone prolactin amounted to $(156.7 \pm 29.4 \text{ ng/ml})$ in the infections compared to the control, while the progesterone hormone was not affected by the initiation of Toxoplasmosis, as it was found that there was a significant increase in the level of IL-27 amounting to $(121.1 \pm 29.2 \text{ pg/ml})$ in the infected compared with the control group. The study objectives also included the effect of toxoplasmosis on the level of antibodies, the level of hormones, and the level of IL-27, depending on the age groups. The study also showed the highest frequency of abortions in women who have had one recurrent miscarriage compared to those who have had two or three miscarriages.

Keywords Miscarriage, Immunological tests, Toxoplasmosis

Introduction

Toxoplasmosis arises as a result of infection with the parasite *T. Gondii* found in the feces of infected cats with Oocysts or eating contaminated meat that is undercooked and containing the infectious phase in the form of tissue cysts, which has a complex and multiple life cycles, and the asexual life cycle occurs in humans and mice. As for the sexual life cycle, it occurs only in cats that are the final host of the parasite, and the parasite can be transmitted directly from the mother to the fetus, especially during the first trimester of pregnancy, leading to miscarriages. It can primarily infect the central nervous system of the fetus and this leads to underdevelopment, Mental illness or death that ends with the pregnant woman's miscarriage of that fetus (Emilie et al., 2017). Toxoplasma parasite *T. gondii* is an obligatory zoonotic

the parasite that can infect living organisms and the infection may be without clinical symptoms. This parasite also causes a variety of clinical diseases in humans and animals. Therefore, this disease is considered an opportunistic disease for weak immunity (Mahfouz et al., 2019). There is also a close relationship between chronic toxoplasmosis and the age of infected persons (Zhou et al., 2011; Shakir et al., 2020). The percentage of infected persons ranges between 65-30% in human societies, and the rate of infection varies in countries depending on several factors, including health, social and other factors such as gender and age and other environmental factors. The most common source of infection is the consumption of raw or undercooked meat, as well as when sanitary conditions are poor (Balasudaram et al., 2010; Vas et al., 2011).

The hormones of the human body change during pregnancy and thus affect the immune response of women, and this increases the chance of infection due to the diminished initial inflammatory response of the body, especially the antibodies to the parasite. Also, the progesterone hormone has a different effect on toxoplasmosis disease, as it leads to exacerbation of infection or to limit the reproduction of the parasite (Leticia *et al.*, 2014) Since progesterone is produced in the ovaries, uterus, and brain (Speroff *et al.*, 1999), the decrease in the concentration of progesterone during miscarriages comes in response to the mother's immune system to reject the fetus by suppresses modulates uterine contraction, and the decrease in the concentration of progesterone is associated with abortion during the first three months From pregnancy (Naji & Tahrr, 2015) As for the hormone prolactin, it was observed that the infection of women with this parasite decreases, as this hormone is secreted from the lactotrophic cells of the anterior lobe of the pituitary gland (Kaur *et al.*, 2003) As for the role of IL-27 during toxoplasmosis, it gave an important insight into its biological activity, as well as confirmed its importance in immune regulation during infection, as IL-27 inhibits the differentiation of Th17 cells during toxoplasmosis because Th17 cells work to increase pathogenicity during toxoplasmosis (Fitzgerald *et al.*, 2007).

Materials and Methods

100 serum samples were collected to determine the antibodies (IgG, IgM) to toxoplasmosis using test by cobas E411 and using Elecsys Toxo IgG Test Kit and Elecsys Toxo IgM Test Kit produced by the Indian company Roche and its effect on the levels of the hormones prolactin and progesterone and the level of IL-27 where depends. The principle of the test is on the interaction between the immune antibodies present in the patient's serum with antigens. The AFIAS technique was also used to measure hormones, using the PRL AFIA kit, progesterone kit, and ELIZA technique to measure the level of IL-27. Also, a test kit for interleukin 27 from the American company Elabscience was used. It was found that 75 samples were infected with the disease Toxoplasma and 25 non-infected control samples, ages ranged between 19-45 years.

Statistical Analysis

The results were statistically analyzed according to the analysis of variance (ANOVA), the (F test) and the (T-test) and using the statistical program (minitab), and the arithmetic means were compared to determine the significant differences between them using the (drabken) multinomial test with the probability level of 0.05 and 0.01.

Results

A study of 75 samples of aborted women infected with Toxoplasmosis in the city of Tikrit and conducted a serological examination for them using the test by Cobas E411 to detect antibodies (IgG, IgM). The results of the current study show in Table 1. that patients with age group 25-34 severely injured or infected compared to another group where they reported 42.7% and age group 19-24 reported 32.0%, age

group 35-45 reported 25.3% of infection based on a P-value of 0.627.

Table 1. Number and percentage of infection, distributed by age groups

Age group (Years)	Patient		control	
24 – 19	24	32.0	9	36.0
25 – 34	32	42.7	8	32.0
35-45	19	25.3	8	32.0
Sum	75	100	25	100
Ns Chi-Square = 0.933 P-Value = 0.627				

The results of the statistical analysis using the ANOVA Table at the 0.01 probability level showed that toxoplasmosis is closely associated with abortion based on the examined immunoglobulin IgG, IgM. A significant increase in the concentration of IgG was observed, amounting to 1.037 ± 0.107 in the aborted women compared to the control, and an increase in the concentration of IgM was also observed. It was 3.6 ± 0.3 as shown in Table 2.

Table 2. Concentrations of IgG, Igm antibodies for Toxoplasmosis in the study groups.

Groups	Toxoplasmosis	
	Positive IgG Mean \pm SD	Positive IgM Mean \pm SD
Patient	1.037 ± 0.107	3.6 ± 0.3
Control	0.381 ± 0.017	0.348 ± 0.065
P-Value	0.0004	0.305

A variation in the level of hormones was observed in women suffering from toxoplasmosis as shown in Table 3.

There were significant differences if the prolactin hormone was recorded 156.7 ± 29.4 ng/ml and progesterone (0.465 ± 0.012 pg/ml) compared to the hormones of non-toxoplasmic women who reported prolactin levels (209.7 ± 43.4 ng/ml) and progesterone (0.875 ± 0.115 pg/ml).

Table 3. Evaluation of the level of the hormones prolactin and progesterone in the study groups.

Hormone	Positive	Negative	P-Value	Normal value
Prolactin	156 ± 29.4 ng/ml	209.7 ± 43.4 ng/ml	0.010	318-3.2ng/ml
Progesterone	0.465 ± 0.012 pg/ml	0.875 ± 0.115 pg/ml	0.0003	0.1- 12.0 ng/ml

P<0.01**

A variation in the level of IL-27 was also observed in women suffering from toxoplasmosis, as shown in Table 4. The

results of the statistical analysis using the ANOVA Table at the 0.01 probability level showed significant differences, as the average concentration of IL-27 was (121.1 ± 29.2pg/ml). in the female patients while in the control group (78.2 ± 15.0 pg/ml).

Table 4. Relationship of kinetics

Cytokines	Positive	Negative	P-Value
IL-27	121.1 ± 29.2 ml/pg	78.2 ± 15.0 ml/pg	0.0003

Table 5. shows the hormone levels in women with toxoplasmosis, as the results of the statistical analysis using the ANOVA Table at the probability level of 0.05 showed that there were significant differences if the prolactin hormone recorded a decrease (137.4 d ± 28.1pg/ml) in the age group (Hamoud et al., 2021; Hussein et al., 2014; Kadhim & Al-awadi, 2013) as well. The results of the statistical analysis at the 0.01 possibility level showed that there were no major variations between the three age groups of the patients, as the progesterone hormone recorded a significant decrease in the three age groups.

Table 5. The effect of injury on the level of the hormones prolactin and progesterone and its relationship to age groups

Hormone	19-24	25-34	45-35	P-Value
PRL	137.4d ± 28.1 ng/ml	176.0bc ± 40.30 ng/ml	151.7cd ± 34.7ng/ml	0.044
Progesterone	0.4039b ± 0.1422pg/ml	0.4611b ± 0.114pg/ml	0.5470 b ± 0.135 pg/ml	0.0003

Table 6. shows the level of interleukin 27 in women with toxoplasmosis, as the results of the statistical analysis using the ANOVA table at the 0.01 likelihood level showed that there were important changes if IL-27 recorded its highest elevation (125.78 a ± 30.43pg/ml) in the age group (19- 25) and below (117.09 a ± 28.99 pg/ml) in the age group (25-34).

Table 6. The effect of infection on the ratios of interleukin 27 and its relationship to age groups.

Cytokines	24- 19	34-25	45-35	P-Value
IL-27	125.78a ± 30.43 ml/pg	117.09a ± 28.99ml/pg	122.70a ± 29.87 ml/pg	0.0004

P<0.01**

Discussion

The rate of IgM antibody indicates To acute infection, while IgG antibodies may increase in 2-4 weeks after infection and gradually rise for several weeks and then remain at a low level for rest time, while repeated exposure to infection may lead to a high rate of antibodies for a longer time In the current study we found that the proportion of women Abortions are higher In the age group between 25-34 years (42.7%). These results are supporting the findings of other study (Abdul-Aziz, 2015; Kadhim, 2020). In addition, (Anwar & Al-Bayati, 2018) suggested that the highest abortion rate is in the age group 21-30 years. Various studies have stated that the risk of miscarriage and infertility increases with the age of the woman, the occurrence of chromosomal abnormal eggs increases significantly with age. It also showed that elderly women have fertility.

PRL P<0.05*

Progesterone P<0.01**

Problems were due to the deterioration of egg quality and others. The results also supported by other study (Al-Doury, 2018; Al-Rawi, 2019; Al-Shammary, 2014; Chiad & Hama, 2019). Where a clear decrease in the level of the hormone prolactin was found in women with toxoplasmosis, and a decrease in the level of the hormone progesterone was found. This result is identical to what was reached (Naji & Tahrr, 2015), (Zamil, 2017).

The levels of hormones in women with toxoplasmosis, depending on the age groups, showed that the level of the hormone prolactin reached the lowest value (137.4 d ± 28.1 ng/ml) within the age group (Kadhim, 2020), while the progesterone hormone was normal, and this result was identical to what was reached by (Bedir et al., 2015) where many of the defensive functions of the immune system are affected by sex hormones through the effect of these hormones It stimulates immune cells and produces cytokines to trigger an immune response (Foitikova et al., 2010). Where progesterone plays an important role in reproductive and non-reproductive tissues, including immune cells, as it has a role in development, differentiation, and reproduction (Elizabeth et al., 2013) where there is a relationship between sex hormones and infection with microbes that affect autoimmune diseases that often affect women. The current study also recorded significant differences between the group of women infected with toxoplasmosis and the control group, as it was proven that the average IL-27 concentration in the patients reached the highest value 125.78 a ± 30.43 pg/ml compared to the control (78.2 ± 15.0 pg/ml) and this is consistent with what was reached by (Kadhim, 2020) and (Al-Taei et al., 2015). It is one of the anti-inflammatory cytokines and is important in immunity against the parasite. It works on balancing the immune response to reduce immune pathology and get rid of pathogenic infections.

It also plays a major role in eliminating intracellular microbes during infection. It is also important in passive immune modulation during the chronic phase of inflammation. Which is important in reducing the severity of tissue injury and dysfunction of the organs (Yoshida, 2015). It acts as an anti-inflammatory, which has an inhibitory role, and acts as an anti-inflammatory in the immune response of Th1, Th2, and Th17 (Belle et al., 2016). The results of the current study showed at the 0.01 probability level that there were significant differences between parasite infection and the number of abortions. The highest percentage was 46.7% when the number of miscarriages was 1, and the lowest percentage was 21.3% when the number of abortions was 3, and the reason for the emergence of the highest infection rate among women who suffer From a one-time abortion to the rupture of the cyst located in the wall of the uterus due to the expansion that occurs during pregnancy, leading to the release of the parasite and infection of the fetus. Also, the suppression of immunity in the mother during pregnancy causes reactivation of chronic infection and release of the parasite from the cyst and penetration into the tissues of the placenta and infection of the fetus, which leads to abortion, and that the rise in the rate of single abortion may be due to the ignorance of most women of their infection with *Toxoplasma gondii* before marriage, and that their pregnancy and the accompanying problems at its inception necessitated conducting various diagnostic tests to determine the causes of this pregnancy threatened with abortion, which confirmed that he had *Toxoplasma* infection and required rapid treatment periodic. This result is consistent with the findings of both researchers (Agrawal et al, 2016; Ahmed, 2017; Mahmood & Shareef, 2019).

Table 7. Number and percentage of infection, distributed according to the number of abortions

The number of miscarriages	Infected	%	Not infected	%
0	0	0.0	22	88.0
1	35	46.7	2	8.0
2	24	32.0	1	4.0
3	16	21.3	0	0.0
Total	75	100	25	100
**Chi-Square = 84.790 P-Value = 0.00002				

References

- Abd-ul-Aziz, S. (2015). Sero-prevalence of anti-CMV-IgM and anti-CMV-IgG in Iraqi Aborted Women Infected with Human Cytomegalovirus in Nasiriyah city. *University of Thi-Qar Journal*, 10(4), 55-60.
- Agrawal A., Singh S. K., Maheshwari R. K. and Goya J. K.(2016). Study of Serological Profile of Torch Infections in Women with Bad Obstetric History. *Microbiology*. 6 (5):2249-555X.
- Ahmad, A. S., & Kareem, Y. K. (2020). Frequency of cytomegalovirus, rubella, and herpes simplex virus in embryonic tissues of women with missed abortion. *Mosul Journal of Nursing*, 8(1), 68-88.
- Ahmed, R. I. (2017). Detection of Cytomegalovirus Infection in Pre-Marital Women in Al-Khalis City. *Diyala Journal For Pure Science*, 13(4-part 1).
- AL-doury, S. N. M. (2018). Prevalence of *Toxoplasma gondii*, Cytomegalovirus and Rubella virus among aborted women in Samarra city. *Tikrit Journal of Pure Science*, 23(7), 32-35.
- (2019). Knowledge and attitude regarding toxoplasmosis among Jazan University female students. *Saudi J Med Med Sci* .7:28-32.
- Al-Rawazq, H. S. A. M. (2017). Seroprevalence of Immunoglobulin G (IgG) and Immunoglobulin M (IgM) and Risk Factors of Toxoplasmosis for A sample of Pregnant Women in Baghdad. *Al-Kindy College Medical Journal*, 13(2), 40-45.
- Al-Rawi, Z. A. (2019). Immunological and molecular diagnosis of Toxoplasmosis and the impact of infection on interleukin levels IL- 17, IL-8 and the third and fourth complement .College of Education for pure sciences University of Tikrit The Degree of Master.
- Al-shammery, R. N. (2014). Prevalence of Cytomegalovirus among pregnant women relation to congenital abnormalities in embryos and children in Wasit province. *Journal of Kerbala University*, 12(1).
- Al-Taei, N. H., Al-Aboody, B. A., & Al-Temimi, M. B. (2015). Serological and immunological study to the prevalence of Toxoplasmosis among sewage workers, soil workers and sellers of fruits and vegetables in the province of Thi-Qar-Iraq. *Journal of THI-QAR Science*, 5(3).
- Anwar, S. A. & Al-Bayati, N. S. (2018). Prevalence of *Toxoplasma gondii* and Cytomegalovirus in Sera of Aborted Women in Samaraa city. *Tikrit Journal of Pure Science*, 22(6), 34-38.
- Balasundaram, M. B., Andavar, R., Palaniswamy, M. and Venkatapath, Y. N. (2010). Outbreak of acquired ocular toxoplasmosis involving 248 patients. *Arch. Ophthalmol.*, 128(1):28-32.
- Bedir, M. Alazawi., Farah, M. Sh. (2015). Studies on the effect of infected cases of parasite *Toxoplasma gondii* on some sex hormones. *Wor.j.ph.research.V.4,issus 10*.2413-2423.
- Belle, L., Agle, K., Zhou, V., Yin-Yuan, C., Komorowski, R., Eastwood, D. (2016). Blockade of interleukin-27 signaling reduces GVHD in mice by augmenting Treg reconstitution and stabilizing Foxp 3 expression. *Blood*.128 (16):2068–2082.
- Castro-Filice, L. S., Barbosa, B. F., Angeloni, M. B., Silva, N. M., Gomes, A. O., Alves, C. M., ... & Ferro, E. A. (2014). Azithromycin is able to control *Toxoplasma gondii* infection in human villous explants. *Journal of translational medicine*, 12(1), 1-12.
- Chiad, I. A. & Hama, A. A. (2019). Knowledge of Cytomegalic Inclusion Disease among a Sample of Pregnant Women in Baghdad City/Iraq. *Al-Nisour Journal for Medical Sciences*, 1(2).
- Elizabeth, G. Gomez., Bertha, G. Pedrajo., Ignacio, C. Arroyo. (2013). Role of Sex Steroid Hormones in Bacterial-Host Interactions. *Bio R International*.Article ID 928290, pages 10
- Émilie, B., Rajnish, Sh., Nicholas, B., Alvin, A. and Emily, J. (2017). Pathology, clinical signs, and tissue distribution of *Toxoplasma gondii* in experimentally infected reindeer (*Rangifer tarandus*). *International Journal for Parasitology: Parasites and Wildlife* . 6(3); 234-240.
- Fitzgerald, D. C., Ciric, B., Touil, T., Harle, H., Grammatikopolou, J., Das Sarma, J., Gran, B., Zhang, G. X. and Rostami, A. (2007). Suppressive effect of IL-27 on encephalitogenic Th17 cells and the effector phase of Th1qar province. *Journal of education of college*. 5(1):2-5.
- Foitikova, M., Cerna, M., Paveika, K. (2010). A review of the effects of prolactin hormone and cytokine on the development and pathogenesis of autoimmune diseases. *Na.int.of health*. 56 (5): 402.13.
- Hamoud, H. R., Al-Kashwan, T. A. J. & Tarish, H. R. (2021). Cytomegalovirus seropositivity among Iraqi women suffering from recurrent pregnancy loss. *Al-Kufa University Journal for Biology*, 13(1)
- Hussein, A., Mohammed, A., and Rebah, N. (2014). seroprevalence of human cytomegalovirus (HCMV) in aborted women in Baghdad province. *Int. J. Curr. Microbiol. App. Sci*, 3(2): 97-102 .
- Kadhim, R. A., & AL-awadi, H. M. (2013). Changes in testosterone, progesterone and prolactin levels in pregnant women with chronic toxoplasmosis. *Medical Journal of Babylon*, 10(3), 699-708.
- kadhim, wael. dheaa. (2020). immunological profile of women with recurrent abortion due to microbial causes in thi-qar government, (master) of technology in medical laboratory science technology, middle technical university college of health and medical technology.
- Kaur, K., Singh, M. & Virk, S. P. (2003) . prolactinomasin infertility . Rev . Gynaecol . pract 3: 180 – 187 . Speroff, L.; Glass, R. H.; Kase, N.G. (1999). Clinical Gynecologic Endocrinology and infertility, 6th Edn.Philadeiphia,PA: Lippincott Williams & Wilkins.1/70.
- Khudhair, M. K., Mohammed, M. R. & Jassim, N. A. S. (2017). The Serologicalrates of Cytomegalovirus Among Women in Diyala Province, With a Study of Some The Immunological Markers. *Diyala Journal For Pure Science*, 13(3-part 3).
- Mahfouz, M., Elmahdy, M., Bahri, A., Mobarki, Y., Altalhi, A., Barkat, N., Al-Essa, H., Ageely, A., Faqeeh, N., Areeshi, N. and Al-Hassan, S. Mahmood, M. N. & Shareef, A. Y. (2019). Detection of infection by rubella and cytomegalovirus among women exposed to abortion in Ninavah province. *Tikrit Journal of Pure Science*, 24(1), 52-56.

- Naji, N. A. & Tahrr, G. N. (2015). The effect of Activin A and Steroid Hormones on the Recurrent and single Abortion. *Tikrit Journal of Pure Science*, 20(5).
- Paliwal, A., Agarwal, M. L., Chacko, K. M., Singh, A., Chauhan, A., & Jindal, T. (2017). Alteration in Physiological and Haematological profile of female albino wistar rats over 90 days oral repeated exposure by Fomesafen. *Advances in Bioresearch*, 8(5).
- Paliwal, A., Agarwal, A. C. M., & Jindal, T. (2019). Fomesafen (diphenyl ether herbicide) toxicity in male albino wistar rats: physiological and biochemical assessment. *Plant Archives*, 19(2), 1881-1885.
- Paliwal, A., Chauhan, A., Agarwal, M. L., & Jindal, T. (2019). Persistence of fomesafen herbicide residues in soybean crop. *Plant Archives*, 19(2), 1974-1979.
- Shakir, O. M., Jasim, M. M. & Al-Abodi, H. R. J. (2020). Diagnosis of *Toxoplasma gondii* by Using ANA Test with Study of the Effect of the Parasite on Ceruloplasmin Enzyme. *Journal of Cardiovascular Disease Research*, 11(4), 141-145.
- Speroff, L., Glass, R. H., Kase, N. G. (1999). *Clinical Gynecologic Endocrinology and infertility*, 6th Edn. Philadelphia, PA: *Lippincott Williams & Wilkins*.1/70.
- Vas, R. S., Rauli, P., Mello, R. G. and Cardoso, M. A. (2011). Congenital toxoplasmosis: A Neglected Disease-Current Brazilian public health policy. *Field actions science reports. Special Issue 3 Brazil*.
- Yoshida, H., Hunter, C. A. (2015). The immunobiology of interleukin-27. *Annu Rev Immunol*. 33:417-443.
- Zamil, A. (2017). Study of the relationship between Toxoplasmosis disease and progesterone, Testosterone, Estradiol and Hormone Prolactin Among for abortion women in Diyala government. *Diyala Journal For Pure Science*, 13(1-part 1).
- Zhou, P., Chen, Z., Li, H., Zheng, H. H., He, S., Lin, R. and Zhu, X. (2011). *Toxoplasma gondii* infection in humans in China. *Parasites and Vectors*, 4(165):1-9.

This work is licensed under a [Creative Commons Attribution 4.0 International License](https://creativecommons.org/licenses/by/4.0/).

