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Research Article

Implications of Toxoplasma Infection on Women's Immune Status in Baghdad Province, Iraq

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I N F O

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A B S T R A C T

Introduction: Worldwide, there are 500 million cases of toxoplasmosis, which is caused by a member of the Coccidae family, Toxoplasma gondii. This study aimed to assess the immune status of women with toxoplasmosis in the Baghdad province.

Method: Blood samples (105) were taken from women who had had abortions or threatened abortions and were admitted to the clinic in the province of Baghdad during 2021–2022 and 20 samples were taken as control. The samples were examined for *T. gondii* IgM and IgG using the ELISA method (Biotech, USA), with the Latex Agglutination Test (LAT) serving as a screening test, which was done in a previous study. Using sterile, disposable hypodermic traveller needles and tubes, around 3 ml of venous blood samples were collected from patients' arms. The serum was obtained by centrifuging the obtained venous blood at 14,000 rpm for 20 minutes; it was then stored at 80°C. ELISA was used to evaluate serum levels of IFN-γ, IL-1α, IL-4, IL-6, IL-8, IL-10, and IL-12 (MyBioSource, USA).

Results: IL-1 exhibited a non-significant increase in infected women as compared to the control group. As compared to the control group, levels of IL-8 were significantly higher, levels of IL-12 in the adaptive cellular immunity cytokines were not significantly higher, and levels of IL-6 and IFN were significantly decreased in infected women. The blood levels of adaptive humoral immune cytokines IL-4 and IL-10 exhibited a non-significant rise and decline, respectively in the test subjects.

Conclusion: Toxoplasmosis may have a substantial role in altering the innate and adaptive immune response and in regulating the cellular and humoral immune components. Significant and non-significant changes in levels of examined variables were discovered. The ability of the parasite to avoid detection and eradication by the immune system, sustaining its survival and multiplication, may be explained by immune response disruption brought on by toxoplasmosis.

Keywords: Toxoplasma, Women, Baghdad, Immunity

Introduction

Coccidae includes the vicious intracellular parasite Toxoplasma gondii. There are three different types of T. gondii: tachyzoites, bradyzoites (found in tissues), and sporozoites. The parasite often lives in lymph nodes, although it may also be found in the brain, heart, and lungs. There are 500 million cases of toxoplasmosis globally. The seroprevalence ranges from 5% to 90% depending on factors including age, region, and habits like eating unclean produce and uncooked meat. Infection rates rise with age and are greater in warmer, more humid climates. Congenital or acquired illnesses are both possible.[1,4] After entering the body of the host, the parasite multiplies within the cell, harming the reticuloendothelial system. The acute phase of invasion is characterised by the parasite's rapid growth and the production of so-called pseudocysts.[5]

Ige antibody production is shown to rise during parasite invasions, particularly during helminth infections. This flaw is caused by problems with how Th cells control the synthesis of antibodies, which encourages a local inflammatory response. IgE takes part in the response of antibody-dependent cellular cytotoxicity (ADCC) by releasing mediators from mast cells. Mast cells, lymphocytes, and macrophages (Mϕ), all produce cytokines (TNF and IL-5) that affect eosinophil cytotoxicity.6 Specific cytokines (IL-4, IL-5, IL-6, IL-10, IL-13, and IL-14) produced by Th2 cells are important in the pathophysiology of parasite illnesses. The main cytokine that causes the eosinophil population to rise in parasites is IL-5, whereas IL-6 promotes the formation of antibodies and has pro-inflammatory effects by promoting the creation of acute-phase proteins.

This kind of immune response is regulated by IL-10 and IL-12. The former reduces cytokine production and by preventing the creation of IL-6 and TNF, enhances the response that occurs when Th2 is involved and B cells are activated. However, IL-12 promotes the development of a Th1 response.[7,10]

This study aimed to assess the immune status of women with toxoplasmosis in the Baghdad province.

Materials and Methods

A diagnostic and prospective study was performed from September 2021 to January 2022. Ethical clearance was obtained from the Baghdad Province Health Coordinate, Ministry of Health, Iraq. One hundred and five blood samples were taken from women who had had abortions or threatened abortions and were admitted to the clinic in the province of Baghdad and 20 samples were taken as control. Following protocol, the blood samples were examined for *T. gondii* IgM and IgG using the ELISA method (Biotech, USA), with the Latex Agglutination Test (LAT) serving as a screening test, which was done in a previous study. Using sterile, disposable hypodermic traveller needles and tubes, around 3 ml of venous blood samples were collected from patients' arms. The serum was obtained by centrifuging obtained venous blood at 14,000 rpm for 20 minutes; it was then stored at 80 °C. All the necessary variables for analysis were included in the questionnaire that was created for data collection.

ELISA was used to evaluate serum levels of IFN-γ, IL-1α, IL-4, IL-6, IL-8, IL-10, and IL-12 (MyBioSource, USA). Statistical analysis was done using the SPSS version.[23]

Results and Discussion

An essential outcome (cytokines level) for the immune response associated with toxoplasmosis was shown by statistical analysis of the collected findings. Additionally, IL-1 exhibited a non-significant increase when compared to the control group, while IL-8 showed a significant rise in level. Levels of IL-12 in the adaptive cellular immunity cytokines were not significantly higher, while IFN was significantly reduced in the infected subjects than in the control group. In comparison to control groups, blood levels of adaptive humoral immune cytokines IL-4 and IL-10 exhibited a non-significant rise and decline, respectively in the infected subjects. In contrast, levels of IL-6 were significantly decreased as compared to the control group (Table 1).

Table 1.Levels of Cytokines among Infected and Control Groups

Test	Control	Infected
IFN-γ	432.10 ± 7.28[a]	306.24 ± 12.70[b]
IL-1α	19.06 ± 1.28[a]	28.80 ± 1.20[a]
IL-4	14.40 ± 0.74[a]	17.65 ± 1.03[a]
IL-6	82.40 ± 4.90[a]	49.66 ± 2.00[b]
IL-8	129.22 ± 17.10[b]	1833 ± 18.51[a]
IL-10	8.94 ± 0.09[a]	8.02 ± 0.73[a]
IL-12	21.46 ± 1.76[a]	24.1 ± 0.70[a]

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The present study's elevated IL-8 levels showed that the inflammatory response in aborted women was intensifying and that neutrophils and lymphocytes were drawn to the endometrium. This finding is consistent with that of Zicari et al., who suggested that neutrophils and lymphocytes in the endometrium may play a key part in the process of protease-induced neurogenic inflammation that results in labour or abortions.[11] Furthermore, Madhappan et al. hypothesised that IL-8 levels in foetal tissue samples from miscarriage cases were higher than those from a group of women who had elective abortions.[12] In contrast, Koumantaki et al. reported that women who spontaneously aborted their babies had much lower plasma levels of IL-8 than those who were carrying healthy babies.[13] Furthermore, Soriano et al. found no differences in serum levels between prospectively included women who had miscarriages and those who had normal pregnancies.[14] Variations in results across these studies may be attributed to the amount of data gathered or the genetic and ethnic makeup of the research group.

The present study's non-significant rise in IL-1 levels might be due to an increase in macrophage, neutrophil, epithelial, and endothelial cell secretion. As a result, inflammatory cells are drawn to the site of inflammation.

According to Hunter and Sibley, who reported that elevated levels of IL-1 may be thought of as the starting point for inflammation and consequently abortion in pregnant women with active toxoplasmosis infection, levels of IL-1 were elevated during an abortion but these levels dropped shortly after an abortion.[15]

According to Dimitriadis et al., IL-1 is involved in early implantation and reproduction.16 On the other hand, according to Kapoor et al., epithelial cells may synthesise IL-1 on demand, which indicates that both infected people and healthy people have considerable levels of this cytokine.[17]

Regarding cytokines of adaptive immunity, IL-12 is a master regulator of the immune response, particularly against intracellular pathogens like T. gondii, by inducing naive T-cells to develop into Th1 cells and inducing the production of IFN by such cells as well as NK cells.[18] The present research found no statistically significant variations in IL-12 levels between patients and controls, which may indicate that the immune system failed to recognise toxoplasma, ultimately leading to an intensification of infection.

The current study's significantly lower IFN levels may indicate a path for an internal parasite to evade cell-mediated immunity, which is bolstered by IFN. In contrast to abortion, which is linked to a shift towards the Th1 immune response that results in the loss of the foetus due to an increase in IL-12 levels that stimulate the NK cells to produce INF and then TNF, normal pregnancy is associated with an enhancement of the Th2 immune response and with suppression of the Th1 immune response to maintain the viability of the foetus, according to Piccinni et al., who also reported that Th2 cytokines inhibit Th1 responses.[19] Thus, the detection of *T. gondii* danger signals triggers a series of intrinsic cellular and humoral reactions. Strong NK cell activation, maturation of dendritic cells, activation of macrophages, and production of IFN, IL-12, TNF, and iNOS all work together to inhibit tachyzoite parasite reproduction. As a result, these marginal variations in IL-12 and the decline in IFN may be related to the time at which blood samples were taken from women who had abortions; samples were taken at least four weeks following the procedure. In a mouse model infected with T. gondii, Kaňková et al. demonstrated that IL-12 levels rose while IL-10 levels dropped.[20]

Genetic variances and variations in the immune system's sturdiness and capacity to combat such pathogenic invaders may contribute to discrepancies in study outcomes.

When it comes to Th2 cytokines, IL-4 encourages immature T lymphocytes to develop into Th2, which subsequently skews the immune response in favour of humoral immunity. IL-4 levels in the present research did not significantly increase, although IL-10 levels in the patients and controls almost matched. After the foetal loss, there was a typical rise in IL-10 levels and a minor reduction in IL-4 levels since the baby no longer needed them to survive. This is because IL-4 and IL-10 prevent the generation of Th1 cytokines by certain cells, which helps to sustain the foetus throughout pregnancy. According to Wilson et al., IL-10 inhibits the synthesis of IFN and *T. gondii's* persistence in the tachyzoite stage while increasing IL-4, which stimulates B-cell class switching and the production of IgE, the primary antibody against parasite infection. The reason for insignificant variations in IL-4 and IL-10 levels after abortion, however, could be related to parasites' ability to hide from the immune system as one of their escape methods.21 According to Butcher et al., *T. gondii* infection of macrophages (Mϕ) causes fast and long-lasting STAT3 phosphorylation irrespective of host IL-10. According to another research, STAT3 is essential for the efficient inhibition of endotoxin-induced IL-12 and TNF responses by tachyzoites. These findings identified a biological mechanism underpinning the parasite's capacity to inhibit the production of Mϕ pro-inflammatory cytokines.[22]

Several different types, including macrophages, endothelial cells, and Th2 cells, generate the crucial cytokine IL-6. This cytokine promotes the development of B cells into plasma cells and boosts the generation of antibodies. It also increases the cytotoxicity of NK cells and cytotoxic T lymphocytes. In the present research, IL-6 levels significantly

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decreased in the case group compared to the controls. When toxoplasmosis-positive women have an abortion, this outcome is possible. In women who have had abortions, a shift towards a Th1 immune response causes IL-6 levels that had risen during pregnancy to fall. According to Makhseed et al., the immune system will start to switch from a Th2 immune response during pregnancy to a Th1 immunological response following abortion.[23] On the other hand, Mousa and Bakhiet noted that IL-6 levels in aborted women rose during *T. gondii* infection.[24] The timing of sample collection following abortion, the immunological status of volunteer individuals, the volume of data used in the research, and other factors may have affected the outcomes of these investigations.

Conclusion

Toxoplasmosis may have a substantial role in altering the innate and adaptive immune response as well as in regulating both the cellular and humoral immune components. Significant and non-significant changes in levels of examined variables were discovered. The ability of the parasite to avoid detection and eradication by the immune system, sustaining its survival and multiplication, may be explained by immune response disruption brought on by toxoplasmosis.

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References

1. Evering T, Weiss LM. The immunology of parasite infections in immunocompromised hosts. Parasite Immunol. 2006;28(11):549-65. [PubMed] [Google Scholar]
2. Hegab SM, Al-Mutawa SA. Immunopathogenesis of toxoplasmosis. Clin Exp Med. 2003;3(2):84-105. [PubMed] [Google Scholar]
3. Lappalainen M, Hedman K. Serodiagnosis of toxoplasmosis. The impact of measurement of IgG avidity. Ann Ist Super Sanita. 2004;40(1):81-8. [PubMed] [Google Scholar]
4. Suzuki LA, Rocha RJ, Rossi CL. Evaluation of serological markers for the immunodiagnosis of acute acquired toxoplasmosis. J Med Microbiol. 2001;50(1):62-70. [PubMed] [Google Scholar]
5. Biesiada G, Kalinowska-Nowak A, Czepiel J, Mach T. [Toxoplasmosis—epidemiology, clinical manifestation and infection in pregnant women]. Przegl Lek. 2006;63(2):97-9. Polish. [PubMed] [Google Scholar]
6. Nickdel MB, Roberts F, Brombacher F, Alexander J, Roberts CW. Counter-protective role for interleukin-5 during acute Toxoplasma gondii infection. Infect Immun. 2001;69(2):1044-52. [PubMed] [Google Scholar]
7. Lang C, Gross U, Lüder CG. Subversion of innate and adaptive immune responses by Toxoplasma gondii. Parasitol Res. 2007;100(2):191-203. [PubMed] [Google Scholar]
8. Romagnani S. Understanding the role of Th1/Th2 cells in infection. Trends Microbiol. 1996;4(12):470-3. [PubMed] [Google Scholar]
9. Vilcek J, Lee TH. Tumor necrosis factor: new insights into the molecular mechanisms of its multiple actions. J Biol Chem. 1991;266(12):7313-6. [PubMed] [Google Scholar]
10. Zaccone P, Fehervari Z, Phillips JM, Dunne DW, Cooke A. Parasitic worms and inflammatory diseases. Parasite Immunol. 2006;28(10):515-23. [PubMed] [Google Scholar]
11. Zicari A, Ticconi C, Realacci M, Cela O, Santangelo C, Pietropolli A, Russo MA, Piccione E. Hormonal regulation of cytokine release by human fetal membranes at term gestation: effects of oxytocin, hydrocortisone and progesterone on tumour necrosis factor-alpha and transforming growth factor-beta 1 output. J Reprod Immunol. 2002;56(1-2):123-36. [PubMed] [Google Scholar]
12. Madhappan B, Kempuraj D, Christodoulou S, Tsapikidis S, Boucher W, Karagiannis V, Athanassiou A, Theoharides TC. High levels of intrauterine corticotropin-releasing hormone, urocortin, tryptase, and interleukin-8 in spontaneous abortions. Endocrinology. 2003;144(6):2285-90. [PubMed] [Google Scholar]
13. Koumantaki Y, Matalliotakis I, Sifakis S, Kyriakou D, Neonaki M, Goymenou A, Koumantakis E. Detection of interleukin-6, interleukin-8, and interleukin-11 in plasma from women with spontaneous abortion. Eur J Obstet Gynecol Reprod Biol. 2001;98(1):66-71. [PubMed] [Google Scholar]
14. Soriano D, Hugol D, Quang NT, Darai E. Serum concentrations of interleukin-2R (IL-2R), IL-6, IL-8, and tumor necrosis factor alpha in patients with ectopic pregnancy. Fertil Steril. 2003;79(4):975-80. [PubMed] [Google Scholar]
15. Hunter CA, Sibley LD. Modulation of innate immunity by Toxoplasma gondii virulence effectors. Nat Rev Microbiol. 2012;10(11):766 78. [PubMed] [Google Scholar]
16. Dimitriadis E, White CA, Jones RL, Salamonsen LA. Cytokines, chemokines and growth factors in endometrium related to implantation. Hum Reprod Update. 2005;11(6):613-30. [PubMed] [Google Scholar]
17. Kapoor M, Martel-Pelletier J, Lajeunesse D, Pelletier JP, Fahmi H. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. Nat Rev Rheumatol. 2011;7(1):33 42. [PubMed] [Google Scholar]

18. Wilson DC, Matthews S, Yap GS. IL 12 signaling drives CD8+ T cell IFN gamma production and differentiation of KLRG1+ effector subpopulations during Toxoplasma gondii infection. J Immunol. 2008;180(9):5935-45. [PubMed] [Google Scholar]
19. Piccinni MP, Lombardelli L, Logiodice F, Kullolli O, Romagnani S, Le Bouteiller P. T helper cell mediated-tolerance towards fetal allograft in successful pregnancy. Clin Mol Allergy. 2015;13(1):9. [PubMed] [Google Scholar]
20. Kaňková S, Holáň V, Zajícová A, Kodym P, Flegr J. Modulation of immunity in mice with latent toxoplasmosis – the experimental support for the immunosuppression hypothesis of toxoplasma-induced changes in reproduction of mice and humans. Parasitol Res. 2010;107(6):1421-7. [PubMed] [Google Scholar]
21. Wilson EH, Wille Reece U, Dzierszinski F, Hunter CA. A critical role for IL 10 in limiting inflammation during toxoplasmic encephalitis. J Neuroimmunol. 2005;165(1-2):63 74. [PubMed] [Google Scholar]
22. Butcher BA, Kim L, Panopoulos AD, Watowich SS, Murray PJ, Denkers EY. IL-10-independent STAT3 activation by Toxoplasma gondii mediates suppression of IL 12 and TNF alpha in host macrophages. J Immunol. 2005;174(6):3148-52. [PubMed] [Google Scholar]
23. Makhseed M, Raghupathy R, Azizieh F, Omu A, Al-Shamali E, Ashkanani L. Th1 and Th2 cytokine profiles in recurrent aborters with successful pregnancy and with subsequent abortions. Hum Reprod. 2001;16(10):2219-26. [PubMed] [Google Scholar]
24. Mousa A, Bakhiet M. Role of cytokine signaling during nervous system development. Int J Mol Sci. 2013;14(7):13931-57. [PubMed] [Google Scholar]

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