ORIGINAL ARTICLE

Effect of some immunological markers on the level of anti-Müllerian hormone (AMH) in women infected with *Toxoplasma gondii*: further investigations

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ABSTRACT

Aim: To explore the effects of *T. gondii* on immune levels and try to find out correlations that maybe manifest later on women who have had the infection and to assess the direct relationship between the infection and a rise in the value of anti-Müllerian hormone (AMH). Specifically, we examined the relationship between AMH and IL-1 β, IL-6, and TNF-α.

Materials and Methods: Blood samples were collected from two identical groups of 80 (40 healthy control and 40 infected with *T. gondii*). The participants were women at an age ranging from 20 to 25 years; Group 1, healthy women who were not infected with Toxoplasma comprised the control series; Group 2, women who were Toxoplasma-infected and who visited medical facilities. Toxoplasma infection was diagnosed using the Latex Agglutination Test (LAT). Serum human interleukins (IL-1β and IL-6), tumor necrosis factor alpha (TNF-α) and anti-Müllerian hormone (AMH) were detected by Enzyme Linked Immunosorbent Assay (ELISA) method.

Results: Compared with the control group, infected women had significantly higher levels of human IL-1 β, IL-6, and tumor necrosis factor alpha (TNF-α). AMH concentrations correlated significantly in a positive manner with human IL-1β, IL-6, and tumor necrosis factor alpha (TNF-α).

Conclusions: Three immune parameters (IL-1 β, IL-6, and TNF-α) had elevated circulating levels, which implied the strong association between AMH and these immune variables.

KEY WORDS: toxoplasmosis, IL-1 β, IL-6, tumor necrosis factor alpha (TNF-α), anti-Müllerian hormone

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INTRODUCTION

Toxoplasma gondii (*T. gondii*) is a parasite belonging to the group of inner parasites of cats, for adults are the intermediate host. Symptoms in most instances, patients are often asymptomatic [1]. The parasite *T. gondii* frequently invades the central nervous systems of reptiles, birds and mammals [2], furthermore, the disease may extend to the vaginal tract and skeletal muscles [3-4]. This parasite has a potential to be deadly, as it may lead to acquired toxoplasmosis in organ recipient patients [5]. It also causes congenital toxoplasmosis in the offspring of some domestic and wild animals, such as goats, sheep and pigs [6]. This disease has now been thought to occur in about a third of the population in the whole world. Toxoplasma gondii (the etiological agent of toxoplasmosis), a protist most commonly found in those that are also organisms from Apicomplexa, is ubiquitous and well-known [7-8]. It has almost unique ability to behave as a parasite of mammal cells including human and farm animals as well as birds and various marines. Tomasina and colleagues extensively discussed the pathogenesis of *T. gondii* [9]. The basic mechanism of pathogenesis is that in order to complete it's indefinitely multiplying and disseminating stage within an isolated infected cell, the parasite needs to make the lysis of cells. However, it is precisely this capacity to change from a fast-dividing, disease-causing form (the tachyzoite) to a slow-dividing 'encysted'/latently-infected mode (the bradyzoite) that allows this cunning and canny organism to coexist in relative equilibrium with its host without actually doing it in. Acute toxoplasmosis is caused by the former, but chronic toxoplasmosis can be caused by the latter. In farm animals, especially sheep, toxoplasmosis costs millions of dollars in lost production. Similarly, it has been demonstrated that toxoplasmosis has a significant impact on threatened wild animal populations, with catastrophic ecological consequences and effects of particular severity in marine life [10]. Eating undercooked meat contaminated with bradyzoites that are encysted in the brain or skeletal muscle is a common method by which this parasite is passed to humans and other carnivores [11]. When a naive

host contracts the disease while pregnant, it may also be passed on to the fetus. Besides that, unintentional contact with infective oocysts produced by feline species in their droppings could bring about transmission. Human infertility is the most common clinical manifestation of acute toxoplasmosis. Chronically infected immunocompromised patients may other clinical manifestations including oral, cervical, or uterine sores, bleeding abnormalities [12], and still other symptoms; ocular hypertension is one such clinical manifestation in a renal transplant recipient diagnosed with molluscum contagiosum [13]. Ophthalmic and neurological complications also occur in persons with chronic toxoplasmosis and HIV. Those with normal immune systems who are congenitally infected or become chronically infected are also at risk of developing ocular toxoplasmosis [14]. In the small intestine, *T. gondii* further develops into rapidly multiplying tachyzoites [15]. Two components of the immune response elicited by this approach anchor the parasite's life cycle. *T. gondii* replicates within immune cells it invades. Following infection and dissemination, the parasite extravasates into a new host where it invades the brain, muscles and other organs [16]. The majority of tachyzoites are cleared in the course of a chronic infection and the parasites differentiate and express a bradyzoite transcriptional profile [17]. In order to survive as the parasite pass through the intestines of the next host a cyst wall is produced that is sugar-based [18]. Therefore, the window of transmission is limited, as the parasite kills the host before this transformation takes place in the absence of a strong immune response. Tumor necrosis factor alpha (TNF-α), interleukin 1 (IL-1 β) and interleukin-6 (IL-6) are key molecules in the onset and progression in innate as well as in adaptive immune response in cells such as endothelium or epithelial cells [19-20]. Inflammasomes also facilitate immunity against microbes, multimolecular interactions, and a variety of cytokines [21]. These kinds of cytokines are secreted by the cells of the innate immune system, e.g. monocytes, dendritic cells, and macrophages [22-23]. Anti-Müllerian hormone (AMH) is an ovarian hormone produced in growing follicles recruited from the primordial follicle pool but have not undergone dominance selection [24]. In view of its ability to reflect ovarian follicular pool volume in a woman of reproductive age, it is considered to be a reliable marker of ovarian reserve. In contrast to other hormonal indexes such as serum FSH, there is little intra- and intermenstrual cycle variability proposed for AMH [25]. In the male fetus, the physiologic degeneration of the Mullerian ducts is induced by AMH. According to Cedars and colleagues AMH can be used as a therapeutic option for screening reduced ovarian reserve [26]. This article following our published work that dealt with AMH level's possible relationship with specific immune markers (IL-2, IL-10, and IL-12) [27].

AIM

The aim of the present study is to explore the effects of *T. gondii* on immune levels and try to find out correlations that maybe manifest later on women who have had the infection and to assess the direct relationship between the infection and a rise in the value of anti-Müllerian hormone (AMH) and to evaluate its putative correlation with other immune markers. Specifically, we examined the relationship between AMH and IL-1 β, IL-6, and TNF-α.

MATERIALS AND METHODS

PARTICIPANTS, ETHICAL APPROVAL AND SCOPE OF THE STUDY

Eighty venous blood samples were obtained from women (20 to 25 years). Women were assigned into two groups (40 women per group; healthy control group and infected group. Women with toxoplasma involved in this study are those who visited used medical care services. Exclusion Criteria: Women with PCOS, autoimmune diseases, hormonal therapies, pregnant or recently pregnant women, women with ovarian pathologies, ovarian malignancies, chronic systemic illnesses, immunosuppressant drugs or corticosteroids or substance abuse.

The study was performed during the period 15th of January -23rd of April 2023. An ethical approval was obtained from the ethical committee in the College of Pharmacy/ University of Alkafeel (protocol number 544, 25/11/2022).

ASSESSMENT OF THE STUDY PARAMETERS

Toxoplasma infection was determined through LAT and AMH as well as inflammatory markers were measured using ELISA. Blood samples were collected in sterile plain tubes. After a 5-minute centrifugation of the blood at 3000 rpm, the serum was transferred into plastic numbered containers and stored at -20°C until several immunological and serological investigations could be performed.

STATISTICAL ANALYSIS

Data are presented as mean ± standard error of mean (SEM). GraphPad Prism 9.3.1 was used in the analysis and presentation of data. The number of participant (n) is mentioned in the legend of each figure. Student`s t-test was performed to compare between healthy controls and infected women. A p-value < 0.05 was considered significant.

RESULTS

This study adds a piece of information supporting our previous published data. Both papers deal with the impact

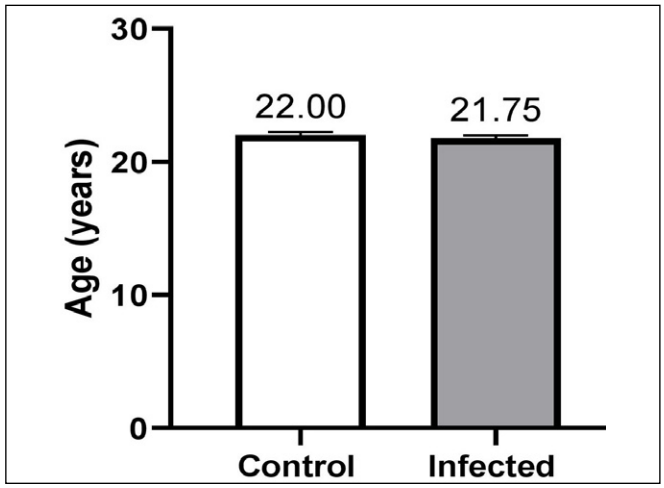

Fig. 1. Age-related distribution of participants in control and infected group, no significant difference was detected (n=40±SEM, t-test)
Source: Own materials

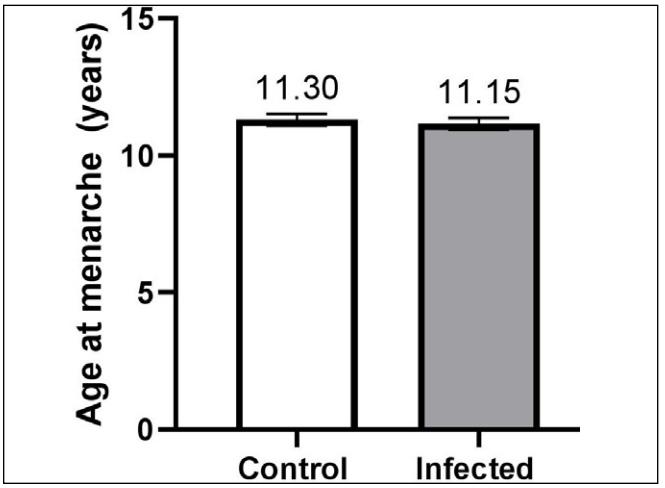

Fig. 3. Age of participants at menarche in control and infected group, no significant difference was detected (n=40±SEM, t-test)
Source: Own materials

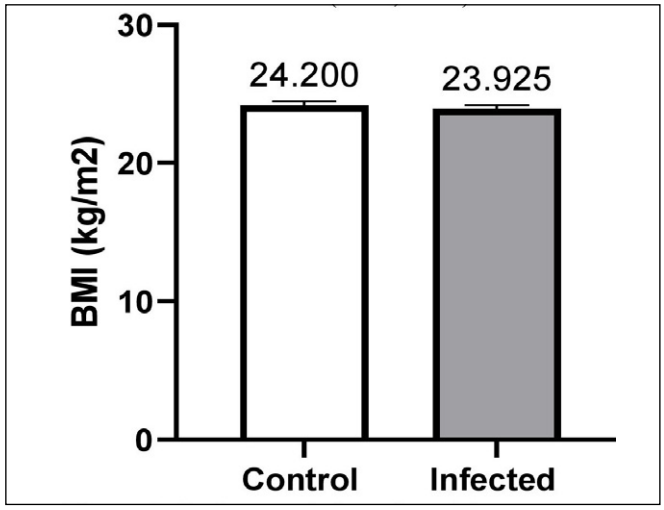

Fig. 2. Body mass index of participants in control and infected group, no significant difference was detected (n=40±SEM, t-test)
Source: Own materials

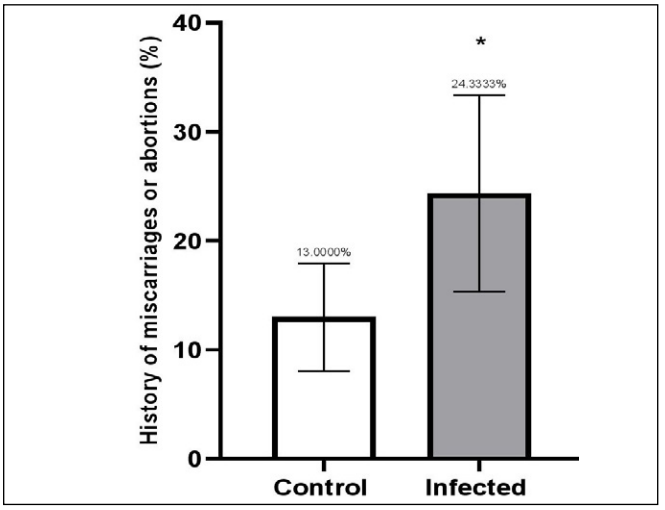

Fig. 4. History of miscarriages or abortions among married women in healthy control and infected women (n=21 and 22±SEM, respectively, *=significantly different $p<0.05$ when compared to control, Chi-square test)
Source: Own materials

of *Toxoplasma gondii* infection on a host of inflammatory biomarkers and their association with Anti-Müllerian Hormone (AMH) in women. Similar findings were found that increased AMH is correlated with an increase in the risk of one or more reproductive morbidities. Both studies test the theory that an immune response following *T. gondii* infection changes the levels of AMH, which could be indicative for a possible risk of reproductive disturbances at any later instance in time. This study represents, therefore, also a strong progression and validation of those previous investigations in which is now demonstrating that by using unrelated group of topically relevant proinflammatory markers, the linkage with observed AMH association may be confirmed together with direct clinical evidence for adverse reproductive outcome (history of miscarriage/abortion). Identification also included in this study emphasized the pre-eminence of the higher frequency of miscarriages/abortions really reinforcing the original idea, that both infection and its associated inflammatory/endocrine profile were involved in adverse reproductive outcomes.

AGE-RELATED DISTRIBUTION OF PARTICIPANTS

As it is mentioned above, participants involved in this study aged 20-25 years. However, the age made no significant difference between healthy and women infected with *T. gondii* as mentioned in figure (1).

BODY MASS INDEX OF PARTICIPANTS

Body mass index showed no significant difference between healthy and women infected with T. gondii as mentioned in figure (2).

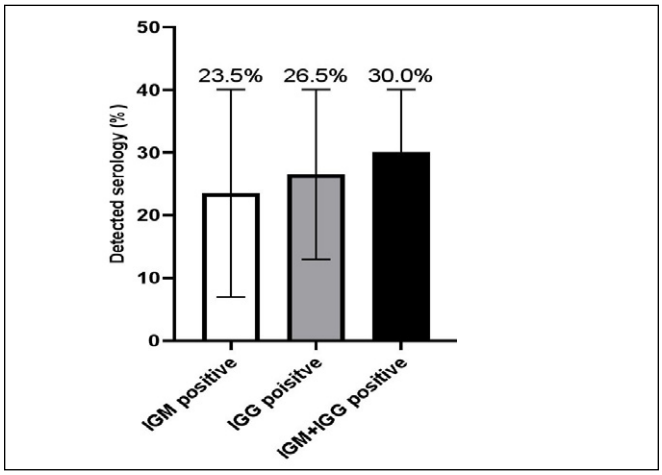

Fig. 5. Serological characterization of antigens against Toxoplasma in infected women. It shows that 23.5% of infected women showed serum IGM immunoglobulin, 26.5% of them showed serum IGG immunoglobulin and 30% of women in disease group showed both IGM and IGG immunoglobulin (n=40±SEM).
Source: Own materials

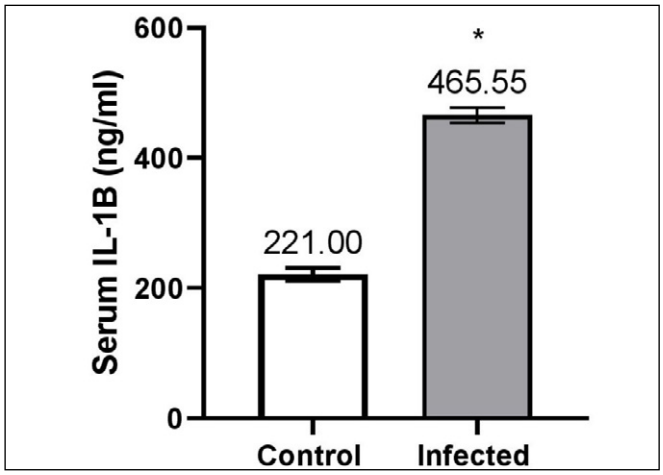

Fig. 6. Serum level of IL-1 β in healthy control and infected women (n=40±SEM, *= significantly different ($p<0.05$) when compared to control, t-test)
Source: Own materials

AGE AT MENARCHE

There was no significant difference between control and infected women regarding the age of participants at menarche as mentioned in figure (3).

HISTORY OF MISCARRIAGES OR ABORTIONS AMONG MARRIED WOMEN

Our results showed that 13% of married women in the healthy control group subjected to miscarriages or abortion while it accounted to 24.3% in infected women representing a significant difference between these two groups as shown in figure (4).

SEROLOGICAL TEST FOR TOXOPLASMOSIS

It was found that 23.5% of infected women showed serum IGM immunoglobulin while 26.5% of them showed serum IGG immunoglobulin. On the other hand, 30% of women in disease group showed both IGM and IGG immunoglobulin as shown in figure (5).

SERUM LEVEL OF IL-1B

It was found that the serum level of IL-1 β in infected women is significantly higher than its level in healthy control group as shown in figure (6).

SERUM LEVEL OF IL-6

It was found that the serum level of IL-6 in infected women is significantly higher than its level in healthy control group a s shown in figure (7).

SERUM LEVEL OF TNF-A

A higher level of serum TNF-α was reported in infected women compared to healthy control group as shown in figure (8).

SERUM LEVEL OF AMH

A higher level of serum AMH was reported in infected women compared to healthy control group as shown in figure (9).

DISCUSSION

This study documented higher serum levels of IL-1, IL-6 and TNF-α in the infected group with a high AMH levels as compared to the control group. These results may be due to a function of those inflammatory markers involved in host's resistance to *T. gondii* infection, since we have shown that *T. gondii* infection promotes IL-2 release which could be due to the activation of primary human monocytes [28]. This increase might occur because CD4 and CD8 T lymphocyte secrete IFN-gamma spontaneously; as well as the natural killer cells secrete IFN- γ when the infection is starting to encounter dendritic cells and neutrophil leukocyte early in the production of IL-1 [29]. As a consequence, it stimulates natural killer cells to produce interferon (IFN-γ) and is produced in high concentration by T-lymphocyte during chronic infection of toxoplasmosis for prevention of reactive parasite's tissue cyst, and for stimulation of macrophages to which they provide antigen presentation and increase the effectiveness of lysosomes in macrophage cell [30]. In other words, it stimulates the effectiveness of natural killer cells. In a previous study, we reported a relationship between elevated level of human cytokines and elevated level

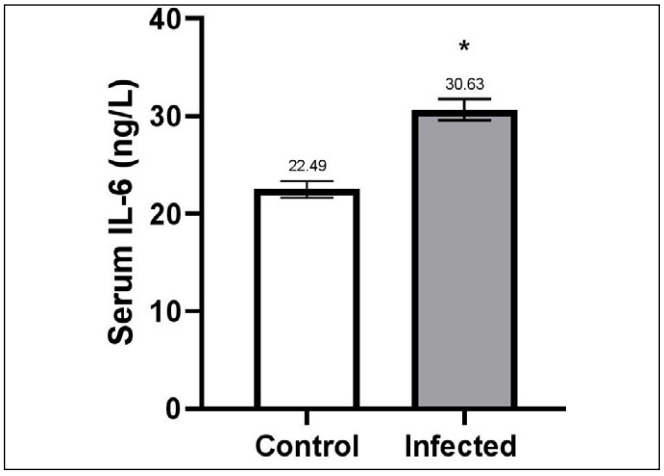

Fig. 7. Serum level of IL-6 in healthy control and infected women (n=40±SEM, *= significantly different (p<0.05) when compared to control, t-test)
Source: Own materials

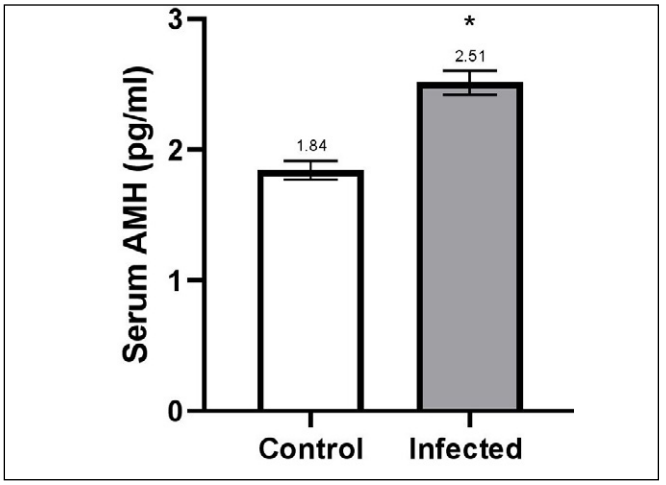

Fig. 9. Serum level of AMH in healthy control and infected women (n=40±SEM, *= significantly different p<0.05 when compared to control, t-test)
Source: Own materials

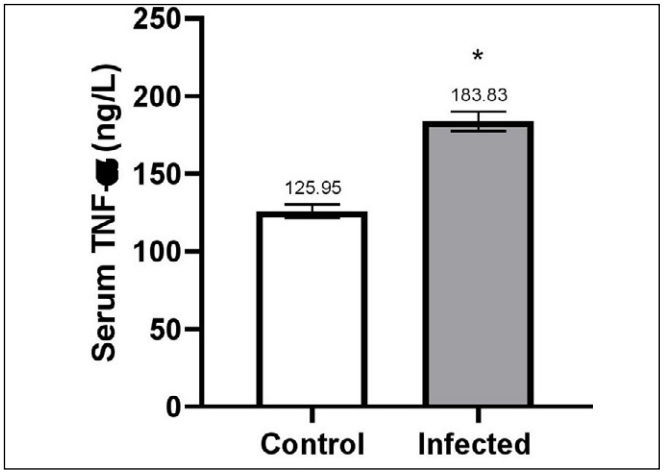

Fig. 8. Serum level of TNF-α in healthy control and infected women (n=40±SEM, *= significantly different (p<0.05) when compared to control, t-test)
Source: Own materials

of AMH in t. gondii infection [27]. Elevated level of cytokines in women infected with *T. gondii* was also reported in another study [31]. Higher level of sex hormone has been reported in infected women compared to control whether concurrent increase or decrease [32-33] findings that support the hypothesis that there is a relationship between elevated level of AMH and increased production of inflammatory markers. High levels of immune markers can be linked to the fact that aborted women inflammatory response was increasing and that the neutrophils and lymphocytes were attracted to the endometrium. Zicari and colleagues reported that that both neutrophils and lymphocytes in the endometrium can have a pivotal role in the phenomenon of protease induced neurogenic inflammation leading to labor or abortions [34], furthermore, Madhappan and colleagues also hypothesized that the levels interleukins (particularly IL-8) in fetal tissue samples obtained from miscarriage cases were considerably above the inflammatory threshold than from elective abortion women [35], however, the findings obtained by Koumantaki and co-workers contradicted with those belong to Madhappan's team which showed that women who underwent spontaneous abortion had much lower plasma IL-8 levels compared with women carrying normal babies [36]. In addition to that, another research showed that serum levels in women prospectively include with miscarriage women and normal pregnancy women detected no difference [37]. This inconsistency may reflect the amount of data collected or may also be related to the genetic and ethnic variation in the study samples. In addition, the low level of IL-1 may be due to an increased release induced by macrophage, neutrophil, epithelial, and by endothelial cells. As a result, inflammatory components are recruited to the inflamed area. However, Saud and colleagues reported that the concentration of IL-1 was 19.06 ± 1.28 (pg/ml) in control versus 28.80 ± 1.20 (pg/ml) in infected women which still higher regardless of significance [38], it seems more than one factor can influence the serum level of immune markers. Several studies have investigated the relationship between inflammatory markers and AMH. For example, in women with regular menses, Schon and colleagues found that CRP and IL-6 are associated with levels of AMH [39]. In another work, however, where the correlation between serum IL-6 and IL-2l levels and AMH was further studied, it was found that IL-6 and IL-2 levels were negatively correlated with AMH indicating that their level was

higher, and the lower the level of AMH, the worse ovarian reserve function. Such contradictory findings could be related to the diseases itself since Sun and colleagues evaluated the level of inflammatory markers in women with premature ovarian failure not with T. gondii infection [40]. It seems that toxoplasma infection participated in the stimulation of immune system including the release of immune markers. The influence of T. gondii infection on mast cells was also studied. EunAh and colleagues focused on the generation of pro-inflammatory cytokines (TNF-α, IL-4), chemokines (CXCL8, MCP-1) and NO by mast cells following stimulation with soluble lysate of T. gondii tachyzoites [41]. They used RT-PCR and ELISA to measure the production of CXCL8 (IL-8), MCP-1, TNF-α, IL-4. For CXCR-1 and CXCR-2 detection, western blot analysis was carried out. They demonstrated that T. gondii lysates induced mast cells of releasing CXCL8, MCP-1, TNF-α, IL-4 and generating NO. This indicates that mast cells are critical to inflammatory responses to *T. gondii*. The results of the current study demonstrate no difference in mean age, body mass index, and age of menarche among control and infection women; however, differences were found in some reproductive and immune parameters. Miscarriages/abortions in married *T. gondii* infected women were significantly higher suggesting a potential deleterious reproductive effect due to the infection. In addition, infected females also presented increased plasma levels of pro-inflammatory cytokines IL-1β, IL-6 and TNF-α, indicating the presence of an immune response. The serum levels of Anti-Müllerian Hormone (AMH) were also notably higher in the infected compared to the uninfected group, which could be indicative of disturbed ovarian reserve or immune-mediated endocrine regulation. Taken together, these data highlight the potential role of *T. gondii* in the reproductive health of women and the importance of immune-inflammatory markers in T. gondii-induced reproductive dysfunction. Further studies may need to focus on prospective studies to establish causal relationships between *T. gondii* infection, immune parameters, and reproductive outcomes over time. In addition, mechanistic Investigations may be required to explore the molecular and cellular mechanisms by which *T. gondii* influences reproductive hormones, ovarian reserve markers like AMH, and immune responses.

CONCLUSIONS

Three immune parameters (IL-1 β, IL-6 and TNF-α) were circulating with increased concentrations in addition to the already reported raised pro-inflammatory markers, again suggesting a tight link between AMH levels and these cytokines. The study confirms the main assumption that immune response post T. gondii infection modifies Anti-Müllerian Hormone (AMH) secretion. Through establishing a confirmed link between AMH and another distinct but important set of proinflammatory markers, the current investigation strongly validates the identified linkage for AMH. Importantly, the finding of more miscarriages/abortions in the infected group is a direct clinical proof of an unfavorable reproductive outcome. This result complements the previous assumption that both infection and its related inflammatory/endocrine profile contribute to the etiopathogenesis of the observed reproductive disorders, predicting potential future morbidities.

REFERENCES

1. Sanchez SG, Besteiro S. The pathogenicity and virulence of Toxoplasma gondii. Virulence. 2021;12(1):3095-3114. doi:10.1080/21505594.2021.2012346 DOI
2. Mendez OA, Koshy AA. Toxoplasma gondii: Entry, association, and physiological influence on the central nervous system. PLOS Pathog. 2017; 13(7): e1006351. doi: 10.1371/journal.ppat.1006351. DOI
3. ElShewy K. Parasites of the Reproductive System BT - Medical Parasitology: A Body System Approach. In: Mahmud R (ed.). Medical Parasitology. Springer Nature Switzerland. 2024, pp. 199-210. doi:10.1007/978-3-031-64736-9_14. DOI
4. Jaiswal AK, Kumar P, Agrawal V, Singh A, Singh SK. Chapter 10 - Parasites of the musculoskeletal system. In: Rana TB (ed.). Developments in Microbiology. Academic Press. 2023, pp. 265-295. doi:10.1016/B978-0-323-95352-8.00012-6. DOI
5. Fabiani S, Fortunato S, Bruschi F. Solid Organ Transplant and Parasitic Diseases: A Review of the Clinical Cases in the Last Two Decades. Pathogens. 2018;7(3). doi:10.3390/pathogens7030065. DOI
6. Singh S. Congenital toxoplasmosis: Clinical features, outcomes, treatment, and prevention. Trop Parasitol. 2016;6(2). doi:10.4103/2229-5070.190813. DOI
7. Dubey JP. The History and Life Cycle of Toxoplasma gondii. In: Weiss LM, Kim KB (eds). Academic Press. chap. 1, 2014, pp.1-17. doi:10.1016/B978-0-12-396481-6.00001-5. DOI
8. Torgerson PR, Mastroiacovo P. The global burden of congenital toxoplasmosis: a systematic review. Bull World Health Organ. 2013;91(7):501-508. doi:10.2471/blt.12.111732. DOI

9. Tomasina R, Francia ME. The Structural and Molecular Underpinnings of Gametogenesis in Toxoplasma gondii. Front Cell Infect Microbiol. 2020;10(December):1-8. doi:10.3389/fcimb.2020.608291. DOI
10. Shapiro K, VanWormer E, Packham A, Dodd E, Conrad PA, Miller M. Type X strains of Toxoplasma gondii are virulent for southern sea otters (Enhydra lutris nereis) and present in felids from nearby watersheds. Proc R Soc B Biol Sci. 2019;286(1909):20191334. doi:10.1098/rspb.2019.1334. DOI
11. Pinto-Ferreira F, Caldart ET, Pasquali AKS, Mitsuka-Breganó R, Freire RL, Navarro IT. Patterns of transmission and sources of infection in outbreaks of human toxoplasmosis. Emerg Infect Dis. 2019;25(12):2177-2182. doi:10.3201/eid2512.181565. DOI
12. Wang ZD, Wang SC, Liu HH, et al. Prevalence and burden of Toxoplasma gondii infection in HIV-infected people: a systematic review and meta-analysis. Lancet HIV. 2017;4(4):e177-e188. https://doi:10.1016/S2352-3018(17)30005-X.
13. Sanders AP, dos Santos T, Felipe CKK, et al. Ocular Lesions in Congenital Toxoplasmosis in Santa Isabel do Ivaí, Paraná, Brazil. Pediatr Infect Dis J. 2017;36(9). doi:10.1097/INF.0000000000001614. DOI
14. Commodaro AG, Chiasson M, Sundar N, Rizzo LV, Belfort R, Grigg ME. Elevated toxoplasma gondii infection rates for retinas from eye banks, Southern Brazil. Emerg Infect Dis. 2016;22(4):691-693. doi:10.3201/eid2204.141819. DOI
15. Dubey JP, Lindsay DS, Speer CA. Structures of Toxoplasma gondiiTachyzoites, Bradyzoites, and Sporozoites and Biology and Development of Tissue Cysts. Clin Microbiol Rev. 1998;11(2):267-299. doi:10.1128/cmr.11.2.267. DOI
16. Harker KS, Ueno N, Lodoen MB. Toxoplasma gondii dissemination: a parasite's journey through the infected host. Parasite Immunol. 2015; 37(3): 141-149. doi:10.1111/pim.12163. DOI
17. Skariah S, McIntyre MK, Mordue DG. Toxoplasma gondii: determinants of tachyzoite to bradyzoite conversion. Parasitol Res. 2010;107(2):253-260. doi:10.1007/s00436-010-1899-6. DOI
18. Shapiro K, Bahia-Oliveira L, Dixon B, et al. Environmental transmission of Toxoplasma gondii: Oocysts in water, soil and food. Food Waterborne Parasitol. 2019;15. doi:10.1016/j.fawpar.2019.e00049. DOI
19. Silva LB, dos Santos Neto AP, Maia SMAS, et al. The Role of TNF-α as a Proinflammatory Cytokine in Pathological Processes. Open Dent J. 2019;13(1):332-338. doi:10.2174/1874210601913010332. DOI
20. Kany S, Vollrath JT, Relja B. Cytokines in Inflammatory Disease. Int J Mol Sci. 2019;20(23). doi:10.3390/ijms20236008. DOI
21. Rathinam VAK, Fitzgerald KA. Inflammasome Complexes: Emerging Mechanisms and Effector Functions. Cell. 2016;165(4):792-800. doi:10.1016/j.cell.2016.03.046. DOI
22. Germic N, Frangez Z, Yousefi S, Simon HU. Regulation of the innate immune system by autophagy: monocytes, macrophages, dendritic cells and antigen presentation. Cell Death Differ. 2019;26(4):715-727. doi:10.1038/s41418-019-0297-6. DOI
23. Iwasaki A, Medzhitov R. Control of adaptive immunity by the innate immune system. Nat Immunol. 2015;16(4):343-353. doi:10.1038/ni.3123. DOI
24. La Marca A, Grisendi V, Griesinger G. How Much Does AMH Really Vary in Normal Women? Int J Endocrinol. 2013;2013(1):959487. doi:10.1155/2013/959487. DOI
25. Shrikhande L, Shrikhande B, Shrikhande A. AMH and its clinical implications. J Obstet Gynecol India. 2020;70(5):337-341. doi:10.1007/s13224-020-01362-0. DOI
26. Cedars MI. Evaluation of female fertility - AMH and ovarian reserve testing. J Clin Endocrinol Metab. 2022;107(6):1510-1519. doi:10.1210/clinem/dgac039. DOI
27. Mushattat SJ, ALAridi JA, Kadhim S. Effect of Some Immunological Markers on The Level of Anti- Mullerian Hormone (AMH) in Women Infected with Toxoplasma gondii. Wiad Lek. 2024;77(10):2020-2026. doi:10.36740/WLek/193199. DOI
28. Tosh KW, Mittereder L, Bonne-Annee S, et al. The IL-12 Response of Primary Human Dendritic Cells and Monocytes to Toxoplasma gondii Is Stimulated by Phagocytosis of Live Parasites Rather Than Host Cell Invasion. J Immunol. 2016;196(1):345-356. doi:10.4049/jimmunol.1501558. DOI
29. Mullangi PK, Shahani L, Koirala J. Role of Endogenous Biological Response Modifiers in Pathogenesis of Infectious Diseases. Infect Dis Clin. 2011; 25(4): 733-754. doi:10.1016/j.idc.2011.07.003. DOI
30. Kapse B. Role of IFN-γ in the Immunity and Control of Gastrointestinal Nematode Infections. 2023. doi:10.17169/refubium-40336. DOI
31. Salomão Lopes C, Carvalho RJV, da Silva TL, et al. Pregnant Women Chronically Infected by Toxoplasma gondii with Depressive Disorder: Differential Modulation of Pro-Inflammatory and Anti-Inflammatory Cytokines. Pathogens. 2025;14(4):330. doi:10.3390/pathogens14040330. DOI
32. Aziz MJ, Ali AA, Hameed MF, Abdullah BA. Effect of Toxoplasma gondii Infection on the Level of Luteinizing and Follicle Stimulating Hormones in Women with Polycystic Ovary Syndrome. Med J Babylon. 2024; 21(Suppl 2). doi:10.4103/MJBL.MJBL_818_23. DOI
33. Wessman M, Korsholm AS, Bentzen JG, et al. Anti-müllerian hormone levels are reduced in women living with human immunodeficiency virus compared to control women: a case–control study from Copenhagen, Denmark. J Virus Erad. 2018;4(2):123-127. doi:10.1016/S2055-6640(20)30256-9. DOI
34. Zicari A, Ticconi C, Realacci M, et al. Hormonal regulation of cytokine release by human fetal membranes at term gestation: Effects of oxytocin, hydrocortisone and progesterone on tumour necrosis factor-α and transforming growth factor-β 1 output. J Reprod Immunol. 2002;56(1-2):123-136. doi:10.1016/S0165-0378(02)00038-4. DOI

35. Madhappan B, Kempuraj D, Christodoulou S, et al. High levels of intrauterine corticotropin-releasing hormone, urocortin, tryptase, and interleukin-8 in spontaneous abortions. Endocrinology. 2003;144(6):2285-2290. doi:10.1210/en.2003-0063. DOI
36. Koumantakis E, Matalliotakis I, Kyriakou D, Fragouli Y, Relakis K. Increased levels of interleukin-8 in human seminal plasma. Andrologia. 1998;30(6):339-343. doi:10.1111/j.1439-0272.1998.tb01180.x. DOI
37. 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):975-980. doi:10.1016/S0015-0282(02)04853-7. DOI
38. Saud MJ, Abd M, Adnan A, Omar TM, Alsaraf KM, Toama MA. Implications of Toxoplasma infection on women's immune status in Baghdad province, Iraq. Journal of Communicable Diseases 2023;55(03):62-66. doi:10.24321/0019.5138.202340. DOI
39. Schon SB, Jiang C, Fortin CN, Neff LM, Wise LA, Marsh EE. the association of adipokines and inflammatory markers with anti-mullerian hormone (AMH) levels in a Latina/Latinx population. Fertil Steril. 2023;120(4):e283. doi:10.1016/j.fertnstert.2023.08.828. DOI
40. Sun S, Chen H, Zheng X, Ma C, Yue R. Analysis on the level of IL-6, IL-21, AMH in patients with auto-immunity premature ovarian failure and study of correlation. Exp Ther Med. 2018; 16(4): 3395-3398. doi:10.3892/etm.2018.6592. DOI
41. Park EA, Han IH, Kim JH, Park SJ, Ryu JS, Ahn MH. Production of inflammatory cytokines and nitric oxide by human mast cells incubated with toxoplasma gondii lysate. Korean J Parasitol. 2019; 57(2): 201-206. doi:10.3347/kjp.2019.57.2.201. DOI

CONFLICT OF INTEREST

The authors declare no conflict of interest

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