Egyptian Journal of Veterinary Sciences

https://ejvs.journals.ekb.eg/

The Role of Pro-Inflammatory Cytokines IL-12 and TNF-α Against Toxoplasmosis among Aborted Women

Sarwin S. M. Mizuri[1,2], Wijdan M. S. Mero[1,3] and Haval M. Khalid[1,2]

[1]*Department of Biology, College of Science, University of Zakho, Duhok, Iraq.*

[2]*Biology Research Center, Research Center, University of Zakho, Duhok, Iraq.*

[3]*Department of Medical Microbiology, College of Science, Knowledge University, Erbil, Iraq.*

Abstract

TOXOPLASMA gondii is an opportunistic intracellular protozoan parasite which causes toxoplasmosis by using its surface proteins that evade the immune system of the host, leading to restricted immune signaling routes. This alteration has various influences on infected individuals, specifically pregnant women, which leads to repeated abortion. The aim of this study was to examine the correlation between systemic inflammatory biomarkers and abortion. Serum samples were collected from 224 aborted women and screened for anti-*T. gondii* immunoglobulin G and M (IgG, IgM) followed by quantification of Interleukin 12 (IL-12) and Tumor Necrosis Factor-alpha (TNF-α) levels using Enzyme Linked Immunosorbent Assay (ELISA) and some inflammatory tests such as C Reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR). The total seropositivity was 25%, which involved 19.6% IgG and 5.4% IgM antibodies with a highly significant (P<0.001) difference. Furthermore, significant differences (P<0.002) are only present regarding IgG test with the number of abortions. Besides, the ESR test showed significant differences (P=0.006, P<0.001) with anti-Toxoplasma IgG and IgM antibodies. While, for the CRP test, highly significant (<0.001) differences were observed for IgG Abs only. Moreover, higher mean concentrations of IL-12 and TNF-α were observed, which were (19.10±2.80, 7.92±0.45 pg/mL) and (99.13±17.62, 62.00±39.54 pg/mL), respectively, among seropositive patients in comparison to the control group, and the difference was statistically significant(P<0.001) for IL-12 only. The study concluded that *T. gondii* significantly boosted the cellular immune response. In addition, it highlights the importance of routine screening for anti-*Toxoplasma* antibodies prior to marriage**,** early immunological screening for pregnant females who are at high risk and raising public awareness about toxoplasmosis and its reproductive consequences through media campaigns and educational programs suggested.

Keywords: *Toxoplasmosis, IL-12, TNF-α, Zakho, aborted women.*

Introduction

One of the significant zoonotic illnesses that affects both humans and animals is toxoplasmosis. This illness is caused by the obligate intracellular protozoan parasite *Toxoplasma gondii* [1], which have a wide host specificity [2]. Toxoplasmosis usually is asymptomatic in healthy individuals, but in immunocompromised people, it can cause serious illnesses [3]. Geographically, there are significant differences in the composition and diversity of the *T. gondii* population [4]. Diagnosing the infection in both human and animal populations is crucial to comprehending the epidemiology of *T. gondii* transmission [5].

In fact, *T. gondii* can spread vertically from mother to the fetus or horizontally through the consumption of tissue cysts or sporulated oocysts in tainted food or water [6]. Toxoplasmosis in pregnant women can result in chorioretinitis, hydrocephalus, nervous system abnormalities, and sensory system problems, as well as newborn death. Depending on social and cultural norms, geographic circumstances, and mechanisms of transmission, the sickness can present in a variety of ways [7]. Pregnancy outcomes and the treatment of the mother and fetus can be

*Corresponding authors: Sarwin Sultan Muhamad, E-mail: sarwin.sultan@yahoo.com, Tel.: 07503295991
(Received 04 May 2025, accepted 12 June 2025)
DOI: 10.21608/ejvs.2025.381738.2824

affected in different ways by this infection [8]. *Toxoplasma gondii* enters host cells by introducing its so-called "invasion machinery" into the plasma membrane of the host cell and can infiltrate without the use of a particular host protein or receptor [9].

Parasite proteins, immunostimulatory molecules, and other biological debris that function as antigens and/or ligands are released when tachyzoites infiltrate and destroy infected cells and/or are digested, the range of proteins that are available varies as the organism is transformed into bradyzoites [10]. Innate immune mechanisms are activated to lower the parasite burden in tissues and produce a pro-inflammatory milieu where the Th1 response develops to ensure survival once a host is infected with *T. gondii* [11]. Furthermore, several immune cells, including T cells and macrophages, release pro-inflammatory cytokines and chemokines such TNF-α, IFN-γ, IL-6, and IL-12 in reaction to infection, by stimulating macrophages to eradicate the parasite and encouraging the recruitment of more immune cells to the infection site, this component is essential to the immunological response against *T. gondii,* these chemicals also play a role in tissue inflammation and degradation [12].

The host's genetic background, fetal gestational age, dose, and infection timing all play a role. The placenta's inflammatory reaction might hinder placental function, lower fetal blood flow, and ultimately lead to miscarriage [13,8]. Findings demonstrated that TNF α might contribute to the pathogenesis of abortion [14]. However, the parasite *T. gondii* is a strong inducer of IL-12 production by dendritic cells (DC), that is why the earlier study found that the sera of toxoplasmosis-affected women had higher levels of IL-12 than the control group [15]. Thus, the immune response to toxoplasmosis is characterized by interplay between pro-inflammatory and anti-inflammatory cytokines. Cytokine profiles are useful markers for estimating the patho-immunological effects of toxoplasmosis [8]. The immune response may be influenced and motivated by an acute or chronic infection with the *T. gondii*. The current study was conducted to determine the presence of any relationship between toxoplasmosis and inflammatory factors and how this relationship affects the immune response modulation, more specifically the role of pro-inflammatory cytokines (IL 12, TNF α) in aborted women who visited Zakho Maternity Hospital, Zakho City/Kurdistan Region, Iraq.

Material and Methods

Study Design

From June 2024 to February 2025, this study was conducted by randomly selecting 224 aborted women, aged 18 to 55, who visited maternity hospital in Zakho City, Duhok Province, Iraq.

Sample Collections

Five millilitres of venous blood were withdrawn from each contributor, and each sample was divided into two parts. To estimate the Erythrocyte Sedimentation Rate (ESR) test using the Westergren's tube method (China), one portion was placed into a tube that was fully labelled with the patient's entire information. To separate the serum, the leftover blood was placed in a separate labelled tube with clot activator. It was then centrifuged for five minutes at 4000 rpm and stored for serological testing. Every serum sample was kept in a 2-ml Eppendorf tube, and all sample tubes were kept for further processing in the lab's deep freezer at -20 °C.

Serological Testing

The serological tests conducted in this study included the use of enzyme linked immunosorbent assay (ELISA) kits for the detection of anti-*Toxoplasma* IgG and IgM antibodies (Bioactive Diagnostica, Germany) and immunological profiles such as pro-inflammatory cytokines (IL12, TNF-α) using DRG, Biocheck Company (Germany). Additionally, titter kits from MISPA-i3/AGAPPI DIAGNOSTIC (Switzerland GmbH) were used to determine (CRP). The test showed positive results in response to inflammation, and all procedures were completed in accordance with the instructions included with each test kit.

Statistical Assessment

The SPSS version 27 was used to assess the data. The link between IgG and IgM antibody seropositivity and various covariates was examined using the Pearson chi-squared test; Fisher's exact test was used in place of the chi-squared test when the "expected values were less than five" surpassed 20% of the cells in a table. The McNemar test was applied to the matched data (IgG and IgM cross-tabulation). Once the p-value equalled or was less than 0.05, the results were deemed statistically significant.

Results

The total rate of seropositive cases was %25 (56/224) which involves 19.6% (44/224) for IgG Abs and 5.4% (12/244) for IgM Abs, besides statistically high significant ($P < 0.001$) differences were observed both tests (Table 1). Concerning to age groups (Table 2), the maximum rate was recorded among age group (26-35) which was 21.4% (24/112) regarding to IgG and 10% (4/40) for IgM. Statistically there was non-significant relations documented concerning to both tests with age groups. Table (3) indicate the relation of seropositivity rate with gestational age, which recorded the highest rate among women who aborted at third trimester 33.3% (4/12) for IgG. While for IgM the highest rate recorded among women during second trimester 6.7% (4/60) and not significant

differences achieved statistically. Relating to to number of abortions the maximum rate represented among women who had experienced one abortion was 54.5% (8/16), 66.7% (8/112) for IgG and IgM respectively, and statistically there was significant differences only between seropositive IgG cases and number of abortions (Table 4). Concerning to inflammatory tests, the increased mean level of ESR were detected between seropositive and control groups related to IgG 21±1.6,16±0.9 mm/hr, and IgM 32±2.0,16±0.8 mm/hr respectively and statistically shows significant differences between seropositive and control groups for both tests (IgG and IgM). Furthermore, concerning CRP the increased level of the mean indicated among seropositive cases than control group which was 23±2.7, 14±1.0 mg/dl, respectively and statistically highly significant (Table 5). The results also showed that the infection with *T. gondii* has a significant effect at the level of IL 12 in the rate of concentration of seropositive Anti-*Toxoplasma* Abs and seronegative (control) group which was 19.10±2.80, 7.92±0.45 pg/mL, respectively and this difference was statistically significant (P< 0.001). Similarly, for TNF-α shows higher rate in the mean concentration among seropositive anti-*Toxoplasma* antibodies than control group which was 99.13±17.62, 62.00±39.54 pg/mL, respectively but statistically was not significant (Table 6).

Discussion

Toxoplasmosis stays a significant public health concern globally. The study observes the total seropositive cases which was %25 (56/224) that involves of 19.6% (44/224) for IgG Abs and 5.4% (12/244) for IgM Abs, besides statistically shows significant differences among both tests. In comparison to the earlier study conducted in Zakho City among women of reproductive age, this result showed a twofold higher prevalence rate. The study found that the overall prevalence of anti-*Toxoplasma* Abs was 12.38% (78/630), with 11.58% (73) for IgG and 0.63 % (4) for IgM antibodies [16]. Similarly, Mahmood *et al*. (2013) [17] found that only 2.5% (10) of 400 samples had recent toxoplasmosis, which was indicated by the presence of positive IgM antibodies. They also found high significant (p<0.001) differences between the two tests. However, according to the frequency of positive IgG antibodies, latent toxoplasmosis was present in 30.25% (121) of the samples. The sources of the samples may be the cause of this high outcome [16]. As a result, samples for this study were only taken from women who had spontaneous abortions, who are more vulnerable to infections because of their weakened immune systems [18]. Moreover, the results showed the non-significant highest seropositivity rate among the age group of 26-35 years which was 21.4% (24/112) regarding to IgG and 10% (4/40) for IgM. These findings differ with the research conducted by Mustafa *et al*. (2024) [19], who found that people aged 36–45 and 46–55 years had the highest rates of seropositivity for IgG, at 41.73% (53) and 47.73% (22), respectively. On the other hand, people between the ages of 18 and 25 years had the highest seroprevalence of IgM antibodies, 10.05% (20). However, only the IgG Abs showed significant (P=0.008) difference. Additionally, another study in Pakistan showed that middle-aged population (25–32 years) had the highest seropositivity of IgG Abs [19, 20], attributed the high seropositivity of anti- *Toxoplasma* antibodies among middle aged females to the lifestyle activities. Furthermore, the main probable cause of the change in infection rates among age groups is probably the difference in exposure levels to *T. gondii* oocysts across persons in different age groups [21]. As regard to different gestational ages, the highest rate 33.3% (4/12) for IgG Abs was displayed among women who aborted at the third trimester, while for IgM the highest rate 6.7% (4/60) was among women during second trimester. These results are consistent with a study conducted in Turkey that found mothers with congenital toxoplasmosis had a higher rate in the third trimester (56.2%), followed by the second trimester (25.2%) [22]. While in a study conducted in the same city, the highest rates of 20% and 6.7%, respectively for both IgG and IgM were found in the third trimester, but the differences were ere statistically non-significant between trimesters [23]. This might be attributed to the reason that most expectant mothers seek medical attention and care facilities early in their pregnancy; otherwise, as the gestation period lengthens, the danger of fetal loss would increase, and miscarriages can occur due to the infections [24]. As related to abortion numbers, the maximum rate was represented among women who had experienced one abortion which was 54.5% (8/16), 66.7% (8/112) for IgG and IgM respectively, with statistically significant differences between only IgG seropositive cases. The current study's findings contradicted with a study in Diyala City that found a proportion of women who had two abortions was more than twice that of women who had only one abortion [25]. Additionally, the present findings contradict with a study conducted in Baghdad City, which claimed that a substantially higher percentage of patients (55.3%) had two abortions [7]. Numerous factors, such as livestock production and management practices, the cleanliness of slaughterhouses and food processing facilities, the density of cats, consumer behavior, geographic location, altitude, and weather, can influence the prevalence of toxoplasmosis [7, 26]. About inflammatory tests, the increased mean level of ESR were detected between seropositive and control groups related to IgG (21±1.6,16±0.9 mm/hr), and IgM (32±2.0,16±0.8 mm/hr) respectively and statistically shows significant differences. This result is consistent with an Egyptian

study by El-Henawy *et al*. (2017) [27] that found patients with high ESR levels had higher seropositivity of anti-*Toxoplasma* Abs than patients with low ESR levels. While Mizuri *et al.* (2024) [28] in a study performed in Zakho City among both males and females also, showed significant (P=0.049) in ESR level for patients seropositive for IgM Abs only. Our results also concur with a study conducted in Kirkuk City that found elevated ESR levels in anti-*Toxoplasma* seropositive individuals [29]. Furthermore, the ESR value displays noteworthy correlations with both gender and age, as its level rises with both. In addition, women are more vulnerable than men [30]. Also, for CRP the increased level of the mean indicated among seropositive cases than control group which was 23±2.7, 14±1.0 mg/dl, respectively, with highly significant differences between them. In a comparable direction, another study found a strong correlation (P = 0.027) between IgG Abs and CRP tests [28]. Also, the current study result is consistent with a study conducted in Egypt where a high CRP rate was accompanied by a high IgG Abs seropositivity rate of 99.9% [27]. As a result, either a primary or secondary infection with the parasite *T. gondii* may stimulate the immune system, or alter it, and raise inflammatory markers [27, 28]. he results also showed that the infection with *T. gondii* has a significant effect at the level of IL 12 in seropositive Anti-*Toxoplasma* Abs and seronegative (control) group which was 19.10±2.80, 7.92±0.45 pg/mL respectively with statistically highly significant (P< 0.001) differences. Likewise, a study conducted by Kanash and Yousif (2021) [15], demonstrated that *T. gondii* infection strongly impacts the rate of IL-12 concentration at the P < 0.05 level, for seropositive anti-*Toxoplasma gondii* antibodies, the rate was 21± 2.4, and for the control group, it was 8± 1.04 pg/mL. The *T. gondii* parasite is a strong inducer of IL-12 production by dendritic cells (DC), which may be the cause of the elevated IL-12 levels in the sera of women infected with toxoplasmosis as compared to control once [31]. Concerning, TNF-α, this cytokine showed higher non-significant mean concentration among seropositive anti-*Toxoplasma* antibodies than control group which was 99.13±17.62, 62.00±39.54 pg/Ml, respectively. Moghaddami *et al.* (2024) [8] stated that women who have a spontaneous miscarriage or stillbirth from congenital toxoplasmosis had higher TNF α levels in their placenta and peripheral blood, which may indicate that TNF plays a part in fetal loss. In addition to the need for additional research, the TNF α-mediated pathway is critical for the immunological response to *T. gondii* infection and may be involved in abortion linked to congenital toxoplasmosis. A study showed that neutralizing TNF-α increases sensitivity and parasite loads reveal the crucial involvement of this cytokine [32]. While the present study contradicts with a study performed in Erbil City which found that the control group had higher levels of TNF alpha than those with seropositive toxoplasmosis (350, 120 pg/mL) [33]. Therefore, the identification of *T. gondii* danger signals trigger a series of humoral and innate cellular reactions. The production of IFN-γ, IL-12, TNF-α, and inducible nitric oxide synthase (iNOS), along with robust NK cell activation, dendritic cell maturation, and macrophage activation, all work together to restrict the reproduction of parasite tachyzoites [3].

Conclusion

A significant systemic and local inflammatory response is implied by the raised levels of pro-inflammatory cytokines IL-12 and TNF-α, as well as increased levels of ESR and CRP, observed in women who have had spontaneous abortions. These results provide credence to the theory that the pathophysiology of pregnancy loss may involve immune dysregulation and increased inflammatory action. Elevated IL-12 and TNF-α, which are identified for their contribution in triggering Th1-type immune responses, may possibly impair maternal-fetal tolerance. These biomarkers cooperatively have the potential to be indicators of immune-mediated pathways that underlie abortion and may direct upcoming therapeutic and diagnostic approaches meant to avoid inflammation-associated pregnancy problems. Correspondingly, to minimize potential reproductive complications, it is suggested that preventive strategies be integrated into public health policy, including routine screening for anti-*Toxoplasma* antibodies prior to marriage, raising public awareness about toxoplasmosis and its reproductive implications through media campaigns and educational programs, Besides, where necessary, early treatment and immunological monitoring of infected individuals to prevent long-term consequences.

Acknowledgement: Not applicable

Funding statements:

This study didn't receive any funding support.

Declaration of Conflict of Interest

The authors declare that there is no conflict of interest.

Ethical of approval

Participants gave their verbal and written consent, and the study was approved by the Duhok General Health Directorate's (Reference number: 26062024-5-2) and the University of Zakho's (College of Medicine) (MAY2024/E06) ethical committees.

TABLE 1. The seropositivity of anti-*Toxoplasma* IgG and IgM Abs among aborted women

Study Group	No. tested	Total Positives		IgG+		IgM+		*P*-value
		No.	%	No.	%	No.	%	
Aborted Women	224	56	25	44	19.6	12	5.4	< 0.001***

*** highly significant statistically

TABLE 2. The relationship of anti-*Toxoplasma* IgG and IgM Abs seropositive and age

Age (years)	No. tested	IgG+		*P*-value	IgM+		*P*-value
		No.	%		No.	%	
18 - 25	40	8	20.0		4	10.0	
26 - 35	112	24	21.4	0.728	4	3.6	0.317
36 - 45	72	12	16.7		4	5.6	
Total	224	44	19.6		12	5.4	

TABLE 3. The relationship between anti-*Toxoplasma* IgG and IgM Abs seropositive and stage of gestation

Gestational age	No. tested	IgG+		*P*-value	IgM+		*P*-value
		No.	%		No.	%	
1st trimester	152	28	18.4		8	5.3	
2nd trimester	60	12	20.0	0.455	4	6.7	0.870
3rd trimester	12	4	33.3		0	0.0	
Total	224	44	19.6		12	5.4	

TABLE 4. The relationship between number of abortions and the seropositivity of IgG and IgM Abs

No. of Abortions	No. tested	IgG+		*P*-value	IgM+		*P*-value
		No.	%		No.	%	
Once	112	24	54.5		8	66.7	
Twice	76	12	27.3	0.002***	4	33.3	0.709
≥ Three times	36	8	18.2		0	0.0	
Total	224	44	100.0		12	100.0	

*** highly significant statistically

TABLE 5. Relationship of CRP and ESR with the seropositivity of IgG and IgM Abs

Inflammatory Tests	IgG+ (n=44)	IgG- (n=180)	*P*-value	IgM+ (n=12)	IgM- (n=212)	*P*-value
	Mean±SE	Mean±SE		Mean±SE	Mean±SE	
ESR mm/hr	21±1.6	16±0.9	0.006***	32±2.0	16±0.8	< 0.001***
CRP mg/dl	23±2.7	14±1.0	<0.001***	12±4.2	16±1.0	0.363

*** highly significant statistically

TABLE 6. The relationship between seropositivity of anti-*Toxoplasma* IgG and IgM Abs and some immunological parameters

Immunological Parameters	Anti-*Toxoplasma* Abs (Positives) (n= 20)	Anti-*Toxoplasma* Abs (Negatives=Control) (n= 10)	*P*-value
	Mean±SE	Mean±SE	
IL12 pg/mL	19.10±2.80	7.92±0.45	< 0.001***
TNF-α pg/mL	99.13±17.62	62.00±39.54	0.327

*** highly significant statistically

References

1. Mikaeel, F. B., Abdo, J. and Omer, L. T. Diagnosis of toxoplasmosis in sheep using serological (ELISA) and molecular technique in Duhok Governorate-Kurdistan region. *SJUOZ*, **3**(1), 32-38 (2015). Retrieved from https://sjuoz.uoz.edu.krd/index.php/sjuoz/article/view/83

2. Al-Atroshi, A. M. A. and Mero, W. M. Seroprevalence of Anti-Toxoplasma antibodies among women of childbearing age in Duhok Province. *SJUOZ*, **1**(1), 44-49 (2013). Retrieved from https://sjuoz.uoz.edu.krd/index.php/sjuoz/article/view/35

3. Aldabagh, M. A. G. H., Hachim, S. K., Qassim, K. W., Al-Mayah, Q. S., Hassan, J. S. and Salloom, D. F. Immune profile in aborted Iraqi women with toxoplasmosis. *MJB*, **15**(1), 48-52 (2018). DOI: 10.4103/MJBL.MJBL_13_18

4. Amouei, A., Sarvi, S., Sharif, M., Aghayan, S. A., Javidnia, J., Mizani, A. and Daryani, A. A systematic review of *Toxoplasma gondii* genotypes and feline: Geographical distribution trends. *Transbound. Emerg. Dis*, **67**(1), 46-64 (2020). https://doi.org/10.1111/tbed.13340

5. Mawlood, H. H., Mero, W. M. S., Su, C. and Isa, A. M. Comparison of Mat with Elisa and Lat Tests in Detecting *Toxoplasma gondii* Antibodies in Human Sera. *SJUOZ*, **5**(1), 28–31(2017). https://doi.org/10.25271/2017.5.1.296

6. Khairullah, A. R., Kurniawan, S. C., Widodo, A., Effendi, M. H., Hasib, A., Silaen, O. S. M. and Afnani, D. A. A comprehensive review of toxoplasmosis: Serious threat to human health. *Open Public Health J.*, **17**(1). (2024). http://dx.doi.org/10.2174/0118749445281387240202094637

7. Fadhil, A. A., Ramadan, G. M., Hameed, N. A., Alhassona, Z. H., Qasim, H. B., Nasir, N. Y. J., & Al-Jassani, M. J. Identification of toxoplasmosis in women by serology in the Baghdad province, *JCD* ***55***(2), 72-72 (2023) DOI: https://doi.org/10.24321/0019.5138.202327

8. Moghaddami, R., Mahdipour, M., & Ahmadpour, E. Inflammatory pathways of *Toxoplasma gondii* infection in pregnancy. *Travel Med. Infect. Dis*, **62**, (2024). 102760. https://doi.org/10.1016/j.tmaid.2024.102760

9. Kochanowsky, J. A., & Koshy, A. A. *Toxoplasma gondii*. *Curr. Biol*, **28**(14) (2018). R770-R771. https://www.cell.com/current-biology/fulltext/S0960-9822(18)30671-7

10. Olatunde, A., Ogunro, O., Tijjani, H., Obidola, S. M., Akpaki, M. A., Yadav, A., ... & Mishra, A. P. Immune Response against Protozoan Parasites. Parasitic Infections: *Imm. Res.& Therapeut.* 73-99 (2023). https://doi.org/10.1002/9781119878063.ch4

11. Uzelac, A., Klun, I., & Djurković-Djaković, O. Early immune response to *Toxoplasma gondii* lineage III isolates of different virulence phenotype. *Front. cell. infect. microbiol.* ***14***, (2024). 1414067. https://doi.org/10.3389/fcimb.2024.1414067

12. Al-Qahtani, A. A., Alhamlan, F. S., & Al-Qahtani, A. A. Pro-inflammatory and anti-inflammatory interleukins in infectious diseases: *Trop. med. infect*, **9**(1), 13 (2024). https://doi.org/10.3390/tropicalmed9010013

13. Denkers, E. Y., & Gazzinelli, R. T. Regulation and function of T-cell-mediated immunity during *Toxoplasma gondii* infection. *Clin Microbiol Rev*, **11**(4), 569-588 (1998)..https://doi.org/10.1128/cmr.11.4.569

14. Marchioro, A. A., Colli, C. M., de Souza, C. Z., da Silva, S. S., Tiyo, B. T., Evangelista, F. F., ... & Falavigna-Guilherme, A. L. Analysis of cytokines IFN-γ, TNF-α, TGF-β and nitric oxide in amniotic fluid and serum of pregnant women with toxoplasmosis in southern Brazil. *Cytokine*, **106**, 35-39 (2018). https://doi.org/10.1016/j.cyto.2018.02.023

15. Kanash, A. K., & Yousif, J. J. The association of toxoplasmosis and the levels of IL-10 and IL-12 in women with breast cancer. *Int. J. Drug Deliv. Technol.*, 11(2), 265-268 (2021). DOI: 10.25258/ijddt.11.2.4

16. Mizuri, S. S. M., & Mero, W. M. S. Seroprevalence of anti-*Toxoplasma gondii* antibodies among women of childbearing age in Zakho City, Kurdistan Region/Iraq. *ZJPAS*, **32**(3), 75-84 (2020). http://dx.doi.org/10.21271/zjpas

17. Mahmood, S., Ban, A. Q., & Zghair, K. Prevalence of toxoplasmosis of male's blood donors in Baghdad. *Iraqi J. Sci.*, **54**(4), 832-841(2013). https://ijs.uobaghdad.edu.iq/index.php/eijs/article/view/12340

18. Ahmad, A. S., & Raad, A. Z. Immunological Study of Unexplained Recurrent Spontaneous Abortion. *Cent. Asian J. Med. Sci.* **5**(3), 285-294 (2024). https://creativecommons.org/lice nses/by/4.0

19. Mustafa, K. M., Mohammed, A. B., Mero, W. M., Mustafa, K., & Mohammed, A. B. Seroprevalence of *Toxoplasma gondii* antibodies and associated risk factors among women in Zakho City, Iraq. *Cureus*, **16**(3) (2024). DOI: 10.7759/cureus.56328

20. Sadiqui, S., Shah, S. R. H., Almugadam, B. S., Shakeela, Q., & Ahmad, S. Distribution of *Toxoplasma gondii* IgM and IgG antibody seropositivity among age groups and gestational periods in pregnant women. *F1000Res* **7**, 1823 (2019). https://doi.org/10.12688/f1000research.15344.3

21. Abdullah, A. M., Abdullah, M. K., Rasheed, R. M., Azko, A. J., Younis, Y. I., Ahmad, H. O., & Majeed, S. A. The Prevalence of *Toxoplasma gondii* Infection in Duhok, Kurdistan Region, Iraq. *Mikrobiol. Z.*, **86**(3), 70-75 (2024). https://doi.org/10.15407/microbiolj86.03.070

22. Gundeslioglu, Ö. Z. D. E. N., HAYTOĞLU, Z., Esen, E., Alabaz, D., ÇAY, Ü., ÖZLÜ, F., ... & Cetiner, S. Konjenital Toksoplazmozis ve Uzun Dönem Sonuçları Congenital Toxoplasmosis and Long-term

Outcomes. *Turkiye Parazitol Derg*. **48**(1) (2024). DOI: 10.4274/tpd.galenos.2024.74046

23. Abdulla, C., Sultan, S., & Mohammed, W. (2022). The impact of *Toxoplasma gondii* antibodies on haematological parameters among women in Zakho District/Iraq. *HIV. Nur.***22**(2), 2713-7. http://doi.org/10.31838/hiv22.02.506
24. Al- Atroshi, A.A.M and Mero, W.M. Seroprevalence of Toxoplasmosis among women of childbearing age from different socioeconomic classes in Duhok City and some nearby villages. *A Master Thesis*, University of Zakho (2011).
25. Darweesh, N. H., Hussein, R. A., Salman, S. T., & Shaker, M. J. Immunological and Molecular study of *Toxoplasma gondii* from aborted women in Diyala/Iraq. *J. Med. Sci.*, **2**(6), 75-82 (2018). http://www.sjomr.org/
26. Hall, S., Ryan, M., & Buxton, D. The epidemiology of toxoplasma infection. *Toxoplasmosis: A comp. clin. guide*, **1**, (58). (2001). https://doi.org/10.1017/CBO9780511527005.005
27. El-Henawy, A. A., Hafez, E. A. R., Nabih, N., Shalaby, N. M., & Mashaly, M. (2017). Anti-Toxoplasma antibodies in Egyptian rheumatoid arthritis patients. *Rheumatol. Int.*, **37**, 785-790 (2017). https://doi.org/10.1007/ s00296-017-3703-8
28. Mizuri, S. S. M., Ramadhan, C. A., & Mero, W. M. S. Associations between toxoplasmosis and rheumatoid arthritis among patients in Zakho City, Kurdistan Region/Iraq. *Zanco J Med Sci* **28**(3), 518-525 (2024). https://doi.org/10.15218/zjms.2024.052
29. Salman, Y. J., & Mohammed, K. A. Relationship between *Toxoplasma gondii* and arthritis among patients in Kirkuk City. *Int. J. Curr. Res. 3*(8), 175-87 (2015).
30. Singh, G. C-reactive protein and erythrocyte sedimentation rate: Continuing role for erythrocyte sedimentation rate. *Adv Biol Chem*, **4**(1), 5-9 (2014). http://dx.doi.org/10.4236/abc.2014.41002
31. Oppmann, B., Lesley, R., Blom, B., Timans, J. C., Xu, Y., Hunte, B., ... & Kastelein, R. A. Novel p19 protein engages IL-12p40 to form a cytokine, IL-23, with biological activities similar as well as distinct from IL-12. *Immunity*, **13**(5), 715-725 (2000). https://www.cell.com/AJHG/fulltext/S1074-7613(00)00070-4
32. Dupont, C. D., Christian, D. A., & Hunter, C. A. Immune response and immunopathology during toxoplasmosis. In *Semin. Immunopathol.* **4**(6): 793–813 (2012). doi:10.1007/s00281-012-0339-3. I
33. Bakr, H. M. Role of Toxoplasma surface proteins in host-parasite immune modulation. *Cell. Mol. Biol.*, **71**(3), 146-150 (2025). Doi: http://dx.doi.org/10.14715/cmb/2025.71.3.17

دور السيتوكينات المحفزة للالتهاب IL-12 وTNF-α ضد داء المقوسات بين النساء اللواتي تعرضن للإجهاض

سروين سلطان محمد مزوري[2،1]، وجدان م. س. ميرو[3،1]، وهفال م. خالد[2،1]
[1] قسم علوم الحياة، كلية العلوم، جامعة زاخو، دهوك، العراق.
[2] مركز أبحاث علوم الحياة، مركز الأبحاث، جامعة زاخو، دهوك، العراق.
[3] قسم الأحياء الدقيقة الطبية، كلية العلوم، جامعة نولج، أربيل، العراق.

الملخص

توكسوبلازما غوندي هي طفيلي أولي داخل الخلايا انتهازي يسبب داء المقوسات، وذلك من خلال استخدام بروتيناته السطحية التي تُمكّنه من التهرب من جهاز المناعة لدى المضيف، مما يؤدي إلى تعطيل مسارات الإشارات المناعية. هذا التغيير له تأثيرات متعددة على الأفراد المصابين، وخاصة النساء الحوامل، حيث قد يؤدي إلى حالات إجهاض متكررة. هدف هذه الدراسة هو فحص العلاقة بين مؤشرات الالتهاب الجهازية والإجهاض .تم جمع عينات مصل الدم من 224 امرأة تعرضن للإجهاض، وتم فحصها للكشف عن الأجسام المضادة من النوع IgG و IgMضد *T. gondii* ، تلاها قياس مستويات الإنترلوكين-12 (IL-12) وعامل نخر الورم-ألفا (TNF-α) باستخدام تقنية الامتصاص المناعي المرتبط بالإنزيم(ELISA) ، بالإضافة إلى بعض اختبارات الالتهاب مثل البروتين المتفاعل C (CRP) ومعدل ترسيب كريات الدم الحمراء .(ESR) بلغت النسبة الكلية للإيجابية المصلية 25%، شملت 19.6% للأجسام المضادة IgG و5.4% للأجسام المضادةIgM ، مع فروقات معنوية عالية .(P<0.001) كما ظهرت فروقات معنوية (P<0.002) فقط فيما يتعلق باختبار IgGوعدد حالات الإجهاض. وأظهر اختبار ESR فروقات معنوية (P=0.006, P<0.001) مع الأجسام المضادة IgG و IgMضد المقوسات. أما اختبار CRP فأظهر فروقات معنوية عالية (P<0.001) مع IgG فقط .علاوة على ذلك، لوحظت تركيزات مرتفعة من IL-12 و TNF-αوالتي كانت (19.10±2.80، 7.92±0.45 بيكوغرام/مل) و(99.13±17.62، 62.00±39.54 بيكوغرام/مل) على التوالي بين المصابات مقارنةً بمجموعة السيطرة، وكانت الفروقات معنوية إحصائيًا (P<0.001) فقط بالنسبة لـ IL-12 .خلصت الدراسة إلى أن طفيلي التوكسوبلازما (*T. gondii*) يعزز بشكل ملحوظ الاستجابة المناعية الخلوية. بالإضافة إلى ذلك، تُبرز النتائج أهمية إجراء الفحص الروتيني للأجسام المضادة للتوكسوبلازما قبل الزواج، وضرورة إجراء الفحص المناعي المبكر للنساء الحوامل المعرضات لخطر الإصابة، كما توصي بـ تعزيز الوعي المجتمعي حول التوكسوبلازما وتبعاتها الإنجابية من خلال الحملات الإعلامية والبرامج التوعوية التعليمية.

الكلمات الدالة: داء المقوسات، إنترلوكين-12 (IL-12)، عامل نخر الورم-ألفا (TNF-α)، زاخو، النساء المُجهضات.