Impact of Toxoplasmosis on Liver and Kidney Function in Women

Doaa A. Abdulwahab [1*], Dina A. A. Abdullah [2]

Abstract

Background: Toxoplasma gondii infection shows significant health risks, particularly in women of childbearing age. Understanding its impact on liver and kidney function is crucial. This study aimed to investigate the prevalence of Toxoplasma gondii IgG and IgM antibodies in a cohort of women and assess their liver and kidney function through biochemical markers. Method: Blood samples from 88 women (aged 14-43 years) were analyzed for IgG and IgM antibodies against T. gondii. Liver and kidney function markers were assessed using biochemical tests. Result: Out of the specimens, 14 (16%) tested positive for IgG and 9 (10%) for IgM antibodies. Notably, the highest antibody rates were observed in the second age group (20-29 years), with 52%, followed by the first and third age groups (<20 / 30-39 years) with 24% each. Significant elevations in creatinine and urea concentrations were observed in patients ($P < 0.05$), along with elevated levels of Aspartate amino-transferase, Alanine transaminase, and Alkaline Phosphatase ($P < 0.001$). Conclusion: The study highlights a significant association between Toxoplasma gondii IgG and IgM antibodies and altered liver and kidney function markers. These findings underscore the importance of screening and managing Toxoplasma infections, especially in women of reproductive age, to mitigate potential health complications.

Keywords: Toxoplasmosis, liver function, kidney function, IgG, IgM

Significance | This study determined the relationship between Toxoplasma infection and liver and kidney dysfunction, aiding in early diagnosis and treatment.

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Introduction

Toxoplasmosis, a critical protozoal illness caused by the parasite Toxoplasma gondii, affects over a billion people worldwide. Humans can contract it through two main pathways: horizontally via inadvertent consumption of T. gondii oocysts in tainted foods and drinks, or vertically through the placenta from mother to unborn child (Mikaeel, 2020). T. gondii, an obligate intracellular parasite, is widespread and can harm tissues and infiltrate sensitive parts of the human body (Babekir et al., 2022). Factors such as age, demographics, and immunologic efficiency influence individuals' susceptibility to T. gondii infections and associated health problems (CDC, 2022). The parasite presents in three contagious varieties: tachyzoite (rapid-replicating type), bradyzoite (encased within cellular cysts), and sporozoite (found inside oocysts) (Khryanin et al., 2015).

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demographics, and immunologic efficiency influence individuals' susceptibility to T. gondii infections and associated health problems (CDC, 2022).

Despite cats being the primary hosts, intermediary hosts in its life cycle include birds and mammals; when cats consume tiny animal parts carrying T. gondii cysts, the cyst membranes disintegrate in the gut, liberating bradyzoites. These bradyzoites subsequently proliferate in the small intestinal walls and develop into oocysts, and cats can excrete millions of oocysts in their stool following 3–14 days of infection (Babekir et al., 2022). The discharged oocysts survive ecological circumstances, sporulate within 1–5 days, and pollute the environment and water. T. gondii is thus spread to intermediate hosts by consuming tainted food or water, and it can survive in their organs for a long time (Ahmed et al., 2016).

This parasite was first divided into three primary clonal kinds by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) indicators. Also, T. gondii strains were divided into more than two hundred separate genotypes by the same technique (Schumacher et al., 2021). Cardiac conditions, severe renal and liver disorders, and other illnesses are all linked to Toxoplasmosis (Nayeri Chegeni et al., 2019). Each essential organ may contain T. gondii, which is particularly obvious in the acute period in blood, cerebrospinal fluid, semen, tears, saliva, and urine. Numerous studies have investigated the various medical manifestations of Toxoplasmosis, revealing a connection between the illness and abnormal liver function tests (Hassen et al., 2019). Any alteration in liver enzymes resulting in dysfunction is termed liver disease, as the liver plays a crucial role in several bodily processes, and its impairment can lead to severe bodily harm; hepatocellular disease is another term for liver disease. The term "liver disease" encompasses a wide range of conditions that impede the liver from performing its essential functions. Typically, three-quarters or more of the liver's tissue must be affected before liver function declines (Abdullah & AL-Aubaidi, 2019).

Several organic and chemical alterations occur during Toxoplasmosis, affecting various bodily functions (Dupont et al., 2012; Akinrotoye et al., 2018). Both genders can be affected by Toxoplasmosis, necessitating clinical testing to assess the extent of the illness. Biochemical tests reveal differences between individuals with Toxoplasmosis and healthy individuals, particularly in kidney function and liver enzyme concentrations such as Aspartate amino-transferase (AST), Alanine amino-transferase (ALT), and alkaline phosphatase (ALP) (El-Sayed et al., 2016). The parasite affects numerous organs in the body, including the liver, spleen, kidneys, and brain, underscoring the importance of comprehensive diagnostic exams for these organs (Muhsin et al., 2016; Mokhtari et al., 2016).

AST, ALT, and ALP are commonly used indicators to assess liver damage caused by Toxoplasmosis (Fu et al., 2020). For renal disorders, albumin and creatinine are pivotal biomarkers (NIDDK, 2021). T. gondii infection induces immunological alterations, including the development of immune-globulins IgM and IgG (Hassen et al., 2019; Gavali et al., 2024). IgM antibodies against T. gondii indicate acute illness, whereas IgG antibodies suggest both acute and latent illness, aiding in clinical diagnosis (Mousavi et al., 2018). The objective of this study was to investigate the impact of Toxoplasmosis on kidney and liver functions.

Materials and methods

Study Design

The study involved 88 human females aged between 14 and 43 years. Between September and December 2022, 5 ml of blood was collected from each participant. Blood samples were transferred to gel tubes and left to stand at room temperature for approximately 30 minutes. Subsequently, they were centrifuged at 3000 rpm for 5 minutes to separate the serum for further analysis. This study was conducted following ethical standards and guidelines. All participants provided informed consent, and the University of Diyala Institutional Review Board approved the study protocol. Confidentiality of participant information was strictly maintained throughout the study.

Evaluation of Toxoplasma IgG and IgM

The initial immunological assessment aimed to detect anti-Toxoplasma antibodies (IgG and IgM) using an enzyme-linked immunosorbent assay (ELISA), following the manufacturer's instructions (Foresight, Germany). Other biochemical analyses, including urea, creatinine, AST, ALT, and ALP levels, were determined using kits supplied by Mindray, China.

Statistical Analysis

The mean and standard deviation were calculated to assess the levels of biochemical markers. An independent t-test was employed to compare these markers between patients with T. gondii infection and their uninfected counterparts. A significance level of less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS Version 26.

Results and discussion

Our study provided insights into the prevalence and impact of Toxoplasmosis on kidney and liver functions. Further research is needed to elucidate the mechanisms underlying T. gondii-induced renal and hepatic damage and develop targeted treatment strategies. The present study examined specimens from eighty-eight women aged 14 to 43 years, assessing IgG and IgM immunoglobulins for T. gondii, along with kidney and liver function tests including urea, creatinine, AST, ALT, and ALP.

Participants were categorized into patient and control groups based on the presence or absence of Toxoplasma antibodies. The mean

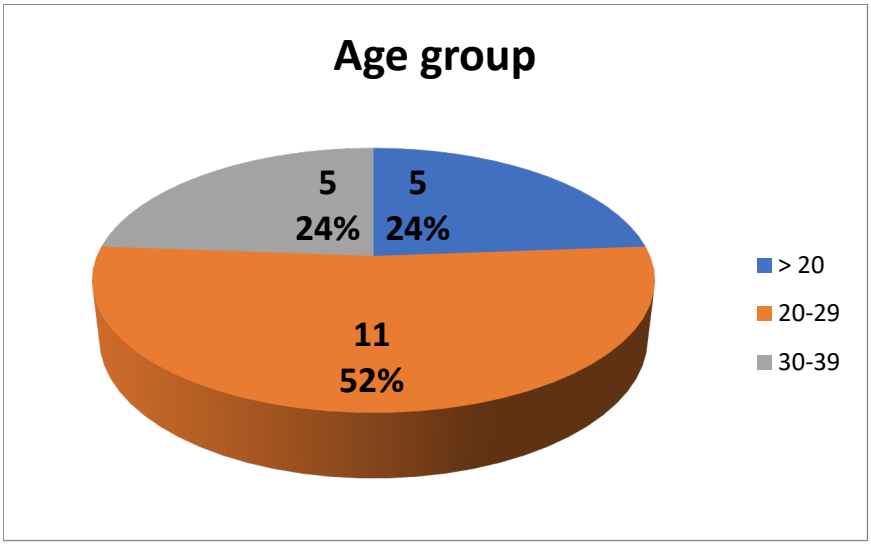

Figure 1. Prevalence of Toxoplasmosis among age groups

Table 1. Detection of Toxoplasma gondii antibodies

			Immunoglobulins		*P* value
			IgG	IgM	
T. gondii	(+)	N	14	9	< 0.001
		%	16 %	10 %	
	(-)	N	74	79	
		%	84 %	90 %	

Table 2. Comparative parameters between patients and control group. N., non-significant; Sig, significant; H., high significant.

Parameter	Control		Patients		*P* _ value
	Mean.	Std. Deviation.	Mean.	Std. Deviation.	
Age	25.96	6.85	23.62	5.88	N. Sig ($p > 0.05$)
Urea	25.22	5.96	33.10	9.34	Sig ($p < 0.05$)
Creatinine	0.61	0.06	0.67	0.09	Sig ($p < 0.05$)
AST	24.66	6.47	35.57	11.63	H. Sig ($p < 0.001$)
ALT	24.75	6.22	34.10	15.17	Sig ($p < 0.05$)
ALP	47.33	19.85	87.52	40.14	H. Sig ($p < 0.001$)

age for the patient group was 25.22±5.88 years, while it was 25.96±6.85 years for the healthy control group. Results revealed that 14 (16%) specimens were positive for IgG, 9 (10%) for IgM, and 2 specimens were positive for both IgG and IgM.

Hassen et al. (2019) reported a higher IgG positivity rate (49.4%) than our study, while their IgM positivity rate (13.6%) was similar to ours.

Quantification of coloration by an ELISA reader enables accurate identification of Toxoplasma biomarkers via antigen-antibody interactions. ELISA technology's simplicity and suitability for both field and research laboratory settings have been documented (Vikrant et al., 2013).

When both IgM and IgG tests for Toxoplasma are negative, it indicates the absence of current or previous infestation. In such cases, preventive measures, such as avoiding consumption of raw meat, are recommended. If IgM is negative but IgG is positive, it suggests a past illness has occurred, posing no risk to the unborn child. However, when both IgM and IgG are positive (or negative), it implies an acute infection. It's noteworthy that IgM titers may remain elevated for an extended period, even beyond the initial two weeks of infection, hence IgM antibodies alone may not always signify an acute toxoplasmosis infection (Inceboz et al., 2021).

Regarding age groups, our study revealed the highest occurrence of Toxoplasmosis in the second age category (20-29) at 52%, followed by the first and third age groups (>20 / 30-39), as depicted in Figure 1.

This finding aligns with Abdulwahhab et al. (2022), who also observed the highest occurrence of Toxoplasmosis in the age category (20-29). However, it contradicts Elsaid's findings, which indicated the highest occurrence in the age category (35-45). The increased seroprevalence in the mid-age category may be attributed to greater exposure to cats, contaminated objects, and foods compared to other age categories.

The analysis of kidney function tests revealed elevated levels of urea and creatinine in patients compared to the control group. The mean±SD for urea in patients was 33.10±9.34, while in the control group, it was 25.22±5.96, demonstrating a significant difference ($P < 0.05$). Similarly, the mean±SD for creatinine in patients was 0.67±0.09, whereas in the control group, it was 0.61±0.06, also showing a significant difference ($P < 0.05$), as presented in Table 2. These findings corroborate with those of Mikaeel in 2022, who observed a slight increase in urea and creatinine levels among patients, although without significant differences (P 0.352, 0.337), respectively.

The liver function tests revealed elevated levels of AST, ALT, and ALP in patients compared to the control group. The mean±SD for AST in patients was 35.57±11.63, whereas in the control group, it was 24.66±6.47, showing highly significant differences ($P < 0.001$). Similarly, the mean±SD for ALT in patients was 34.10±15.17, while in the control group, it was 24.75±6.22, indicating significant differences ($P < 0.05$). Moreover, the mean±SD for ALP in patients was 87.52±40.14, compared to 47.33±19.85 in the control group, displaying highly significant differences ($P < 0.001$), as illustrated in Table 2.

These results are consistent with Mahmood and Dawood (2012) and Mikaeel (2022), who also observed increased concentrations of AST, ALT, and ALP in the patient group with significant differences ($P < 0.001$). Babekir et al. (2022) reported a slight increase in AST, ALT, and ALP levels, while Hassen et al. in 2019 noted a decrease in these concentrations in the patient group, which aligns with the findings of the present study.

While T. gondii has the capability to infiltrate tissues such as the renal and induce persistent illnesses and cell death, the majority of Toxoplasmosis cases remain asymptomatic (Babekir et al., 2022). Exposure to T. gondii can lead to acute or long-term renal disease, affecting individuals throughout their lives. Research has identified a correlation between undergoing dialysis and an increased incidence of T. gondii infections (Saadat et al., 2020).

The mechanisms through which T. gondii affects the renal system remain uncertain. Studies have shown that toxoplasma infection triggers an increase in nitric oxide and reactive oxygen species (ROS) generation within cells, leading to oxidative stress (Dincel et al., 2016). This oxidative stress initiates an inflammatory response mediated by pro-inflammatory mediators such as TNF-alpha, IL-1b, and the transcriptional factor NF-kB, which are associated with renal failure. Chronic oxidative stress exacerbates inflammation, leading to tissue damage and eventual organ dysfunction. Furthermore, the later stages of inflammation contribute to an increase in TGF-beta production, which stimulates the synthesis of the extracellular matrix (Pizzino et al., 2017).

Glomerulonephritis or tubular necrosis are the two primary kidney disorders associated with parasite illnesses (Toporovski et al., 2012). In comparison to the toxoplasmosis-infected healthy control group, the liver enzyme group exhibited a significant increase of 28% in AST levels (El-Sayed et al., 2016). Chronic liver disease (CLD) is a hepatic condition characterized by persistent inflammation, infiltrative immunological responses, structural changes, or metabolic insults lasting for at least six months before complete healing due to the compromised immune system. Patients with CLD, particularly those with elevated AST levels, are highly susceptible to opportunistic parasite infections (El-Sayed et al., 2016).

Conclusions

In conclusion, Toxoplasmosis, caused by the parasite Toxoplasma gondii, affects a significant portion of the global population, with transmission occurring through various pathways, including ingestion of contaminated food or transmission from mother to

fetus (Mikaeel, 2020). T. gondii's widespread presence and ability to invade tissues pose health risks (Babekir et al., 2022). Factors such as age, demographics, and immune status influence susceptibility to T. gondii infections (CDC, 2022). Diagnostic methods, including ELISA, aid in identifying Toxoplasma biomarkers accurately (Vikrant et al., 2013).

Age-wise, our study noted a higher prevalence of Toxoplasmosis in the 20-29 age group, attributed to increased exposure to risk factors (Abdulwahhab et al., 2022). The analysis of kidney and liver function tests revealed significant alterations in patients compared to controls, indicating potential organ damage (Mikaeel, 2022). These findings align with previous studies reporting similar trends in liver enzyme levels (Mahmood & Dawood, 2012; Mikaeel, 2022). The IgG and IgM of T. gondii were significantly related to the elevation levels of kidney and liver function.

T. gondii's impact extends beyond acute infection, potentially leading to chronic renal and liver diseases (Babekir et al., 2022). The underlying mechanisms involve oxidative stress, inflammatory responses, and tissue damage (Dincel et al., 2016; Pizzino et al., 2017). Notably, individuals with chronic liver disease are particularly vulnerable to opportunistic parasite infections due to compromised immunity (El-Sayed et al., 2016).

Moreover, Toxoplasmosis presents varied clinical manifestations, emphasizing the importance of comprehensive diagnostic approaches (Hassen et al., 2019). Further research is warranted to elucidate the pathophysiological mechanisms of T. gondii-induced organ damage and develop targeted interventions. Overall, understanding the complexities of Toxoplasmosis is crucial for effective prevention, diagnosis, and management of this parasitic infection.

Author contributions

D.A.A. worked on specimen collection and Analysis, D.A.A.A. provided referencing and statistical analysis.

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Competing financial interests

The authors have no conflict of interest.

References

Abdullah, R. S., and AL-Aubaidi, I. K. (2019). Seroprevalence of Toxoplasmosis in Iraqi Patients with Liver Diseases. Infection (new or had an infection in the past), 2, 16.

Abdulwahhab, A. R., Nooruldeen, M. Y., and Muhsin, S. S. (2020). Genetic change and biochemical variations occurrence in patients with Toxoplasma gondii infections. EurAsian Journal of BioSciences, 14, 1309-1313.

Ahmed, H., Malik, A., Arshad, M., Mustafa, I., Khan, M. R., Afzal, M. S., and Simsek, S. (2016). Seroprevalence and spatial distribution of Toxoplasmosis in sheep and goats in North-Eastern Region of Pakistan. The Korean journal of parasitology, 54(4), 439.

Akinrotoye, K. P., Bankole, M. O., and Oluwole, S. (2018). Occurrence of Pathogenic bacteria on public surfaces within community schools in Abeokuta Environs, Ogun State. Journal of Environmental Treatment Techniques, 6(3), 47-52.

Babekir, A., Mostafa, S., Minor, R. C., Williams, L. L., Harrison, S. H., & Obeng-Gyasi, E. (2022). The Association of Toxoplasma gondii IgG and Liver Injury in US Adults. International Journal of Environmental Research and Public Health, 19(12), 7515.

Centres for Disease Control and Prevention. Parasites – Toxoplasmosis (Toxoplasma Infection) Epidemiology & Risk Factors Cited 2022. Available online: https://www.cdc.gov/parasites/toxoplasmosis/epi.html (accessed on 18 June 2022).

Dincel, G. C., and Atmaca, H. T. (2016). Role of oxidative stress in the pathophysiology of Toxoplasma gondii infection. International journal of immunopathology and pharmacology, 29(2), 226-240.

Dupont, C. D., Christian, D. A., & Hunter, C. A. (2012, November). Immune response and immunopathology during Toxoplasmosis. In Seminars in immunopathology (Vol. 34, No. 6, pp. 793–813). Springer-Verlag.

Elsaid, M. M. A., Azbedah, A. G., Dia Eddin, E. E. A., & Alkout, A. (2014). The prevalence of Toxoplasma gondii infection in psychiatric patients in Tripoli, Libya. Journal of American Science, 10(5), 135–140.

El-Sayed, N. M., Ramadan, M. E., and Ramadan, M. E. (2016). Toxoplasma gondii infection and chronic liver diseases: evidence of an association. Tropical medicine and infectious disease, 1(1), 7.

Fu, S., Wu, D., Jiang, W., Li, J., Long, J., Jia, C., and Zhou, T. (2020). Molecular biomarkers in drug-induced liver injury: challenges and future perspectives. Frontiers in pharmacology, 10, 1667.

Gavali, L. V., Mohammed, A. A., Al-Ogaili, M. J., Gaikwad, S. H., Kulkarni, M., Das, R., & Ubale, P. A. (2024). Novel terephthalaldehyde bis (thiosemicarbazone) Schiff base ligand and its transition metal complexes as antibacterial Agents: Synthesis, characterization and biological investigations. Results in Chemistry, 7, 101316.

Hassen, A. H., Ali, M. S., and Ekhnafer, A. M. (2019). Effect of Toxoplasma gondii Infection on Haematological and liver function parameters among abortive women in El-Beida City. Publisher Full Text.

Inceboz, T., Korkmaz, M., Erdoğan, D. D., and İnceboz, Ü. (2021). Acute Toxoplasmosis During Pregnancy: A Hard Call. Türkiye Parazitolojii Dergisi, 45(3), 223.

Khryanin, A. A., Reshetnikov, O. V., and Kuvshinova, I. N. (2015). Toxoplasmosis: epidemiology, diagnosis, treatment. Antibiotiki i Khimioterapiia= Antibiotics and Chemoterapy [sic], 60(5-6), 16-21.

Mahmood, N. A., & Dawood, M. N. (2012). Liver function tests in Toxoplasmosis. Annals of the College of Medicine Vol, 38(2).

Mikaeel, F. B. (2020). The effect of Toxoplasma gondii infection in women on some biochemical and hormonal parameters in Duhok province, Iraq. International Journal of Research in Medical Sciences, 8(10), 1.

Mokhtari, E., Khamehchian, M., Montazer, G., and Nikudel, M. (2016). Landfill site selection using Simple Additive Weighting (SAW) and artificial neural network methods; a case study from Lorestan province, Iran. International Journal of Geography and Geology, 5(10), 209-223.

Mousavi, P., Mirhendi, H., Mohebali, M., Shojaee, S., Valian, H. K., Fallahi, S., & Mamishi, S. (2018). Detection of Toxoplasma gondii in acute and chronic phases of infection in immunocompromised patients and pregnant women with real-time PCR assay using TaqMan fluorescent probe. Iranian Journal of Parasitology, 13(3), 373.

Muhsin, S. S., Jafar, E. H., and Jafar, N. S. (2013). Biochemical study on the effect of Toxoplasma gondii on Liver Function in Women. Iraqi J. Vet. Med, 37(2), 257-260.

National Institute of Diabetes and Digestive and Kidney Diseases. Albuminuria: Albumin in the Urine. 2021. Available online: https://www.niddk.nih.gov/health-information/kidney-disease/chronic kidney-disease-ckd/tests-diagnosis/albuminuria-albumin-urine (accessed on 11 November 2021).

Nayeri Chegeni, T., Sarvi, S., Amouei, A., Moosazadeh, M., Hosseininejad, Z., A. Aghayan, S., and Daryani, A. (2019). Relationship between Toxoplasmosis and obsessive-compulsive disorder: A systematic review and meta-analysis. PLoS Neglected Tropical Diseases, 13(4), e0007306.

Pizzino, G., Irrera, N., Cucinotta, M., Pallio, G., Mannino, F., Arcoraci, V., and Bitto, A. (2017). Oxidative stress: harms and benefits for human health. Oxidative medicine and cellular longevity, 2017.

Saadat, F., Mahmoudi, M. R., Rajabi, E., Roshan, Z. A., Shad, B. M., and Karanis, P. (2020). Seroepidemiology and associated risk factors of Toxoplasma gondii in hemodialysis patients. Acta Parasitologica, 65(4), 906-912.

Schumacher, A. C., Elbadawi, L. I., DeSalvo, T., Straily, A., Ajzenberg, D., Letzer, D., and Kazmierczak, J. J. (2021). Toxoplasmosis outbreak associated with Toxoplasma gondii-contaminated venison—high attack rate, unusual clinical presentation, and atypical genotype. Clinical Infectious Diseases, 72(9), 1557-1565.

Toporovski, J., Romano, S., Hartmann, S., Benini, W., and Chieffi, P. P. (2012). Síndrome nefrótica associada à toxoplasmose: relato de sete casos. Revista do Instituto de Medicina Tropical de São Paulo, 54(2), 61-64.

Vikrant, S., Amit, K. J., and Daya, S. (2013). Recent trends in the diagnosis of Toxoplasmosis. Clinical Reviews and Opinions, 5(2), 11-17.