



Impact of serum level concentrations of IgG and IgM on abortion in women who had both risk factors diabetes and hypertension

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ABSTRACT

Abortion is a significant global public health concern affecting millions of women each year. Factors such as maternal diabetes and hypertension have been recognized as major contributors to increased abortion risk. Immunoglobulins, specifically IgG and IgM, play crucial roles in pregnancy outcomes and have been studied extensively. This study aimed to assess the levels of *Toxoplasma* IgG and IgM in aborted women with and without diabetes or hypertension. This cross-sectional study examined 64 women who experienced *Toxoplasma gondii*-induced abortions at Erbil Maternity Teaching Hospital between January 2021 and May 2021. Their medical history, including diabetes and hypertension status, was collected through interviews. Blood samples were analyzed using VIDAS technology to measure serum IgG and IgM levels. The mean IgG and IgM antibody levels were compared between groups of women based on the number of abortions, diabetes status, and hypertension status. In women with a history of abortion, IgM antibody levels differed significantly among the five groups ($P \leq 0.01$). While the average serum *Toxoplasma* IgG concentration varied between diabetic and non-diabetic women, these differences were not significant ($P > 0.05$). Conversely, there were highly significant differences in the concentration of serum *Toxoplasma* IgM ($P < 0.01$). Comparing women with and without hypertension, no significant differences were found in the mean concentrations of serum *Toxoplasma* IgG and IgM ($P > 0.05$). The IgM antibody had a significant impact on the number of performed abortions, and these effects were also observed in abortion in women with diabetes.

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Introduction

The word "abortion" refers to ending a pregnancy (expulsion or extraction of the embryo or fetus) before 20 weeks or when the fetus weighs less than 500g. Abortion comes in two flavors: spontaneous and induced. Spontaneous abortion occurs naturally before the 20th completed week of pregnancy and can be either complete or incomplete. Induced abortion, in contrast, is a deliberate choice to terminate a pregnancy and can be carried out for various reasons, such as unintended pregnancies (1).

Miscarriage, also known as spontaneous abortion, is a common complication during early pregnancy, happening in approximately 15-20% of all pregnancies that are clinically recognized (2). Recurrent pregnancy loss (RPL), defined as the loss of three or more consecutive pregnancies, affects about 2-5% of couples trying to conceive (3). The causes of spontaneous abortion are intricate and varied, involving genetic, anatomical, hormonal, immune, and environmental factors, all contributing to its occurrence (4,5).

Two prevalent medical disorders that have been linked to the etiology of spontaneous abortion are diabetes and hypertension. The metabolic condition diabetes, which is defined as hyperglycemia, raises the risk of prenatal morbidity and mortality. On the other hand, with an estimated frequency of 5-10% among pregnant women, hypertension is a major cause of maternal and fetal morbidity and mortality. The combination of these two risk factors can

exacerbate pregnancy complications and raise the chances of experiencing an abortion (6,7).

Immunoglobulins (Ig), which are immune system components, have also been linked to the pathophysiology of pregnancy problems. Immunoglobulin G (IgG) and immunoglobulin M (IgM), which are both important in the humoral immune response, are of particular importance (8,9). IgG is the most abundant kind of immunoglobulin in human serum, accounting for approximately 75% of the total immunoglobulin pool and 10-20% of the total circulating plasma proteins, whereas IgM is the first type of immunoglobulin produced during an immune response. Changes in these immunoglobulin levels have been linked to a variety of pregnancy problems, including spontaneous abortion (10-12).

Toxoplasma as a single-celled organism has global distribution (13). Getting this infection during pregnancy increases the risk of miscarriage, fetal death and congenital abnormalities. Also, maternal infection is associated with a four-fold increase in preterm delivery (14). The annual incidence of *Toxoplasma gondii* in the world is about 200,000, which is mostly seen in less developed countries (15). The results of previous studies show different prevalences in different regions of the world. There were limited studies on the prevalence of anti-*Toxoplasma* antibodies (16).

Based on the information found in the search results, there is limited evidence suggesting a potential link

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between the levels of immunoglobulins (specifically IgG and IgM) and abortion. Hiwa et al. (2018), study discovered notable variations in IgG concentrations between abortion cases and normal pregnancies, but no significant differences were observed in IgM and IgA serum levels across the groups (17). The results of Berger et al.'s study (2020) showed that in conclusion, combinations of diabetes mellitus (D), obesity (O), and chronic hypertension (H) significantly magnify the risk of preterm birth (PTB), especially provider-initiated PTB (piPTB), and PTB with altered fetal growth or preeclampsia (18).

Considering that very limited studies have investigated the effect of these variables on abortion and that no specific study has been done in the Middle East country; therefore, it was necessary to conduct this study with the aim of evaluating the concentration of Toxoplasma IgG and IgM in diabetic, non-diabetic, hypertensive and non-hypertensive aborted women.

Materials and Methods

Study design and participants

This observational, cross-sectional study was conducted on a group of 64 Toxoplasma gondii aborted women, aged between 22 and 45 years, attending Erbil Maternity Teaching Hospital between January 2021 and May 2021. All participants were subjected to a personal interview using a specially designed questionnaire format to collect information on their medical history, including diabetes and hypertension status.

Blood sample collection and processing

Five milliliters (ml) of venous blood were taken from each participant using an aseptic procedure and a disposable syringe. The blood samples were collected in anticoagulant-free tubes and allowed to clot at room temperature. The serum was produced by centrifuging the samples for 5 minutes at 4500 rpm. The serum was then divided into several Eppendorf tubes and immediately stored at -20°C until further analysis.

Measurement of serum IgG and IgM levels

Toxoplasma IgG and IgM concentrations in serum were measured using the VIDAS technology, as directed by the manufacturer. The mean IgG and IgM antibody levels were compared between groups of women based on the number of abortions, diabetes status, and hypertension status.

Statistical analysis

The results were expressed as mean \pm standard error (SE). Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software version

26. Statistical differences between groups were determined using the Least Significant Difference (LSD) test for multiple comparisons after ANOVA. In association with Excel version 5, both descriptive and analytical tests were utilized, and the data were presented using simple frequency distribution tables for each variable. The mean, standard error, standard deviation (SD), and range were calculated for different parameters.

The difference in proportions of qualitative data was tested using Pearson's Chi-square (X^2) test. Statistical significance was defined as a p-value of less than 0.05.

Ethical considerations

The ethical standards outlined in the Helsinki Declaration were followed in the conduct of this investigation. The hospital's institutional review board examined and approved the study protocol. Participants provided informed consent, and the confidentiality of their personal information was ensured.

Results

This study was designed to investigate certain serological biomarkers (Toxoplasma IgG and IgM) in aborted women in conceders to some risk factors. One of these factors is the sequence of abortion. Toxoplasma IgG and IgM in aborted women revealed higher Mean \pm SE of serum toxoplasma IgG concentration in aborted women was 32.50 ± 0.50 when the sequence of abortion was five, however, the lower was 14.67 ± 4.70 when the sequence of abortion was three. No statistically significant differences were reported when comparing mean serum toxoplasma IgG concentration in aborted women in a different sequence of abortion ($p > 0.05$) (Table 1).

The analysis of Toxoplasma IgM antibody levels in relation to the number of abortions revealed interesting findings. Women who had experienced one abortion had an average IgM antibody level of 0.29 ± 0.17 . For women with a history of two abortions, the average IgM antibody level was 0.15 ± 0.17 . Women who had three abortions had an average IgM antibody level of 0.24 ± 1.40 . The mean IgM antibody levels for women with four and five abortions were 21.60 ± 2.20 and 75.50 ± 0.10 , respectively. These results indicate a statistically significant difference in the mean IgM antibody concentrations among the five groups of women ($P \leq 0.01$). (Table 2)

The study examined the levels of toxoplasma IgG and IgM in women who had experienced abortion, comparing those with and without diabetes. The results showed that the average serum concentration of toxoplasma IgG was 23.14 ± 8.87 in non-diabetic women, which was not significantly different from the concentration of 18.00 ± 9.14 in diabetic women ($P > 0.05$). However, there were highly

Table 1. Toxoplasma IgG concentrations according to the No. of abortion sequence.

No. of abortion sequence	No.	Toxoplasma IgG concentrations	F Test	p-value
One	25	$23.23 \pm 11.17^*$		
Two	17	24.99 ± 15.38		
Three	12	14.67 ± 4.70	0.157	$P > 0.05$
Four	6	22.50 ± 0.60		
Five	4	32.50 ± 0.50		

*Mean \pm SE

Table 2. Toxoplasma IgM according to No. of abortion sequence.

No. of abortion sequence	No.	Toxoplasma IgM concentrations	F Test	p-value
One	25	0.29± 0.17		
Two	17	0.15±0.17		
Three	12	0.24±1.40	4.30	P < 0.01
Four	6	21.60±2.20		
Five	4	75.50±0.10		

*Mean ± SE

Table 3. Toxoplasma IgG and IgM concentrations in diabetic and non-diabetic aborted women.

Parameters	Aborted women		p-value**
	Non Diabetic n = 44	Diabetic N = 20	
Toxoplasma IgG Concentration	23.14±8.87*	18.00±9.14	P>0.05
Toxoplasma IgM concentration	0.05 ± 0.01	0.40 ± 0.12	P<0.01

*Mean ± SE **t-test

Table 4. Toxoplasma IgG and IgM in hypertensive and non-hypertensive aborted women.

Parameters	Aborted women		p-value**
	Hypertension n = 12	Non Hypertension n = 52	
Toxoplasma IgG	10.60±4.39*	26.42±3.36	P>0.05
Toxoplasma IgM	0.52 ± 0.25	0.38 ± 0.41	P<0.01

*Mean ± SE **t-test

significant differences (P<0.01) in the serum concentration of toxoplasma IgM between the two groups, as shown in Table 3.

The study investigated the association between serum levels of toxoplasma IgG and IgM in women who had experienced abortion and had hypertension. The results indicated that there were no significant differences in the mean serum concentrations of both toxoplasma IgG and IgM between hypertensive and non-hypertensive women. These findings were supported by statistical analysis, with p-values greater than 0.05 for both markers, as shown in Table 4, Figures 1 and 2.

Discussion

The present study was conducted to investigate the levels of toxoplasma IgG and IgM antibodies in women who had experienced abortion. The results revealed a significant difference in the levels of IgM antibodies in women with a history of abortion, with an increase observed in the average level of IgM antibodies with an increase in the number of abortions. Additionally, pregnant women with diabetes showed a significant difference in the mean level of IgM antibodies. These findings suggest that IgM antibodies may play a crucial role in miscarriage among pregnant women.

Toxoplasma gondii, an intracellular parasite, often causes no symptoms or only mild illness (19,20). However, when a pregnant woman becomes infected with the parasite, it can be transmitted to the fetus, potentially leading to miscarriage and severe neurological and chorioretinal damage in the newborn (21).

In their systematic review and meta-analysis, Nayeri et al. (2020) sought to investigate the prevalence of Toxoplasma gondii antibodies and their association with spontaneous abortion. The study utilized various databases to

identify relevant studies and calculated both the odds ratio (OR) and seroprevalence of T. gondii. The results revealed a higher prevalence of IgM and IgG antibodies in affected women, and the odds ratio indicated that both types of antibodies significantly increased the risk of spontaneous abortion (22). The present study found that the presence of IgM antibodies significantly increased the likelihood

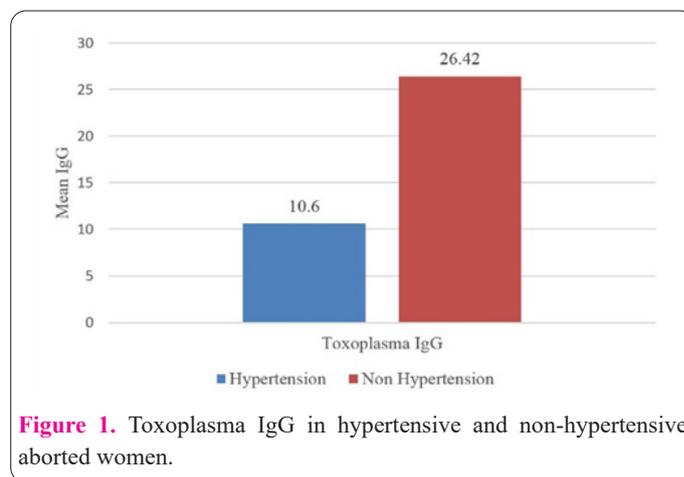


Figure 1. Toxoplasma IgG in hypertensive and non-hypertensive aborted women.

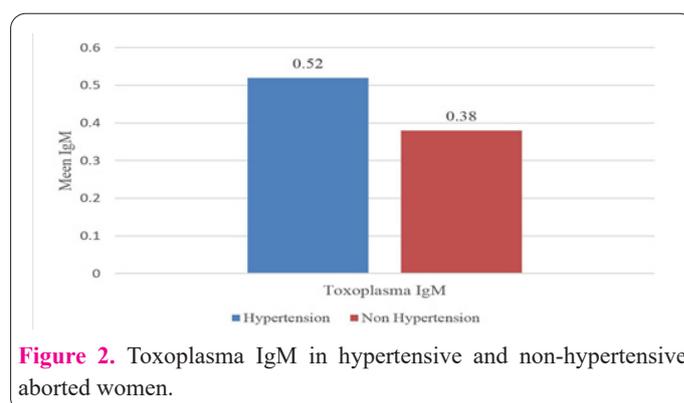


Figure 2. Toxoplasma IgM in hypertensive and non-hypertensive aborted women.

of spontaneous abortion, whereas IgG antibodies did not have a significant effect on such abortions.

Naqid et al. (2019) conducted a study in Zakho City, Iraq, to investigate the prevalence of toxoplasma gondii IgM and IgG antibodies and their association with spontaneous abortions. The four-year study revealed a high prevalence of anti-toxoplasma antibodies among pregnant women. The study's findings were intriguing as they contradicted those of the present study, indicating that IgG antibodies had a more substantial effect on the occurrence of spontaneous abortions, while the impact of IgM antibodies was relatively minor (23). However, the present study found that IgM antibodies had a significant impact on spontaneous abortions, indicating the need for further research to determine the impact of these antibodies on pregnancy outcomes.

Ahmed et al. (2021) study, which was conducted in Kitkuk city hospital, Iraq, examined 60 pregnant women with a history of miscarriage. The study found a significant difference in IgG antibodies among the participants, which had a significant impact on miscarriage in the women under investigation (24). In contrast, the present study found that IgM antibodies had a greater impact on spontaneous abortions. These findings highlight the importance of further research to understand the role of different antibodies in pregnancy outcomes.

Shakiba and colleagues (2020) conducted a study in Sanandaj, West Iran, to investigate the prevalence of serum toxoplasmosis infection in pregnant women with diabetes. The study analyzed 136 serum samples from pregnant women with diabetes. The findings indicated a higher prevalence of IgG antibodies than IgM antibodies in women, and there was a significant difference in the amount of IgG antibodies between diabetic and non-diabetic women, which differed from the results of the present study. However, no significant difference was observed in IgM antibodies between the two groups of women under investigation (25). These discrepancies in the results could be attributed to differences in the methodology and sample size of the studies.

Saki et al. (2016) conducted studies that found a significant difference in IgG antibodies between diabetic and non-diabetic individuals (26), whereas the present study found a significant difference in IgM antibodies between the two groups. To clarify the reason for this divergence, further research is essential. There are many genetic, biochemical, physiological, and epigenetic findings related to diarrhea (27-31).

The present study found no significant difference in IgM and IgG antibodies between women with a history of miscarriage and high blood pressure, compared to those with a history of miscarriage and normal blood pressure. However, a study by Ubaid Hamza et al. (2022) in Iraq revealed a significant difference in IgG antibodies between the two groups of women (32). These results are consistent with a study by de Araujo Andrade et al. (2020) in Brazil, which found a significant difference in IgG antibodies between women with a history of miscarriage and those without (33).

Toxoplasma gondii is a prevalent zoonotic parasite that poses a significant clinical threat, particularly to pregnant women and immunocompromised individuals. Its importance in public health and its widespread prevalence across various human populations necessitates greater at-

tention to be paid to this disease. Despite describing this pathogen for over a century, a comprehensive and all-encompassing understanding of toxoplasmosis remains elusive, leaving numerous avenues for further research. This includes designing various diagnostic kits and vaccination strategies utilizing immunoprotein cells, identifying multiple parasite genotypes, examining clinical and therapeutic outcomes, and investigating the anti-tumor effects of *T. gondii*.

In this study, it was shown that IgM antibodies had a significant effect on the number of miscarriages, particularly in women with diabetes. The findings suggest that future research should focus more on the disease course and other epidemiological aspects of the disease, given the impact of IgM antibodies on recurrent miscarriages and the absence of evidence for the effect of IgG antibodies on miscarriages in the study participants.

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Competing interests

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Availability of data and materials

The data of this study will be made available to other researchers upon request from the corresponding author.

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