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# Relationship between toxoplasma IgG avidity levels and abortion risk

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**Abstract**---Abortion is still a problem that receives special attention because based on data from the World Health Organization (WHO), abortion accounts for 15-50% of the causes of maternal death in the world. One of the risk factors for abortion is infection during pregnancy, including toxoplasmosis. The aim of this study was to analyze whether there was a relationship between toxoplasma IgG avidity levels and the risk of abortion. The research uses a literature review study to identify, analyze, and evaluate scientific papers through MDPI, PubMed, and ScienceDirect data sources. 60 articles were produced from the four data sources, there were 7 articles that passed the inclusion criteria which are summarized in the PRISMA diagram. The results in one article mentioned two abortions and the other article mentioned 17 abortions, both in first trimester pregnant women with low toxoplasma IgG avidity levels. Both articles show the results that women who have low toxoplasma IgG avidity levels experience more abortions in the early trimester than women who have medium or high toxoplasma IgG avidity levels. The conclusion of this study was that there was a relationship between toxoplasma IgG avidity levels and the risk of abortion.

**Keywords**---Abortus, IgG Avidity, Toxoplasma Gondii, Toxoplasmosis.

**Introduction**

Abortion is still a problem that receives special attention because of the high probability of occurrence (Al-Yami et al., 2021). Based on data from the World Health Organization (WHO), abortion accounts for 15% to 50% of the causes of maternal death in the world. Abortion occurs in around 5% of 208 million pregnancies globally and especially in Indonesia, abortion occurs in 10% to 15% of five million pregnancies every year (Fallahi et al., 2018). Abortion is the expulsion of a fetus through the birth canal before the gestational age reaches 20

to 22 weeks (154 days) starting from the first day of the last menstrual period (HPHT) or before the fetus' weight reaches 500 grams (Bieńkowski et al., 2022).

Risk factors for abortion are divided into three groups, namely fetal factors, maternal factors and external factors (Khan & Khan, 2018). One of the mother's risk factors for abortion is infection during pregnancy. Infections in pregnant women can be caused by viruses, bacteria, or other infectious agents (Abdallah et al., 2019). Types of infections in pregnant women that are associated with abortion include syphilis, pelvic inflammation, and TORCH (Toxoplasmosis, Other agents, Rubella, Cytomegalovirus, and Herpes simplex). This infection can cross the placenta and cause morbidity and even mortality in the fetus (Meroni et al., 2022).

Toxoplasmosis is an infection caused by the protozoan *Toxoplasma gondii*, including one of the TORCH infections that can attack pregnant women and is ranked ninth out of the 15 most common diseases in pregnancy. Individuals with toxoplasmosis may have no symptoms or they may resemble other infectious diseases (Rostami et al., 2021). Organs affected by infection include lymph nodes, eyes and brain. Mild and moderate symptoms depend on the number of *T. gondii* and the individual's immune status. *T. gondii* infection is very dangerous if it occurs in pregnant women or immunocompromised patients (Siddiqui et al., 2014). Toxoplasmosis in pregnant women can cause abortion, stillbirth, premature birth, and other adverse events in pregnancy. Congenital infections such as hydrocephalus, microcephaly, intracranial calcification, chorioretinitis, mental retardation, and other growth abnormalities appear (Radoi et al., 2023).

The diagnosis of toxoplasmosis requires a laboratory examination, namely a serological examination to see the toxoplasma IgG and IgM antibody titers. IgM is an antibody that appears in the early stages as a primary antibody response, while IgG appears as a secondary antibody response (Grada et al., 2024). Detection of IgM toxoplasma has a sensitivity indicator of 93.3% to 100% for diagnosing primary toxoplasmosis, but has a specificity of around 77.5% to 99.1% because IgM toxoplasma may still be positive after several weeks or even months after primary infection. To assess the possibility of abortion through the onset of infection, an IgG avidity examination is important for pregnant women.

IgG avidity is the aggregate strength of anti-*T. gondii* IgG to react with protein epitopes. Progressively, the functional binding affinity of anti-*T. gondii* IgG increases after maturation of the humoral immune response, which is called affinity maturation, so that antibodies produced earlier have a lower affinity than antibodies formed later (Milne et al., 2020). High toxoplasma IgG avidity results indicate the infection appeared in the previous 3-5 months, while low toxoplasma IgG avidity indicates the infection appeared in the last 3 months. In pregnant women, high toxoplasma IgG avidity indicates infection acquired before pregnancy (Vueba et al., 2020).

Management of pregnant women with toxoplasmosis is almost the same as other patients, giving only pyrimethamine can be teratogenic, especially if given in the first trimester, so its administration must be prevented (Yuriah, 2024). Management in the early prenatal period is based on two regimens: spiramycin 3

mg orally once a day or a combination of pyrimethamine with sulfonamide and folic acid to reduce the risk of pyrimethamine toxicity. This research was conducted with the aim of assessing the relationship between toxoplasma IgG avidity levels and the risk of abortion using the literature review method.

## **Method**

This research uses the Literature Review method. Researchers use a focus on reviewing, identifying relevant studies, describing the process, identifying literature using PRISMA flowcharts, data extraction, and mapping/scoping (Yuriah et al., 2022).

### *Search Strategy*

Article search procedure uses journals published between 2013 and 2024. The articles obtained were taken from the electronic databases *MDPI*, *PubMed*, and *ScienceDirect*. The article search was performed using the keywords (((("Relationship") OR ("correlation")) AND ("Toxoplasma")) OR ("Toxoplasma IgG")) OR ("toxoplasmosis")) OR ("Toxoplasma gondii")) AND ("Avidity Levels ") AND ("Abortion ") OR ("Abortions").

### *Inclusion Criteria*

The inclusion criteria used were articles published in English, articles published between 2013-2024, using qualitative and quantitative research methods, and no country-specific criteria were intended.

### *Exclusion Criteria*

The Exclusion criteria used are opinion articles, review *articles* (*systematic review* and *literature review*), reports and *commentary*, as well as letters and book reviews.

### *Search Results*

PRISMA results show that there are 60 articles obtained from three databases. Article selection was carried out based on predetermined inclusion and exclusion criteria. This research produced seven related articles. The stages of selecting research journals are depicted in the PRISMA diagram shown in Figure 1.

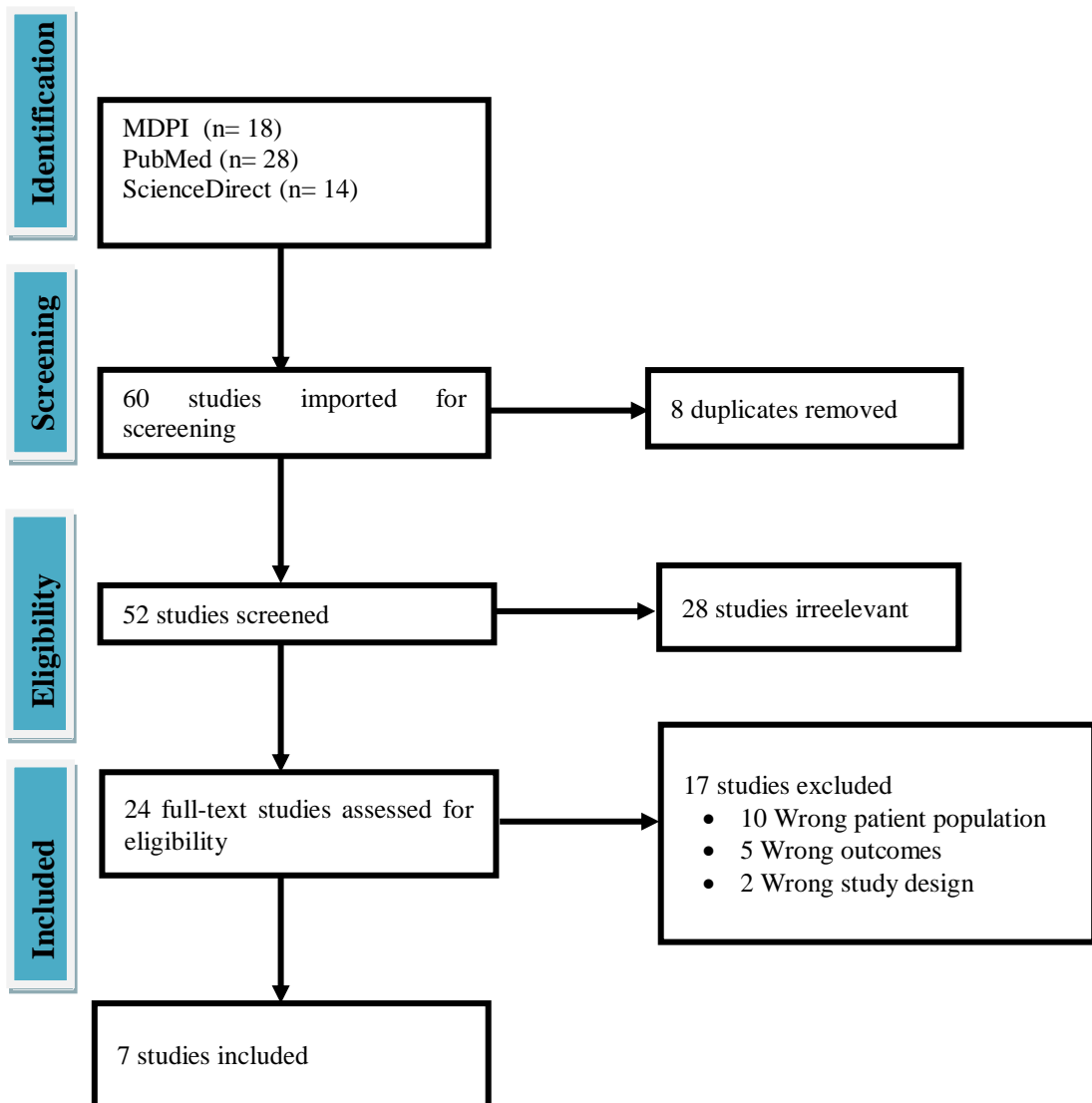


Figure 1. PRISMA Flow Diagram

## Results and Discussion

### Results

#### *Extraction Data*

The articles that have been obtained are then extracted. The articles are extracted based on the article's author, the year of publication, the country, the number of samples used, method, and the study's findings.

Table 1. Extraction Data

No	Author/Year/Title	Country	Research Design	Sample	Result
1	(Machumi et al., 2017)/ Factors Associated With Toxoplasma gondii IgG and IgM Antibodies, and Placental Histopathological Changes Among Women With Spontaneous Abortion in Mwanza City, Tanzania	Tanzania	Quantitative, Cross-sectional	260 women	The mean age of the enrolled women was 2665.9 years. The seropositivity of IgG and IgM antibodies were 144/260 (55.4%; 95% confidence interval [CI], 49–61) and 6/260 (2.3%; 95% CI, 3–8), respectively. IgG seropositivity was significantly high among women in the first trimester (59.1% vs.43.5%; P=.03). Only low gestation age (odds ratio [OR] 1.11; 95% CI, 1.02–1.20; P=.02) and keeping a cat (OR 11.80; 95% CI, 1.32–10.5; P=.03) independently predicted IgG and IgM seropositivity, respectively. Presence of inflammation (OR 1.95; 95% CI, 1.05–3.64; P=.03), calcification (OR 3.28; 95% CI, 1.01–10.63; P=.04), necrosis (OR 2.86; 95% CI, 1.39–5.89; P=.04), and lymphocyte infiltrations (OR 2.24; 95% CI, 1.17–4.24; P=.01) were significantly associated with T. gondii IgG seropositivity. Almost half of women with spontaneous abortion in the city of Mwanza have specific T. gondii IgG antibodies. Placental histopathological changes suggestive of toxoplasmosis were significantly found among IgG seropositive women.

2	(Valladares-Garrido et al., 2022)/ Toxoplasma gondii Infection and Threatened Abortion in Women from Northern Peru	Northern Peru	Quantitative, Cross-sectional	218 pregnant women	Of 218 pregnant women, 35.8% presented positive serology for T. gondii and 14.7% had threatened abortion in their current pregnancy. Pregnant women with positive T. gondii infection had 2.45-fold higher frequency of threatened abortion (PR: 2.45, 95% CI:1.15-5.21). In addition, the frequency of threatened abortion decreased by 9% for each additional year of age (PR: 0.91, 95% CI: 0.86-0.97). A previous history of threatened abortion also showed a higher frequency of threatened abortion (PR: 5.22, 95% CI: 2.45-11.12). T. gondii infection is associated with threatened abortion. An early age of pregnancy and a previous history of abortion are also associated with this condition.
3	(Kheirandish et al., 2019)/ Toxoplasma Serology Status and Risk of Miscarriage, A Case-Control Study among Women with A History of Spontaneous Abortion	Iran	Quantitative, Case Control Study	240 serum samples from women experiencing spontaneous abortion for the first time as the case group and 240 serum samples from women who had a normal delivery with no history of abortion as the control group	The Toxoplasma IgM antibody was detected in 3.3% (8/240) of the case group and 0.4% (1/240) of the control group, which was a statistically significant difference between the two groups [P=0.019, odds ratio (OR)=10.266]. Of all samples 47.5% and 46.3% of the case and control groups were positive for Toxoplasma IgG antibody, respectively. Seven out of 8 (87.5%) IgM-positive serum samples from the case group had low IgG avidity, indicating acute infections, whereas all IgG-positive sera and 1 IgM-positive serum, which was related to the control group, showed a high IgG avidity, indicating chronic infections. Maternal acute toxoplasmosis during pregnancy is raised as one of the factors that increase the chance of spontaneous abortion.

4	(Mocanu et al., 2022)/ The Impact of Latent Toxoplasma gondii Infection on Spontaneous Abortion History and Pregnancy Outcomes: A Large-Scale Study	Romania	Quantitative, retrospective study	806 pregnant women	This study did not show differences between groups regarding the history of spontaneous abortion (OR = 1.288, p = 0.333), cesarean section (OR = 1.021, p = 0.884), placental abruption (OR 0.995, p = 0.266), pregnancy-induced hypertension rate (OR 1.083, p = 0.846), secondary sex ratio (1.043, p = 0.776), 10 APGAR score at birth (p = 0.544), gestational age at birth (p = 0.491) or birth weight (p = 0.257). The observed differences between the rate of pregnancy complications in the two groups of pregnant women with and without latent infection with TG, did not reach a statistical significance.
5	(Alsammani, 2013)/ Seroepidemiology of Toxoplasma Gondii Infection in Women with First Trimester Spontaneous Miscarriage in Qena Governorate, Egypt	Egypt	Quantitative, Cross-sectional	76 women	Of 76 women with spontaneous abortion screened for Toxoplasma-specific IgG and IgM antibodies with ELisa, 35 were IgG seropositive, of which, 14 samples were IgM seropositive. Therefore, seropositivity rates of 46.1% (95% CI: 35.1%, 57.3%), and 18.4% (95% CI: 10.89%, 28.32%) for IgG and IgM, respectively were found. These indicate that, 27.6 % (21 cases) of studied women (IgG+/IgM-) were immune to toxoplasmosis and 53.94 % (41 cases) were susceptible to primary infection (IgG-/IgM-). Mean while acute toxoplasmosis (IgG+/IgM+) was 18.4 % (14 cases) with one case (1.3%) confirmed for recent infection as she had Tachyzoites on histopathology study. On the basis of multivariate logistic regression, living in a rural area was found to be the only independent predictor of toxoplasmosis (OR=3.800, CI= 1.100-10.813, p=0.034). The seroprevalence of T. gondii infection in women with first trimester abortion in Qena governorate of Egypt is high.
6	(Zeinali et al., 2023)/ Prevalence and risk factors of Toxoplasma gondii infection among women with miscarriage	Iran	Quantitative, Cross-sectional	215 women with abortion and their aborted fetuses	Among 215 serum samples of women with abortion, 70 (32.6%) were positive for anti-Toxoplasma IgG, and three (1.4%) were positive for IgM. The RE-529 sequence of T. gondii was positive in three (1.4%) of the aborted fetuses. The analysis of GRA6 gene indicated that all three positive samples carried a GRA6 allele (GRA6I) of T. gondii type I genotype. Our findings suggest that T. gondii is one of the causative agents of

	and their aborted fetuses in the northwest of Iran				spontaneous abortion in West Azerbaijan Province, the northwest of Iran.
7	(Siddiqui et al., 2015)/ Role of Toxoplasma gondii serology in patients with habitual abortions	India	Qualitative	A 400 patients with history of multiple spontaneous abortions.	Most of the patients were in the age group of 20-30 years. About 78.2% of females were from rural background. History of contact with cats was present in 56.5% of patients. About 91.3% of patients were non-vegetarian. Maximum number of patients with positive results in all the three serological tests had 2 spontaneous abortions. The prevalence of toxoplasmosis in pregnant females with history of habitual abortions were found to be 47.9%. IgM was positive in 35.4% while 16.6% of the patients had low IgG avidity antibodies indicating acute infection.

## Discussion

The research results contain descriptions of research articles that have been reviewed based on predetermined criteria for inclusion criteria, exclusion criteria and eligibility criteria for the seven articles analyzed in this literature review. Of the selected articles, the method used was quantitative, one article was a case study, one was retrospective, and five were cross-sectional. Two studies came from Iran, one from India, one from Egypt, one from Tanzania, one from Romania, and one from Northern Peru. All studies reviewed used samples of pregnant women.

From (Siddiqui et al., 2015) research, most of the patients were in the age group of 20-30 years. About 78.2% of females were from rural background. History of contact with cats was present in 56.5% of patients. About 91.3% of patients were non-vegetarian. Maximum number of patients with positive results in all the three serological tests had 2 spontaneous abortions. The prevalence of toxoplasmosis in pregnant females with a history of habitual abortions was found to be 47.9%. IgM was positive in 35.4% while 16.6% of the patients had low IgG avidity antibodies indicating acute infection.

Of 218 pregnant women, 35.8% presented positive serology for *T. gondii* and 14.7% had threatened abortion in their current pregnancy. Pregnant women with positive *T. gondii* infection had 2.45-fold higher frequency of threatened abortion (PR: 2.45, 95% CI:1.15-5.21). In addition, the frequency of threatened abortion decreased by 9% for each additional year of age (PR: 0.91, 95% CI: 0.86-0.97). A previous history of threatened abortion also showed a higher frequency of threatened abortion (PR: 5.22, 95% CI: 2.45-11.12). *T. gondii* infection is associated with threatened abortion. An early age of pregnancy and a previous



history of abortion are also associated with this condition (Valladares-Garrido et al., 2022).

#### *Factors Associated with Toxoplasmosis*

Serological screening for acute toxoplasmosis is recommended for prenatal screening, especially in countries with a high prevalence of toxoplasmosis (Milne et al., 2020). However, there are several obstacles to carrying out this screening. Therefore, it is necessary to know the risk factors associated with toxoplasmosis for prevention (Briciu et al., 2023).

#### *Contact with Cats*

Previous research articles showed that there was a significant association between the presence of anti-T.gondii antibodies and women having a history of contact with cats. This is supported by a higher seropositivity rate in women who have cats as pets compared to women without cats at home (Radoi et al., 2023). As previously known, cats are the definitive host which produces non-sporulating oocyst stages of *Toxoplasma gondii* which appear in their feces. Domestic cats can shed millions of oocysts in the soil and survive for months or even years in the environment. After becoming infective, oocysts sporulate which will later develop in the environment such as soil, water, or plant material, then be ingested by birds or rodents as intermediate hosts until they eventually form cysts. Humans can become infected when they come into contact with cat feces which have *Toxoplasma gondii* oocyst stage in their feces and at this cyst stage it will live in skeletal muscle tissue, heart muscle, brain and human eyes and can then cross the placenta if experienced by pregnant women (Yuriah & Kartini, 2022).

#### *Consuming Raw Meat, Vegetables, Fruit and Unhygienic Water*

Cat feces are not the only medium for the growth and transmission of *Toxoplasma gondii*. Soil, plants, and even water are places where sporulating oocysts develop before being consumed by birds or rodents (Silva-Díaz et al., 2020). Consuming vegetables and fruit if they are not cleaned first or if they are washed less cleanly so that they become unhygienic, can contain sporulated oocysts obtained from soil or water (Yuriah et al., 2023). Humans who consume pork, beef and/or goat meat that is not cooked well enough may be at risk of contracting *Toxoplasma gondii* infection (Al-Adhroey et al., 2019). These animals whose lives are connected to the soil or are omnivores such as pigs can eat plants or drink water containing sporulating oocysts without being noticed. As soon as the sporulating oocyst is ingested by an animal, the oocyst turns into tachyzoites which will be present in nerve and muscle tissue. When tachyzoites cannot be eliminated by immunity, it only takes a maximum of eight hours to turn into bradyzoites and then into cysts, this cyst stage will develop in the human body after the animal's flesh is eaten (Zeinali et al., 2023).

#### *Low Socioeconomic Status*

Serological screening for toxoplasmosis is recommended once a month for women who are non-reactive to *Toxoplasma gondii* and live in countries with a high

prevalence of toxoplasmosis, but one of the obstacles to this screening is that it is expensive and is not always available in developing countries, this is associated with low socioeconomic factors with prenatal screening (Muthoharoh et al., 2022).

## **Conclusion**

Based on the results of the analysis and discussion of the descriptions of the two research articles reviewed, it was concluded that there was a relationship between Toxoplasma IgG avidity levels and the risk of abortion, so that the risk of abortion could be assessed from Toxoplasma IgG avidity levels during early pregnancy screening.

Hence, emphasize on health education especially on the Toxoplasma transmission routes in the childhood, and performance of screening program using regular serologic tests during pregnancy could help physicians in the diagnosis, prevention, and treatment of toxoplasmosis and reduction of the economic burden of the disease on society

### *Conflict of interest statement*

The authors declared that they have no competing interests.

### *Statement of authorship*

The authors have a responsibility for the conception and design of the study. The authors have approved the final article.

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