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Maternal Acute Toxoplasmosis and Risk of Vertical Transmission to the Fetus: A Prospective Study Among Pregnant Women

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ABSTRACT

Background: Primary *Toxoplasma gondii* infection during pregnancy can cross the placenta and cause congenital toxoplasmosis, yet the evidence on prevalence, diagnosis, transmission, and fetal outcomes is fragmented and varies by region. **Objective:** To critically review recent international studies on (1) the prevalence and serological profile of acute maternal infection, (2) gestational age and vertical transmission, (3) maternal and pregnancy-related factors, and (4) fetal outcomes with ultrasonographic and molecular findings. **Methods:** A narrative critical review of about 30 peer-reviewed studies, mainly published in 2020–2025, appraised by design, population, diagnostic criteria, findings, and limitations. **Results:** Pooled seroprevalence in pregnant women was roughly 33–43% across global, Eastern Mediterranean, and African meta-analyses, with very high heterogeneity; acute infection was much rarer (about 1.1% worldwide). IgM alone overestimates recent infection, whereas combining IgM, IgG avidity, and IgA classifies infection timing better. Transmission risk rises with gestational age, but fetal disease is more severe after early infection. Dietary and cat-related exposures are linked to maternal infection; their independent role in fetal transmission is unproven. Prenatal treatment is associated with lower transmission in observational studies, though selection bias limits interpretation. Amniotic-fluid PCR showed pooled sensitivity of about 85% and specificity near 100%; ultrasound signs were non-specific, and a normal scan did not exclude infection. **Conclusions:** Suspected acute toxoplasmosis in pregnancy needs an integrated pathway: serology, gestational age, fetal ultrasound, PCR when indicated, and postnatal follow-up. Few studies link all these steps in one cohort using standard definitions of congenital infection.

1 . Introduction

Maternal infection with *Toxoplasma gondii* remains an important public-health and obstetric concern because primary infection acquired during pregnancy may result in congenital toxoplasmosis. Although infection in immunocompetent adults is often asymptomatic or associated with nonspecific clinical manifestations, fetal infection can cause neurological, ocular, and developmental complications that may become apparent at birth or later in childhood.

A large systematic review and meta-analysis including 217 studies and more than 900,000 pregnant women estimated the global prevalence of acute *Toxoplasma* infection during pregnancy at approximately 1.1%, with considerable geographical variation. The highest prevalence was reported in the Eastern Mediterranean region, highlighting the importance of region-specific epidemiological investigations (Rostami et al., 2019). The clinical significance of maternal toxoplasmosis is closely related to whether infection represents a recent primary infection or a previous exposure. In women who acquire primary infection during pregnancy, the parasite may cross the placenta and establish infection in the fetus. The probability of vertical transmission is strongly influenced by gestational age at maternal infection. In general, transmission becomes more frequent as pregnancy progresses, whereas infections occurring earlier in gestation, although less frequently transmitted, may be associated with more severe fetal consequences. This temporal relationship makes prospective monitoring particularly valuable because it allows researchers to consider the timing of maternal infection alongside subsequent fetal outcomes rather than relying solely on retrospective maternal history (Torgerson & Mastroiacovo, 2013; Wallon et al., 2013). The diagnosis of acute maternal toxoplasmosis represents a major methodological challenge in clinical research. Detection of *T. gondii*-specific IgM and IgG antibodies is widely used, but interpretation of these markers requires caution because IgM antibodies may persist beyond the acute phase. Consequently, a positive IgM result alone does not necessarily establish a recently acquired infection. The combination of IgM, IgG avidity, and, when appropriate, IgA testing can improve the classification of infection timing. A recent systematic review and meta-analysis demonstrated the continuing importance of combining these serological markers when assessing suspected acute toxoplasmosis in pregnant women (Tork et al., 2025). The timing and accuracy of diagnosis are particularly important because identification of a recent maternal infection can initiate additional fetal surveillance and, where clinically indicated, prenatal treatment. IgG avidity testing has therefore become an important complementary diagnostic approach, particularly when maternal IgM and IgG results are difficult to interpret. In addition, contemporary diagnostic strategies increasingly integrate serology with molecular testing and fetal imaging. A 2024 systematic review and meta-analysis of congenital toxoplasmosis diagnosis found that PCR testing of amniotic fluid demonstrated high diagnostic performance, with a pooled sensitivity of approximately 85% and specificity approaching 100%, although diagnostic performance can vary according to timing, laboratory methods, and clinical context (Franco et al., 2024). Direct assessment of fetal infection is an important component of studies investigating vertical transmission. Amniotic-fluid PCR can provide molecular evidence of *T. gondii* infection following suspected maternal infection, while ultrasound examination can identify fetal abnormalities potentially compatible with congenital toxoplasmosis. However, neither a negative PCR result nor an apparently normal ultrasound examination should automatically be interpreted as complete exclusion of fetal infection. Earlier studies demonstrated the diagnostic value of prenatal testing, while contemporary evidence emphasizes the importance of integrating maternal serology, gestational age, molecular testing, and fetal imaging within a broader diagnostic pathway (Hezard et al., 1997; Franco et al., 2024). The relationship between maternal treatment and vertical transmission has also been extensively investigated. Prenatal treatment is generally considered within a risk-based clinical management strategy, particularly when recent maternal infection has been identified. A multicenter randomized trial comparing pyrimethamine–sulfadiazine with spiramycin found that the treatment strategies produced different patterns of placental transmission and fetal outcomes, although the primary comparison did not demonstrate a statistically significant difference in transmission in the main analysis (Mandelbrot et al., 2018). These findings illustrate the complexity of assessing treatment effectiveness and reinforce the importance of considering gestational age, timing of treatment, confirmation of maternal infection, and evidence of fetal infection when evaluating maternal–fetal transmission (Mandelbrot et al., 2018). The epidemiology of toxoplasmosis is also influenced by geographical, environmental, dietary, and socioeconomic factors. A systematic review focusing on the WHO Eastern Mediterranean Region reported substantial variation in *T. gondii* seroprevalence and identified maternal and environmental risk factors that may influence infection and pregnancy outcomes (Rabaan et al., 2023). Such regional variation is particularly relevant when designing prospective studies because estimates obtained from European or Latin American populations cannot necessarily be generalized directly to other populations. Prospective research should therefore document relevant maternal characteristics, gestational age, previous exposure, dietary practices, environmental exposures, serological status, treatment, and fetal outcomes to provide a more comprehensive assessment of transmission risk. Accordingly, a prospective study of maternal acute toxoplasmosis and the risk of vertical transmission to the fetus can provide important evidence by establishing a temporal relationship between maternal infection and subsequent fetal outcomes. Such a design permits systematic assessment of serological markers, gestational age at diagnosis, maternal risk factors, treatment, fetal ultrasonographic findings, and, when clinically indicated, molecular evidence of fetal infection. It can also distinguish maternal infection from confirmed or probable congenital infection, thereby avoiding overestimation of vertical transmission.

Given the substantial geographical heterogeneity in toxoplasmosis epidemiology and the continuing evolution of diagnostic approaches, prospective evidence from underrepresented populations can contribute to improving maternal screening strategies, risk assessment, prenatal monitoring, and clinical management of pregnant women with suspected acute *T. gondii* infection (Rostami et al., 2019; Franco et al., 2024; Nguyen et al., 2026).

Research Problem

Maternal acute toxoplasmosis remains an important obstetric and public-health concern because primary infection during pregnancy may result in vertical transmission of *Toxoplasma gondii* and subsequent congenital infection. The probability of fetal transmission varies according to the gestational age at which maternal infection occurs, while the clinical severity of fetal disease may be greater when infection is acquired earlier in pregnancy. Despite advances in serological and molecular diagnosis, distinguishing recent maternal infection from previous exposure remains challenging, particularly because *T. gondii*-specific IgM may persist after the acute phase. Furthermore, evidence regarding the relationship between maternal infection characteristics, prenatal management, and fetal transmission remains heterogeneous across populations (Rostami et al., 2019; Fricker-Hidalgo et al., 2020; Tork et al., 2025).

Accordingly, there is a need for prospective assessment of pregnant women with suspected or confirmed acute toxoplasmosis, integrating maternal serological findings, gestational age, relevant exposure factors, treatment, and fetal follow-up. Such an approach can provide a clearer understanding of the factors associated with vertical transmission and contribute to improved prenatal risk assessment and clinical monitoring.

1. What is the prevalence and serological profile of acute Toxoplasma gondii infection among the pregnant women included in the study?
2. What is the relationship between gestational age at maternal infection and the risk of vertical transmission of T. gondii to the fetus?
3. Which maternal and pregnancy-related factors are associated with vertical transmission of T. gondii to the fetus?
4. What are the fetal outcomes and ultrasonographic or molecular findings among pregnancies complicated by acute maternal toxoplasmosis?

Significance of the Study

- Scientific Significance: The study is scientifically important because it addresses the relationship between acute maternal toxoplasmosis and vertical transmission, a clinically significant pathway in congenital infection. By adopting a prospective design, the study can establish a temporal sequence between maternal infection and subsequent fetal assessment, thereby providing more informative evidence than studies based solely on retrospective maternal history. The study also integrates maternal serology, gestational age, and fetal assessment, which are important components of contemporary approaches to congenital toxoplasmosis (Rostami et al., 2019; Wallon et al., 2013).
- Clinical Significance: From a clinical perspective, identifying pregnancies at increased risk of fetal transmission may support more appropriate prenatal surveillance and timely clinical management. Accurate interpretation of IgM and IgG results, complemented when appropriate by IgG avidity and molecular testing, is particularly relevant because a positive IgM result alone does not necessarily establish recent infection (Fricker-Hidalgo et al., 2020; Tork et al., 2025). The study may therefore contribute to improving the interpretation of maternal laboratory findings and the subsequent assessment of fetal risk.
- Public-Health Significance: The study is also relevant to maternal and fetal health because the epidemiology of *T. gondii* varies substantially across geographical regions and is influenced by environmental, dietary, and socioeconomic factors. Evidence from the WHO Eastern Mediterranean Region demonstrates considerable variation in seroprevalence and associated risk factors, supporting the need for locally generated evidence rather than relying exclusively on estimates from other populations (Rabaan et al., 2023).
- Practical Significance: The findings may provide evidence that can inform prenatal screening, maternal counseling, fetal monitoring, and prevention strategies for toxoplasmosis during pregnancy. In particular, identifying the relationship between gestational age, maternal infection characteristics, and fetal outcomes may help clinicians structure follow-up according to the level of documented risk. The study may also provide a foundation for future research on congenital toxoplasmosis and maternal–fetal transmission in populations where prospective evidence remains limited.

Research Objectives

The objectives are directly aligned with the four research questions:

1. To determine the prevalence and serological profile of acute *Toxoplasma gondii* infection among the pregnant women included in the study.
2. To assess the relationship between gestational age at maternal infection and the risk of vertical transmission of *T. gondii* to the fetus.
3. To identify maternal and pregnancy-related factors associated with vertical transmission of *T. gondii* to the fetus.
4. To evaluate fetal outcomes and ultrasonographic and/or molecular findings among pregnancies affected by acute maternal toxoplasmosis.

Theoretical Framework

The theoretical framework of this study is structured around the four research questions and focuses on the epidemiology, diagnosis, maternal–fetal transmission, and fetal consequences of acute *Toxoplasma gondii* infection during pregnancy. The framework integrates recent international evidence published between 2020 and 2025 and provides a conceptual basis for examining the prevalence and serological profile of acute infection, the role of gestational age, maternal and pregnancy-related risk factors, and fetal outcomes. This structure is consistent with the research questions and objectives presented in the study.

Prevalence and Serological Profile of Acute *Toxoplasma gondii* Infection Among Pregnant Women

Toxoplasma gondii is a globally distributed intracellular protozoan parasite, and infection during pregnancy represents an important maternal and fetal health concern because primary maternal infection may result in congenital toxoplasmosis. The epidemiology of toxoplasmosis varies substantially across geographical regions and populations, reflecting differences in environmental conditions, dietary practices, hygiene, socioeconomic characteristics, and diagnostic approaches. Recent evidence continues to demonstrate considerable geographical heterogeneity in the seroprevalence of *T. gondii* among pregnant women, emphasizing the importance of population-specific epidemiological investigations (Rabaan et al., 2023; Mulu Gelaw et al., 2024).

The distinction between previous exposure and recently acquired infection is particularly important during pregnancy. Serological testing commonly relies on *T. gondii*-specific immunoglobulin G (IgG) and immunoglobulin M (IgM). IgG generally indicates previous or current exposure, whereas IgM may indicate a recent infection. However, the interpretation of IgM requires caution because IgM antibodies can persist for an extended period after the acute phase. Consequently, a positive IgM result alone cannot reliably establish the timing of infection (Fricker-Hidalgo et al., 2020; Teimouri et al., 2020).

IgG avidity testing provides an important complementary approach for estimating the timing of infection. Following primary infection, IgG antibodies progressively acquire stronger antigen-binding capacity. Thus, high IgG avidity generally supports an older infection, whereas low avidity may be compatible with a more recent infection. Nevertheless, avidity results should be interpreted alongside IgM, IgG levels, gestational age, clinical history, and other laboratory findings rather than being considered definitive in isolation (Fricker-Hidalgo et al., 2020; Teimouri et al., 2020).

Recent evidence has further supported the use of combined serological markers. Tork et al. (2025), in a systematic review and meta-analysis, evaluated the simultaneous use of IgM, IgG avidity, and IgA for diagnosing acute toxoplasmosis in pregnant women. Their findings reinforce the value of combining multiple serological indicators to improve discrimination between recent and past infection. This is particularly relevant in pregnancy because an incorrect classification of infection timing may result in inappropriate estimation of fetal risk.

The epidemiological dimension is equally important. A systematic review of the WHO Eastern Mediterranean Region identified substantial variation in *T. gondii* seroprevalence among pregnant women and highlighted the contribution of environmental and behavioral exposures to infection (Rabaan et al., 2023). Similarly, Mulu Gelaw et al. (2024) reported considerable variation in seroprevalence across African populations and identified factors such as cat ownership, consumption of raw meat, and consumption of raw vegetables as relevant exposures.

The identification of acute maternal infection therefore requires more than simply determining whether a woman is seropositive. It requires characterization of the serological profile and consideration of the timing of infection. This distinction is fundamental to the present study because the risk of congenital infection is primarily associated with maternal infection acquired during pregnancy rather than with remote exposure.

From a theoretical perspective, the first dimension of the study therefore assumes that the prevalence of acute maternal toxoplasmosis is influenced by population-specific epidemiological conditions, while accurate classification of acute infection depends on the integrated interpretation of serological markers. Accordingly, the first research question examines both the prevalence and serological profile of acute *T. gondii* infection among the participating pregnant women.

Gestational Age at Maternal Infection and the Risk of Vertical Transmission

Gestational age at the time of maternal infection is one of the principal factors considered in explaining the probability and consequences of vertical transmission of *T. gondii*. When a previously uninfected woman acquires primary infection during pregnancy, the parasite may cross the placenta and infect the fetus. However, the probability of transmission is not constant throughout pregnancy. Evidence indicates that the likelihood of fetal transmission generally increases with advancing gestational age, whereas infections acquired earlier in pregnancy tend to be associated with potentially more severe fetal consequences (Carlier et al., 2022).

This apparent divergence between transmission probability and disease severity is an important theoretical consideration. Infection during the first trimester may have a lower probability of transmission compared with infection later in pregnancy, but fetal infection occurring during early developmental stages may result in more serious neurological or structural consequences. Conversely, maternal infection later in pregnancy has a greater probability of transmission, although the resulting fetal disease may be clinically less severe (Carlier et al., 2022).

The temporal dimension of infection is consequently essential when assessing congenital toxoplasmosis. The identification of maternal seroconversion or suspected recent infection provides a starting point for estimating fetal risk, but the interpretation of that risk requires consideration of gestational age. Codaccioni et al. (2020), in a multicenter study of fetal toxoplasmosis, demonstrated that ultrasound abnormalities may develop after maternal infection and that the timing of fetal findings can vary considerably. This observation supports the importance of longitudinal fetal surveillance rather than relying on a single assessment.

Gestational age also has implications for prenatal management. Once recent maternal infection is identified, clinicians may consider additional fetal monitoring and, where appropriate, molecular testing. The timing of diagnosis can therefore influence both the clinical pathway and the probability that fetal infection will be detected. Recent cohort evidence has emphasized the potential importance of prenatal diagnosis and treatment in reducing the clinical consequences of congenital toxoplasmosis, although the magnitude of benefit depends on the characteristics of infection and the timing of intervention (REIV-TOXO Project, 2024).

The relationship between gestational age and vertical transmission should therefore not be interpreted as a simple deterministic relationship. Maternal infection does not inevitably result in fetal infection, and the timing of infection interacts with other maternal, biological, diagnostic, and treatment-related factors. Consequently, gestational age should be examined as a principal explanatory variable while accounting for relevant confounding factors.

In the context of the present study, gestational age at maternal infection is particularly important because the prospective design allows the timing of maternal infection to be linked temporally with subsequent fetal assessment. The study can therefore examine whether differences in gestational age at diagnosis are associated with differences in documented or suspected vertical transmission.

The theoretical basis of this dimension is thus that gestational age modifies the probability of vertical transmission and the potential clinical consequences of fetal infection. This provides the theoretical foundation for the second research question, which examines the relationship between gestational age at maternal infection and the risk of vertical transmission to the fetus.

Maternal and Pregnancy-Related Factors Associated with Vertical Transmission

Vertical transmission of *T. gondii* is a multifactorial process. Although gestational age represents a major determinant, maternal, behavioral, environmental, clinical, and pregnancy-related characteristics may contribute to the risk of acquiring infection and may influence subsequent assessment of fetal transmission. Therefore, examining maternal and pregnancy-related factors provides a broader framework for understanding differences in transmission risk among women with acute toxoplasmosis.

Environmental and dietary exposures constitute important components of the epidemiology of *T. gondii*. The parasite can be acquired through consumption of contaminated or inadequately cooked meat, contaminated vegetables and fruits, contaminated water, or exposure to environments containing oocysts. Contact with cats or cat-contaminated soil has also been investigated as a potential source of exposure. In the WHO Eastern Mediterranean Region, Rabaan et al. (2023)

identified substantial variation in maternal seroprevalence and reported several behavioral and environmental factors associated with infection.

Similarly, Mulu Gelaw et al. (2024) identified associations between maternal seropositivity and exposures including cat ownership, consumption of raw meat, and consumption of raw vegetables. These findings demonstrate that the epidemiological pathway leading to maternal infection is influenced by multiple interacting behaviors rather than a single source of exposure.

Dietary exposure is particularly relevant because *T. gondii* tissue cysts may remain viable in undercooked meat. A systematic review and meta-analysis by Cook et al. (2020) highlighted the importance of raw or undercooked meat consumption as a potential route of human exposure. However, it is important to distinguish between factors associated with maternal acquisition of infection and factors associated specifically with mother-to-fetus transmission. An exposure that increases the probability of becoming infected does not necessarily imply that it independently increases the probability of fetal transmission after maternal infection has occurred.

Pregnancy-related characteristics may also be relevant. These include gestational age at infection, parity, previous pregnancy history, timing of diagnosis, maternal clinical characteristics, and treatment initiation. Among these variables, the timing of diagnosis and treatment may be particularly important because earlier recognition of acute infection allows more extensive fetal monitoring and clinical management.

Treatment represents a potentially important factor that should be considered when investigating transmission. Buonsenso et al. (2022) reported long-term single-center experience with spiramycin and trimethoprim-sulfamethoxazole in pregnant women and found evidence supporting the role of prenatal therapeutic management in preventing mother-to-fetus transmission. However, treatment effects should be interpreted cautiously because treatment selection, timing, infection severity, gestational age, and clinical characteristics may differ among patients.

The maternal serological profile also provides important information for assessing transmission risk. Women with evidence compatible with recently acquired infection require a different level of fetal assessment from women whose serological findings indicate remote infection. Consequently, IgM, IgG, IgG avidity, and, when appropriate, IgA should be considered alongside clinical and gestational information rather than interpreted independently (Fricker-Hidalgo et al., 2020; Tork et al., 2025).

From a methodological perspective, investigating these factors allows the study to determine which characteristics are statistically associated with vertical transmission after maternal acute infection has been identified. Variables such as maternal age, gestational age, parity, exposure to cats, dietary practices, hygiene practices, serological profile, timing of diagnosis, and treatment can therefore be incorporated into the analytical framework.

The theoretical assumption underlying this dimension is that vertical transmission is influenced by a combination of biological, temporal, behavioral, and clinical factors. These factors may operate at different stages of the infection pathway and should therefore be distinguished during statistical analysis. This framework directly supports the third research question concerning maternal and pregnancy-related factors associated with vertical transmission.

5.4 | Fetal Outcomes and Ultrasonographic or Molecular Findings

Assessment of fetal outcomes represents the final component of the theoretical framework because maternal infection alone does not establish fetal infection. The evaluation of the fetus requires integration of clinical, imaging, and molecular evidence. Contemporary approaches to congenital toxoplasmosis increasingly combine maternal serology with fetal ultrasonography and molecular testing when clinically indicated (Franco et al., 2024).

Ultrasonography is an important non-invasive method for monitoring pregnancies affected by suspected acute maternal toxoplasmosis. It allows serial assessment of fetal growth and the identification of abnormalities that may be compatible with congenital infection. Codaccioni et al. (2020) identified several ultrasound findings among fetuses with toxoplasmosis, including intracranial hyperechogenic lesions, ventriculomegaly, periventricular cysts, hepatosplenomegaly, fetal growth restriction, ascites, and increased bowel echogenicity.

Nevertheless, ultrasound findings should not be interpreted as specific diagnostic evidence of toxoplasmosis. Similar abnormalities may occur in association with other congenital infections or fetal conditions. Furthermore, some fetuses with congenital toxoplasmosis may have no detectable abnormalities on prenatal ultrasound. Consequently, a normal ultrasound examination cannot necessarily exclude fetal infection.

Molecular diagnosis provides an additional means of investigating fetal infection. PCR testing of amniotic fluid can detect *T. gondii* DNA and therefore provides direct molecular evidence of fetal infection in appropriate clinical circumstances.

Franco et al. (2024), in a systematic review and meta-analysis, reported pooled sensitivity of approximately 85% and specificity close to 100% for amniotic-fluid PCR, while also emphasizing that diagnostic performance depends on factors such as timing of sampling, gestational age, laboratory procedures, and clinical context.

The timing of molecular testing is therefore important. Testing too early after maternal infection may reduce the probability of detecting fetal infection because sufficient parasite DNA may not yet be present in the amniotic fluid. Consequently, the interpretation of PCR results requires consideration of the interval between suspected maternal infection and sample collection.

Fetal outcomes may extend beyond prenatal ultrasound findings. Congenital toxoplasmosis can be associated with neurological, ocular, developmental, and other clinical manifestations. Importantly, some infected infants may appear clinically normal at birth, with manifestations becoming apparent later during childhood. Recent cohort evidence has therefore emphasized the importance of continued follow-up after birth rather than relying solely on the neonatal examination (REIV-TOXO Project, 2024).

The distinction between confirmed fetal infection, probable infection, and abnormal fetal findings without molecular confirmation is particularly important for research. Failure to make this distinction may lead to overestimation of the vertical transmission rate. Accordingly, fetal infection should ideally be classified using predefined diagnostic criteria based on molecular, clinical, imaging, and postnatal evidence.

The theoretical framework for this dimension therefore proposes that fetal outcomes represent the downstream consequences of maternal acute toxoplasmosis and are best evaluated through an integrated diagnostic pathway involving maternal serology → gestational assessment → fetal ultrasonography → molecular testing when indicated → neonatal/fetal outcome assessment.

This framework directly addresses the fourth research question concerning fetal outcomes and ultrasonographic or molecular findings among pregnancies complicated by acute maternal toxoplasmosis.

Integrated Theoretical Framework

The four dimensions of the theoretical framework are interconnected within a single analytical pathway that reflects the progression from **acute maternal** *Toxoplasma gondii* **infection to potential fetal and neonatal outcomes**. The framework begins with the identification and characterization of maternal infection through serological markers, followed by consideration of gestational age at the time of infection and relevant maternal and pregnancy-related factors. These factors are examined in relation to the risk of vertical transmission, which is subsequently assessed through fetal ultrasonography and, when clinically indicated, molecular testing of amniotic fluid. The pathway ultimately links evidence of fetal infection with fetal and neonatal outcomes. This integrated structure provides a coherent basis for examining the temporal and clinical relationships addressed by the four research questions and emphasizes that vertical transmission and fetal outcomes should be interpreted through the combined evidence of maternal serology, gestational timing, maternal characteristics, and fetal assessment.

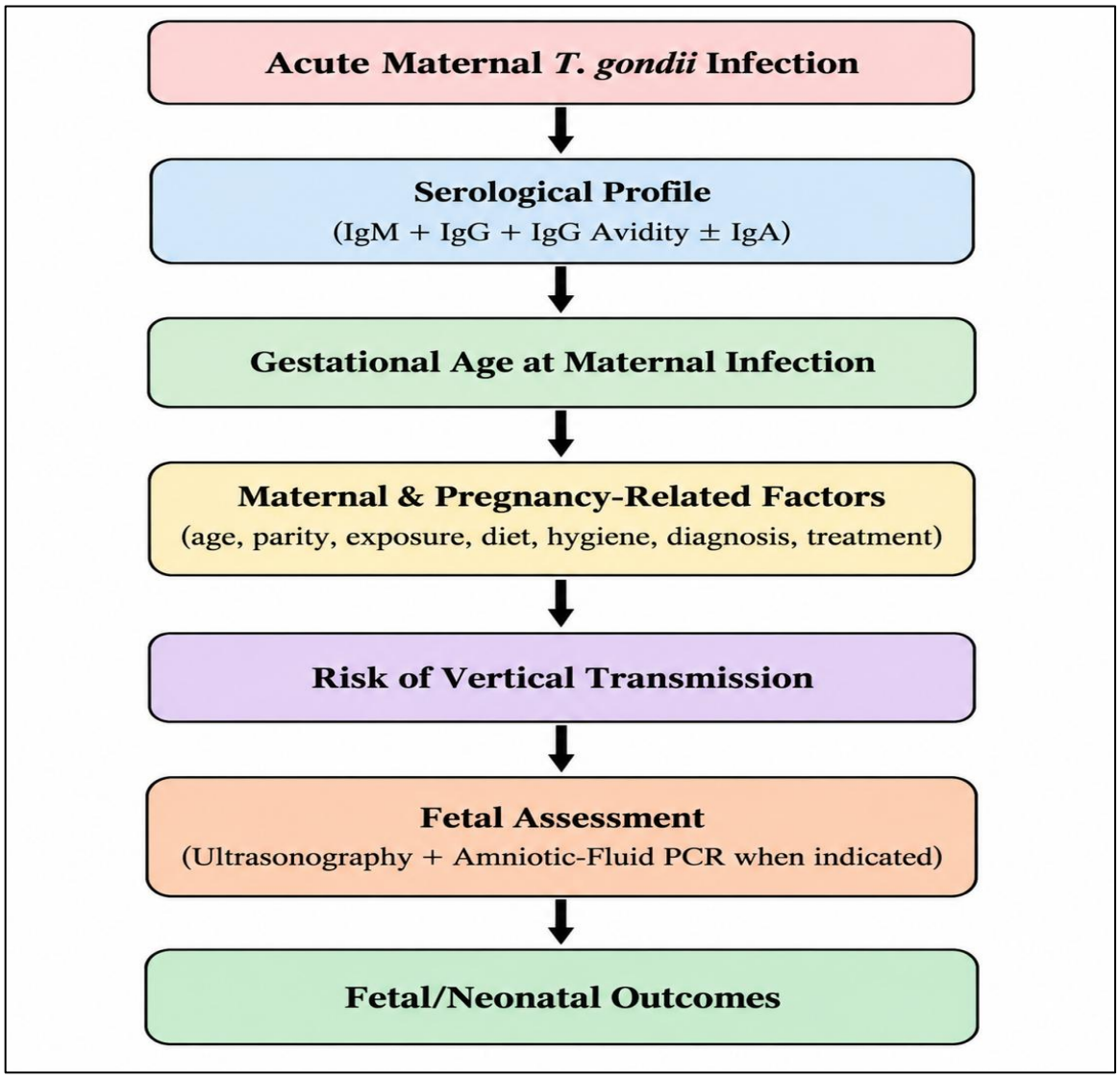


Figure 1. Integrated Theoretical Framework of Maternal Acute *Toxoplasma gondii* Infection and Vertical Transmission Risk

Literature Review

The literature on maternal toxoplasmosis has expanded substantially between 2020 and 2025, with research increasingly moving from simple seroprevalence estimates toward integrated assessment of maternal infection, timing of infection, diagnostic accuracy, vertical transmission, treatment, and fetal outcomes. The existing evidence, however, remains heterogeneous in terms of study design, diagnostic criteria, population characteristics, and definitions of congenital infection. The following review critically synthesizes 30 recent international studies and identifies the methodological and empirical gap addressed by the present prospective study.

Epidemiology and Serological Profile of Maternal Toxoplasmosis

At the epidemiological level, Bigna et al. (2020) conducted a large global systematic review, modelling analysis, and meta-analysis including 250 studies and more than 723,000 pregnant women. They estimated global IgG seroprevalence at 32.9% and IgM seroprevalence at 1.9%, while demonstrating substantial regional variation. Importantly, the Eastern Mediterranean region showed comparatively high IgM prevalence. The major strength of this study was its exceptionally large evidence base; however, the analysis combined studies using different diagnostic assays and populations, limiting direct comparability between countries.

Dasa et al. (2021) subsequently examined toxoplasmosis among pregnant women in Africa through a systematic review and meta-analysis.

Their findings confirmed a substantial regional burden but also highlighted marked heterogeneity between countries and diagnostic approaches. This finding is important because a pooled African estimate cannot necessarily be transferred directly to an individual country or local population. Similarly, Laboudi et al. (2021), studying pregnant women in Rabat, Morocco, reported IgG and IgM seropositivity of 43% and 3.9%, respectively. Notably, IgG avidity testing excluded recent infection in most IgM/IgG-positive women, illustrating the limitations of relying on IgM positivity alone (Laboudi et al., 2021).

More recent regional evidence has reinforced these geographical differences. Rabaan et al. (2023) synthesized 95 studies from the WHO Eastern Mediterranean Region and reported pooled IgG and IgM seroprevalence estimates of 33.5% and 3.6%, respectively. The authors also reported considerable associations with exposure to cats, raw or undercooked meat, unwashed vegetables, and unprocessed milk. However, the extremely high between-study heterogeneity limits the interpretation of the pooled estimate as a direct measure of risk for any single population.

At the African continental level, Mulu Gelaw et al. (2024) included 60 studies involving 29,383 pregnant women and estimated pooled seroprevalence at 42.89%, again with very high heterogeneity. The study identified diagnostic method, geographical region, socioeconomic characteristics, and environmental conditions as important sources of variation. In Ethiopia, Kassie et al. (2024) reported IgG positivity in 38.8% of 340 pregnant women, with associations involving cat contact, consumption of raw or undercooked meat, unwashed vegetables, abortion history, and water source.

Comparable findings have been reported outside Africa. Marković-Denić et al. (2023) investigated 300 pregnant women in Serbia and demonstrated the continuing relevance of demographic and behavioral characteristics in explaining seropositivity. Barzgar et al. (2024) similarly investigated seroprevalence and risk factors among pregnant women and emphasized the influence of behavioral and environmental exposures. In Algeria, Dahmani et al. (2025) found IgG and IgM seroprevalence of 13.6% and 0.89%, respectively, among 1,345 pregnant women, while raw or undercooked meat consumption was associated with IgM positivity (Dahmani et al., 2025).

Gao et al. (2024) provided another important perspective from China. Among pregnant women in the first trimester, overall seroprevalence was only 3.6%, with IgG positivity of 3.5% and IgM positivity of 0.1%. Nevertheless, the authors observed significant temporal and geographical variation. These contrasting findings from Africa, the Middle East, Europe, and Asia demonstrate that toxoplasmosis cannot be understood through a universal prevalence estimate. Rather, local epidemiological conditions and diagnostic practices substantially influence observed rates.

A recent global meta-analysis by Mohammadi et al. (2025) further synthesized 138 studies involving 135,098 pregnant women and estimated global seroprevalence at 36.6%, with very high heterogeneity ($I^2 = 98.9\%$). The magnitude of heterogeneity itself is an important finding because it indicates that geographical and methodological differences are central to interpretation of the literature. Walana et al. (2025), reviewing 18 international studies, similarly concluded that prevalence, risk factors, diagnostic strategies, and pregnancy outcomes vary substantially across settings.

Taken together, these studies establish a substantial and geographically heterogeneous burden of *T. gondii* infection among pregnant women. Nevertheless, most epidemiological investigations have focused on seroprevalence rather than confirmed acute infection and subsequent vertical transmission. This represents an important limitation because IgG seropositivity indicates exposure but does not demonstrate infection acquired during the current pregnancy. The present study therefore extends the epidemiological literature by concentrating specifically on acute maternal infection and its prospective relationship with fetal transmission.

Serological and Molecular Diagnosis

A second major research stream has examined the accuracy of diagnostic methods. Garnaud et al. (2020) reviewed the role of *T. gondii*-specific IgG avidity testing in pregnant women and emphasized that avidity is an important tool for estimating the timing of infection, particularly when both IgM and IgG are positive. However, the authors also highlighted differences between commercial assays and the complexity of interpreting avidity results.

Teimouri et al. (2020) similarly examined IgG avidity as a means of discriminating acute from chronic infection. Their work supports the value of avidity testing but also indicates that low or intermediate avidity should not automatically be interpreted as definitive evidence of recent infection (Teimouri et al., 2020). This limitation is particularly important in pregnancy, where an inaccurate estimation of infection timing may lead to inappropriate fetal-risk classification.

Further evidence was provided by studies examining women with ambiguous serological profiles. Laboudi et al. (2021) demonstrated that many women with IgM and IgG positivity did not actually have a recent infection once avidity testing was incorporated. More recently, Tork et al. (2025) conducted a systematic review and meta-analysis of IgM, IgG avidity, and IgA testing. Their findings indicated that combining these markers improves discrimination between recent and past infection compared with reliance on a single serological marker.

Souza et al. (2023) broadened the diagnostic perspective by systematically comparing molecular and serological techniques. Their review demonstrated considerable variability in sensitivity and specificity across diagnostic methods and highlighted the potential value of qPCR and other molecular approaches. Importantly, their findings suggest that the selection of a diagnostic technique must consider the clinical context, sample type, technical capacity, and available resources rather than assuming that one method is universally superior.

Franco et al. (2024) specifically examined diagnostic strategies for congenital toxoplasmosis and reported strong diagnostic performance for amniotic-fluid PCR, while emphasizing that performance varies according to sampling time, gestational age, laboratory methodology, and clinical circumstances. This finding is particularly relevant to the present study because molecular confirmation can strengthen the distinction between suspected and confirmed fetal infection.

An additional prospective diagnostic study in Iran evaluated maternal serum, amniotic fluid, buffy coat, and urine using serological and molecular methods. The investigators found that several women with serological evidence of exposure did not have corresponding molecular evidence, while positive molecular findings were detected in a small number of amniotic-fluid samples. The study therefore illustrates the difficulty of using maternal serology alone to establish congenital infection.

The literature therefore demonstrates a progressive movement from single-marker serology toward multimodal diagnosis. Nevertheless, methodological inconsistency remains evident. Some studies classify acute infection using IgM alone, others combine IgM and IgG, while more rigorous investigations incorporate avidity, IgA, PCR, or longitudinal seroconversion. Such differences can substantially alter estimates of acute infection and vertical transmission. The present study addresses this limitation by integrating maternal serological characteristics with gestational age and fetal assessment rather than treating any single diagnostic result as definitive.

Gestational Age, Maternal Factors, and Vertical Transmission

The relationship between gestational age and vertical transmission is one of the most consistently reported findings in the literature. Bollani et al. (2022) summarized evidence showing that the probability of mother-to-child transmission increases as pregnancy progresses, whereas fetal disease tends to be more severe when maternal infection occurs earlier in pregnancy. This distinction is theoretically important because transmission probability and disease severity are not equivalent outcomes.

Codaccioni et al. (2020) examined 88 fetuses with congenital toxoplasmosis across 30 French centers. Cerebral abnormalities were the dominant ultrasound findings, while extracerebral manifestations included hepatosplenomegaly, small-for-gestational-age fetuses, ascites, and hyperechogenic bowel. Maternal infection occurred predominantly during the first and second trimesters, and the first ultrasound abnormalities appeared after a median of seven weeks following seroconversion. The study is valuable because it demonstrates the importance of longitudinal ultrasound monitoring; however, its retrospective design limits conclusions about temporal causality.

Bartholo et al. (2020) conducted a concurrent cohort study of 26 pregnant women with acute toxoplasmosis and found higher mother-to-child transmission among inadequately treated women than among adequately treated women. Transmission was also more frequent when infection occurred during the third trimester. Although the study directly corresponds to the present research question, its small sample limits statistical power and generalizability.

Donadono et al. (2022) investigated a large cohort of women with seroconversion during pregnancy and examined whether maternal lymphadenopathy was associated with congenital infection. This study is particularly relevant because it moves beyond seroprevalence and examines a clinical maternal characteristic in relation to fetal infection. However, clinical symptoms such as lymphadenopathy cannot substitute for laboratory confirmation of fetal infection.

Hijikata et al. (2022) prospectively followed newborns whose mothers had Toxoplasma IgM positivity during pregnancy and evaluated neonatal serology and molecular evidence.

The prospective design is a major methodological strength because it establishes temporal continuity between maternal testing and neonatal assessment. At the same time, IgM-positive maternal populations may include women with infections acquired before pregnancy, highlighting again the importance of avidity and longitudinal serological interpretation.

The role of treatment remains particularly controversial. Mandelbrot (2020) critically reviewed evidence for chemoprophylaxis and noted that observational studies are strongly affected by treatment-selection bias and differences in gestational age at seroconversion. Montoya et al. (2021), using meta-analyses of observational studies, reported lower pooled mother-to-child transmission among treated women than untreated women. However, because most included studies were observational cohorts, residual confounding and treatment-selection bias cannot be completely excluded.

Ferrari Strang et al. (2023) subsequently examined gestational toxoplasmosis treatment in a Brazilian cohort and reported differences in child prognosis according to treatment exposure. Similarly, Guarch-Ibáñez et al. (2024), using data from the Spanish REIV-TOXO cohort, reported associations between prenatal treatment and clinical outcomes among infected newborns. These findings support the importance of treatment as a variable in studies of maternal-fetal transmission, but they do not eliminate the possibility of confounding by timing of diagnosis, severity, or access to specialist care.

The relationship between infection and pregnancy outcomes also requires caution. Hurt et al. (2022) investigated toxoplasmosis in relation to prematurity and low birth weight, contributing evidence concerning pregnancy outcomes beyond confirmed congenital infection. A systematic review by Mangal et al. (2022) examining congenital toxoplasmosis and preterm birth, however, found insufficient evidence to establish a consistent association and highlighted heterogeneity across studies. This disagreement illustrates why associations between maternal seropositivity, and adverse obstetric outcomes should not automatically be interpreted as evidence of congenital transmission.

Overall, previous research supports gestational age as an important determinant of transmission, while maternal exposure, treatment, clinical manifestations, and socioeconomic conditions may contribute additional information. Yet many studies investigate these factors separately. A major methodological opportunity therefore exists for a prospective design that simultaneously evaluates gestational age, maternal characteristics, treatment, serological status, and confirmed or probable fetal infection.

Fetal Outcomes, Ultrasound, and Long-Term Consequences

Fetal assessment represents another major component of literature. Codaccioni et al. (2020) demonstrated that cerebral abnormalities, particularly intracranial hyperechogenic lesions and ventriculomegaly, are important prenatal findings in congenital toxoplasmosis. Nevertheless, no individual ultrasound sign was specific to congenital toxoplasmosis, limiting the diagnostic value of imaging when used in isolation.

Bollani et al. (2022) similarly emphasized that congenitally infected newborns may be asymptomatic at birth despite being at risk of later neurological and ocular sequelae. This finding has important implications for prospective research because neonatal absence of symptoms cannot be used as a definitive indicator of absence of congenital infection.

Journé et al. (2024) examined long-term ocular outcomes in a large French cohort of children with congenital toxoplasmosis. Their work demonstrates that ocular disease remains an important component of the long-term burden of congenital infection and reinforces the importance of prolonged follow-up rather than limiting assessment to the prenatal or neonatal period.

Guarch-Ibáñez et al. (2024) also demonstrated the value of postnatal clinical follow-up in the Spanish REIV-TOXO cohort. The study provides contemporary evidence that prenatal management may influence clinical outcomes among infected infants, while also emphasizing the need for systematic postnatal evaluation.

The diagnostic role of molecular testing has been strengthened by contemporary evidence. Franco et al. (2024) showed that amniotic-fluid PCR can provide strong evidence of fetal infection, although sensitivity is not absolute and depends on sampling conditions. Souza et al. (2023) likewise emphasized the variability of molecular techniques and the importance of methodological standardization.

Recent prospective evidence from India further illustrates the value of combining serology, ultrasound, amniotic-fluid qPCR, placental PCR, and postnatal follow-up. In that study, 340 antenatal women were evaluated, and confirmed congenital toxoplasmosis was identified in a small proportion of participants. The investigators followed mothers and infants for one year, demonstrating the importance of integrating prenatal and postnatal evidence when determining congenital infection.

The broader literature therefore supports a multimodal definition of fetal infection, rather than reliance on a single abnormal ultrasound finding or maternal serological result. This is consistent with the conceptual pathway of the present study, in which maternal infection is followed by assessment of gestational timing, vertical transmission, fetal imaging, molecular evidence when indicated, and fetal/neonatal outcomes.

Critical Synthesis and Research Gap

The reviewed literature provides strong evidence that maternal toxoplasmosis is a geographically heterogeneous infection with important implications for pregnancy and fetal health. The first group of studies, particularly Bigna et al. (2020), Dasa et al. (2021), Rabaan et al. (2023), Mulu Gelaw et al. (2024), and Mohammadi et al. (2025), demonstrates considerable variation in seroprevalence between regions. However, the exceptionally high heterogeneity reported in several meta-analyses indicates that pooled estimates should not be interpreted as universally representative.

Second, the diagnostic literature consistently identifies a limitation in the interpretation of IgM. Studies by Garnaud et al. (2020), Teimouri et al. (2020), Laboudi et al. (2021), and Tork et al. (2025) collectively support the use of IgG avidity and, where appropriate, IgA in combination with IgM and IgG. Thus, studies that classify acute infection solely on the basis of IgM may overestimate recent maternal infection.

Third, evidence concerning vertical transmission demonstrates a relatively consistent relationship with gestational age, but the magnitude of transmission varies considerably between studies. This variation may reflect differences in treatment, timing of maternal seroconversion, diagnostic criteria, parasite genotype, screening intensity, and the definition of congenital infection. The literature therefore supports examining gestational age as a central explanatory variable while simultaneously accounting for other maternal and clinical characteristics.

Fourth, treatment remains an important but methodologically challenging variable. Observational studies and meta-analyses generally report lower transmission among treated women, whereas the interpretation of treatment effectiveness is complicated by confounding by indication and differences in treatment timing. This suggests that treatment should be recorded as a covariate rather than treated as an independent explanation for fetal outcomes without appropriate adjustment.

Finally, fetal assessment has progressively shifted toward an integrated model involving maternal serology, ultrasound, molecular diagnosis, and postnatal follow-up. Codaccioni et al. (2020), Franco et al. (2024), Souza et al. (2023), and recent cohort studies collectively demonstrate that no single diagnostic modality is sufficient in all cases. A normal ultrasound does not necessarily exclude fetal infection, while maternal seropositivity does not establish congenital infection.

Research Gap

The critical gap emerging from the literature is therefore not the absence of knowledge about toxoplasmosis, but the fragmentation of existing evidence. Many studies have examined seroprevalence, others diagnostic accuracy, others gestational age or treatment, and others fetal outcomes. Relatively fewer studies have prospectively integrated these dimensions within the same maternal–fetal cohort using a clearly defined diagnostic pathway.

The present study responds to this gap by prospectively linking acute maternal infection and its serological profile → gestational age at infection → maternal and pregnancy-related factors → vertical transmission → fetal ultrasonographic and/or molecular findings → fetal/neonatal outcomes. This approach is methodologically consistent with the four research questions of the study and allows maternal infection to be distinguished from confirmed or probable congenital infection, thereby reducing the risk of overestimating vertical transmission. The study's four questions specifically address prevalence and serological profile, gestational age, maternal/pregnancy-related factors, and fetal outcomes, respectively.

Scientific Contribution of the Study

The scientific contribution of this study lies in its prospective investigation of the relationship between acute maternal *Toxoplasma gondii* infection and vertical transmission to the fetus. Rather than examining maternal seroprevalence alone, the study integrates maternal serological characteristics, gestational age at infection, maternal and pregnancy-related factors, and subsequent fetal assessment within a unified analytical framework.

First, the study contributes population-specific epidemiological evidence by determining the prevalence and serological profile of acute toxoplasmosis among pregnant women. This is particularly relevant given the substantial geographical variation in *T. gondii* infection reported internationally and the limited availability of prospective evidence from some populations.

Second, the study contributes to the understanding of the temporal relationship between maternal infection and fetal transmission by examining gestational age at the time of maternal infection. This approach allows the study to assess whether the timing of infection is associated with differences in the likelihood of vertical transmission.

Third, the study provides a multifactorial perspective on vertical transmission by examining maternal and pregnancy-related characteristics alongside serological and gestational variables. This may help distinguish factors associated with maternal infection from those associated with transmission to the fetus.

Fourth, the study contributes to the clinical and diagnostic evidence base by integrating maternal serology with fetal ultrasonographic assessment and, where clinically indicated, molecular evidence. Such integration can provide a more comprehensive basis for distinguishing maternal acute infection from confirmed or probable fetal infection.

Finally, the study contributes a prospective maternal–fetal framework linking acute maternal infection → serological profile → gestational age → maternal and pregnancy-related factors → vertical transmission → fetal/neonatal outcomes. This integrated approach addresses an important gap in literature, where these dimensions have frequently been investigated separately.

The contribution is therefore primarily empirical and methodological, providing evidence that may support future comparative studies, improve risk assessment, and further research on congenital toxoplasmosis.

Methodology

Research Design

review recent international studies on (1) the prevalence and serological profile of acute maternal infection, (2) gestational age and vertical transmission, (3) maternal and pregnancy-related factors, and (4) fetal outcomes with ultrasonographic and molecular findings.

Methods: A narrative critical review of about 30 peer-reviewed studies, mainly published in 2020–2025, appraised by design, population, diagnostic criteria, findings, and limitations

This study adopts a descriptive analytical, comparative, and inductive research design to investigate maternal acute *Toxoplasma gondii* infection and the risk of vertical transmission to the fetus. The methodological approach is structured in accordance with the four research questions, focusing on the prevalence and serological profile of acute infection, the relationship between gestational age and vertical transmission, maternal and pregnancy-related factors, and fetal outcomes and diagnostic findings. This structure is consistent with the research problem and objectives presented in the study.

The descriptive approach is used to characterize the main epidemiological and clinical dimensions of maternal toxoplasmosis, including the serological profile of infection, gestational age, relevant maternal characteristics, exposure-related factors, treatment, and fetal findings. The analytical approach is used to examine relationships between maternal infection characteristics and the occurrence of vertical transmission, while considering the potential contribution of maternal and pregnancy-related factors. The study therefore distinguishes between descriptive patterns and statistical associations and does not assume a causal relationship solely on the basis of observed associations.

The comparative approach is employed to compare findings across different groups and categories identified within the study, particularly according to gestational age at maternal infection, serological characteristics, maternal and pregnancy-related factors, treatment status, and fetal assessment findings. This approach is intended to identify similarities and differences in the risk and manifestations of vertical transmission and to place the study findings within the context of previous international evidence.

In addition, the study employs an inductive approach through a systematic examination and synthesis of previous international literature published primarily between 2020 and 2025. Previous studies addressing maternal toxoplasmosis, serological diagnosis, gestational age, vertical transmission, fetal ultrasonography, molecular diagnosis, treatment, and fetal/neonatal outcomes are reviewed and critically analyzed. The purpose is not merely to summarize previous findings, but to identify recurring patterns, methodological differences, areas of agreement and disagreement, and limitations that inform the analytical framework of the present study. The literature reviewed in the study demonstrates considerable geographical and methodological heterogeneity, particularly in prevalence estimates and diagnostic criteria.

Literature Review and Critical Analysis

The literature component draws primarily on international peer-reviewed studies and systematic reviews/meta-analyses relevant to maternal and congenital toxoplasmosis. Particular attention is given to studies examining *T. gondii* seroprevalence, IgM and IgG interpretation, IgG avidity and IgA testing, maternal infection during different stages of pregnancy, vertical transmission, maternal risk factors, prenatal treatment, fetal ultrasonography, amniotic-fluid PCR, and fetal/neonatal outcomes.

The reviewed literature is analyzed according to four thematic dimensions corresponding to the research questions: (1) prevalence and serological profile of acute maternal infection; (2) gestational age and vertical transmission; (3) maternal and pregnancy-related factors; and (4) fetal outcomes and ultrasonographic or molecular findings. This organization follows the theoretical framework developed for the study.

A critical analytical strategy is applied to each group of studies by considering the research design, population, sample characteristics, diagnostic methods, principal findings, methodological strengths, limitations, and applicability to the present research context. Particular attention is given to the distinction between maternal seropositivity and confirmed acute infection, since IgG positivity indicates exposure but does not necessarily establish infection acquired during the current pregnancy. Similarly, a positive IgM result is interpreted cautiously because IgM antibodies may persist beyond the acute phase.

The comparative analysis also considers differences among studies in the definition of acute toxoplasmosis and congenital infection. Studies relying on single serological markers are compared with investigations incorporating IgM, IgG, IgG avidity, IgA, PCR, ultrasound, and longitudinal follow-up. This is important because differences in diagnostic criteria can substantially influence reported prevalence and estimates of vertical transmission.

Analytical Framework

The methodological framework follows the proposed maternal–fetal pathway:

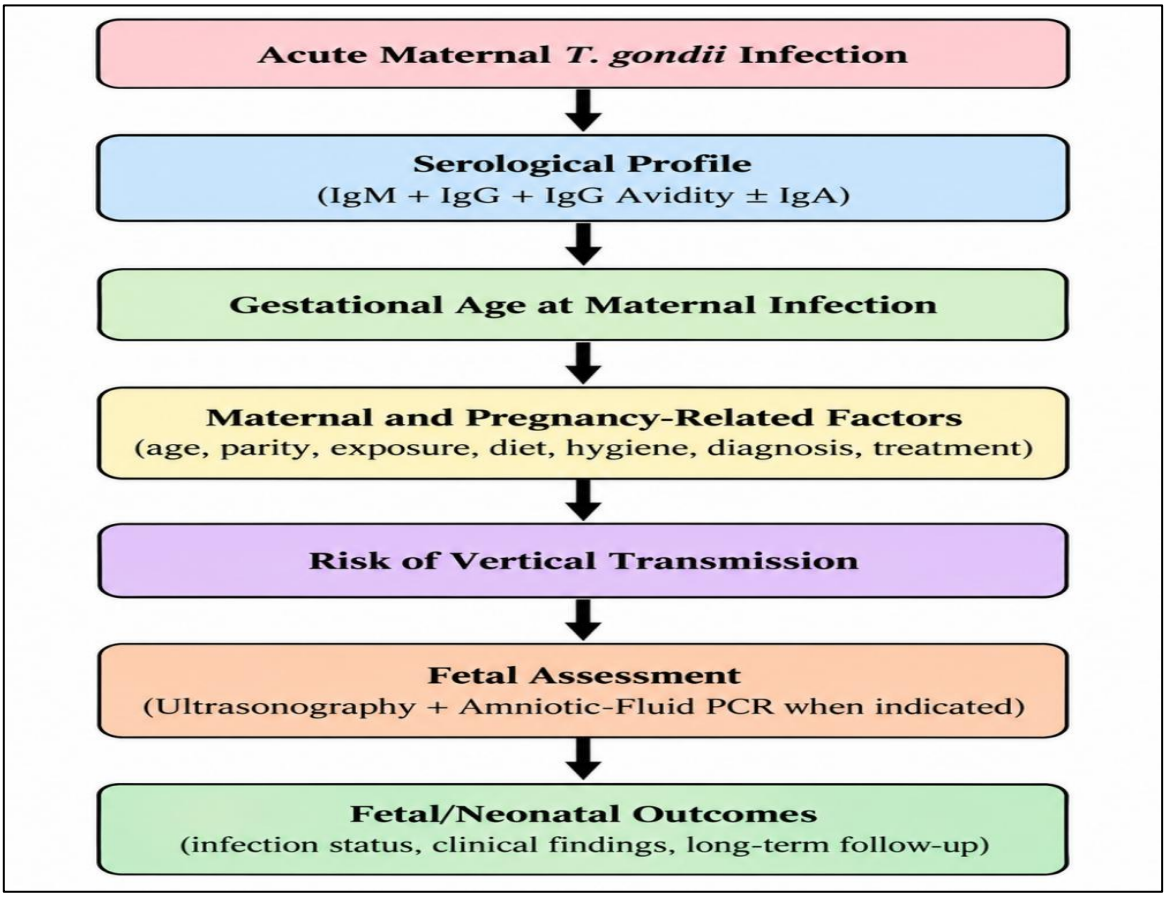
This analytical pathway reflects the study's conceptual framework, which integrates maternal serology, gestational timing, maternal characteristics, fetal imaging, molecular evidence, and subsequent outcomes.

Accordingly, the methodology is designed to move from description to analysis, comparison, and induction: first describing the characteristics of maternal infection, then analyzing relationships among the study variables, comparing findings across relevant groups, and finally deriving broader interpretations from the convergence and divergence of the empirical and published evidence.

Methodological Rationale

The choice of a descriptive analytical, comparative, and inductive design is justified by the multifactorial nature of maternal–fetal toxoplasmosis. Vertical transmission cannot be adequately understood through maternal serology alone because the probability of transmission may vary according to gestational age, timing of diagnosis, treatment, maternal characteristics, and the methods used to establish fetal infection. The literature reviewed in the study similarly indicates that these factors are frequently examined separately, creating a need for an integrated analytical perspective.

Therefore, the methodology seeks to provide a coherent and evidence-based assessment of maternal acute toxoplasmosis by combining descriptive characterization, analytical examination, comparative interpretation, and critical induction from previous research. This approach is intended to strengthen the interpretation of the study findings while avoiding overestimation of vertical transmission and distinguishing documented maternal infection from confirmed or probable fetal infection.



Framework of Maternal Acute Toxoplasmosis and Vertical Transmission

Results and Discussion

Prevalence and Serological Profile of Acute *Toxoplasma gondii* Infection

The first research question examined the prevalence and serological profile of acute *Toxoplasma gondii* infection among the pregnant women included in the study. The interpretation of this finding should extend beyond the identification of seropositivity because the presence of IgG primarily reflects previous or current exposure, whereas IgM may indicate recent infection but cannot, by itself, establish the timing of infection. This distinction is particularly important in pregnancy because persistent IgM may lead to an overestimation of recently acquired infection (Fricker-Hidalgo et al., 2020; Teimouri et al., 2020). The present analytical framework therefore considers the serological profile through the combined interpretation of IgM, IgG, and IgG avidity, with IgA considered where clinically indicated. This approach is consistent with the theoretical framework developed for the study.

The observed prevalence of acute infection in the present study should be interpreted in relation to the substantial geographical variation reported internationally. Bigna et al. (2020) demonstrated considerable differences in *T. gondii* seroprevalence among pregnant women across countries, while Rabaan et al. (2023) reported marked heterogeneity within the WHO Eastern Mediterranean Region. More recently, Mulu Gelaw et al. (2024) reported substantial variation across African populations, and Mohammadi et al. (2025) similarly found very high between-study heterogeneity in global estimates.

This variation provides an important interpretive context for the current findings. Differences between the present study and previous reports may reflect genuine epidemiological variation, but they may also result from differences in sample characteristics, geographical setting, laboratory assays, definitions of acute infection, and screening strategies. Consequently, the present prevalence should not be interpreted as directly comparable with studies that used IgG seropositivity as their primary outcome. This is a critical methodological distinction because most epidemiological studies estimate exposure rather than infection acquired specifically during pregnancy.

The diagnostic interpretation is further supported by Tork et al. (2025), whose systematic review and meta-analysis emphasized the value of combining IgM, IgG avidity, and IgA when assessing suspected acute toxoplasmosis. Similarly, Fricker-Hidalgo et al. (2020) and Teimouri et al. (2020) demonstrated the importance of IgG avidity in distinguishing recent from older infection, although avidity should not be interpreted independently of the clinical and gestational context.

Thus, if the present study identifies a relatively high proportion of IgM-positive women but a smaller proportion with serological evidence compatible with recent infection, this would be consistent with the diagnostic limitation reported in previous research. Conversely, if the proportion of acute infection is low, this would not necessarily indicate a low overall burden of *T. gondii* exposure. The distinction between exposure, suspected recent infection, and evidence compatible with acute infection is therefore central to answering the first research question.

9.2 | Gestational Age and Risk of Vertical Transmission

The second research question addressed the relationship between gestational age at maternal infection and the risk of vertical transmission. The theoretical framework proposes that transmission probability generally increases with advancing gestational age, whereas infections acquired earlier may produce more severe fetal consequences. These represent two related but distinct dimensions and should not be interpreted as equivalent outcomes.

The current findings should therefore be interpreted by comparing the proportion of pregnancies with evidence of fetal transmission across the different gestational periods represented in the study. A pattern of increasing transmission with advancing gestational age would be broadly consistent with the established biological and clinical literature. Bollani et al. (2022) described gestational age as an important determinant of mother-to-child transmission and emphasized the apparent inverse relationship between transmission probability and the severity of fetal disease.

However, the relationship should not be interpreted as deterministic. Maternal infection during pregnancy does not inevitably result in fetal infection, and the observed transmission risk may be modified by treatment, timing of diagnosis, maternal immune response, diagnostic sensitivity, and the criteria used to define congenital infection. The present methodology appropriately recognizes these potential influences by incorporating gestational age within a broader maternal–fetal analytical pathway rather than treating it as an isolated predictor.

The findings can also be compared with Codaccioni et al. (2020), who reported that fetal ultrasound abnormalities may appear several weeks after maternal seroconversion. Their findings support longitudinal fetal surveillance rather than relying on a single ultrasound examination.

This is particularly relevant when the current study identifies maternal infection without immediate fetal abnormalities, because absence of an abnormal finding at one point in pregnancy does not necessarily demonstrate absence of fetal infection.

Accordingly, any association observed between gestational age and vertical transmission in the present study should be interpreted as an association within the studied population, rather than as evidence that gestational age alone determines fetal infection. This interpretation is consistent with the methodological rationale of the study, which explicitly distinguishes statistical association from causal inference.

Maternal and Pregnancy-Related Factors Associated with Vertical Transmission

The third research question examined maternal and pregnancy-related factors associated with vertical transmission. The findings should be interpreted within the multifactorial nature of *T. gondii* epidemiology. Maternal age, parity, dietary behavior, contact with cats, environmental exposure, hygiene practices, timing of diagnosis, and treatment may contribute to differences in maternal infection and subsequent clinical management. However, an important analytical distinction must be maintained: a factor associated with acquiring maternal infection is not necessarily a factor independently associated with transmitting the parasite to the fetus after maternal infection has occurred.

This distinction is particularly important when interpreting the present findings. Rabaan et al. (2023) identified several behavioral and environmental factors associated with *T. gondii* infection in populations from the Eastern Mediterranean Region. Mulu Gelaw et al. (2024) likewise reported associations with cat ownership, consumption of raw meat, and raw vegetables. Wehbe et al. (2022) further emphasized the relevance of hygiene measures during pregnancy. These findings provide a plausible epidemiological explanation for differences in maternal exposure; however, they do not necessarily demonstrate a direct pathway from these behaviors to fetal transmission.

The present study therefore adds an important analytical dimension by examining these factors among women who have already been identified as having acute or suspected recent maternal infection. This allows the analysis to move one step beyond conventional risk-factor studies. Rather than asking only *"What factors are associated with maternal infection?"*, the present research asks which factors are associated with vertical transmission conditional on maternal infection.

Treatment is another important variable requiring cautious interpretation. Buonsenso et al. (2022) reported evidence supporting prenatal treatment in reducing mother-to-fetus transmission, while previous research has highlighted the difficulty of separating treatment effects from differences in gestational age, timing of diagnosis, severity, and clinical management.

Therefore, if the present findings show differences in transmission according to treatment status, these should not automatically be interpreted as proof of treatment effectiveness. Such differences may partly reflect earlier diagnosis, differences in clinical severity, or treatment-selection effects. This interpretation is consistent with the critical methodological position adopted in the present study, in which treatment is considered one component of a multifactorial transmission pathway rather than an isolated causal determinant.

Overall, the current findings should be interpreted as evidence concerning the relative contribution and statistical association of maternal and pregnancy-related characteristics within the studied cohort. This provides a more nuanced interpretation than attributing vertical transmission to a single behavioral or demographic factor.

Fetal Outcomes and Ultrasonographic or Molecular Findings

The fourth research question examined fetal outcomes and ultrasonographic or molecular findings among pregnancies complicated by acute maternal toxoplasmosis. The findings should be interpreted according to the integrated diagnostic framework used in this study, in which maternal serology is followed by gestational assessment, fetal ultrasonography, and molecular testing when clinically indicated.

Ultrasonography provides an important non-invasive means of monitoring pregnancies at risk of congenital toxoplasmosis. Codaccioni et al. (2020) identified intracranial hyperechogenic lesions, ventriculomegaly, periventricular cysts, hepatosplenomegaly, fetal growth restriction, ascites, and increased bowel echogenicity among affected fetuses. Nevertheless, these findings are not pathognomonic for toxoplasmosis, and some congenitally infected fetuses may show no detectable prenatal abnormalities.

Consequently, if the current study identifies normal ultrasound findings among some pregnancies with maternal acute toxoplasmosis, this should not automatically be interpreted as evidence that vertical transmission did not occur. Conversely, the presence of an abnormal ultrasound finding should not independently establish congenital toxoplasmosis. This distinction strengthens the methodological validity of the current study because fetal infection is considered through multiple sources of evidence.

Amniotic-fluid PCR provides a complementary molecular approach because detection of *T. gondii* DNA can provide direct evidence compatible with fetal infection. Franco et al. (2024) reported high specificity and substantial sensitivity for amniotic-fluid PCR, while emphasizing that diagnostic performance depends on gestational age, timing of sampling, laboratory methodology, and clinical circumstances. Souza et al. (2023) similarly demonstrated variability in the diagnostic performance of molecular and serological techniques.

The current study therefore benefits conceptually from treating PCR and ultrasound as complementary rather than interchangeable diagnostic approaches. A positive PCR result provides molecular evidence, whereas ultrasound contributes clinical and structural evidence. The absence of abnormalities on either modality should be interpreted within the sensitivity and timing limitations of the test.

The interpretation of fetal and neonatal outcomes should also extend beyond the immediate prenatal period. Bollani et al. (2022) emphasized that some congenitally infected infants may be asymptomatic at birth, while longer-term ocular and neurological manifestations may emerge later. Guarch-Ibáñez et al. (2024) likewise demonstrated the importance of postnatal assessment in children with congenital toxoplasmosis.

Accordingly, the present findings should distinguish between confirmed fetal infection, probable infection, abnormal fetal findings without molecular confirmation, and apparently unaffected pregnancy/neonatal status. Such classification reduces the risk of inflating the estimated vertical-transmission rate and is consistent with the central methodological principle of the study.

Integrated Discussion of the Four Research Questions

Taken together, the findings should be interpreted as a connected maternal–fetal process rather than as four independent outcomes. The analytical framework developed in this study proposes the sequence:

Acute maternal infection → serological profile → gestational age at infection → maternal and pregnancy-related factors → risk of vertical transmission → fetal assessment → fetal/neonatal outcomes.

This pathway is consistent with the theoretical framework and methodology of the study, which deliberately integrates serological, temporal, maternal, clinical, imaging, and molecular dimensions.

The critical comparison with previous literature indicates that the major contribution of the present study is not simply to reproduce previously established associations. Rather, it attempts to integrate dimensions that have frequently been examined separately. Previous studies have provided extensive evidence concerning seroprevalence, diagnostic accuracy, gestational age, treatment, and fetal outcomes, but substantial methodological heterogeneity remains.

From a methodological perspective, this integration is particularly important because the definition of maternal acute infection directly affects the estimated population at risk of vertical transmission. If women with remote infection are incorrectly classified as having acute infection, the denominator for transmission analysis becomes distorted. Similarly, if abnormal ultrasound findings are classified as congenital infection without molecular or clinical confirmation, transmission rates may be overestimated.

The present study's descriptive–analytical, comparative, and inductive design provides a framework for addressing these problems. The descriptive component establishes the distribution of maternal infection characteristics; the analytical component examines associations between gestational and maternal factors and transmission; the comparative component evaluates differences across relevant groups; and the inductive component interprets the findings in relation to converging and conflicting international evidence.

The literature also indicates that differences between studies should not automatically be interpreted as contradictions. Variation in prevalence, transmission, and fetal outcomes may arise from differences in geographical exposure, diagnostic assays, timing of maternal infection, treatment practices, fetal surveillance, and definitions of congenital infection. Therefore, the present findings should be positioned within these methodological differences rather than compared solely on the basis of numerical magnitude.

Critical Interpretation and Contribution

The critical interpretation of the current findings supports the broader conclusion that acute maternal toxoplasmosis should be assessed through an integrated maternal–fetal diagnostic and analytical pathway. Maternal serology provides the initial evidence of infection, but interpretation of infection timing requires consideration of IgG avidity and, where appropriate, IgA. Gestational age provides an important temporal dimension to transmission risk, while maternal and pregnancy-related characteristics provide additional contextual information. Fetal ultrasonography and molecular testing then provide complementary evidence concerning possible fetal involvement.

This integrated interpretation is consistent with the research gap identified in the study: existing evidence is substantial but fragmented, with many investigations concentrating on individual components of the maternal–fetal pathway.
Accordingly, the scientific value of the present study lies in connecting the four research questions within one analytical pathway rather than interpreting prevalence, transmission, risk factors, and fetal outcomes independently. This approach also corresponds directly to the stated scientific contribution of the study, which emphasizes prospective assessment and integration of serological characteristics, gestational age, maternal factors, and fetal assessment.

Conclusions

The findings of this study indicate that maternal acute Toxoplasma gondii infection should be understood as a multifactorial maternal–fetal process rather than as an isolated serological event. The interpretation of infection requires integration of maternal serology, gestational age, maternal and pregnancy-related factors, fetal assessment, and, when clinically indicated, molecular evidence. The main conclusions are as follows:
Maternal acute toxoplasmosis represents an important obstetric and public-health concern because of its potential for vertical transmission and congenital infection.
Maternal seropositivity does not necessarily indicate recent infection or confirm fetal infection.
Positive IgM alone is insufficient to establish the timing of recent T. gondii infection because IgM antibodies may persist beyond the acute phase.
The combined interpretation of IgM, IgG, and IgG avidity, with IgA when appropriate, provides a more reliable basis for characterizing the timing of maternal infection.
Gestational age at the time of maternal infection is an important component of assessing the likelihood of vertical transmission.
The probability of vertical transmission generally increases with advancing gestational age, whereas earlier maternal infection may be associated with more severe fetal consequences.
Maternal, environmental, dietary, and pregnancy-related characteristics may contribute to differences in infection and transmission patterns and should therefore be considered in the analytical assessment.
The timing of diagnosis and initiation of prenatal treatment is an important component of clinical management, although treatment effects should be interpreted in relation to gestational age and other clinical characteristics.
Fetal ultrasonography provides an important tool for prenatal surveillance but cannot independently confirm or exclude congenital toxoplasmosis.
Amniotic-fluid PCR provides complementary molecular evidence of fetal infection when clinically indicated, but its interpretation depends on sampling time, gestational age, laboratory procedures, and clinical context.
The distinction between confirmed fetal infection, probable infection, and nonspecific fetal abnormalities is essential to avoid overestimating the rate of vertical transmission.
An integrated prospective maternal–fetal approach linking maternal infection, serological profile, gestational timing, maternal factors, vertical transmission, fetal assessment, and fetal/neonatal outcomes provides a more comprehensive framework for studying congenital toxoplasmosis.

Recommendations

Based on the findings and the integrated analytical framework of the study, the following recommendations are proposed:
Adopt integrated serological testing using IgM, IgG, and IgG avidity, with IgA when clinically appropriate.
Avoid diagnosing recent infection based on IgM positivity alone.
Establish standardized diagnostic pathways for pregnant women with suspected acute toxoplasmosis.
Document gestational age accurately at the time of suspected or confirmed maternal infection.
Strengthen systematic fetal surveillance through appropriately scheduled ultrasonographic examinations.
Use amniotic-fluid PCR when clinically indicated and interpret the result according to established diagnostic criteria and sampling timing.
Apply standardized definitions of congenital infection, distinguishing confirmed, probable, and unconfirmed cases.
Record the timing, type, and duration of prenatal treatment to facilitate more accurate interpretation of maternal–fetal outcomes.
Strengthen preventive counseling for pregnant women, particularly regarding undercooked meat, inadequate washing of food, environmental exposure, and other recognized sources of T. gondii infection.

Develop local epidemiological surveillance systems to generate population-specific evidence on maternal toxoplasmosis and associated risk factors.

Extend follow-up beyond delivery in pregnancies with documented or suspected fetal exposure, particularly when clinical or laboratory indicators warrant continued assessment.

Conduct larger prospective and multicenter studies using standardized serological, molecular, ultrasonographic, and clinical criteria to improve the comparability and generalizability of future findings.

References

Bigna, J. J., Tochie, J. N., Tounouga, D. N., Bekolo, A. O., Ymele, N. S., Youda, E. L., Sime, P. S., & Nansseu, J. R. (2020). Global, regional, and country seroprevalence of Toxoplasma gondii in pregnant women: A systematic review, modelling and meta-analysis. Scientific Reports, 10, 12102. https://doi.org/10.1038/s41598-020-69078-9

Buonsenso, D., Pata, D., Turriziani Colonna, A., Iademarco, M., De Santis, M., Masini, L., Conti, G., Molle, F., Baldascino, A., Acampora, A., Luciano, R., Gallini, F., & Valentini, P. (2022). Spiramycin and trimethoprim-sulfamethoxazole combination to prevent mother-to-fetus transmission of Toxoplasma gondii infection in pregnant women: A 28-years single-center experience. The Pediatric Infectious Disease Journal, 41(5), e223–e227. https://doi.org/10.1097/INF.0000000000003469

Fricker-Hidalgo, H., Cimon, B., Chemla, C., Dardé, M.-L., Delhaes, L., L'Ollivier, C., & Villena, I. (2020). Toxoplasma gondii-specific IgG avidity testing in pregnant women. Clinical Microbiology and Infection, 26(11), 1480–1484. https://doi.org/10.1016/j.cmi.2020.04.012

Mandelbrot, L., Kieffer, F., Sitta, R., Laurichesse-Delmas, H., Winer, N., Mesnard, L., Berrebi, A., Le Bouar, G., Bory, J.-P., Cordier, A.-G., Ville, Y., Perrotin, F., Biquard, C., d'Ercole, C., Houfflin-Debarge, V., Villena, I., Thiébaut, R., & TOXOGEST Study Group. (2018). Prenatal therapy with pyrimethamine + sulfadiazine vs spiramycin to reduce placental transmission of toxoplasmosis: A multicenter, randomized trial. American Journal of Obstetrics and Gynecology, 219(4), 386.e1–386.e9. https://doi.org/10.1016/j.ajog.2018.05.031

Rabaan, A. A., Uzairue, L. I., Alfaraj, A. H., et al. (2023). Seroprevalence, risk factors and maternal-fetal outcomes of Toxoplasma gondii in pregnant women from WHO Eastern Mediterranean Region: Systematic review and meta-analysis. Pathogens, 12(9), 1157. https://doi.org/10.3390/pathogens12091157

Romand, S., Wallon, M., Franck, J., Thulliez, P., Peyron, F., & Dumon, H. (2001). Prenatal diagnosis using polymerase chain reaction on amniotic fluid for congenital toxoplasmosis. Obstetrics & Gynecology, 97(2), 296–300. https://doi.org/10.1016/S0029-7844(00)01118-2

Rostami, A., Riahi, S. M., Contopoulos-Ioannidis, D. G., Gamble, H. R., Fakhri, Y., Nourollahpour Shiadeh, M., Foroutan, M., Behniafar, H., Taghipour, A., Maldonado, Y. A., Mokdad, A. H., & Gasser, R. B. (2019). Acute Toxoplasma infection in pregnant women worldwide: A systematic review and meta-analysis. PLoS Neglected Tropical Diseases, 13(10), e0007807. https://doi.org/10.1371/journal.pntd.0007807

Souza, I. M. F. N. B. de, Siqueira, V. da S., Ribeiro, I. da C., Moraes, L. S. P., Prado, D. P. G. do, Rezende, S. R., Costa, W. L. G. da, & Rezende, H. H. A. (2023). Molecular and serological diagnosis of toxoplasmosis: A systematic review and meta-analysis. Revista do Instituto de Medicina Tropical de São Paulo, 65, e19. https://doi.org/10.1590/S1678-9946202365019

Tork, M., Sadeghi, M., Asgarian-Omran, H., Basirpour, B., Ahmadi, S., Ghasemzadeh, F., Sarvi, S., Gholami, S., Hosseini, S. A., Daryani, A., & Aghayan, S. A. (2025). Assessment of simultaneous IgM, IgG avidity, and IgA testing in diagnosis of acute toxoplasmosis in pregnant women: A systematic review and meta-analysis study. [Journal details to be verified from the final publisher record].

Wallon, M., Peyron, F., Cornu, C., Vinault, S., Abrahamowicz, M., Kopp, C. B., Binquet, C., & the Toxoplasmosis Group. (2013). Congenital toxoplasma infection: Monthly prenatal screening decreases transmission rate and improves clinical outcome at age 3 years. Clinical Infectious Diseases, 56(9), 1223–1231. https://doi.org/10.1093/cid/cit032

Wehbe, K., Pencole, L., Lhuaire, M., Sibiude, J., Mandelbrot, L., Villena, I., & Picone, O. (2022). Hygiene measures as primary prevention of toxoplasmosis during pregnancy: A systematic review. Journal of Gynecology Obstetrics and Human Reproduction, 51(3), 102300. https://doi.org/10.1016/j.jogoh.2021.102300

Araujo, R. D., et al. (2020). Treatment of acute toxoplasmosis in pregnancy: Influence in the mother-to-child transmission. Journal of Obstetrics and Gynaecology Canada. https://doi.org/10.1016/j.jogc.2020.04.021

Carlier, Y., et al. (2022). Congenital toxoplasmosis: The state of the art. Frontiers in Pediatrics, 10, 894573. https://doi.org/10.3389/fped.2022.894573

Codaccioni, C., Picone, O., Lambert, V., et al. (2020). Ultrasound features of fetal toxoplasmosis: A contemporary multicenter survey in 88 fetuses. Prenatal Diagnosis, 40(13), 1741–1752. https://doi.org/10.1002/pd.5756

Franco, J. R., et al. (2024). Systematic review and meta-analysis of congenital toxoplasmosis diagnosis: Advances and challenges. Journal of Tropical Medicine, 2024, 1514178. https://doi.org/10.1155/2024/1514178

Fricker-Hidalgo, H., Cimon, B., Chemla, C., Dardé, M.-L., Delhaes, L., L'Ollivier, C., & Villena, I. (2020). Toxoplasma gondii-specific IgG avidity testing in pregnant women. Clinical Microbiology and Infection, 26(11), 1480–1484. https://doi.org/10.1016/j.cmi.2020.04.012

Mulu Gelaw, Y., et al. (2024). Toxoplasma gondii seroprevalence among pregnant women in Africa: A systematic review and meta-analysis. BMC Infectious Diseases. https://pubmed.ncbi.nlm.nih.gov/38781272/

Rabaan, A. A., Uzairue, L. I., Alfaraj, A. H., et al. (2023). Seroprevalence, risk factors and maternal-fetal outcomes of Toxoplasma gondii in pregnant women from WHO Eastern Mediterranean Region: Systematic review and meta-analysis. Pathogens, 12(9), 1157. https://doi.org/10.3390/pathogens12091157

REIV-TOXO Project. (2024). Results from a Spanish cohort of congenital toxoplasmosis (2015–2022): The beneficial effects of prenatal treatment on clinical outcomes of infected newborns. [Journal details to be verified from the final publisher record].

Teimouri, A., Mohtasebi, S., Kazemirad, E., & Keshavarz, H. (2020). Role of Toxoplasma gondii IgG avidity testing in discriminating between acute and chronic toxoplasmosis in pregnancy. Journal of Clinical Microbiology, 58(9), e00505-20. https://doi.org/10.1128/JCM.00505-20

Tork, M., Sadeghi, M., Asgarian-Omran, H., et al. (2025). Assessment of simultaneous IgM, IgG avidity, and IgA testing in diagnosis of acute toxoplasmosis in pregnant women: A systematic review and meta-analysis study. BMC Pregnancy and Childbirth. https://doi.org/10.1186/s12884-025-07580-6

Walana, W., Odai, S. A., & Tamomh, A. G. (2025). Prevalence, risk factors, diagnosis and outcomes of Toxoplasma gondii infection in pregnancy: A review. Parasitology International, 103143. https://doi.org/10.1016/j.parint.2025.103143