Screening for Toxoplasmosis in Pregnant Women in an Effort to Prevent Congenital Toxoplasmosis

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Abstract: This literature review aims to describe toxoplasmosis screening in pregnant women and its relevance in preventing congenital toxoplasmosis. Toxoplasmosis in pregnancy is a serious global health problem, as it can be transmitted transplacentally and cause congenital toxoplasmosis. This condition can cause miscarriage, neurological damage, ocular disorders, and even fetal death, with an estimated 190,100 cases per year. As the disease is usually asymptomatic, toxoplasmosis screening in pregnancy is essential to prevent congenital transmission. The screening strategies vary by country. The United States, Canada, and the United Kingdom do not recommend routine screening, while France, Italy, Austria, and Slovenia have implemented mandatory antenatal screening, and other European countries use a selective approach. In Indonesia, there has been no literature review specifically discussing toxoplasmosis screening during pregnancy. A literature search in English and Indonesian was conducted using PubMed-MEDLINE, Google Scholar, university databases, electronic journals, medical textbooks, and official websites of health organizations. Publications were limited to the last thirty years, focusing on toxoplasmosis screening in pregnancy. Toxoplasmosis screening programs for pregnant women are beneficial in preventing the transmission of *Toxoplasma gondii* infection from mother to fetus, but their effectiveness is greatly influenced by regional prevalence. In countries with low prevalence, routine screening is considered inefficient because it may cause anxiety in pregnant women and unnecessary medical intervention. Conversely, in regions with moderate to high prevalence, screening can provide added value, especially when combined with appropriate therapy and monitoring.

1 INTRODUCTION

Toxoplasmosis is a zoonotic disease caused by the obligate intracellular protozoan *Toxoplasma gondii* (*T. gondii*) that is widespread throughout the world (Stelzer, 2019). Domestic and wild felids are definitive hosts that shed infectious oocysts *T. gondii* in their feces, while humans and warm-blooded animals are intermediate hosts with the infective forms as tachyzoites (acute phase) and bradyzoites (within tissue cysts) (FKUI SPDP, 2021). Transmission to humans occurs through various routes, ranging from ingesting tissue cysts in undercooked meat (commonly pork, lamb, venison), consumption of food or beverages contaminated with environmental oocysts, direct contact with soil contaminated with infected cat feces, to direct human-to-human routes such as transmission of tachyzoites through blood transfusions or transplasental transmission during pregnancy, and transmission of tissue cysts through organ transplantation from infected donors (Araujo, 2024; Naeem, 2023).

Toxoplasma gondii infection affects approximately one-third of the global human population, with low prevalence in North America and Northern Europe, moderate to high prevalence in some Southern and Central European countries, and the highest prevalence was reported in Latin America and tropical African countries (Salari, 2025; Mueller 2021). Globally, the seroprevalence among pregnant women shows 1.9% for IgM and 32.9% for IgG, with the highest prevalence in the Eastern Mediterranean and the Americas and the lowest in the Western Pacific (Bigna, 2020).

Toxoplasmosis during pregnancy is a serious global health problem, as it can cause miscarriage, fetal death, and neurological disorders and disabilities in children. Globally, it is estimated to account for approximately 190,100 congenital toxoplasmosis cases are reported annually, or about 1.5 cases per 1,000 live births (Torgerson, 2013). Prevention of congenital toxoplasmosis is crucial because infection in mothers is generally asymptomatic but can cause serious complications. Systematic screening of all pregnant women, particularly those at increased risk,

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such as cat owners, is not yet a global policy, and in Indonesia there is no literature review specifically addressing this issue. This literature review aims to describe the practice of toxoplasmosis screening in pregnancy and its relevance in congenital toxoplasmosis prevention.

2 LITERATURE REVIEW

A comprehensive search was conducted through electronic database, including PubMed-MEDLINE, Google Scholar, university databases, electronic journals, medical textbooks, and official websites of health organizations. The results of this review are expected to provide a scientific basis for the development of more effective prevention strategies.

Inclusion criteria were articles published in English or Indonesian, focusing on toxoplasmosis in pregnancy, particularly screening and diagnosis, including original research, systematic reviews, meta-analyses, and clinical guideline published within the last 30 years. Exclusion criteria included studies not related to pregnancy, those without full-text access, and duplicate publications. A total of approximately 27 articles were ultimately included in this review.

Epidemiology of Toxoplasmosis in Pregnancy

The seroprevalence of *T. gondii* in pregnant women varies widely across countries and regions, influenced by social, economic, and cultural factors (Salari, 2025; Perdana, 2025). Various systematic reviews and meta-analyses have demontrated that the prevalence of toxoplasmosis remains high, varying between regions and countries. Globally, the seroprevalence of latent infection (IgG positive) in pregnant women has been reported to range from 32.9–36.6%, with an average of around 33–34%, while the prevalence of latent infection from the largest meta-analysis reached 33.8% (95% CI: 31.8–35.9) (Salari, 2025; Bigna, 2020; Rostami, 2020). Acute infection (IgM positive) is relatively lower, around 1.1–4.1% depending on the region, with a global average of 1.9% (Bigna, 2020). Regional distribution shows a consistent pattern, with the highest prevalence in South America (52.8–56.2%) and Africa (around 46.8%), moderate to high in Southern and Central Europe (24–40%), lower in North America (19.7%) and Northern Europe, and the lowest in the Western Pacific region (11.2–11.8%) (Salari, 2025; Bigna, 2020; Rostami, 2020). In Southeast Asia, the prevalence of toxoplasmosis ranges from 4% to 39% (Bigna, 2020). A national systematic review and meta - analysis of *T. gondii* IgG antibody seroprevalence in Indonesia reported 60.1% with a prevalence in pregnant women is 29.4% (Perdana, 2025). A local study in Makassar involving 184 pregnant women reported a latent prevalence of 32.6%, with the main risk factors including contact with cats, consumption of undercooked chicken satay, and drinking of unboiled water (Polanunu, 2021).

Pathophysiology of Toxoplasmosis in Pregnancy

Transmission of *T. gondii* from mother to fetus occurs gradually through the placental barrier, beginning with infection of maternal leukocytes, which act as “Trojan horses” by carrying the parasite to the endometrial layer that forms the maternal part of the placenta (decidua) (Arranz-Solís, 2020). The parasite then invades trophoblast cells, disseminates into the villi core, and finally enters the fetal bloodstream (Arranz-Solís, 2020; Faral-Tello, 2023). The highest risk of vertical transmission is in the third trimester due to thinning of the placental barrier (Faral-Tello, 2023; Robert-Gangneux, 2011). The level of virulence is also influenced by *T. gondii* strains differences (types I, II, III), which have different abilities in invasion, inflammation induction, and immune system evasion (Moghaddami, 2024). Type I strains are highly virulent, easily penetrate the placenta, suppress IL-12 leading to excessive parasite replication, cause tissue damage, increase the risk of miscarriage, and result in severe congenital toxoplasmosis (Arranz-Solís, 2020; Moghaddami, 2024). Type II strains, which are common in humans, have moderate virulence and are associated with chronic infection with the possibility of periodic reactivation (Arranz-Solís, 2020; Moghaddami, 2024). Type III strains are relatively less virulent and generally result in chronic infection without severe symptoms, although vertical transmission may still occur, particularly in immunocompromised mothers (Arranz-Solís, 2020; Moghaddami, 2024).

Immunologically, neutrophils provide the initial defense, followed by dendritic cell activation and a Th1 response that produces IFN-γ to suppress parasite replication (Moghaddami, 2024). Excessive IFN-γ production can trigger trophoblast cell

apoptosis, inhibit trophoblast invasion into decidua, and result in impaired fetal growth or miscarriage (Moghaddami, 2024). A predominant Th2 response supports *T. gondii* replication, but infection can shift the immune balance toward a pro-inflammatory states, characterized by increased cytokines and adhesion molecules, potentially leading to placental damage (Moghaddami, 2024). Maintaining a balance between pro- and anti-inflammatory cytokines is crucial for maintaining pregnancy and preventing complications of congenital toxoplasmosis (Araujo, 2024).

Clinical Manifestations of Toxoplasmosis in Pregnancy

More than 80% of *T. gondii* infections are asymptomatic (Ahmed, 2020). Patients who do experience symptoms generally have mild and nonspecific symptoms, such as a short fever lasting 2-3 days, headache, muscle pain, pharyngitis, hepatosplenomegaly, diffuse non-pruritic maculopapular rash, or painless bilateral cervical lymphadenopathy, while severe cases may present with retinocoroiditis and visual impairment (Ahmed, 2020; Paquet 2018) Toxoplasmosis acquired during pregnancy can cross the placenta and cause congenital toxoplasmosis (Dunn, 1999).

The manifestations of congenital toxoplasmosis depend on the gestational age at the time of infection. The first trimester often results in more severe clinical manifestations, such as abortion, hydrocephalus, mental retardation, and ocular lesions, while in the later trimesters, manifestations are generally milder or subclinical (Durdu, 2023). One rare complication with a poor prognosis is hydranencephaly, which is the absence of the cerebral cortex due to vascular damage, usually resulting in intrauterine death or a life expectancy of <1 year (Hermawan, 2022). Approximately 80% of infants with congenital toxoplasmosis are born without symptoms (Paquet, 2028). In early 1952, Dr. Albert Sabin introduced the classical tetrad describing the clinical minifestations of congenital toxoplasmosis in humans, consisting of retinocoroiditis, intracranial calcifications, hydrocephalus or microcephaly, and psychomotor disorders (FKUI SPDP, 2021). The most common manifestation is retinocoroiditis, while the most severe is hydrocephalus (±4% of cases), with retinocoroiditis that may appear late, even during childhood or adulthood (Dubey, 2021).

Screening of Toxoplasmosis in Pregnancy

Toxoplasmosis screening practices during pregnancy vary across countries. In low prevalence regions (e.g., United Kingdom, United States, Canada), routine screening is not recommended due to cost-effectiveness concerns (Dubey, 2021). In contrast, some European countries and Brazil implement routine or periodic screening for at-risk (seronegative) pregnant women due to higher risk and the presence of more virulent strains (Durdu, 2023). If toxoplasmosis prenatal screening during is not routinely performed in a country or region, testing for *T. gondii* infection is necessary in certain clinical conditions. This approach is known as "opportunistic" screening, which is performed based on maternal or fetal indications, as detailed in Table 1 (Ratha, 2020).

Table 1. Opportunistic Screening Approach for Toxoplasmosis in Pregnancy

Maternal Indication	Fetal Indication
a. Previous history of toxoplasmosis	a. Severe intrauterine growth restriction
b. Fever with lymphadenopathy or rash during pregnancy	b. Polyhydramnios with no identifiable fetal anomalies
c. Immunocompromised condition	c. Placental thickening
d. Engaging in activities with a high risk of infection, such as taking care of cats, eating raw meat or salads, or visiting endemic areas	d. Fetal visceral calcification
	e. Ventriculomegaly with echogenic nodules in the brain parenchyma
	f. Ascites or non-immune fetal hydrops

Diagnosis of Toxoplasmosis During Pregnancy

The definitive diagnosis of acute toxoplasmosis is made by finding tachyzoites in tissue biopsy, bone marrow, cerebrospinal fluid, or ventricles. However, in clinical practise, tachyzoites are difficult to detect using routine staining technique and require a long examination time (FKUI SPDP, 2021). In pregnancy, the diagnosis of toxoplasmosis primarily relies on several tests, including serological tests as the main approach, amniocentesis with polymerase chain reaction (PCR) for *T. gondii*, and ultrasonography (USG) to detect fetal abnormalities (Azis 2022). Serological tests are an important tool because infection induces the production of specific antibodies that can persist for life, thereby enabling both detection of current infection and identification of past exposure (FKUI SPDP, 2021; Kodym 2023).

Serological testing is the first step in screening by detecting IgG, IgM, and IgA antibodies (Fig. 1) (Kodym, 2023; Azis, 2022). IgM appears about one week after infection, peaks at 4–12 weeks, and declines within 9–10 months, although 9–27% may persist for more than 2 years (Ratha, 2020). IgA appears similarly to IgM, peaks slightly later, and persists for 3–4 months (Ratha, 2020). IgG appears 1–2 weeks after infection, peaks at week 12, remains stable for up to 6 months, then declines but persists for life due to the presence of tissue cysts (Paquet, 2018; Ratha, 2020).

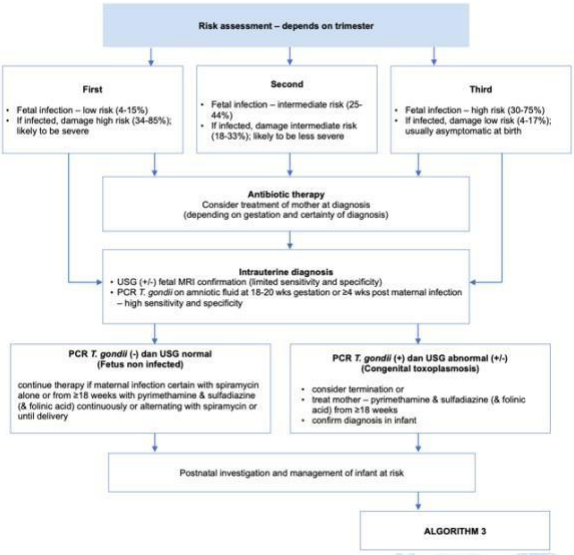

Fig.1 Algorithm I: Antenatal evaluation of toxoplasmosis in pregnancy (Azis, 2022).

Interpretation of serology results determines the phase of infection. Negative IgG and IgM results indicate either no history of infection or a very recent acute infection, but prevention education is necessary and some protocols recommend retesting after 1–6 months or at delivery to detect seroconversion (Azis, 2022; Haslam, 2003). Positive IgG and negative IgM indicate a past infection and no further follow-up is required (Azis, 2022). A positive result for both IgG and IgM antibodies indicates that the infection is a recent infection or it is a false-positive result. A diagnosis of acute toxoplasmosis is confirmed by fourfold rise IgG titers on the second test with an interval of ≥ 3 weeks after the first test, or by seroconversion from negative to positive (FKUI SPDP, 2021). Commercial serological assay may occationally yield inaccurate result, therefore positive antibody findings should be confirmed in a reference toxoplasmosis laboratory (Azis, 2022).

Classically, IgM and IgA antibodies are considered markers of the acute phase, but these antibodies can persist for a long time, leading to potential misinterpretation (Kodym, 2023). To overcome this limitation, additional confirmation is required, namely the IgG avidity test. This test measures the binding affinity of IgG antibodies to the *T. gondii* antigen, which progressively increases after infection as the humoral immune response matures (Kodym, 2023). A high avidity value indicates that the infection occurred at least 3– 4 months prior, making it reliable for ruling out acute infection (Garnaud, 2020).

For pregnant women who are suspected of having or have been diagnosed with toxoplasmosis, a risk assessment for the fetus should be conducted according to the trimester of pregnancy (Fig. 2). It is crucial to explain the risks of vertical transmission to pregnant women, as this can help them decide whether to proceed with amniocentesis or consider terminating the pregnancy, even though they may interpret these risks differently (Azis, 2022).

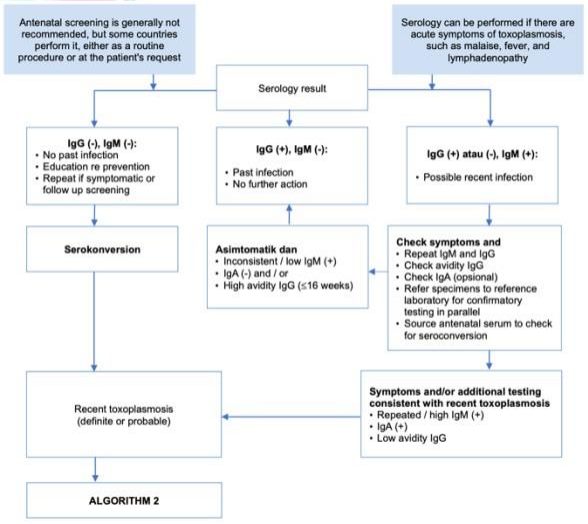

Fig. 2 Algorithm II: Investigation and management of toxoplasmosis in pregnancy (Azis, 2022).

If infection is detected at ≤18 weeks of gestation, immediate administration of spiramycin should be considered (Paquet, 2018). Spiramycin is a macrolide antibiotic that accumulates in the placenta but does not easily cross the placental barrier; therefore, it is useful for preventing vertical

transmission of the parasite to the fetus and is indicated only before infection occurs in the fetus (Paquet, 2018). This medication is administered at a dose of 1 g orally every 8 hours and must be accompanied by regular fetal ultrasound examinations at least once a month to monitor fetal development; treatment must be continued until delivery or until amniocentesis results are available (Azis, 2022). If the amniocentesis result is negative, spiramycin is continued until delivery, but if it is positive or the mother is in the third trimester without amniocentesis, treatment is switched to a combination of pyrimethamine-sulfadiazine with folinic acid supplementation at the recommended dose, namely 50 mg of pyrimethamine once daily, 500 mg of sulfadiazine three tablets twice daily, and 25 mg of folinic acid two capsules weekly (Ahmed, 2020). Pyrimethamine and sulfadiazine have the potential to be toxic in the first trimester (Azis, 2022). Pregnancy termination is considered only in the presence severe anomalies detected on USG, such as hydrocephalus (Azis, 2022).

Ultrasonography findings are not specific for toxoplasmosis, as they may be observed in other congenital infections or genetic diseases, therefore require confirmation through laboratory tests (Moghaddami, 2020). Prenatal diagnosis of toxoplasmosis is most accurate when performed using PCR on amniotic fluid during the second trimester (weeks 17–21) (Romand, 2001). A positive result is sufficient to confirm the presence of congenital toxoplasmosis, whereas a negative result does not completely rule out the possibility of infection because

T. gondii may remain in the placenta and cross the placental barrier several days to several weeks later. Consequently, serial USG monitoring, prophylactic spiramycin therapy, and neonatal evaluation are still required (Dubey, 2021; Ratha, 2020). Amniocentesis is indicated if the mother is diagnosed with a primary infection, serological results are inconclusive for acute infection, or abnormal ultrasound findings suggest congenital toxoplasmosis (Paquet, 2018). This test should be performed at 18 weeks or more of gestation and at least 4 weeks after the mother's suspected infection to reduce the risk of false-negative results (Paquet, 2018).

Screening and Management of Neonates at Risk for Toxoplasmosis

Neonatal screening is not routinely performed, but it can be an alternative if antenatal screening is not available (Azis, 2022). In mothers with suspected or confirmed toxoplasmosis, whether they have received treatment or not, and in cases of negative or positive amniotic fluid PCR, further investigation is required. Tests include neonatal serology (IgM and/or IgA), placental histology, and PCR from blood or cerebrospinal fluid (Fig. 3) (Azis, 2022). Neonatal serum samples should be taken after 10 days of birth to avoid contamination from maternal antibodies (Azis, 2022).

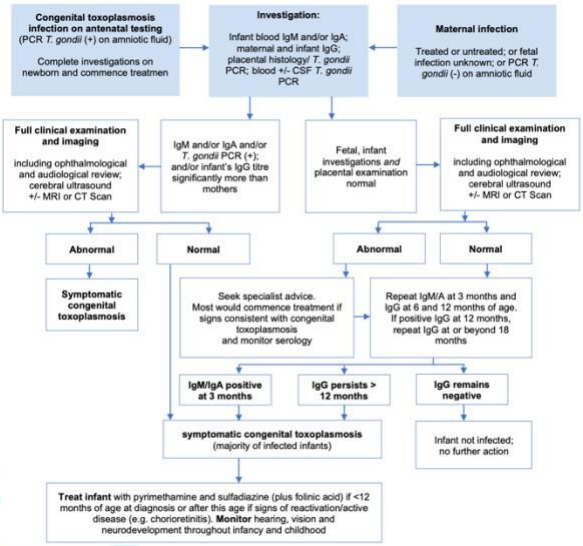

Fig. 3 Algorithm III: Investigation and management of infants at risk of toxoplasmosis (Azis, 2022).

The diagnostic criteria for congenital toxoplasmosis include one of the following: (1) a positive IgG result persisting for more than 12 months (gold standard); (2) a positive IgM and/or IgA result at three months of age; (3) a positive PCR test result for *T. gondii* in amniotic fluid, peripheral blood, cerebrospinal fluid, urine, or other bodily fluids; and (4) positive IgG in the neonate (but negative IgM and IgA) along with serological evidence of acute *T. gondii* infection in the mother during pregnancy with clinical evidence indicative of congenital toxoplasmosis (Azis, 2022; Maldonado, 2017).

Clinical evaluation of infants with suspected congenital toxoplasmosis includes a complete physical examination, neurological, ophthalmological, and audiological evaluation, as well as imaging evaluation (CT scan/MRI/head ultrasound and

abdominal ultrasound) (Azis, 2022; Maldonado, 2017). If congenital toxoplasmosis has not been confirmed, monitoring is performed through a complete clinical evaluation and IgG titer testing every 4-6 weeks until IgG disappears (Maldonado, 2017). The incidence of long-term sequelae, such as chorioretinitis, is high in infants who do not receive therapy, even if they are born without symptoms. Treatment has been shown to reduce the risk of these complications (Azis, 2022). Suspected cases of congenital toxoplasmosis in infants are treated for 12 months with a combination of pyrimethamine, sulfadiazine, and folinic acid. The recommended dosage is as follows (Azis, 2022; Maldonado, 2017):

1. Pyrimethamine: 1-2 mg/kg/12 hours for the first two days, followed by 1 mg/kg/day for 2-6 months, then finally 1 mg/kg/day (three times a week) for a total duration of 12 months.
2. Sulfadiazine: 50-100 mg/kg/12 hours
3. Folinic acid (leucovorin): 10 mg three times a week, to be continued for up to one week after discontinuing pyrimethamine.

Impact of Screening Programs on Pregnant Women

The preventive impact of toxoplasmosis screening programs on pregnant women shows varying results, ranging from no preventable cases to approximately 40 cases of disease per 100,000 pregnancies, influenced by the prevalence of infection, the risk of vertical transmission, the proportion of symptomatic children, the sensitivity of serological tests, and the compliance of pregnant women in following the screening program (Eskild, 1996). The benefits of screening programs also need to consider a number of negative risks, such as induced abortion due to misdiagnosis or maternal anxiety about the risk of disability due to positive or false positive results (Eskild, 1996; Gilbert, 2002). Anxiety in pregnant women may increase cortisol hormones in the body, which can trigger spontaneous abortion (James, 2023; Sastra, 2016). Side effects of drugs during prenatal care (spiramycin, pyrimethamine, and sulfadiazine) can also cause gastrointestinal complaints, skin rashes, and bone marrow depression (Gilbert, 2002). In addition, a nationwide screening program will require high costs, especially in countries with low prevalence, so its efficiency and benefits are still being debated (Eskild, 1996; Gilbert 2002).

Studies conducted in southern Taiwan and Saudi Arabia show that periodic prenatal toxoplasmosis screening is ineffective due to low prevalence, high false positives, and high costs, making prevention education a more appropriate strategy for pregnant women (Lee, 2022; Almogren 2011). In contrast, programs in France and Austria emphasize periodic serological screening with high compliance rates, prenatal diagnosis with amniotic fluid PCR, and monitoring of newborns, which has proven to be more cost-effective, while educating pregnant women remains key to prevention (Dubey, 2021; Prusa, 2017).

3 CONCLUSIONS

Based on the available evidence, the implementation of toxoplasmosis screening during pregnancy should be tailored to regional epidemiological conditions and the availability of healthcare resources. In areas with low prevalence, universal screening is not recommended due to limited cost-effectiveness as well as the risk of false-positive results, unnecessary interventions, and increased anxiety among pregnant women. Therefore, a selective (risk-based) screening approach is preferred, targeting pregnant women with identified risk factors or clinical and ultrasound findings suggestive of possible infection. Conversely, in areas with moderate to high prevalence, universal or periodic screening of seronegative pregnant women may be considered, particularly if supported by adequate diagnostic facilities, confirmatory testing, and appropriate treatment protocols.

For countries such as Indonesia, where seroprevalence is relatively high but national screening policies have not yet been established, a phased approach is recommended. This includes implementing selective screening as an initial strategy, strengthening education for pregnant women to prevent primary infection, and improving access to diagnostic and confirmatory tests. Overall, toxoplasmosis screening during pregnancy can help reduce vertical transmission, but its effectiveness depends on local prevalence as well as the integration of accurate diagnosis, timely treatment, and continuous monitoring.

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