

Toxoplasmosis in Pregnancy: An Integrated Review of General Perspectives and the Sri Lankan Context

NL De Silva, TC Yahathugoda

Department of Parasitology, Faculty of Medicine, University of Ruhuna, Sri Lanka

Correspondence: lalindidesilva@med.ruh.ac.lk

Page | 82

Abstract. *Toxoplasma gondii* is a cosmopolitan zoonotic protozoan with significant public health implications. Recognised primarily as a leading foodborne pathogen, humans can also acquire the infection through other routes. A critical concern arises when primary infection occurs during pregnancy, as this may result in congenital toxoplasmosis, often leading to fetal complications. This review presents a brief overview of global and Sri Lankan studies on toxoplasmosis during pregnancy, with data sourced from PubMed and Google Scholar, alongside a focused examination of Sri Lankan literature. Timely diagnosis and accurate determination of the timing of acute infections are vital for managing acute maternal infections, as prompt treatment can significantly reduce vertical transmission and mitigate long-term fetal consequences. Despite its importance, Sri Lankan literature on the subject remains limited. Available studies indicate substantial exposure to the parasite, alongside a considerable proportion of non-immune pregnant women vulnerable to primary infections during gestation. Furthermore, awareness about toxoplasmosis among this population is notably low, highlighting the need for targeted health education to prevent primary infections during pregnancy. This review also addresses the specific challenges faced in Sri Lanka, including the absence of universal antenatal and neonatal screening programs, limited access to diagnostic facilities, and restricted availability of effective treatments. Strengthening these areas is essential to improve maternal and fetal outcomes. The findings highlight the need for more research and public health interventions in the Sri Lankan context to address the gaps in awareness, prevention, and management of toxoplasmosis during pregnancy.

Keywords. *Toxoplasma gondii*, Pregnancy, Congenital toxoplasmosis, Seroprevalence, Sri Lanka.

INTRODUCTION

Toxoplasma gondii is a zoonotic protozoan with a significant global impact on public health. It is recognised as a leading foodborne infection, although humans can also contract the parasite through other routes. *T. gondii* has an extensive host range, infecting numerous mammalian and avian species. In humans, *T. gondii* is associated with diverse clinical manifestations, including lymphadenitis, ocular complications, and encephalitis, primarily influenced by the immune status of the host [1]. Most immunocompetent individuals remain asymptomatic following infection. However, a unique challenge arises when primary infection occurs during pregnancy as this can lead to congenital toxoplasmosis with severe fetal outcomes [2]. Such morbidities may manifest at birth or emerge later in life, ranging from congenital malformations and prematurity to perinatal death [3]. The consequences are devastating and have a lasting impact on the affected children and

their families. Consequently, toxoplasmosis during pregnancy represents a critical concern that necessitates focused prevention and management efforts.

Toxoplasmosis is a cosmopolitan infection with widespread prevalence worldwide. In 2020, the global seroprevalence of *Toxoplasma* IgM among pregnant women was estimated at 1.9%, whereas IgG seroprevalence was markedly higher at 32.9%. Regionally, the Eastern Mediterranean exhibited the highest IgM seroprevalence, while the American region recorded the lowest. Lower prevalence rates were generally observed in high-income countries [4].

Data on congenital transmission of toxoplasmosis are primarily derived from countries with established prenatal or postnatal surveillance programs, such as France [5]. Despite the significance and ubiquity of toxoplasmosis in Asia, data on congenital transmission in this region remain scarce or nonexistent [5]. Challenges in

diagnosis and the limited availability of suitable diagnostic tools likely contribute to the under-detection of many prenatal infections.

Felids are the only known definitive hosts of *T. gondii*, with domestic cats playing the most significant role in the peri-domestic transmission cycle [6]. The parasite reproduces sexually in the small intestines of felids, releasing oocysts into the environment. Intermediate hosts, including humans, become infected by ingesting material contaminated with oocysts. Inside the body, oocysts release sporozoites which transform into tachyzoites (active and multiplying stage), which spread to various tissues through the bloodstream. Tachyzoites then become dormant bradyzoites in tissue cysts, which persist for life. Felids become infected by consuming tissue cysts through carnivorousism or by ingesting oocysts [6].

Humans can acquire this infection through various means, influenced by cultural practices, dietary habits, maternal lifestyles, and environmental factors that support oocyst survival. Key sources include contact with contaminated soil (often from cat faeces) and consuming raw or undercooked meat, unwashed vegetables, or raw milk. All types of meat—pork, poultry, beef, lamb, game, and processed meats—pose potential risks. Contaminated water and poor food hygiene also increase transmission risk [7]. The infection can spread vertically from mother to fetus during pregnancy [3], through organ transplants, blood transfusions [8, 9] or, rarely, accidental exposure in laboratories [10].

METHODS

A comprehensive search was conducted on PubMed and Google Scholar to identify studies for this literature review. Publications from 2000 onward were included, restricted to free full-text articles in English. Studies were assessed for relevance to the following objectives: (1) providing an overview of toxoplasmosis in pregnancy, including its global impact, transmission, clinical manifestations, diagnosis, treatment, and prevention through health education; (2) summarising the literature on toxoplasmosis in pregnancy in Sri Lanka; and (3) exploring challenges related to toxoplasmosis in Sri Lanka. The number of references was selected per the journal's policy.

TRANSPLACENTAL TRANSMISSION AND ACUTE TOXOPLASMOSIS DURING PREGNANCY

Transplacental transmission of *T. gondii* occurs when a woman acquires a primary infection during pregnancy. Rare cases involve persistent parasitemia from infections shortly before pregnancy, reactivated disease in HIV-infected mothers, or reinfection with a different strain in an immune mother during pregnancy [1]. The gestational age at the time of infection is a critical factor influencing both transplacental transmission and the severity of the disease [1, 11]. Early pregnancy transmission is less efficient, with negligible risk near conception, rising to 10% by the end of the first trimester, 30–54% by the second trimester, and over 60%, or even 90%, in the final weeks of gestation [1, 12]. The severity of congenital infection is inversely proportional to the gestational age at infection. Early gestational infections are more likely to result in severe fetal outcomes compared to those occurring later in pregnancy [1, 3].

Most pregnant women with acute *T. gondii* infection remain asymptomatic [13, 14]. Only a minority exhibit mild flu-like symptoms, including malaise, fatigue, fever, lymphadenopathy, or, rarely, visual disturbances due to chorioretinitis [13]. Consequently, acute infections often go unnoticed and untreated, complicating efforts to prevent congenital transmission [15]. Notably, many mothers of affected children do not recall a febrile illness during gestation which could be attributed to acute toxoplasmosis [16].

THE BURDEN OF CONGENITAL TOXOPLASMOSIS

A 2013 systematic review estimated the annual global burden of congenital toxoplasmosis at 190,100 cases, corresponding to a total of 1.20 million disability-adjusted life years (DALYs). The burden was particularly significant in South America, the Middle East, and low-income regions [17]. More recent studies indicate a decline in seroprevalence, suggesting a reduced rate of congenital toxoplasmosis [18]. Several factors contribute to this decline: improved farming practices, such as vaccinating sheep and properly cooking or freezing meat, have reduced exposure to

tissue cysts and bradyzoites. Better hygiene in food and water, fewer stray cats, keeping pet cats indoors, feeding them commercial food, and securing play areas have minimised oocyst exposure. Screening of blood and organ donors, milk pasteurisation, and health education and screening programs have further contributed [18]. However, much of this data has been generated in high- and middle-income countries, with limited contributions from low and lower-middle-income nations. Consequently, these findings may not fully apply to regions like Asia including Sri Lanka, where robust data are still lacking. Therefore, region-specific research is required to generate accurate data.

CLINICAL MANIFESTATIONS OF CONGENITAL TOXOPLASMOSIS

Congenital toxoplasmosis presents a wide range of clinical manifestations, influenced by the timing of maternal infection and host-parasite genetics [1]. Over 85% of affected neonates are asymptomatic at birth, with symptoms often appearing later in life [19]. The condition can affect multiple systems, causing long-term complications like chorioretinitis, seizures, cognitive impairment, motor dysfunction, and cerebellar abnormalities, sometimes emerging months or years after birth [1]. Additional complications include sensorineural hearing loss, nephrosis, hematologic disorders, hepatosplenomegaly, endocrinopathies, and myocarditis [3, 11]. Severity varies, from neonatal symptoms to delayed adolescence manifestations, with over 82% of subclinical cases at birth developing retinal disease. The classic triad—retinochoroiditis, hydrocephalus, and cerebral calcifications—is rare, and symptoms often overlap with other congenital infections like CMV or rubella. Rarely, particularly in HIV-infected mothers or newborns, the infection can progress rapidly, affecting the central nervous system, heart, and lungs [1]. Untreated or poorly treated cases carry a high risk of neurological and developmental complications. The risk of early and long-term morbidity is highest when maternal seroconversion occurs between 24

and 30 weeks of gestation, with significant risks also present during the second and third trimesters [19]. Therefore, accurate dating of maternal infection is critical for assessing fetal impact and initiating proper treatment.

CONFIRMING THE PRIMARY INFECTION AND ESTIMATION OF ITS TIME (DATING) DURING PREGNANCY

Routine prenatal screening and detecting seroconversion during gestation is considered the most reliable indicator of primary infection and provides the best estimation of the timing of acute infection [5, 15, 20]. The absence of prenatal screening programs in many countries, such as Sri Lanka, contributes to the lack of sequential screening data and the underdiagnosis of acute infections during pregnancy.

Diagnosing an acute primary infection during pregnancy mainly relies on serological testing. The presence of anti-*Toxoplasma* IgG antibodies, either preconceptionally or during early prenatal screening, indicates immune protection against an acute primary infection during gestation [1]. In non-immune mothers, diagnosis can be achieved in several ways; (1) Detection of anti-*Toxoplasma* IgM, IgA or IgE antibodies. (2) seroconversion from IgG negative to IgG positive status (usually in combination with the detection of IgM, IgA or IgE antibodies) (3) IgG avidity test (4) greater than 4-fold rise of IgG titers in paired samples collected two weeks apart [15, 19, 21]. After primary infection, IgM and IgA antibodies appear within a week, peak at one month, and decline to undetectable levels within weeks to months, but IgM can persist for years in some cases (Figure 1). IgE peaks at three months and rapidly becomes undetectable. IgG antibodies rise 1–3 weeks after IgM, plateau at 2–3 months, and then gradually decrease, persisting at low levels for life [23]. A positive IgG without IgM rules out recent infection, often eliminating the need for further testing in immunocompetent mothers. Alternatively, repeating IgG titers after 2–3 weeks can identify a recent infection through a rising titer. A negative IgM excludes recent infection, while a positive IgM followed by IgG confirms it.

IgM antibodies can either decline to undetectable levels within several weeks or months or persist for over a year. This variability complicates the interpretation of IgM results, especially in the third trimester, as negative IgM levels at this stage may simply indicate that the antibodies have already appeared and disappeared. Consequently, IgM is considered a more reliable marker for recent infection during the first and second trimesters [19]. Additionally, IgM testing can yield false positives due to cross-reactivity, where natural IgM antibodies react with *Toxoplasma* antigens [22]. The possibility of persistence of IgM for over a year, complicates its interpretation, particularly in the third trimester, where negative IgM may indicate that antibodies have appeared and disappeared. Therefore, IgM is more reliable for detecting recent infections in the first and second trimesters [19]. Additionally, false positives can occur due to cross-reactivity with natural IgM antibodies [22].

The IgG avidity test measures the bond strength between anti-*Toxoplasma* IgG antibodies and antigens, which is weak during acute infection and strengthens over time. It helps estimate the timing of infection from a single serum sample and distinguishes between primary infection and reactivation, particularly in pregnant or immunosuppressed patients [19, 22]. Avidity typically shifts from low to high 5–6 months after acute infection, with low avidity persisting for 3–4 months in primary infections during pregnancy [22]. Most commercial tests use a 16-week cutoff for interpretation [24]. A high avidity result rules out primary infection within the last 16 weeks and, in the first trimester, confirms infection occurred before conception. In cases where IgM serology is difficult to interpret, the avidity test helps by clarifying if the IgM represents a recent infection or a persistent titer from earlier.

Conversely, a low avidity result may indicate a recent primary infection within the past 16 weeks but cannot confirm it, especially early in pregnancy. In the third trimester, low avidity strongly suggests infection occurred during gestation. However, persistent low avidity in

some pregnant women, influenced by immune responses or antibiotics, complicates interpretation [25]. While low avidity indicates a higher risk of congenital transmission, high avidity signifies minimal risk. Decisions on further investigation and management should consider these factors [22].

Maternal acute infections do not always result in fetal infection. Therefore, suspected or confirmed maternal infections should be investigated with PCR testing on amniotic fluid, to confirm foetal infection. PCR has 86.3–98.3% sensitivity and 100% specificity for diagnosing fetal *Toxoplasma* infection [1, 26]. This method minimizes the need for more invasive procedures on the fetus or newborn [19, 27]. Amniocentesis is recommended after 18 weeks of gestation for mothers who have serology of acute infection or ultrasound signs of foetal infection but not for indeterminate serology [26]. It can also confirm or rule out foetal infection in the third trimester, potentially avoiding unnecessary newborn treatment [27]. The procedure carries a low foetal loss risk (1–2%), especially after 18 weeks [28]. The Sri Lanka College of Obstetricians and Gynaecologists advises amniocentesis where expertise is available, delaying it until 21 weeks and 6–8 weeks post-infection to reduce false negatives [29].

TREATMENT OF TOXOPLASMOSIS DURING PREGNANCY

Treating acute infection during pregnancy reduces vertical transmission, lowering the risk and severity of congenital toxoplasmosis in the fetus and newborn [11, 15]. Prenatal treatment decreases severe and mild case numbers, birth manifestations, and late complications, highlighting the importance of early diagnosis and treatment [30]. Similarly, treating infected neonates or infants within the first year significantly improves long-term outcomes [16].

When a primary infection is diagnosed or cannot be ruled out within the first 18 weeks of gestation, spiramycin is recommended to prevent vertical transmission [13, 19].

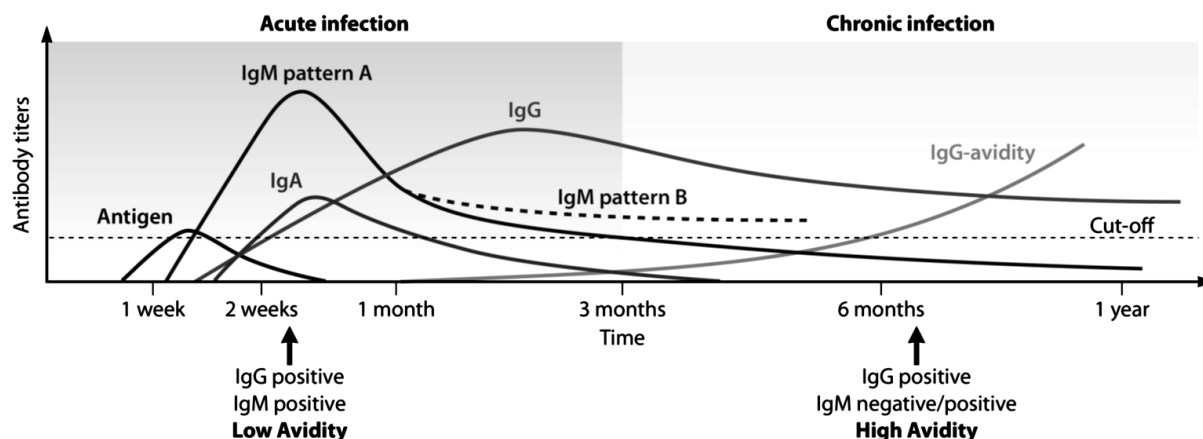


Figure 1. *Toxoplasma* serological profile following acute infection and the changing pattern of IgM, IgG, and IgG avidity over time following primary infection. IgM pattern A depicts the typical IgM response and IgM pattern B depicts the long-term IgM persistence [22].

Spiramycin, a macrolide antibiotic that concentrates in the placenta, reduces parasite load but does not treat the fetus directly. Its efficacy in preventing transmission is estimated at over 60% [1], supported by a recent meta-analysis showing significant reductions in vertical transmission with spiramycin treatment [31]. After 18 weeks of gestation, confirmed foetal infection warrants switching from spiramycin to pyrimethamine and sulfadiazine with folinic acid, continuing through gestation and the infant's first year [1, 31]. This combination achieves higher drug concentrations in foetal tissues, effectively targeting the parasite. Some centres start this therapy earlier, reporting reduced vertical transmission and lower rates of cerebral toxoplasmosis [32]. However, it may lead to negative amniotic fluid PCR results, complicating management decisions. While treatment regimens vary by region, these drugs remain the standard of care to date [31].

THE ROLE OF HEALTH EDUCATION IN PREVENTING ACUTE TOXOPLASMOSIS DURING PREGNANCY

Understanding the life cycle of *T. gondii* is essential for minimising exposure to key risk factors. These include consuming raw or undercooked meat, poor hand hygiene, inadequate cleaning of cooking utensils,

drinking unfiltered water, soil contact, handling cat litter, and travelling to high-risk regions [33]. Pregnant women require special attention, with health education efforts primarily focused on preventing congenital toxoplasmosis. Evidence states that providing dietary guidance, promoting safe behaviours (avoiding risk factors), and taking environmental precautions can significantly reduce the risk of *T. gondii* infection in pregnant women and those of childbearing age [34]. Systematic reviews have confirmed that hygiene measures are effective as the primary prevention method during pregnancy [35].

SRI LANKAN LITERATURE ON TOXOPLASMOSIS IN PREGNANCY

A study published in 1995 examined two groups of pregnant women in Colombo: one group with a history of threatened or habitual abortions and the other with no such history (Table 1). The study tested anti-*Toxoplasma* antibodies in these women and found no significant difference in seropositivity rates between the two groups, nor any association with cat ownership [36]. Only the abstract was available for review of this study, therefore the seroprevalence rates could not be documented (This study, though not meeting the review's inclusion criteria, was included due to the limited available references on toxoplasmosis in Sri Lanka).

Table 1. Summary of studies addressing toxoplasmosis in Sri Lanka

Citation and year	Period of study	Number of participants	Key findings
Ekanayake, 1995 [36]	Data not available	• Pregnant women -418 • Habitual abortions -134	• No significant differences between <i>T. gondii</i> antibody prevalence in women with a history of abortions and those without, or between women with threatened and habitual abortions. • Seropositivity was not related to cat ownership.
Subasinghe, 2011 [37]	2009-2010	• Pregnant women -100 • Spontaneous miscarriage -100	• No significant differences between IgG prevalence among the pregnant group (28%) and the spontaneous miscarriage group (17%) • Significant risk factors: not identified
Iddawela, 2015 [38]	2010-2013	• Total -103 • Pregnant women -30	• In-house ELISA developed (sensitivity: 95.3%, specificity: 98.3%) • <i>Toxoplasma</i> avidity test ELISA could distinguish acute from chronic phases in pregnant mothers
Iddawela, 2017 [39]	2010-2013	• Pregnant women -536	• IgG positivity: 29.9% and IgM positivity: 2(0.37%) • Seroprevalence in T1, T2 & T3: 30.4%, 30.6% and 26.1% respectively • Significant risk factors: preparation/selling raw meat, household gardening
Chandrasena, 2016 [40]	2014	• Pregnant women -293	• IgG positivity: 12.3% and IgM positivity: zero • Significant risk factors: not identified • <i>Toxoplasma</i> awareness: 4.4%

A case-control study in Colombo investigated the seroprevalence of *T. gondii* among a group of healthy pregnant women (within 28 weeks of gestation) and a group who had experienced a spontaneous miscarriage within the previous six months. Among women who tested positive for IgG antibodies, 46.7% had experienced spontaneous miscarriages. In comparison, 58.4% of women who were seronegative for the antibodies had a history of miscarriages. However, the difference between the two groups was not statistically significant [37]. This study also found no significant associations between seropositivity and known risk factors. However, the finding that over 75% of women of childbearing age were non-immune highlighted an important public

health concern with the need for educational programs to prevent infection during pregnancy. ELISA is the most widely used serological assay for screening and diagnosis of toxoplasmosis. In resource-limited settings like Sri Lanka, the high cost of commercially available kits prompted the development of an in-house ELISA assay. This in-house test demonstrated comparable sensitivity and specificity to commercial kits [38]. The study, which involved sera from pregnant mothers, concluded that this ELISA could be effectively used for diagnosing toxoplasmosis in pregnant women. It further evaluated a *Toxoplasma* avidity test ELISA and concluded that it can be used to screen

pregnant mothers successfully for acute infections.

A cross-sectional study conducted among pregnant women attending antenatal care at Teaching Hospital Peradeniya found a 29.9% anti-*Toxoplasma* IgG seroprevalence, while only 0.37% (two mothers) tested positive for IgM antibodies [39]. This study identified handling and selling raw meat and household gardening as significant risk factors. However, no significant associations were found with owning domesticated cats or consuming locally produced meat or dairy products. While the seroprevalence indicated considerable exposure, 70.1% of the women were seronegative.

Another survey evaluated the prevalence, risk factors and awareness of toxoplasmosis among pregnant women in the Gampaha district [40]. Among 293 participants, 12.3% were seropositive for IgG antibodies, while none tested positive for IgM. This study also demonstrated a large non-immune population. Although no significant associations with risk factors were identified, there was a marginally significant link between seroprevalence, and the frequent consumption of commercially prepared meals (weekly or more) based on bivariate analysis. Notably, awareness of toxoplasmosis was strikingly low at 4.4%.

CHALLENGES WITH TOXOPLASMOSIS IN PREGNANCY IN THE SRI LANKAN CONTEXT

This review highlights the limited availability of Sri Lankan literature on toxoplasmosis in pregnancy and the need for further studies to generate essential data. The existing research reveals variability in exposure to the infection across different settings, with IgG seroprevalence rates reported as 12.3%, 22.5%, and 29.9%. Notably, the highest exposure was observed among mothers attending antenatal care in Peradeniya (29.9%), compared to the lowest (12.3%) in Gampaha, highlighting regional differences. However, all studies have shown that most pregnant women (>70%) are non-immune, placing them at significant risk for primary infection during pregnancy. This finding highlights the critical importance of health

education and primary prevention of toxoplasmosis, which should be integral to antenatal care in Sri Lanka. Furthermore, awareness data, available from only one study, reveal alarmingly low awareness levels, indicating that pregnant women are inadequately informed about the risks and preventive measures, leaving them vulnerable to infection during gestation.

There is no universal prenatal screening program for toxoplasmosis in Sri Lanka, making it challenging to detect acute infections in pregnant mothers of which the majority are asymptomatic. Consequently, most infections are likely to remain undiagnosed and untreated. Similarly, the absence of universal newborn screening means that many infected newborns, who are often asymptomatic at birth, are not identified and do not receive timely treatment during their first year of life. This increases the risk of developing sequelae, such as neurological or ocular manifestations and learning difficulties, impacting both the child and the family in the long run. These untreated children may only be diagnosed later in life when complications arise, representing considerable morbidity from a preventable and treatable condition. Furthermore, they remain at risk of reactivation of the latent infection in the event of immunosuppression, because the treatments do not eradicate tissue bradyzoites. As such, toxoplasmosis poses an insidious threat.

The most reliable method of dating a primary *T. gondii* infection is through seroconversion, but without a routine prenatal screening program, seroconversion often goes undetected in Sri Lanka. The diagnosis of a primary infection in Sri Lanka is usually pursued only in symptomatic mothers, in cases where unusual findings are observed in the fetus or following a miscarriage. Diagnosis in the local setting typically relies on detecting IgG and IgM antibodies, although this approach has several limitations, such as the long-term persistence of IgM antibodies, which can complicate interpretation. This routine serological testing is available only in a few centres, making accessibility a significant challenge. The IgG avidity test, a valuable tool for dating recent

primary infections, is not available in Sri Lanka, further complicating the dating process.

For diagnosed or highly suspected maternal infections, the Sri Lanka College of Obstetricians and Gynaecologists recommends confirming fetal diagnosis through amniocentesis, provided that the expertise and resources are available. However, subsequent PCR testing of the amniotic fluid is hindered by its limited availability and cost. Currently, PCR testing is not offered in the government sector, but it may be accessible in a few research centres or private facilities. These challenges highlight the need for improved diagnostic infrastructure and the need for improved access to testing and screening.

Management of toxoplasmosis in Sri Lanka is challenging due to the inconsistent availability of key drugs such as spiramycin, pyrimethamine, and sulfadiazine. The procurement process for these medications is often difficult and time-consuming, which increases the risk of vertical transmission and the likelihood of chronic sequelae in the baby. In the absence of these first-line treatments, alternative options may need to be considered in the Sri Lankan context. These alternatives include other macrolides such as clindamycin, azithromycin, and clarithromycin, or combination drugs like Fansidar (pyrimethamine with sulfadoxine) and co-trimoxazole (trimethoprim with sulfamethoxazole) [41]. Ensuring the availability of first-line therapies to optimize outcomes for both the mother and the baby is important.

Considering the improved hygiene, living standards, and urbanisation in Sri Lanka over recent decades, the seroprevalence of *T. gondii* infections may have decreased. However, this assumption cannot be confirmed without specific data, because similar trends may not apply uniformly across all areas of the country. Stray cats, abundant in Sri Lanka to date, pose a constant risk of exposure to *Toxoplasma* oocysts. Although consuming undercooked meat is not a primary mode of transmission in Sri Lanka, there remains a risk of infection during meat preparation or selling. For instance,

individuals may acquire the infection through handling contaminated meat and consequent accidental contact with mucous membranes or tasting meat curries before they are sufficiently cooked or while meat seasoning [42].

CONCLUSIONS AND RECOMMENDATIONS

Evidence and data on toxoplasmosis in pregnancy are limited in Sri Lanka. More studies are recommended to generate robust evidence regarding the impact of congenital toxoplasmosis. The available data highlight a large non-immune population among pregnant women, while also showing significant exposure rates to the *Toxoplasma* parasite. Non-immune pregnant women are particularly susceptible to acquiring a primary infection during pregnancy, which poses the risk of vertical transmission and harmful fetal outcomes. It is recommended that health education programs be implemented to raise awareness and promote the avoidance of significant risk factors to prevent primary infections during pregnancy.

REFERENCES

1. Farrar J, Hotez PJ, Junghanss T, Kang G, Lalloo D, White NJ. Manson's Tropical Diseases. 23 ed: Saunders Ltd.; 2013 9th December 2013. 1360 p.
2. Centers for Disease Control and Prevention. About toxoplasmosis. Online 2024 [updated 10 September 2024]. Available from: <https://www.cdc.gov/toxoplasmosis/about/index.html>.
3. Hampton MM. Congenital toxoplasmosis: a review. Neonatal Netw. 2015;34(5):274-8.
4. Bigna JJ, Tochie JN, Tounouga DN, Bekolo AO, Ymele NS, Youda EL, et al. Global, regional, and country seroprevalence of *Toxoplasma gondii* in pregnant women: a systematic review, modelling and meta-analysis. Sci Rep. 2020;10(1):12102.
5. Dubey J, Murata F, Cerqueira-Cézar C, Kwok O, Villena I. Congenital toxoplasmosis in humans: an update of worldwide rate of congenital infections. Parasitology. 2021;148(12):1406-16.
6. Prevention CfDCa. Toxoplasmosis [Available from: <https://www.cdc.gov/dpdx/toxoplasmosis/index.html>].
7. Thebault A, Kooh P, Cadavez V, Gonzales-Barron U, Villena I. Risk factors for sporadic toxoplasmosis: a systematic review and meta-

- analysis. Microbial Risk Analysis. 2021; 17:100133.
8. Khurana S, Batra N. Toxoplasmosis in organ transplant recipients: Evaluation, implication, and prevention. Tropical Parasitology. 2016;6(2):123-8.
9. Alvarado-Esquivel C, Sánchez-Anguiano LF, Hernández-Tinoco J, Ramos-Nevarez A, Estrada-Martínez S, Cerrillo-Soto SM, et al. Association between *Toxoplasma gondii* infection and history of blood transfusion: a case-control seroprevalence study. J Int Med Res. 2018;46(4):1626-33.
10. Herwaldt BL. Laboratory-acquired parasitic infections from accidental exposures. Clin Microbiol Rev. 2001;14(4):659-88.
11. Deganich M, Boudreaux C, Benmerzouga I. Toxoplasmosis infection during pregnancy. Tropical Medicine and Infectious Disease. 2022;8(1):3.
12. Blaszkowska J, Górska K. Parasites and fungi as a threat for prenatal and postnatal human development. Annals of parasitology. 2014;60(4).
13. Goldstein EJ, Montoya JG, Remington JS. Management of *Toxoplasma gondii* infection during pregnancy. Clin Infect Dis. 2008;47(4):554-66.
14. Boyer K, Hill D, Mui E, Wroblewski K, Karrison T, Dubey J, et al. Unrecognised ingestion of *Toxoplasma gondii* oocysts leads to congenital toxoplasmosis and causes epidemics in North America. Clin Infect Dis. 2011;53(11):1081-9.
15. Rostami A, Riahi SM, Contopoulos-Ioannidis DG, Gamble HR, Fakhri Y, Shiadeh MN, et al. Acute *Toxoplasma* infection in pregnant women worldwide: A systematic review and meta-analysis. PLoS Negl Trop Dis. 2019;13(10):e0007807.
16. Boyer KM, Holfels E, Roizen N, Swisher C, Mack D, Remington J, et al. Risk factors for *Toxoplasma gondii* infection in mothers of infants with congenital toxoplasmosis: implications for prenatal management and screening. Am J Obstet Gynecol. 2005;192(2):564-71.
17. Torgerson PR, Mastroiacovo P. The global burden of congenital toxoplasmosis: a systematic review. Bull World Health Organ. 2013; 91:501-8.
18. Milne GC, Webster JP, Walker M. Is the incidence of congenital toxoplasmosis declining? Trends in parasitology. 2023;39(1):26-37.
19. Bollani L, Auriti C, Achille C, Garofoli F, De Rose DU, Meroni V, et al. Congenital toxoplasmosis: the state of the art. Frontiers in paediatrics. 2022; 10:894573.
20. Montoya JG. Systematic screening and treatment of toxoplasmosis during pregnancy: is the glass half full or half empty? Am J Obstet Gynecol. 2018;219(4):315-9.
21. Cañedo-Solares I, Ortiz-Alegria L, Figueroa-Damián R, Bustos-Bahena M, González-Henkel H, Calderón-Segura E, et al. Toxoplasmosis in pregnancy: determination of IgM, IgG and avidity in filter paper-embedded blood. J Perinatol. 2009;29(10):668-72.
22. Teimouri A, Mohtasebi S, Kazemirad E, Keshavarz H. Role of *Toxoplasma gondii* IgG avidity testing in discriminating between acute and chronic toxoplasmosis in pregnancy. J Clin Microbiol. 2020;58(9):10.1128/jcm. 00505-20.
23. Dard C, Fricker-Hidalgo H, Brenier-Pinchart M-P, Pelloux H. Relevance of and new developments in serology for toxoplasmosis. Trends in parasitology. 2016;32(6):492-506.
24. Garnaud C, Fricker-Hidalgo H, Evengård B, Álvarez-Martínez MJ, Petersen E, Kortbeek LM, et al. *Toxoplasma gondii*-specific IgG avidity testing in pregnant women. Clin Microbiol Infect. 2020;26(9):1155-60.
25. Findal G, Stray-Pedersen B, Holter EK, Berge T, Jennum PA. Persistent low *Toxoplasma* IgG avidity is common in pregnancy: experience from antenatal testing in Norway. PLoS One. 2015;10(12):e0145519.
26. Robert MG, Brenier-Pinchart M-P, Garnaud C, Fricker-Hidalgo H, Pelloux H. Molecular diagnosis of toxoplasmosis: recent advances and a look to the future. Expert Rev Anti Infect Ther. 2021;19(12):1529-42.
27. Prusa A-R, Kasper D, Pollak A, Olischar M, Gleiss A, Hayde M. Amniocentesis for the detection of congenital toxoplasmosis: results from the nationwide Austrian prenatal screening program. Clin Microbiol Infect. 2015;21(2):191. e1- e8.
28. Padeniya A, Dias T. Invasive prenatal testing at a Tertiary Fetal Medicine referral center in Sri Lanka: A service evaluation audit. 2015.
29. Shemoon Marleen AHB, Mangala Dissanayaka, U.D.P Rathnasiri, T. Kadotgajan, Pradeep De Silva. The investigation and management of the small-for-gestational-age fetus & fetal growth restriction. Sri Lanka Journal of Obstetrics and Gynaecology 2023.
30. McLeod R, Lykins J, Gwendolyn Noble A, Rabiah P, Swisher CN, Heydemann PT, et al. Management of congenital toxoplasmosis. Current Pediatrics Reports. 2014; 2:166-94.
31. Montoya JG, Laessig K, Fazeli MS, Siliman G, Yoon SS, Drake-Shanahan E, et al. A fresh look at the role of spiramycin in preventing a neglected disease: meta-analyses of observational studies. Eur J Med Res. 2021;26(1):143.
32. Mandelbrot L, Kieffer F, Sitta R, Laurichesse-Delmas H, Winer N, Mesnard L, et al. Prenatal therapy with pyrimethamine+ sulfadiazine vs spiramycin to reduce placental transmission of

- toxoplasmosis: a multicenter, randomised trial. Am J Obstet Gynecol. 2018;219(4):386. e1-. e9.
33. Rajapakse S, Weeratunga P, Rodrigo C, de Silva NL, Fernando SD. Prophylaxis of human toxoplasmosis: a systematic review. Pathogens and global health. 2017;111(7):333-42.
 34. Gollub EL, Leroy V, Gilbert R, Chêne G, Wallon M. Effectiveness of health education on Toxoplasma-related knowledge, behaviour, and risk of seroconversion in pregnancy. Eur J Obstet Gynecol Reprod Biol. 2008;136(2):137-45.
 35. Wehbe K, Pencole L, Lhuair M, Sibiude J, Mandelbrot L, Villena I, et al. Hygiene measures as primary prevention of toxoplasmosis during pregnancy: A systematic review. Journal of Gynecology Obstetrics and Human Reproduction. 2022;51(3):102300.
 36. Ekanayake S, Kurukulasuriya N. Prevalence of antibodies to *Toxoplasma gondii* in pregnant women. 1995.
 37. Subasinghe S, Karunaweera N, Kaluarachchi A, Abayaweera C, Gunatilake M, Ranawaka J, et al. *Toxoplasma gondii* seroprevalence among two selected groups of women. Sri Lankan Journal of Infectious Diseases. 2011;1(1).
 38. Iddawela D, Ehambaram K, Kumarasiri P, Wijesundera S. Development and validation of an Enzyme Linked Immunosorbent Assay (ELISA) test for the diagnosis of toxoplasmosis in Sri Lanka. Ceylon Med J. 2015;60(3).
 39. Iddawela D, Vithana SMP, Ratnayake C. Seroprevalence of toxoplasmosis and risk factors of *Toxoplasma gondii* infection among pregnant women in Sri Lanka: a cross-sectional study. BMC Public Health. 2017; 17:1-6.
 40. Chandrasena N, Herath R, Rupasinghe N, Samarasinghe B, Samaranayake H, Kastuririratne A, et al. Toxoplasmosis awareness, seroprevalence and risk behaviour among pregnant women in the Gampaha district, Sri Lanka. Pathogens and global health. 2016;110(2):62-7.
 41. Milewska-Bobula B, Lipka B, Gołąb E, Dębski R, Marczyńska M, Paul M, et al. Recommended management of *Toxoplasma gondii* infection in pregnant women and their children. Przegl Epidemiol. 2015;69(2):291-8.
 42. Mirza Alizadeh A, Jazaeri S, Shemshadi B, Hashempour-Baltork F, Sarlak Z, Pilevar Z, et al. A review on inactivation methods of *Toxoplasma gondii* in foods. Pathogens and Global Health. 2018;112(6):306-19.