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CONGENITAL TOXOPLASMOSIS: A SYSTEMATIC REVIEW ON EPIDEMIOLOGY, CLINICAL MANIFESTATIONS, AND DIAGNOSIS IN PEDIATRICS

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Luiz Eduardo Falqueti Val[1], Julia Sousa Lombardi[2], Rafaela Minatel Prevelato[3], Ana Helisa Cardoso Machado[4], João Vitor Zampieri Pontes[5], Isadora Neves Tasso[6], Maria Eugênia Alves Martins de Araújo Tristão[7].

ABSTRACT

Objective: The general objective of the present study is to analyze the scientific production on congenital toxoplasmosis in pediatrics, seeking to identify the main methods used in the diagnosis and treatment of this pathology. **Methodology:** This is a systematic review focused on understanding the main aspects that permeate congenital toxoplasmosis in the pediatric population. The research was guided by the question: "What are the main aspects that permeate the development of congenital toxoplasmosis in pediatrics, as well as what are the main clinical repercussions and the diagnostic and therapeutic methods used in clinical practice?"element. To find answers, searches were performed in the PubMed database using six descriptors combined with the Boolean term "AND". This resulted in 91 articles. 20 articles were selected for analysis and 10 articles were used to compose the collection. **Results:** Congenital Toxoplasmosis continues to be an important public health problem, due to the potential serious complications it presents for the fetus and the newborn. The reduction in seroprevalence in some regions shows progress, but highlights the need to expand preventive strategies, especially among women of childbearing age. Vertical transmission of *Toxoplasma gondii* is directly related to the gestational age of maternal infection, being more severe when it occurs in early pregnancy. Although treatment with antiparasitic drugs is effective in reducing sequelae, it has limitations and challenges, such as adverse effects and

[1] Graduating in Medicine from the University of Franca (UNIFRAN) - Franca-SP
Email: val.falqueti@hotmail.com
Vacancy filled: TCC
[2] Graduating in Medicine at the University of Franca (UNIFRAN) - Franca - SP
E-mail: juliasouzalombardi@gmail.com
[3] Graduating in Medicine at the University of Franca (UNIFRAN) - Franca - SP
Email: rafaelaminprev@gmail.com
[4] Graduated from the University of Vale do Sapucaí (UNIVAS) - Pouso Alegre - MG
E-mail: dra.anahelisacardosomachado@gmail.com
[5] Graduated from the Faculty of Health Sciences of Barretos (FACISB) - BARRETOS - SP
Email: joaovpontes01@outlook.com
[6] Undergraduate student in medicine at the Municipal University Center of Franca (UNI-FACEF)
E-mail: isadoranevestasso@gmail.com
[7] Guidance counselor
Dr.
Pediatrician, Post graduate in Pediatric Palliative Care, Pediatric and Neonatal ICU and Pediatric Nutrition, acting as a professor of the medical course
University of France
Institution: University of Franca (UNIFRAN)
E-mail: Maria Eugênia _059@hotmail.com

inefficiency against latent stages of the parasite. **Conclusion:** Therefore, it is concluded that efforts combining early screening, population education, access to therapies, and development of new interventions, such as vaccines, are crucial. An integrated, multidisciplinary approach is essential to reduce the global burden of disease and improve outcomes for affected mothers and newborns.

Keywords: Pediatrics. Toxoplasmosis, Congenital. Treatment. Diagnosis.

INTRODUCTION

Toxoplasma gondii (T. gondii) is one of the most common zoonotic agents observed in humans, and its incidence varies according to geography and socioeconomic characteristics. It is especially common in Europe, Central America, Brazil, and Central Africa. In 2013, the World Health Organization (WHO) estimated that there are up to 190,100 new cases of CT and 1.20 million disability-adjusted life years each year globally. The burden of disease is particularly high in Latin America and in certain populations in the US and elsewhere with high exposure (GUNDESLIOGLU, ÖZDEN et al; 2024) (ZHOU et al; 2024).

There are 3 forms of the parasite during infection. These are called tachyzoites (stage where they are found in groups or individually), bradyzoites (stage where they are found in tissue cysts), and sporozoites (stage where they are found in oocysts outside the host). The ingestion of oocysts excreted in cat feces and the consumption of raw or undercooked meat containing forms of bradizoites are considered the most important transmission routes for Toxoplasma infection (GUNDESLIOGLU, ÖZDEN et al; 2024).

Congenital infections, defined here as maternal infections with vertical transmission to the fetus, are a global public health concern and contribute to poor pregnancy outcomes, neonatal diseases, long-term neurodevelopmental sequelae, and health care costs (FORTIN et al; 2023) . Congenital Toxoplasmosis (TC) occurs as a result of T. gondii crossing the placenta and infecting the baby. Congenital infection usually occurs during the pregnancy of a woman previously not exposed to the infection or rarely after reactivation of chronic toxoplasmosis during pregnancy (FORTIN et al; 2023) (SILVA et al; 2022).

Infection during pregnancy can cause serious complications that can lead to stillbirth. Although the infection is usually asymptomatic in the mother, the infected newborn may exhibit a wide spectrum of clinical manifestations, ranging from asymptomatic forms to severe and irreversible defects with ocular, neurological, and/or systemic involvement, miscarriages, stillbirths, seizures, hydrocephalus, auditory disturbances, chorioretinitis, retinal scarring, and visual disturbances in the late period (GUARCH-IBÁÑEZ et al; 2024) (GUNDESLIOGLU, ÖZDEN et al; 2024) . Vertical transmission varies depending on gestational age, the trimester in which the pregnant woman had primary infection, and prenatal treatment. While the rate of transmission to the baby in untreated pregnant women is 10-15% in the first trimester, it has been reported to be 70-80% in the third trimester (GUNDESLIOGLU, ÖZDEN et al; 2024).

The diagnosis of CT depends on the history and serology of the mother's exposure to Toxoplasma during pregnancy, the baby's serology for Toxoplasma, and clinical features.

IgM for Toxoplasma may be negative in 20-50% of CT cases. Positive IgG for Toxoplasma alone is not conclusive, as it may indicate maternal antibody transfer; therefore, its value should be compared with the mother's IgG levels and assessed based on follow-up values. To evaluate the avidity values of anti-T antibodies. gondii, along with IgG and IgM antibodies, in the first trimester of pregnancy can help distinguish between past and recent infections. Effective treatment during pregnancy has been reported to reduce the rate of serious neurological sequelae by 75% in infants who develop CT. Early diagnosis and initiation of effective CT treatment play an important role in indicating prognosis (GUNDESLIOGLU, ÖZDEN et al; 2024).

This systematic review article aims to compile and evaluate the existing scientific evidence on congenital toxoplasmosis in the pediatric population. The intention is to provide a comprehensive and up-to-date view, which not only synthesizes current knowledge about the condition, but also identifies gaps in research and directs future investigations and clinical practices. By offering an in-depth analysis of the evidence, this study aims to serve as a resource for health professionals, researchers, and academics, helping to optimize diagnostic and therapeutic approaches to this condition.

METHODOLOGY

This is a systematic review that seeks to understand the main aspects of congenital toxoplasmosis infection in the pediatric population, as well as to demonstrate the main diagnostic and pharmacological methods used in the treatment of the condition. For the development of this research, a guiding question was elaborated through the PVO (population, variable and objective) strategy: "What are the main aspects that permeate the development of congenital toxoplasmosis in pediatrics, as well as what are the main clinical repercussions and the diagnostic and therapeutic methods used in clinical practice?"

The searches were carried out through searches in the PubMed Central (PMC) databases. 6 descriptors were used in combination with the Boolean term "AND": Congenital Toxoplasmosis, Pediatrics, Congenital Infection, Pregnancy Complications Parasitic, Toxoplasmosis, Congenital and Neonatology. The search strategy used in the PMC database was: Congenital Toxoplasmosis AND Pediatrics AND Congenital Infection , Pregnancy Complications, Parasitic AND Pediatrics AND Congenital Toxoplasmosis AND Congenital Toxoplasmosis AND Toxoplasmosis, Congenital AND Pediatrics AND Neonatology. From this search, 91 articles were found, which were later submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2015 to 2025 and that addressed the themes proposed for this

research, in addition, review, observational and experimental studies, made available in full. The exclusion criteria were: duplicate articles, available in the form of abstracts, that did not directly address the proposal studied and that did not meet the other inclusion criteria.

After associating the descriptors used in the searched databases, a total of 91 articles were found. After applying the inclusion and exclusion criteria, 20 articles were selected from the PubMed database, and a total of 10 studies were used to compose the collection.

DISCUSSION

Toxoplasma gondii is a ubiquitous protozoan parasite that causes infection with Toxoplasmosa, a zoonosis with worldwide distribution. This intracellular parasite infects warm-blooded animals, including humans, and is estimated to have infected more than a third of the world's population. Primary infection is usually (80% of cases) asymptomatic in immunocompetent individuals, however, if a woman becomes infected during pregnancy, toxoploasmosis may occur, with potentially serious sequelae (neurological and/or ocular damage) or a fatal outcome (in utero abortion, fetal/neonatal death). The risk of transmission to the fetus is closely related to the gestational age at infection in the mother, ranging from <15% in the first trimester of pregnancy to nearly 70% in the third trimester. In contrast, congenital toxoplasmosis (TC) is more severe if the mother is infected during the first trimester of pregnancy (KAMUS et al; 2023) .

Although a decrease in seropositivity for T. gondii has been reported in recent decades, it is estimated that one-third of the world's population is infected with T. gondii. In a retrospective study evaluating 1,037 pregnant women in 2022, Toxoplasma seroprevalence was reported as 52.6%, the seroconversion rate as 3.4%, and the congenital infection rate as 0.2% (GUNDESLIOGLU, ÖZDEN et al; 2024). There is a large disparity between countries in the incidence of CT, which is estimated to vary between 0.1 and six cases per 1000 live births. The highest burden of CT is in the Middle East and South America, and the incidence in Europe is estimated to be between 0.5 and 1.6 per 10,000 and in France between two and four per 10,000 live births. In Portugal, according to the latest epidemiological data, the seroprevalence of T. gondii infection has decreased, from a rate of 47% in 1979 to 18% between 2009 and 2020. Therefore, approximately 80% of women of childbearing age are susceptible to toxoplasmosis infection during pregnancy, with a risk of CT in the newborn (LOSA et al; 2024).

Contact of pregnant women with oocysts excreted in cat feces, ingestion of oocysts through food, consumption of raw or undercooked meat, and ingestion of bradyzoite forms

are the most important forms of transmission of congenital Toxoplasma. The high consumption of traditional foods made with raw meat in our region increases the mother's exposure to toxoplasmosis. In a study carried out, it was shown that 31.2% of mothers of babies with congenital Toxoplasma had a history of eating raw or raw meat. In addition, 31.2% of the mothers had contact with cats and animals. The risk of sequelae in the fetus is inversely proportional to gestational age, i.e., the lower the gestational age, the greater the risk of sequelae and injuries, while the higher the gestational age, the lower the risk of sequelae GUNDESLIOGLU, ÖZDEN et al; 2024) .

Although it is subclinical in about 75-90% of infected newborns, CT has a wide range of nonspecific clinical manifestations. Only a small percentage have the complete classic triad (hydrocephalus, intracranial calcifications, and chorioretinitis) (LOSA et al; 2024). The disease manifests itself in intrauterine and extrauterine life. The involvement of those with the infection varies according to the degree of the lesion: from severe and generalized presentation, with maculopapular rash, purpura, pneumonia, prolonged jaundice and hepatosplenomegaly, to alterations of the central nervous system due to hydrocephalus, intracerebral calcifications, epilepsy, microcephaly or microphthalmia with chorioretinitis or sinella, or subclinical infection. In the long term, these patients may experience neurodevelopmental delay or cognitive impairment, motor disorders, hearing loss, and visual disturbances. The risk of sequelae is higher (up to 92%) in patients not treated during the gestational or postnatal period (POSADA-BUSTOS et al; 2024) .

In a study conducted in Brazil, 71.4% of the cases presented chorioretinitis in early childhood, and the probability of developing new lesions in patients treated in the first two months of life and the severity of the disease was lower than in those treated after 4 months of life. In addition to chorioretinitis, patients may have involvement such as microphthalmia, macular atrophy, macular scarring, cataracts, and strabismus. Macular involvement has been reported in 54% of children with CT in North America. One study showed that microphthalmia occurred in 6 (33.3%) patients, macular atrophy and scarring in 5 (27%), and cataract in 2 (11.1%) patients. At follow-up during the period, nystagmus developed in 1 (5.5%) patient. In view of the fact that chorioretinitis can develop into adolescence, eye examination and follow-up were performed at regular intervals (GUNDESLIOGLU, ÖZDEN et al; 2024).

Monthly screening, starting before or near conception until one month after delivery for the development of antibodies to the parasite in previously seronegative women, may allow treatment to prevent transplacental transmission of newly acquired maternal Toxoplasma infection or treat the fetus to prevent sequelae. France, Austria, Slovenia,

Colombia, Panama, Brazil, Argentina, and Morocco have screening programs for CT (ZHOU et al; 2024).

A diagnosis of CT can be reached by combining the following: T. gondii-positive IgG and IgM in the newborn; IgG of the newborn with a value significantly higher than the maternal IgG at birth; positive PCR test in amniotic fluid; positive PCR test in the blood or CSF of the newborn; or the persistence of positive IgG after 12 months, which is the gold standard. However, interpretation of serological testing can be challenging for the following reasons: Positive IgG of the newborn may reflect past or current infection in the mother as it crosses the placenta; small amounts of maternal IgM can cross the placenta, resulting in low IgM levels in uninfected newborns if performed soon after birth; otherwise, if the infection occurs in late pregnancy, cases of false-negative IgM may occur, since IgM appears within 1-2 weeks of exposure; and maternal therapy can alter the serological profile of the newborn, as it can delay IgG production (LOSA et al; 2024).

After discontinuation of treatment, a rebound increase in IgM and/or IgG for T. gondii may be observed in cases of CT , and this situation is thought to be due to a delayed serologic response to infection rather than a relapse. Therefore, a positive IgG beyond 12 months of age is considered the gold standard and confirms the diagnosis of CT (LOSA et al; 2024).

Ultrasound findings associated with fetal toxoplasmosis are ventricular dilatation, cerebral calcifications, hepatomegaly, splenomegaly, ascites, pleural effusion, and pericardial effusion. quarter. Magnetic resonance imaging showed loss of parenchymal volume of both cerebral hemispheres and cerebellum with corticosubcortical cystic degeneration, dilatation of the lateral ventricles and hepatosplenomegaly. Because sonographic findings can only detect very obvious malformations, other subtle findings may be overlooked; Therefore, fetal brain MRI is used to better delineate subtle malformations. Differential diagnostic imaging includes cytomegalovirus and Aicardi-Goutières syndrome; hydrocephalus is also present in aqueductal stenosis, Chiari malformation type 2, and Dandy-Walker malformation, but are not associated with hepatosplenomegaly (LAZARTE-RANTES et al: 2021).

Early identification and treatment of pregnant women with acute infection reduces vertical transmission rates and disease severity in the affected fetus. Prevention and treatment use antiparasitic drugs. Spiramycin concentrates in the placenta and blocks or delays transmission to the fetus, resulting in fewer infections or a milder infection. Current treatment of confirmed fetal infection requires treatment with pyrimethamine, sulfadiazine, and folinic acid, although considered the mainstays of treatment, these medications do not

treat the life stage of latent bradyzoite; therefore, they are effective in active infection, but not definitively curative (EL BISSATI et al; 2018).

Before starting treatment, complete blood counts and liver enzyme tests should be performed. Subsequently, adverse effects should be monitored. Haematological toxicity is the main adverse effect of pyrimethamine and sulfadiazine, and neutropenia is described as occurring in more than half of children treated with these drugs, but the addition of folinic acid reduces the likelihood of this adverse effect (LOSA et al; 2024).

In an increasingly global society, infection with parasites of different virulence is likely to occur in a variety of geographic locations. Modern individuals are highly mobile, and their pathogens travel with them. The transport of agricultural products and bird migration patterns also contribute to the movement of strains globally. The role of animals in the transmission of parasites cannot be underestimated. A role for the interruption of environmental transmission through vaccination programs in domestic and wild cat populations may exist. A vaccine for cats was developed in the 1980s. A laboratory-attenuated strain of T. gondii was used to vaccinate cats and reduced transmission of the disease to pigs (EL BISSATI et al; 2018).

However, methods to effectively vaccinate wild cats on a large scale have so far remained elusive. There is no commercially available vaccine for cats at this time. There are commercially available live vaccines for sheep, which have been designed to reduce abortions associated with T. gondii infection. In addition, therapeutic interventions should be made available more widely in a more cost-effective way, so that those pregnant women and children diagnosed with toxoplasmosis can be adequately treated (EL BISSATI et al; 2018).

Possible approaches include encouraging more widely and easily distributed generic drugs, discovery and development of alternative drugs, or vaccine development. This problem has many solutions on the horizon. An optimal approach is multifaceted. An educated population of pregnant women, doctors, and others who provide care is an important first step. Referral centers can provide expertise in the interpretation, sometimes nuanced, of serological tests. Once a diagnosis is established, experience in treatment is imperative, as well as the availability of medications and knowledge of their appropriate use (EL BISSATI et al; 2018).

CONCLUSION

Congenital Toxoplasmosis represents a significant global public health challenge, especially in regions with high seroprevalence rates and lower access to effective screening

and treatment programs. Infection caused by Toxoplasma gondii, often asymptomatic in immunocompetent individuals, can have devastating consequences when it occurs during pregnancy, including severe neurological and ophthalmological sequelae in the fetus, as well as fatal cases. The impact of gestational age on disease severity and the risk of vertical transmission reinforces the need for early diagnosis and rapid intervention. Epidemiological studies indicate that cultural practices, such as the consumption of undercooked meat and contact with cats, remain significant risk factors, especially in regions where these practices are prevalent. However, challenges still remain, such as the need to improve access to therapeutic interventions and vaccines, which are currently limited in availability and efficacy. Antiparasitic drugs, such as pyrimethamine and sulfadiazine, have shown efficacy in controlling active infection, but have limitations in treating the latent stage of the parasite. Additionally, the adverse effects associated with these treatments highlight the importance of continuous monitoring during use.

To address these challenges, it is necessary to invest in multidimensional solutions. The implementation of educational programs aimed at pregnant women, doctors and caregivers is essential to reduce the risks of primary infection. In addition, the strengthening of reference centers for the interpretation of serological tests and timely treatment are fundamental steps in mitigating the impacts of toxoplasmosis. The availability of medicines in a cost-effective and accessible manner, along with the development of vaccines and therapeutic alternatives, can revolutionize the control of this disease. Thus, global efforts for the prevention and management of Congenital Toxoplasmosis must be coordinated and based on well-structured public health policies, promoting education, screening, and equitable access to interventions. Only through a multifaceted approach will it be possible to reduce the burden of this disease and significantly improve the associated clinical and social outcomes.

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