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Clinical manifestations and management of Congenital Toxoplasmosis: A systematic review

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ABSTRACT
Objective: The general objective of the present study is to analyze the scientific production on Congenital Toxoplasmosis, seeking to identify the main clinical manifestations, as well as the main methods used in the treatment of this pathology. . Methodology: It is a systematic review focused on understanding the main aspects of Congenital Toxoplasmosis. The research was guided by the question: "What are the main signs and symptoms of Congenital Toxoplasmosis in the pediatric population, as well as what are the therapeutic resources used in clinical practice?" . To find answers, searches were performed in the PubMed database using four descriptors combined with the Boolean term "AND". This resulted in 102 articles. 14 articles were selected for analysis. Results: Congenital toxoplasmosis is serious and its consequences for the fetus vary according to the trimester of infection. Infections in early pregnancy are less common but more severe, and can cause neurological and ocular complications. Accurate diagnostics, such as IgG and PCR avidity tests, are essential to identify recent infections and enable timely interventions. Conclusion: Prevention, early treatment, and screening programs are crucial to reduce transmission and negative impacts on the infant, and the combination of early diagnosis, effective treatment, and prevention improves outcomes for pregnant women and infants.

Keywords: Toxoplasmosis, Congenital, Clinical Picture, Pediatrics.

INTRODUCTION

Toxoplasmosis is an infection caused by Toxoplasma gondii, a parasite that affects almost all homeothermic animals, including humans. Considered the most common parasitic zoonotic disease globally, toxoplasmosis affects about 35% of the world's population throughout its lifetime (AKBARI et al; 2022) (TEIMOURI et al; 2022). The pathogen is an obligate intracellular protozoan parasite, whose multiplication occurs in the intestinal tract of cats and other felines, which are the only definitive hosts. Humans can act as intermediate hosts. Infection in humans usually occurs by ingestion of raw food or undercooked meat containing viable cysts, by ingestion of water, fruits, vegetables, shellfish, or by contact with soil contaminated with oocysts present in the feces of infected cats, in addition to vertical transmission from mother to fetus. All cats can be final hosts of T. gondii, and infected cats excrete T. gondii oocytes through feces. (AKBARI et al; 2022)

The parasite manifests itself in three forms: tachyzoites, bradyzoites, and sporozoites. Tachyzoites are the rapidly multiplying forms of T. gondii, while bradyzoites are the latent form, found in tissues as cysts. Sporozoites are the infectious forms of T. gondii that remain dormant in the environment and, due to their resistance, can remain infectious for many years, even when exposed to common disinfectants and extreme environmental conditions. The parasite's sexual cycle occurs in felines, while the asexual cycle occurs in intermediate hosts, where the parasite travels through blood and lymph to reach organs and remain dormant as bradyzoites. (DEGANICH et al; 2022)

After ingestion, oocysts and bradyzoites turn into asexual tachyzoites that spread the infection throughout the body. Although rare, postnatally acquired tachyzoite infection can occur through, for example, ingestion of contaminated unpasteurized milk, transfusion of infected blood, use of contaminated needles, or sexual transmission by infected seminal fluid. Tachyzoites are responsible for vertical transmission in pregnant women who have not previously been infected with T. gondii. (MILNE Colin; WEBSTER, Joanne P; 2023)

In individuals with a normal immune system, toxoplasmosis is usually a mild, self-limiting infection. Only about 10% of people with acute infection develop the disease, which is characterized by flu-like symptoms such as fever, body aches, fatigue, lymph node enlargement and headache. However, toxoplasmosis can be severe in cases of immunosuppression, such as in fetuses and newborns, or in people with HIV and other conditions that affect the immune system. (BOBIĆ et al; 2019)

Different strains of the parasite were identified, three main ones called type I, II and III, in addition to other atypical strains, which vary in virulence and epidemiological pattern. In Europe, 95% of humans infected by T. gondii are type II, while in North America, type II accounts for 43.9%, type III accounts for 18.2%, and atypical strains make up the remainder. The genotype of the

parasite can influence the severity of the disease, and in South America, the strains have greater genetic variability and are generally more virulent. (BOLLANI et al; 2022)

Vertical transmission from pregnant women to fetuses can cause congenital toxoplasmosis (TC), which occurs primarily after primary infection during or shortly before pregnancy. CT can be asymptomatic in about 75% of newborns, but it can cause severe harm to the fetus, such as retinochoroiditis, hydrocephalus, microcephaly, and mental retardation. The risk of vertical transmission varies according to the trimester of maternal infection, being about 10-15% in the first trimester, 30% in the second and 60% in the third. In rare cases, transmission can occur in chronically infected women with immunosuppression. (TEIMOURI et al; 2022) Early detection of primary T. gondii infection is vital for maternal and newborn safety. However, many pregnant women with acute infections have no symptoms, making diagnosis difficult. Seroconversion during pregnancy is the most direct indicator of primary toxoplasmosis, but the lack of antibody screening programs prior to conception limits the effectiveness of this approach. (TEIMOURI et al; 2022)

During pregnancy, the parasite can cross the placenta and infect the developing fetus. Infections in the first and second trimesters can cause serious problems, such as miscarriage, or anomalies, such as intracranial calcifications, low birth weight, hydrocephalus, retinochoroiditis, and microcephaly. Third-trimester infections are usually asymptomatic at birth, but intracranial calcifications, hearing loss, and visual disturbances may arise later. The overall seroprevalence rates of T. gondii infection are 39.3% in the general population and 41.0% in pregnant women. (AKBARI et al; 2022) The risk of transplacental transmission depends on the stage of pregnancy at the time of maternal infection, being low in the first trimester and can reach 90% in the last days of pregnancy. However, fetal disease tends to be more severe when the infection occurs earlier in pregnancy. (BOLLANI et al; 2022)

This systematic review article aims to compile and analyze the scientific evidence on the clinical manifestations and management of Congenital Toxoplasmosis. The objective is to provide a comprehensive and up-to-date view, which synthesizes existing knowledge and identifies gaps in research, guiding future investigations and clinical practices. In-depth analysis of the evidence is intended to be a useful resource for healthcare professionals, researchers, and academics, contributing to the improvement of diagnostic and therapeutic approaches to Congenital Toxoplasmosis.

METHODOLOGY

This is a systematic review that seeks to understand the main aspects of the clinical manifestations of Congenital Toxoplasmosis in pediatric patients, as well as to demonstrate the main methods used in the treatment of the condition, aiming to ensure a greater clinical elucidation of this

pathology. For the development of this research, a guiding question was elaborated through the PVO (population, variable and objective) strategy: "What are the main signs and symptoms of Congenital Toxoplasmosis in the pediatric population, as well as what are the therapeutic resources used in clinical practice?"

The searches were carried out through searches in the PubMed Central (PMC) databases. Four descriptors were used in combination with the Boolean term "AND": Congenital Toxoplasmosis, Toxoplasmosis, Diagnosis Differential and Newborn. The search strategy used in the PMC database was: Congenital toxoplasmosis AND newborn; Congenital toxoplasmosis; Toxoplasmosis congenital AND Diagnosis Differential; Toxoplasmosis AND newborn. From this search, 102 articles were found, which were subsequently submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2019 to 2024 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 102 articles were found. After applying the inclusion and exclusion criteria, 23 articles were selected from the PubMed database, and a total of 14 studies were used to compose the collection.

DISCUSSION

The transmission rate of toxoplasmosis, however, depends mainly, as well as the clinical presentation of congenital toxoplasmosis, on gestational maturity at the time of infection. The protective role of the placenta is most effective in the first trimester, allowing parasites to pass through in less than 10% of cases. With the increase in vascularization, the placental barrier becomes increasingly permeable, leading to the transmission of parasites in about 30% of cases in the second trimester, in 60-70% of cases in the third trimester, even more so in the last weeks of pregnancy. (BOLLANI et al; 2022) (BOBIĆ et al; 2019) Toxoplasma gondii infection can cause destruction of the placental structure, affecting the maternal-fetal interface composed of cytotrophoblasts (CTBs) and syncytiotrophoblasts (SYN). SYN is highly resistant to T. gondii, but damage to this layer allows the pathogen to invade. The infection can lead to necrosis and thrombi formation in the placental villi, resulting in fetal hypoxia and miscarriage. In people with normal immunity, the infection is latent, but it can cause serious illness in fetuses, leading to microcephaly or death. Infection during pregnancy can result in miscarriage due to dysfunction of regulatory T cells, which are crucial for maintaining maternal-fetal immune tolerance. (GAO et al; 2021)

The severity of fetal infection decreases with increasing gestational time. On the other hand, when the infection occurs in early pregnancy, the consequences for the fetus will be the most serious. Although serious consequences can also occur in second and third trimester infections, they are less common. Fetal infections are more likely to occur during the third trimester. (BOLLANI et al; 2022) (BOBIĆ et al; 2019) (OYEYEMI T; 2020)

Given that infection in immunocompetent individuals is usually asymptomatic, even in pregnant women, clinical diagnosis is rarely established without laboratory analysis. The rate of maternal-fetal transmission, without prenatal treatment, is estimated to average 50% throughout pregnancy. Immunological tests for IgG, IgM, IgA, and avidity of IgG-specific antibodies are used for diagnosis of maternal infection, and amniocentesis with molecular analysis is used for diagnosis of fetal infection. Determining the timing of maternal infection is crucial to assess the risk of fetal infection and the need for therapy. (BOBIĆ et al; 2019)

Evaluating specific antibodies to Toxoplasmosis in pregnant women in the first trimester is crucial to prevent congenital infections and allow early interventions. IgG avidity, which increases from low to high at 5 to 6 months after primary infection, helps identify recent infections, with high avidity indicating lower risk of fetal infections. IgG affinity increases after primary infection, resulting in increased antigen-antibody binding. Studies show that pregnant women with primary infections exhibit low avidity for 3 to 4 months after infection, increasing thereafter. The detection of Toxo IgM is sensitive but has low specificity, and may result in positive Toxoplasma IgM avidity tests. Elevated IgG avidity results suggest a low risk of vertical transmission of Toxoplasma, as long as the test is performed in the first trimester. (TEIMOURI et al; 2022)

Avidity tests are valuable when there are no screening programs available and only one serum sample from anti-Toxoplasma IgM positive pregnant women in the first trimester is available. Primary results suggest that low avidity indicates recent infections, increasing the risk of intrauterine transmission. IgG avidity may persist for months after recent infection, making it useful to rule out recent infections. High avidity rules out acute infections in the last 3-4 months, being ideal in the first trimester. Late testing can lead to unnecessary diagnoses. Follow-up samples after 3-4 weeks may improve clinical decisions. High avidity excludes infection in IgM-positive pregnant women in the first 4 months, but intermediate avidity is difficult to interpret and requires further study. (TEIMOURI et al; 2022)

Monthly screening during pregnancy, until delivery, allows for a timely assessment of the diagnosis of maternal infection, to start specific treatment early, in order to try to prevent transmission or reduce the risk of serious injury. (BOLLANI et al; 2022) Although IgG avidity tests are useful during pregnancy, their efficacy in newborns is still unclear. Some studies have reported low avidity values in neonates infected with T. gondii, reflecting maternal values. The IgG avidity

test is effective for diagnosing acute toxoplasmosis in pregnant women, with 100% sensitivity and 92.7% specificity. Neonates with low IgG avidity had higher serum levels of specific IgM and IgG and more severe symptoms of toxoplasmosis compared with those with high IgG avidity. In the literature review, these newborns had a 15-fold higher rate of severe symptoms. IgG avidity, when combined with PCR, is an essential tool for the accurate diagnosis of toxoplasmosis in pregnant women. This combination helps to avoid misdiagnosis and unnecessary treatment, especially in cases of acute infection and congenital toxoplasmosis (CT). (TEIMOURI et al; 2022)

After ingestion of food or water contaminated with T. gondii, parasitemia occurs, and tachyzoites can invade the placenta if the woman is pregnant. The transmission of T. gondii to the fetus is more efficient in the second half of pregnancy due to the decrease in the thickness of the placenta and immunological factors. Infection in early pregnancy is more severe, as the immune response is less effective. Transplacental transmission usually occurs when a woman is infected during pregnancy, and can cause miscarriage, stillbirths, or serious illness in the baby. (DUBEY et al; 2021) Infection in the first trimester can cause miscarriage, stillbirth, and premature birth, while infections in the third trimester usually go unnoticed at birth but can lead to complications such as chorioretinitis later on. Previous maternal infection usually confers protection, but hormonal changes can reactivate toxoplasmosis, resulting in transplacental transmission. In rare cases, reactivation of a previous infection can lead to congenital toxoplasmosis, especially in immunosuppressed women. (DUBEY et al; 2021) (OYEYEMI T; 2020)

A recent global meta-analysis estimated that 0.6% of pregnant women have acute Toxoplasma infection, resulting in about 201,600 children being born with congenital toxoplasmosis annually. Congenital infection can lead to miscarriage, leading to encephalitis, pneumonitis and congenital anomalies, stillbirth, hydrocephalus, microcephaly, and ocular and neurological complications. Latent toxoplasmosis, which can reactivate in cases of immunosuppression, is associated with several neuropathological and psychiatric effects. The global prevalence of latent toxoplasmosis in pregnant women is still unknown, but understanding it is crucial for public health and health policymaking. (ROSTAMI et al; 2020) (RAHMANIAN et al; 2020)

Although the epidemiological importance of T. gondii reinfections remains uncertain, their occurrence is recognized and represents a risk due to the genetic diversity of the strains, especially in South America. Health professionals should be informed about the potential for reinfection and incorporate this knowledge into their preventive advice, especially in endemic areas. (ARAUJO COELHO et al; 2024)

The diagnosis of congenital toxoplasmosis is complex and requires an algorithm that involves serological and molecular methods and biological assays. In newborns with suspected infection, a negative result from any existing laboratory method at birth or in the first six months of life cannot

exclude intrauterine infection. The recognition of late sequelae is hampered by differential diagnostic problems, and in children without clinical signs at birth, sequelae may occur after several years. (BOBIĆ et al; 2019)

PCR techniques for prenatal microbiological diagnosis for the detection of T. gondii DNA in amniotic fluid have revolutionized prenatal care for the diagnosis of congenital toxoplasmosis. First, it allows an anticipation of the diagnosis, since PCR has specificity and a positive predictive value of 100%, in addition, it avoids more invasive procedures to the fetus. However, amniocentesis should be performed only after the 18th week of pregnancy, four weeks after the estimated date of infection in a pregnant woman. A negative result does not completely exclude the presence of congenital toxoplasmosis, as the negative predictive value is 98.1%; No false-negative prenatal diagnoses may be due to delayed transplacental transmission of parasites after amniocentesis or to very low parasite densities in amniotic fluid. The risk of procedure-related fetal loss (or preterm birth, delivery in a more advanced pregnancy) is estimated to be less than 0.1% (BOLLANI et al; 2022)

The first reported case of childhood toxoplasmosis with confirmed vertical transmission dates back to 1942. Currently, it is known that congenital infection is the most severe form of toxoplasmosis and occurs in children of mothers who contracted primary T. gondii infection during pregnancy. (CAMPOS et al; 2020) In South America, mortality in newborns with CT is not uncommon, and 35% of children have severe neurological disease, including hydrocephalus, microcephaly, and mental retardation; 80% of children have eye injuries and up to 40% of children may have hearing loss. (GARWEG G; 2022)

In neonatal age, congenital toxoplasmosis is asymptomatic in 85% of cases. The classic triad described by Wolf in 1939 (hydrocephalus, calcifications, and chorioretinitis) is observed very rarely in modern times. Neonatal manifestations, if present, may include hydrocephalus, microcephaly, intracranial calcifications, chorioretinitis, cataracts, seizures, nystagmus, jaundice, petechiae, anemia, enlargement of the liver and spleen, prematurity, and severe intrauterine growth restriction with abnormally low birth weight. However, none of these symptoms are pathognomonic of toxoplasmosis and may suggest other congenital infections (CMV, Herpes simplex, rubella, syphilis). (BOLLANI et al; 2022)

Among the ocular manifestations, the most frequent is chorioretinitis and retinal lesions are usually located in the posterior pole. It occurs most often after a reactivation of the infection and in cases where the macula is involved there may be loss of visual function The worsening of central vision, due to the involvement of the macula, may recover after the inflammation resolves. Chorioretinitis is commonly recurrent and relapsing, but these episodes are rarely associated with systemic signs or symptoms. For any additional week of gestation, in case of maternal primary infection, the risk of chorioretinitis decreased by 3% but increased 2.1-fold when maternal primary

infection occurred before 20 weeks' gestation and 3.6-fold in infants with additional clinical manifestations at birth. (BOLLANI et al; 2022)

Other eye disorders, reported in addition to recurrent foci of chorioretinitis, that can contribute to visual impairment are strabismus, microphthalmia, cataract, retinal detachment, optic nerve atrophy, iridocyclitis, nystagmus, and glaucoma. Ocular manifestations in infants with congenital infection in Brazil are more severe than in the United States and Europe. Brazilian infants have developed chorioretinitis more frequently and the lesions are multiple, larger, and more likely to be localized to the posterior pole than European infants. Several studies suggest that the marked difference in the prevalence and severity of ocular involvement in Brazil is due to different prevention and infection protocols with more virulent atypical strains of T. gondii that predominate in Brazil but are rarely found in other countries. (BOLLANI et al; 2022) In a follow-up study, 82% of children developed lesions within 20 years, with some affecting vision. Another 14-year study of 327 children in Lyon showed that 29% had injuries despite treatment. In the US, 11 out of 120 congenitally infected children died within 4 years despite treatment. The morbidity of congenital toxoplasmosis is high and may be underestimated. (DUBEY et al; 2021)

There are certain critical periods during pregnancy when the fetus is at high risk of exposure to teratogens. Some microorganisms, including Toxoplasma gondii, are known to have teratogenic effects, interfering with fetal development and causing irreversible disorders. This parasite invades the Central Nervous System (CNS), forming tissue cysts, and can interfere with neurodevelopment, leading to frequent neurological abnormalities associated with T. gondii infection. (CAMPOS et al; 2020). The involvement of the central nervous system is demonstrated by calcifications that accompany the phenomena of vasculitis and necrosis and mainly affect periaqueductal and periventricular regions. Hydrocephalus may sometimes be the only manifestation of congenital toxoplasmosis; Observational data show a frequency of 31% when the mother received no therapy, compared to 0.8% in the newborns of treated women. (BOLLANI et al; 2022)

Untreated neonates with mild or subclinical congenital toxoplasmosis at birth are at increased risk for complications such as chorioretinitis, microcephaly, seizures, sensorineural hearing loss, motor dysfunction, slow growth, and endocrine abnormalities. Chorioretinitis can lead to retinal detachment, vision loss, cataracts, glaucoma, and iris changes, with new retinal lesions appearing in childhood and adolescence. Even with treatment, there is a risk of late sequelae due to the possibility of reactivation of the parasite, especially in the heart and central nervous system. (DEGANICH et al; 2022)

The data show that children with congenital toxoplasmosis may present both hearing loss and alterations in central audit trajectories, with infection being a risk for peripheral and central auditory pathway disorders. Studies indicate that 12.3% to 12.5% of children have transient and conductive

alterations, 3.8% peripheral sensorineural alterations, 27.4% retrocochlear alterations and 33.3% Central Auditory Processing (CAP) alterations. Evaluation of the central auditory nervous system is essential, as children with congenital toxoplasmosis may have changes in the brainstem and subcortical levels. Although there are divergences in the literature regarding the association between congenital toxoplasmosis and hearing loss, the infection significantly increases the risk of hearing impairments, suggesting the need for specific diagnostic procedures. (DEGANICH et al; 2022)

Studies on the knowledge of toxoplasmosis among health professionals in Brazil show a varied understanding, with 97.4% correctly recognizing cats as a source of transmission, but still prevailing significant gaps. Common misconceptions include the belief that dogs can spread the parasite and misguided advice about prevention. Recognition of the risk of raw or undercooked meat is inconsistent, and there are misunderstandings about IgG avidity testing. Doctors and recent graduates demonstrate better knowledge, but uncertainties about treatment guidelines persist. Although there is limited evidence demonstrating a significant correlation between health education measures and reduced seroprevalence of congenital toxoplasmosis, the strategic importance of education in the primary prevention of infectious diseases cannot be ignored. (ARAUJO COELHO et al; 2024)

Preventing toxoplasmosis infection involves educating about preventive measures, such as avoiding sources of infection, not drinking unfiltered water, and maintaining hand hygiene. Washing fruits and vegetables thoroughly and cooking meat properly are essential, as most infections in the U.S. come from undercooked meat. Freezing meat at -12°C or less can also kill tissue cysts. Pregnant women should avoid cleaning cat litter boxes to reduce the risk of exposure. Keeping cats indoors and vaccinating them can decrease the elimination of oocysts. Education and integration of these measures into antenatal programs can reduce seropositivity rates. (DEGANICH et al; 2022)

Due to the complexity of the diagnosis and the need for timely treatment to prevent severe consequences of congenital toxoplasmosis (CT), intervention occurs at three levels: prevention of maternal infection during pregnancy, prevention of transplacental transmission to the fetus, and mitigation of the consequences of fetal infection. Health education is essential to reduce the incidence of primary infection in pregnant women. (BOBIĆ et al; 2019)

Timely treatment of acute infections can prevent or delay transmission to the fetus and mitigate the consequences. Serological screening programs are crucial to identify and treat women at risk. Mitigating the consequences involves continuous treatment of fetuses and newborns with specific medications. In France, the national program for the prevention of congenital toxoplasmosis, in force since 1978, includes screening in the first trimester, monthly surveillance for seronegative women, and treatment with spiramycin in case of seroconversion. If the prenatal diagnosis is positive, a combination of PS and folinic acid is given. This protocol has been shown to be effective

in reducing vertical transmission and the severity of congenital toxoplasmosis. Babies diagnosed receive additional tests and treatment for one year. Since 2007, a surveillance system has been monitoring cases of congenital toxoplasmosis in France. (BOBIĆ et al; 2019)

Treatment of toxoplasmosis during pregnancy is most effective if started less than three weeks after seroconversion, especially with pyrimethamine and sulfadiazine (PS), significantly reducing the risk of congenital infection. Studies show that mothers treated with PS have a lower rate of transmission of the disease to the fetus compared to those treated with spiramycin. In addition, prenatal care decreases the risk of death or the development of severe neurological symptoms in infected infants, improving neurological, cognitive, ocular, and auditory outcomes. (DEGANICH et al; 2022)

In primary maternal toxoplasmosis infection, acquired during the first 18 weeks of gestation, treatment with spiramycin, a macrolide that reaches significant placental concentration and may reduce the frequency of vertical transmission, but is not effective for the treatment of fetal infection, is recommended. Spiramycin prevents the spread of parasites from mother to fetus across the placenta, while PS is used for fetal treatment. Studies indicate that SP therapy may be more effective than spiramycin in preventing transmission of infection to the fetus, although the difference did not reach statistical significance. (DEGANICH et al; 2022) (BOBIĆ et al; 2019) This treatment cannot be used before 14 weeks of gestation due to the potential risks of teratogenicity. In the case of primary maternal Toxoplasma infection, to exclude fetal anomalies, monthly ultrasound monitoring is recommended until term. When amniocentesis is positive, ultrasounds should be checked every 2 weeks to monitor the brain anatomy of the fetus. The main sonographic findings associated with congenital toxoplasmosis are ventriculomegaly and intracranial calcifications. (BOLLANI et al; 2022)

Conventional treatment for acquired and congenital toxoplasmosis includes pyrimethamine, sulfadiazine, and folinic acid. Pyrimethamine inhibits DNA synthesis, and its effectiveness increases when combined with sulfadiazine. However, this combination is not recommended in the first trimester of pregnancy due to teratogenic risk and myelosuppression, which can be mitigated with folinic acid. Serious complications, although rare, can occur. Treatment alternatives include combinations with clindamycin, clarithromycin, azithromycin, or atovaquone, and monotherapy with cotrimoxazole or atovaquone. When PCR is positive due to infection acquired after 18 weeks of gestation, the current gold standard is the association of pyrimethamine, sulfonamides and folinic acid. Steroids can be used in the treatment of ocular toxoplasmosis. There are clinical trials that are underway to determine the optimal dose of dexamethasone. (WILSON et al; 2020) (SILVA da et al; 2021)

Toxoplasmosis is common, and current chemotherapy has limitations in efficacy and safety, with side effects that affect patient compliance. New drugs are being developed, with a focus on improving pharmacokinetic characteristics and reducing side effects, especially in pregnant women and newborns. Optimal drugs must be effective at all stages of infection, bioavailable in target tissues, and globally accessible. (SILVA da et al; 2021)

All neonates at risk of congenital toxoplasmosis (proven maternal infection, with or without prenatal diagnosis) should undergo a complete clinical and neurological check-up at birth, specific immunological serum tests, direct and indirect, dilated fundoscopy, transfontanellar ultrasound (to rule out any ventricular dilation, brain calcifications, porencephaly). Liver and cardiac ultrasound, brain computed tomography (CT) or magnetic resonance imaging (MRI), and electroencephalographic (EEG) monitoring, are useful when clinical and neurological symptoms are severe. (BOLLANI et al; 2022)

Pyrimethamine and sulfonamide, due to their action on the synthesis folate, act synergistically against T. gondii. Both drugs reduce the growth of rapidly proliferating tachyzoites and prevent their transformation into new cysts, which are insensitive to this treatment. Pyrimethamine is absorbed slowly but completely in the gastrointestinal tract. The half-life of serum in the newborn is about 60 hours, and in cerebrospinal fluid it reaches a concentration of about 10–20% of serum levels. Sulfadiazine appears to be the most active sulfonamide; Its plasma half-life of 12 to 19 hours makes it preferable to other sulfonamides and its concentration in cerebrospinal fluid reaches 50% of the plasma concentration. It is excreted by the kidneys and is poor solubility can cause crystalluria, which can be avoided with good hydration of the patient. (BOLLANI et al; 2022)

In a South American population, it has been reported that starting antiparasitic therapy as early as possible, compared with a delay to or later to the fourth month of life, reduces the risk of eye injury in the first 5 years of life from 78% to 33% (GARWEG G; 2022). Treatment should be continued for at least one year, as a shorter period of therapy can lead to severe disability. Prior to initiating therapy, G6PD deficiency should be ruled out and throughout treatment patients should be monitored clinically and serologically to verify the efficacy of therapy and the possible occurrence of adverse reactions. (BOLLANI et al; 2022)

Haematological adverse events can affect up to 30% of newborns. Use of antifolate and sulfonamides may result in gradual bone marrow depression, more frequent in the first two months of life and mostly consistent with reversible neutropenia. Folinic acid should always be associated for prevention and reduction of hematological toxicity of drugs. Sometimes anemia and thrombocytopenia are also present. Patients' blood should therefore be monitored, initially every 15 days and thereafter once a month. When neutrophils are <800/mm3, therapy should be temporarily interrupted and resumed with increased white blood cells. No long-term hematologic toxicity or late-

onset malignancies were found. Gastrointestinal symptoms such as vomiting, diarrhea, and lack of appetite are also occasionally described. A small percentage of studies report dermatological adverse events, including rash. Sulfonamide intolerance causes severe skin manifestations, such as Steven Johnson Syndrome, and treatment should be stopped immediately and permanently. (BOLLANI et al; 2022)

CONCLUSION

The high prevalence of toxoplasmosis in Brazil and the serious consequences of contracting the disease during pregnancy reinforce the need for adequate education on prevention. Congenital toxoplasmosis is a serious condition that can have several consequences for the fetus, varying according to the trimester of pregnancy in which the infection occurs. Transmission is less common in early pregnancy, but infections that occur during this period tend to be more severe. Clinical manifestations may include neurological and ocular complications, which may affect the child's long-term quality of life.

Accurate diagnoses, through IgG and PCR avidity tests, are essential for the identification of recent infections and for the implementation of timely interventions. Prevention and early treatment are crucial to reduce vertical transmission of the parasite and minimize negative impacts on the baby. Education on preventive measures, coupled with serological screening programs, plays a vital role in reducing the incidence of congenital toxoplasmosis. Thus, a combined approach of early diagnosis, effective treatment, and prevention can offer better outcomes for pregnant women and their babies.

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