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CONGENITAL TOXOPLASMOSIS: CURRENT PERSPECTIVES ON DIAGNOSIS AND THERAPEUTIC APPROACHES

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ABSTRACT Congenital toxoplasmosis, caused by Toxoplasma gondii, has a global incidence of approximately 190,000 cases annually. Maternal infection prevalence during pregnancy ranges from 1% to 40%, with European seroprevalence varying between 10% and 60%. Early infections often result in severe fetal outcomes, such as hydrocephalus, intracranial calcifications, and chorioretinitis. Pathogenesis involves the transmission of tachyzoites, the rapidly dividing form of T. gondii, across the placenta, leading to infection of fetal organs. Clinical manifestations are diverse, including neurological and ocular involvement, as well as systemic symptoms like hepatosplenomegaly and jaundice. Diagnosis involves serological tests, PCR, and imaging studies. Treatment typically includes a combination of pyrimethamine, sulfadiazine, and folinic acid, with glucocorticoids for severe inflammation.

KEYWORDS : Toxoplasmosis; Congenital, Pregnancy Complications, Infectious; Serologic Tests; Polymerase Chain Reaction; Anti-Infective Agents.

INTRODUCTION

Congenital toxoplasmosis, caused by the protozoan parasite Toxoplasma gondii, is a significant health concern due to its potential to cause severe complications in infected fetuses and infants. This narrative review aims to provide a comprehensive overview of the current diagnostic methods and therapeutic approaches for congenital toxoplasmosis. While the infection is often asymptomatic in immunocompetent individuals, congenital transmission can lead to serious outcomes, including retinal disease, neurological impairments, and other systemic manifestations. Diagnosis primarily relies on serological testing and polymerase chain reaction (PCR) to detect the presence of the parasite in both the mother and infant. Therapeutic management typically involves antiparasitic treatment with pyrimethamine, sulfadiazine, and folinic acid, tailored to the severity of the infection and the infant's response. This review will explore the latest advancements in diagnostic techniques and treatment protocols, emphasizing the importance of early detection and prolonged therapy to mitigate long-term sequelae in affected children (1,2).

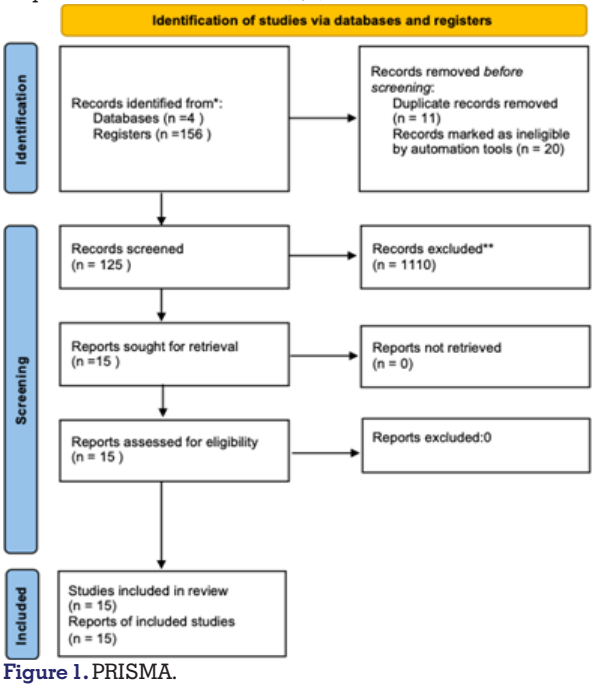

Figure 1. PRISMA.

METHODS

The methodology for this narrative review involved a comprehensive literature search in four main databases: PubMed, Scopus, Web of Science, and Cochrane Library. Keywords such as "congenital toxoplasmosis," "diagnosis," "treatment," and "therapeutic approaches" were used. The search was limited to articles published in English over the past ten years. Titles and abstracts were initially screened, followed by a full-text review of relevant articles. Ultimately, 15 references meeting the inclusion criteria were selected and analyzed.

Epidemiology

Congenital toxoplasmosis, caused by Toxoplasma gondii, has a global incidence estimated at 190,000 cases per year. The prevalence of maternal infection during pregnancy ranges from 1% to 40%, depending on geographic region. In Europe, seroprevalence among pregnant women varies from 10% to 60%. The risk of transmission to the fetus is approximately 30% if the mother is infected during the first trimester, increasing to 60% in the third trimester. However, the severity of fetal outcomes is inversely related to gestational age at the time of infection; early infections often result in more severe complications, such as hydrocephalus, intracranial calcifications, and chorioretinitis (3,4).

Pathogenesis Of Congenital Toxoplasmosis

The pathogenesis of congenital toxoplasmosis involves the transmission of Toxoplasma gondii from an infected mother to her fetus. During primary infection in pregnancy, the parasite crosses the placenta, especially if the mother acquires the infection during the first trimester. T. gondii exists in three forms: tachyzoites, bradyzoites, and sporozoites. Tachyzoites are the rapidly dividing form responsible for acute infection and can disseminate through the bloodstream, reaching various tissues, including the placenta. Once the parasite infects placental tissue, it can invade the fetal circulation and infect fetal organs. The severity of infection in the fetus depends on the timing of maternal infection; earlier infections can lead to more severe outcomes due to the critical stages of fetal development. Common manifestations in the fetus include chorioretinitis, hydrocephalus, and intracranial calcifications. The immune response in the fetus is typically underdeveloped, allowing the parasite to proliferate and cause significant tissue damage (5,6).

Clinical Manifestations

Congenital toxoplasmosis can present with a wide range of clinical manifestations, often depending on the timing of the maternal infection during pregnancy. Early infections, particularly in the first trimester, are more likely to result in severe outcomes due to the critical stages of fetal development during this period (7).

Neurological manifestations are among the most significant and include hydrocephalus, intracranial calcifications, and seizures. These can result from the parasite invading and causing inflammation in the brain. Hydrocephalus is characterized by an abnormal accumulation of cerebrospinal fluid within the brain, leading to increased intracranial pressure and head enlargement. Intracranial calcifications, visible on imaging studies, indicate areas of previous inflammation and tissue damage. Ocular involvement is common and often presents as chorioretinitis, an inflammation of the retina and choroid. This condition can lead to vision impairment or blindness if not adequately treated. Infants with congenital toxoplasmosis may also develop strabismus (misalignment of the eyes) or nystagmus (uncontrolled eye movements) (8,9).

Other systemic manifestations can include hepatosplenomegaly (enlarged liver and spleen), jaundice, and lymphadenopathy (swollen lymph nodes). These symptoms result from the systemic spread of the parasite and the body's immune response to infection. In severe cases, the infection can lead to low birth weight, prematurity, and even stillbirth. Hearing loss is another potential consequence, often identified later in life through routine screening. This is typically due to damage to the inner ear structures. The severity and combination of these clinical manifestations can vary widely, making early diagnosis and treatment crucial to improve outcomes and prevent long-term sequelae. Regular follow-up and monitoring are essential for managing these children and addressing any emerging complications promptly (10).

Diagnosis of Congenital Toxoplasmosis

The diagnosis of congenital toxoplasmosis involves a multi-faceted approach, incorporating serological tests, molecular methods, and imaging studies to confirm the presence of Toxoplasma gondii infection and assess its impact on the fetus or newborn (11).

Maternal Testing:

The initial step in diagnosing congenital toxoplasmosis starts with the pregnant mother. Serological tests are performed to detect specific antibodies against T. gondii. The presence of IgM antibodies indicates a recent infection, while IgG antibodies suggest past exposure. A rising IgG titer over time can also indicate an acute infection. If maternal infection is suspected during pregnancy, further testing is warranted to assess the risk to the fetus (11,12).

Amniocentesis:

For pregnant women with confirmed T. gondii infection, amniocentesis can be performed between 18 and 20 weeks of gestation. Amniotic fluid is obtained and tested using polymerase chain reaction (PCR) to detect T. gondii DNA. A positive result confirms fetal infection, allowing for early intervention and management (11,12).

Neonatal Testing:

After birth, the diagnosis of congenital toxoplasmosis in the newborn involves serological testing for T. gondii-specific IgM and IgA antibodies, which are indicative of congenital infection. Since maternal IgG antibodies can cross the placenta and persist in the infant, IgG testing alone is not diagnostic. PCR testing of blood, cerebrospinal fluid (CSF), or other body fluids can also provide definitive evidence of infection(11,12).

Imaging Studies:

Imaging studies are crucial for identifying the characteristic manifestations of congenital toxoplasmosis. Cranial ultrasound is often used initially to detect intracranial calcifications and hydrocephalus. If abnormalities are found, computed tomography (CT) or magnetic resonance imaging (MRI) may be performed for more detailed evaluation (12).

Ophthalmologic Examination:

An eye examination by an ophthalmologist is essential to detect chorioretinitis and other ocular lesions, which are common in congenital toxoplasmosis (12).

Follow-up Testing:

Serological tests are repeated over the first year of life to monitor for changes in antibody levels, confirming the persistence or resolution of infection (12).

Combining these diagnostic tools ensures a comprehensive evaluation, enabling early diagnosis and prompt treatment to mitigate the adverse effects of congenital toxoplasmosis.

Treatment of Congenital Toxoplasmosis

The treatment of congenital toxoplasmosis is aimed at reducing the severity of symptoms and preventing long-term sequelae. Early diagnosis and prompt initiation of therapy are critical to improving outcomes in affected infants. The standard treatment regimen typically involves a combination of antiparasitic medications and supportive care (13,14).

Antiparasitic Therapy: The primary treatment for congenital toxoplasmosis includes a combination of pyrimethamine, sulfadiazine, and folinic acid. Pyrimethamine is an antiparasitic agent that inhibits the parasite's ability to replicate, while sulfadiazine acts synergistically with pyrimethamine to enhance its efficacy. Folinic acid is administered concurrently to counteract the bone marrow suppression caused by pyrimethamine (14).

Pyrimethamine:

Initially given at a loading dose, followed by a maintenance dose for a prolonged period, usually up to one year. The dosing regimen starts with 2 mg/kg/day for two days, then 1 mg/kg/day for six months, and 1 mg/kg every other day for the remainder of the year.

Sulfadiazine:

Administered at a dose of 50 mg/kg twice daily for the entire treatment duration. It is essential to maintain adequate hydration to prevent crystalluria and renal complications.

Folinic Acid (Leucovorin):

Given at 10 mg three times a week to mitigate the hematologic toxicity of pyrimethamine.

Glucocorticoids:

In cases where there is severe inflammation, such as chorioretinitis or elevated cerebrospinal fluid (CSF) protein levels, glucocorticoids like prednisone or prednisolone may be used. These are administered at a dose of 1 mg/kg/day to reduce inflammation and prevent damage to vital organs.

Monitoring and Supportive Care: Regular monitoring is crucial to assess the effectiveness of treatment and detect potential side effects. This includes routine blood tests to monitor complete blood counts (CBCs), liver and kidney function tests, and regular eye exams to track any changes in vision or the development of ocular lesions. Additionally, neurodevelopmental assessments are important to identify and manage any developmental delays or neurological impairments early on (14,15).

Long-term Follow-up:

Infants treated for congenital toxoplasmosis require long-term follow-up to monitor for late sequelae such as vision impairment, hearing loss, and developmental delays. Regular follow-up visits with a pediatric infectious disease specialist, neurologist, and ophthalmologist are

recommended. By following a comprehensive treatment plan that includes antiparasitic therapy, supportive care, and vigilant monitoring, the adverse outcomes associated with congenital toxoplasmosis can be significantly reduced, enhancing the quality of life for affected infants (15).

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