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Original Research Paper

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CONGENITAL SYPHILIS: COMPREHENSIVE REVIEW OF CLINICAL PRESENTATIONS, DIAGNOSTIC APPROACHES, AND EVALUATION STRATEGIES

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ABSTRACT Congenital syphilis poses a persistent threat to neonatal health despite being a preventable and treatable disease. This comprehensive review examines the clinical presentations, diagnostic approaches, and evaluation strategies for congenital syphilis. Clinical manifestations can range from asymptomatic to severe, affecting multiple organ systems. Diagnosis relies on serological testing, including non-treponemal and treponemal tests, with careful interpretation in neonates due to passive transfer of maternal antibodies. Imaging studies and lumbar puncture may be warranted in certain cases. Treatment with penicillin remains the cornerstone, with regimens varying based on age and clinical severity. Close follow-up and serological monitoring are essential to assess treatment response and prevent long-term sequelae. Despite challenges, early detection, and comprehensive management can significantly reduce the burden of congenital syphilis.

KEYWORDS : Congenital Syphilis, Clinical Presentation, Diagnosis, Evaluation, Treatment

INTRODUCTION

Congenital syphilis is a serious yet preventable condition caused by the transplacental transmission of Treponema pallidum from an infected mother to her fetus. Despite advances in healthcare, the global incidence of congenital syphilis remains a concern, particularly in low- and middle-income countries. This comprehensive review aims to provide a detailed overview of the clinical presentations, diagnostic approaches, and evaluation strategies for congenital syphilis. Key topics include the efficacy of penicillin as the primary treatment, dosing regimens for different age groups, and the importance of follow-up serological testing. Additionally, special considerations for infants born to mothers with HIV coinfection and those with penicillin allergies are discussed (1).

METHODS

The comprehensive literature search was conducted to identify relevant studies on congenital syphilis. Electronic databases including PubMed, Embase, and Cochrane Library were searched using keywords such as "congenital syphilis," "neonatal syphilis," "Treponema pallidum," "diagnosis," "treatment," and "clinical presentation." The search was limited to studies published in English from January 2000 to December 2023. Additional studies were identified through manual searches of reference lists from relevant articles and reviews. Studies were included if they met the following criteria: (1) original research articles reporting on clinical presentations, diagnostic approaches, or evaluation strategies of congenital syphilis, (2) studies conducted on human subjects.

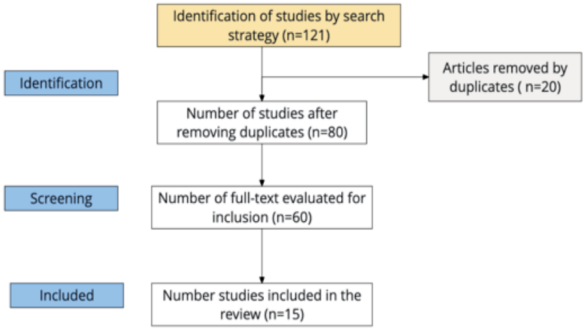

Figure 1. PRISMA.

Clinical Manifestations

Congenital syphilis presents a broad spectrum of clinical manifestations that can affect multiple organ systems. The severity and type of symptoms depend on the stage of the disease and the adequacy of maternal treatment during pregnancy. Early manifestations, which can occur in the first few weeks of life, include hepatosplenomegaly, rash (including maculopapular, vesiculobullous, or pustular), jaundice, and hematological abnormalities such as anemia, thrombocytopenia, and leukocytosis. Skeletal abnormalities, such as osteochondritis and periostitis, may also be present (2).

Late manifestations of congenital syphilis can appear months to years after birth and often involve the development of Hutchinson's triad, which includes interstitial keratitis, eighth nerve deafness, and Hutchinson's teeth (notched incisors). Other late manifestations include frontal bossing, saber shins, and Clutton's joints. Neurosyphilis can manifest as hydrocephalus, seizures, and intellectual disability (3).

Evaluation and Diagnosis

Diagnosing congenital syphilis requires a comprehensive approach that includes a detailed maternal history, physical examination of the newborn, and appropriate laboratory testing. Maternal history should include information on prenatal care, previous syphilis diagnoses and treatments, and serological status during pregnancy. Physical examination of the newborn should focus on identifying signs suggestive of congenital syphilis, such as hepato splenomegaly, rash, jaundice, and skeletal abnormalities (3,4).

Laboratory testing is essential for confirming the diagnosis. Serological tests for syphilis, including non-treponemal tests (e.g., Venereal Disease Research Laboratory [VDRL], Rapid Plasma Reagin [RPR]) and treponemal tests (e.g., fluorescent treponemal antibody absorption [FTA-ABS], Treponema pallidum particle agglutination [TP-PA]), should be performed on both the mother and the newborn. Additionally, cerebrospinal fluid (CSF) analysis should be considered in infants with clinical or laboratory evidence of congenital syphilis to assess for neurosyphilis. Radiographic studies, such as long bone radiographs, may also be indicated to evaluate for skeletal abnormalities (4).

Assessment of Organ System Involvement in Congenital Syphilis

Evaluation of organ involvement in congenital syphilis is paramount for determining the extent of disease and guiding appropriate management. The evaluation should include a thorough physical examination and targeted diagnostic studies. Physical examination should assess for signs of

organ involvement, such as hepatomegaly, splenomegaly, skin lesions, and skeletal abnormalities. Specific attention should be paid to the presence of neurologic symptoms or signs, as neurosyphilis can have serious consequences if not promptly recognized and treated (5).

Diagnostic studies may include imaging studies, such as radiographs and ultrasound, to evaluate for skeletal abnormalities and organ enlargement. Laboratory tests, including complete blood count, liver function tests, and CSF analysis, can help assess the degree of organ involvement and guide treatment decisions. Regular monitoring of organ function during treatment is essential to assess the response to therapy and detect any complications early. Collaboration between pediatricians, infectious disease specialists, and other relevant healthcare providers is crucial for the comprehensive evaluation and management of organ involvement in congenital syphilis (6).

Differential Diagnosis

Diagnosis of congenital syphilis requires consideration of various conditions presenting with similar clinical features. Differential diagnosis includes infections such as cytomegalovirus, toxoplasmosis, and herpes simplex virus, which can cause intrauterine growth restriction, hepato splenomegaly, and jaundice. Other congenital infections like rubella, varicella, and human immuno deficiency virus (HIV) can also mimic some symptoms of congenital syphilis. Non-infectious causes such as metabolic disorders (e.g., galactosemia, tyrosinemia) and genetic syndromes (e.g., trisomy 21, congenital adrenal hyperplasia) should also be considered. A thorough evaluation, including serological testing, imaging studies, and genetic testing, is essential for accurate diagnosis (7).

Treatment Approaches by Category

Congenital syphilis poses a significant public health challenge, requiring a nuanced approach to treatment based on age and clinical presentation. The cornerstone of therapy remains penicillin due to its proven efficacy and safety profile. Treatment regimens are categorized based on age and clinical status, ensuring appropriate management for each patient category (7,8).

Infants < 1 Month of Age

For asymptomatic infants born to untreated or inadequately treated mothers, a single dose of intramuscular (IM) benzathine penicillin G (50,000 units/kg) is recommended. This approach has been shown to be highly effective in preventing congenital syphilis in high-risk newborns. However, for symptomatic infants, a more aggressive approach is warranted, with a 10-day course of aqueous crystalline penicillin G preferred. The dosing is adjusted by weight, with infants ≤7 days old receiving 50,000 units/kg IV every 12 hours, and those >7 days old receiving it every 8 hours (8).

Infants > 1 Month of Age and Children

In symptomatic patients with clinical or radiological findings suggestive of congenital syphilis, a 10-day course of aqueous crystalline penicillin G is recommended. The dosing regimen is similar to that for younger infants, with adjustments made for weight and age. Asymptomatic patients with positive serology but no clinical or radiological evidence of disease should receive three doses of benzathine penicillin G IM weekly. This regimen has been shown to be effective in preventing the progression of latent syphilis to symptomatic disease (9).

Special Considerations

Patients with a penicillin allergy should undergo desensitization followed by penicillin therapy, as there are limited data on the efficacy of alternative agents. Co-infection with syphilis and HIV does not alter the treatment approach for syphilis, and the same evaluation and treatment protocols should be followed as for patients without HIV infection (9,10).

Monitoring and Follow-Up

Regular serological follow-up with non-treponemal tests (e.g., VDRL, RPR) is essential for monitoring treatment response. These tests should be performed every 2-3 months until seronegative. Additionally, clinical and developmental surveillance should be ongoing, including regular auditory and visual assessments (10).

Adverse Effects and Complications

Penicillin is generally well-tolerated, with rare occurrences of local reactions and the Jarisch-Herxheimer reaction. In cases of treatment failure, additional evaluation and a prolonged course of parenteral penicillin are warranted (10).

Evaluation and Follow-Up

Evaluation and follow-up play a crucial role in the management of congenital syphilis, aiming to assess treatment response, monitor for disease progression, and prevent long-term complications. The evaluation process involves a combination of clinical assessments, serological testing, and developmental monitoring, tailored to the age and clinical status of the patient (11).

Clinical Assessment

Regular clinical evaluations are essential to detect any signs or symptoms of disease progression or treatment failure. Infants and children should undergo thorough physical examinations, focusing on identifying manifestations of congenital syphilis, such as skin lesions, hepato splenomegaly, skeletal abnormalities, and neurological findings. Developmental milestones should be monitored closely to detect any delays or abnormalities early on (11,12).

Serological Testing

Serological testing is a key component of the evaluation and follow-up process in congenital syphilis. Non-treponemal tests, such as VDRL or RPR, are commonly used to assess treatment response and monitor disease activity. These tests should be performed every 2-3 months initially, with the frequency decreasing as the titers become non-reactive. Serological testing should continue until the titers are non-reactive or have decreased by at least fourfold from the initial titers (12).

Neuroimaging and CSF Analysis

In cases where there is suspicion of neurosyphilis or inadequate treatment response, neuroimaging studies and cerebrospinal fluid (CSF) analysis may be warranted. Neuroimaging can help detect structural abnormalities or lesions indicative of neurosyphilis, while CSF analysis can provide valuable information on the presence of T. pallidum and inflammatory markers. These tests should be performed based on clinical judgment and may require consultation with a pediatric neurologist or infectious disease specialist (13).

Developmental Monitoring

Developmental surveillance is critical in infants and children with congenital syphilis to detect any delays or abnormalities early on. Regular assessments of developmental milestones, including motor, cognitive, and social skills, should be performed to ensure appropriate intervention and support are provided if needed (14).

Special Considerations

Patients with a history of congenital syphilis should receive ongoing monitoring and follow-up throughout childhood and adolescence, as they may be at increased risk for certain

complications, such as cognitive or developmental delays, hearing loss, or vision problems. These patients may benefit from multidisciplinary care involving pediatricians, infectious disease specialists, developmental pediatricians, and other specialists as needed (15).

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