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CONGENITAL SYPHILIS IN NEWBORNS: CURRENT APPROACHES TO DIAGNOSIS, TREATMENT, AND PREVENTION

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Abstract. Background: Congenital syphilis remains a significant challenge in neonatal medicine and public health because of its association with fetal infection, stillbirth, premature delivery, neonatal mortality, and long-term complications. Despite the availability of effective diagnostic methods and antibiotic treatment, delayed maternal diagnosis, inadequate prenatal care, and insufficient preventive interventions continue to contribute to adverse pregnancy outcomes.

This study aims to critically analyze current scientific evidence regarding the clinical manifestations, diagnostic criteria, therapeutic approaches, and prevention strategies for congenital syphilis in newborns, with particular emphasis on factors influencing early detection and effective clinical management.

Keywords: congenital syphilis; newborns; Treponema pallidum; neonatal infections; vertical transmission; serological diagnosis; antenatal screening; penicillin therapy; perinatal complications; prevention.

Introduction

Congenital syphilis is a potentially severe multisystem infectious disease caused by Treponema pallidum, primarily transmitted from an infected pregnant woman to her fetus through the placenta. The disease continues to represent a major global public health concern despite the availability of inexpensive diagnostic tests and effective antimicrobial treatment.

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Maternal syphilis may result in a wide spectrum of adverse pregnancy outcomes, including spontaneous abortion, stillbirth, premature birth, neonatal death, and congenital infection. The clinical presentation of congenital syphilis ranges from asymptomatic infection to severe systemic involvement affecting the skin, liver, spleen, bones, hematological system, and central nervous system.

One of the principal diagnostic challenges is that infected newborns may appear clinically healthy at birth, while manifestations of the disease can develop during infancy or later childhood. Consequently, clinical examination alone is insufficient to exclude congenital syphilis.

The prevention of congenital infection depends primarily on the timely identification and appropriate treatment of maternal syphilis during pregnancy. However, inequalities in healthcare access, delayed prenatal registration, inadequate screening coverage, and incomplete maternal treatment remain substantial barriers.

The objective of this review is to examine current approaches to the diagnosis, treatment, and prevention of congenital syphilis in newborns and identify key clinical and healthcare-system factors influencing neonatal outcomes.

Literature Review

Epidemiology and Global Burden of Congenital Syphilis

Congenital syphilis remains a major challenge in neonatal medicine, maternal healthcare, and public health. Although effective diagnostic procedures and antimicrobial treatment have been available for decades, the disease continues to contribute substantially to fetal loss, stillbirth, neonatal mortality, and long-term disability.

Gomez et al. (2013), in a systematic review and meta-analysis of untreated maternal syphilis, demonstrated a strong association between maternal infection and adverse pregnancy outcomes. Their findings provided important epidemiological

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evidence supporting the implementation of routine antenatal screening and timely antimicrobial treatment.

More recently, Stafford, Workowski, and Bachmann (2024), in their review published in the New England Journal of Medicine, examined the consequences of syphilis during pregnancy, emphasizing the importance of maternal disease stage, timing of treatment, and prevention of vertical transmission. The authors highlighted that congenital syphilis remains preventable when maternal infection is identified and treated appropriately.

According to World Health Organization estimates, approximately 700,000 cases of congenital syphilis occurred globally in 2022, with an estimated 390,000 associated adverse birth outcomes. These findings indicate that congenital syphilis remains a substantial international health burden despite the availability of effective preventive interventions.

The clinical presentation of congenital syphilis is highly variable, ranging from asymptomatic infection to severe multisystem disease. Salomè et al. (2024), in their review entitled Congenital Syphilis: A Re-Emerging but Preventable Infection, examined the contemporary clinical significance of congenital infection and its association with fetal and neonatal complications. Their work reinforces the importance of timely recognition of infection and appropriate clinical management.

Flores et al. (2026), in a state-of-the-art review published in Clinical Infectious Diseases, emphasized that congenital syphilis may affect nearly every organ system. They also highlighted that many infected infants are asymptomatic at birth, while delayed manifestations may emerge over subsequent years. This variability complicates early diagnosis and makes systematic neonatal evaluation particularly important.

The literature identifies hepatosplenomegaly, cutaneous lesions, rhinitis, hematological abnormalities, skeletal lesions, and neurological complications among the recognized manifestations of early congenital syphilis. However, these findings may

overlap with other neonatal infections, requiring a comprehensive differential diagnostic approach.

Diagnostic Challenges and Serological Assessment

Early diagnosis is essential for preventing serious complications of congenital syphilis. Nevertheless, laboratory confirmation remains challenging because maternal antibodies can cross the placenta and produce reactive neonatal serological results in the absence of confirmed neonatal infection.

The CDC Laboratory Recommendations for Syphilis Testing (2024) emphasize the importance of quantitative nontreponemal tests, including the rapid plasma reagin (RPR) and Venereal Disease Research Laboratory (VDRL) assays. The recommendations explain that treponemal tests performed on neonatal serum are difficult to interpret because passively transferred maternal antibodies may persist for more than one year.

Fanella et al. (2024), in their publication Diagnosis and Management of Congenital Syphilis: Avoiding Missed Opportunities, stressed the importance of assessing maternal treatment history, reinfection risk, paired maternal and infant serological findings, and neonatal clinical manifestations. Their review identifies incomplete information about maternal infection and treatment as an important barrier to appropriate neonatal risk assessment.

Consequently, current diagnostic approaches rely on the integration of clinical observations, maternal medical history, comparative serological testing, and additional investigations such as cerebrospinal fluid examination and long-bone radiography when indicated.An important issue in the literature concerns the limited evidence supporting alternative antibiotic regimens for neonatal congenital syphilis. Accordingly, penicillin-based treatment continues to be the recommended standard.

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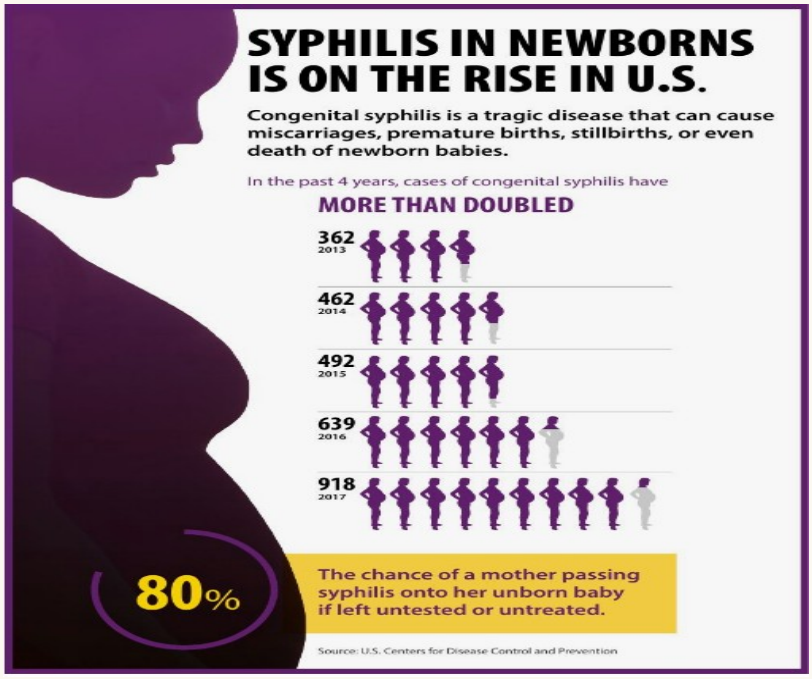

Figure 1. Rising Incidence of Congenital Syphilis in the United States, 2013–2017

Figure 1 illustrates the increasing number of reported congenital syphilis cases in the United States between 2013 and 2017, based on data from the U.S. Centers for Disease Control and Prevention (CDC). The number of reported cases increased from 362 in 2013 to 918 in 2017, representing an approximately 154% increase.

The infographic also highlights the substantial risk of mother-to-child transmission when maternal syphilis remains untreated. These findings emphasize the importance of early prenatal screening, timely diagnosis, appropriate penicillin treatment, and effective public health interventions to prevent congenital syphilis and reduce adverse neonatal outcomes

Results and Analysis

The analysis of international epidemiological reports demonstrates that congenital syphilis remains a significant cause of preventable neonatal morbidity and mortality. Despite the availability of reliable serological screening methods and effective penicillin-based treatment, the global burden of congenital syphilis remains substantial.

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According to estimates published by the World Health Organization (WHO), approximately 700,000 cases of congenital syphilis occurred worldwide in 2022, corresponding to an estimated incidence of 523 cases per 100,000 live births. This figure was more than ten times higher than the WHO elimination threshold of 50 cases per 100,000 live births.

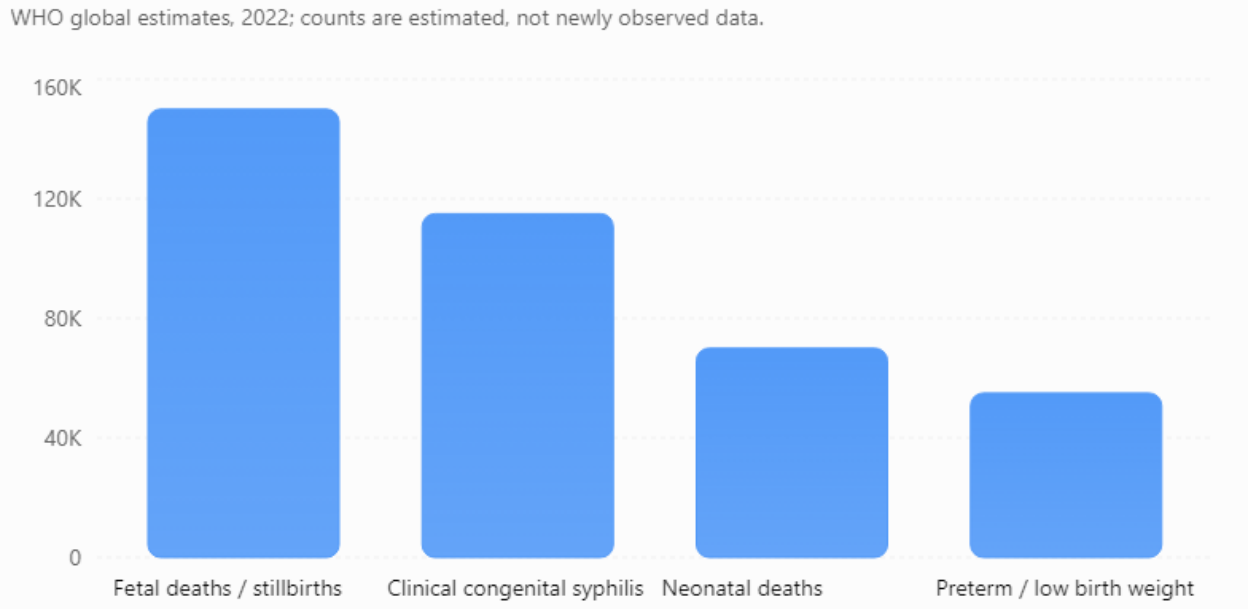

Figure 2. Estimated adverse birth outcomes associated with maternal syphilis worldwide, 2022 (Source: WHO global estimates for 2022).

These findings indicate that congenital syphilis produces consequences extending beyond neonatal infection itself. The substantial number of fetal deaths and stillbirths emphasizes the importance of identifying maternal syphilis before irreversible fetal complications develop.

However, WHO figures represent model-based global estimates rather than a single prospective clinical cohort. Consequently, they should not be interpreted as patient-level outcomes or directly extrapolated to individual countries.

Maternal Risk Factors and Missed Opportunities for Prevention

The analysis identified inadequate maternal screening and treatment as major preventable contributors to congenital syphilis. WHO estimates for 2022 indicate that 21% of syphilis-associated adverse birth outcomes occurred among women who had

not attended antenatal care, while approximately 53% occurred among women who attended antenatal care but were not screened for syphilis. Another 16% occurred among women who tested positive but did not receive treatment or received inadequate treatment.

Further evidence comes from the CDC analysis of congenital syphilis cases in the United States during 2022. Among 3,761 reported cases, 3,302 (87.8%) involved absent or untimely maternal testing, inadequate treatment, or absent or undocumented treatment.

Specifically, 36.8% involved absent or untimely testing, 39.7% inadequate treatment, and 11.2% absent or undocumented treatment.

The comparison of WHO and CDC findings reveals a consistent pattern: failures in maternal screening and treatment contribute substantially to the persistence of congenital syphilis.

Nevertheless, these datasets differ in geographic coverage and methodology. WHO data represent global modeled estimates, whereas the CDC findings are based on reported national surveillance cases. Therefore, their percentages should not be pooled or interpreted as a common study population.

Analysis of Clinical Manifestations in Newborns

The reviewed clinical literature and international guidelines indicate that congenital syphilis is characterized by substantial variation in clinical presentation.

A major diagnostic challenge is the possibility of asymptomatic infection during the neonatal period. The absence of visible abnormalities at birth does not exclude congenital syphilis, particularly when maternal infection remains untreated or inadequately treated.

The principal manifestations identified in clinical guidance are summarized below.

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1-Table

Analysis of Clinical Manifestations in Newborns

Clinical category	Principal manifestations	Diagnostic significance
Dermatological	Maculopapular rash, vesiculobullous lesions	May support early clinical recognition
Hepatobiliary	Hepatomegaly, splenomegaly, jaundice	Suggests possible systemic involvement
Hematological	Anemia, thrombocytopenia	May indicate systemic infection
Skeletal	Osteochondritis, periostitis	Can support diagnosis in conjunction with other findings
Neurological	Abnormal cerebrospinal fluid findings, neurological abnormalities	Requires assessment for possible neurosyphilis
Sensory	Hearing and ocular abnormalities	Important for assessment of complications

These findings suggest that neonatal examination must be integrated with maternal serological history rather than used as an isolated diagnostic procedure. Importantly, the available evidence does not justify ranking these manifestations by frequency without a clearly defined clinical dataset. A comparative cohort study would be necessary to determine their relative prevalence and associations with neonatal outcomes.

Comparative Analysis of Diagnostic Approaches

The diagnostic analysis indicates that the accuracy of congenital syphilis assessment depends on the combined interpretation of maternal treatment history, neonatal physical findings, and quantitative serological testing. CDC recommendations distinguish four clinical scenarios: confirmed or highly probable congenital syphilis, possible congenital syphilis, congenital syphilis less likely, and congenital syphilis unlikely. This classification reflects the recognition that no single serological result can reliably establish or exclude congenital infection in every neonatal presentation.

2-Table

Comparative Analysis of Diagnostic Approaches

Diagnostic parameter	Clinical interpretation
Maternal syphilis history	Establishes infection and treatment context
Adequacy and timing of maternal treatment	Helps determine neonatal infection risk
Neonatal physical examination	Identifies manifestations compatible with congenital syphilis
Quantitative RPR/VDRL comparison	A neonatal titer at least fourfold higher than the maternal titer supports highly probable infection
Cerebrospinal fluid evaluation	Assesses possible central nervous system involvement when indicated
Long-bone radiography	Identifies skeletal abnormalities associated with congenital syphilis
Clinical and serological follow-up	Supports assessment of infection status and treatment response

An important limitation of neonatal serology is the transplacental transfer of maternal IgG antibodies. Consequently, reactive treponemal tests in newborns may reflect passive antibody transfer rather than active congenital infection. These findings support a risk-based diagnostic strategy combining maternal and neonatal information.

The reviewed guidelines consistently identify penicillin G as the preferred treatment for congenital syphilis. According to CDC recommendations, neonates with confirmed or highly probable congenital syphilis generally require a ten-day course of parenteral penicillin G. Management of infants in lower-risk categories depends on clinical findings, maternal treatment adequacy, laboratory evaluation, and the ability to ensure follow-up. From an analytical perspective, three findings are particularly important.

• First, treatment decisions should not depend solely on the presence of neonatal symptoms. Infants without obvious clinical abnormalities may still require treatment when maternal infection history indicates significant risk.

• Second, the adequacy and timing of maternal therapy are central to neonatal risk assessment. Treatment initiated too close to delivery may not provide adequate protection, even when appropriate medication has been prescribed.

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• Third, successful management extends beyond antimicrobial administration. CDC recommends clinical examination and quantitative nontreponemal serological testing every two to three months in neonates with reactive tests until seroreversion occurs. Persistent titers after treatment require reassessment.

The reviewed sources support the established role of penicillin therapy. However, the present narrative analysis does not provide a pooled treatment success rate because comparable patient-level outcomes and follow-up measures were not available for formal meta-analysis.

The combined epidemiological and clinical evidence highlights three interrelated determinants of congenital syphilis outcomes: maternal healthcare access, diagnostic accuracy, and continuity of neonatal care. The epidemiological findings demonstrate that congenital syphilis remains prevalent despite the availability of effective preventive interventions. The high proportion of cases associated with missed screening or inadequate treatment suggests that implementation gaps are a major public health concern. The diagnostic findings demonstrate that congenital syphilis cannot be reliably excluded through neonatal physical examination alone. Appropriate diagnosis requires systematic evaluation of maternal and infant clinical and serological information. The treatment findings support penicillin-based management and structured follow-up as central components of neonatal care. Taken together, the evidence indicates that reducing congenital syphilis requires coordinated interventions throughout pregnancy, delivery, and the neonatal period.The synthesis identifies several priorities for further clinical and epidemiological investigation.

A particularly important research direction is evaluating maternal screening coverage, treatment completion, neonatal diagnostic practices, and follow-up outcomes within regional healthcare systems.

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For Uzbekistan and other Central Asian countries, hospital-based retrospective studies could examine the relationship between maternal antenatal care, infection detection, neonatal clinical manifestations, and treatment outcomes.

Potential research indicators include gestational age at maternal diagnosis, treatment timing, maternal and neonatal RPR titers, birth outcomes, neonatal clinical manifestations, and follow-up serological responses.

Such investigations could provide locally relevant evidence to support improved maternal and neonatal infectious disease prevention.

The reviewed evidence supports the following conclusions:

1. Congenital syphilis remains a significant and largely preventable cause of adverse pregnancy and neonatal outcomes worldwide.

2. Gaps in antenatal screening and maternal treatment account for a substantial proportion of preventable congenital syphilis cases.

3. Neonatal infection may be asymptomatic, making comprehensive maternal and neonatal assessment essential.

4. Penicillin G remains the recommended treatment, with management determined by neonatal risk classification.

5. Continued serological monitoring is necessary to evaluate treatment response and identify infants requiring additional assessment.

The findings reinforce the importance of integrating clinical management with maternal health services and public health prevention strategies.

Conclusion

Congenital syphilis remains a significant global public health challenge, despite being a largely preventable infectious disease. The increasing incidence of congenital syphilis in several countries, particularly the United States, highlights persistent shortcomings in prenatal healthcare services, early detection, maternal treatment, and preventive interventions. Maternal infection with Treponema pallidum can result in

severe adverse pregnancy outcomes, including spontaneous abortion, stillbirth, premature delivery, neonatal mortality, and long-term neurological, auditory, visual, and developmental complications.

The available scientific evidence demonstrates that timely diagnosis and appropriate treatment of maternal syphilis are essential for preventing vertical transmission and reducing congenital infections. Universal syphilis screening during early pregnancy, repeat testing for women at increased risk or according to local epidemiological recommendations, and prompt administration of stage-appropriate penicillin therapy represent fundamental strategies for effective prevention. Furthermore, comprehensive neonatal assessment and timely treatment are necessary to minimize complications among infants with confirmed or suspected congenital syphilis.

The persistence of congenital syphilis is associated not only with biological and clinical factors but also with broader socioeconomic and structural determinants of health. Limited access to antenatal services, inadequate healthcare infrastructure, poverty, social stigma, insufficient public awareness, delayed diagnosis, and barriers to appropriate treatment contribute to preventable maternal and neonatal infections. These findings emphasize that effective congenital syphilis prevention requires an integrated approach combining clinical management, epidemiological surveillance, public health education, and equitable access to reproductive healthcare.

Strengthening maternal and child healthcare systems, improving screening coverage, ensuring the uninterrupted availability of penicillin, and enhancing coordination among obstetricians, neonatologists, pediatricians, and infectious disease specialists are essential components of prevention strategies. Additionally, evidence-based public health policies should prioritize vulnerable populations and address healthcare disparities that increase the risk of untreated maternal syphilis.

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