Review Article

Indian Journal of Maternal-Fetal and Neonatal Medicine
Volume 4 Number 1, January - June 2017
DOI: http://dx.doi.org/10.21088/ijmfnm.2347.999X.4117.11

Clinical Implications of Syphilis in Pregnancy and Dental Manifestations in Neonates

Alka Patil*, Alkesh Shende, Alka Waghmare***, Anuradha Bhatsange****, Lalitha Shiggaon******

Author's Affiliation:
*Professor & Head, Department of Obstetrics & Gynaecology, **Post Graduate Student ***Professor & Head ****Reader, Department of Periodontics, JMF's A.C.P.M. Medical College, Dhule, Maharashtra, India.

Reprint Request:
Alkesh Shende, 9/704 Premsagar Housing Complex, Near Indian oil Nagar, Mankhurd link road, Chembur, Mumbai-400043. Maharashtra, India.
E-mail: alkabpatil@rediffmail.com

Received on 10 January 2017
Accepted on 20 January 2017

Abstract

Syphilis is an infectious disease presenting stages associated with specific orallesions. Therefore, health professionals should be familiar with the different syphilis oral manifestations at each stage and be prepared to refer any suspected patient for further evaluation. Congenital syphilis is a very rare clinical entity,and its early diagnosis and treatment is essential. Dental findings often provide valuable evidence for the diagnosis of late congenital syphilis. It occurs due to the transmission of the disease from an infected mother to her fetus through placenta. This long forgotten disease continues to effect pregnant women resulting in perinatal morbidity and mortality. Congenital syphilis is a preventable disease, and its presence reflects a failure of prenatal care delivery system, as well as syphilis control programs. Although oral manifestations of syphilis are most likely to be observed during secondary disease, all stages of the disease can give rise to oral lesions. Since the prevalence of infective syphilis in heterosexuals has been increasing, there has now been a gradual rise in the number of children born with congenital syphilis. Consequently, the congenital disease gives rise to dental anomalies as well as bone, skin, and neurological anomalies of the face. This review describes the various stages of syphilis, along with its diagnosis and further management.

Keywords: Syphilis; Pregnancy; Congenital.

Introduction

Syphilis infection during pregnancy still represents a worldwide health problem. In which the congenital syphilis is an infectious disease transmitted by an infected mother to her fetus. It is the oldest recognized infection, and continues to account for extensive global perinatal morbidity and mortality [1-4]. Syphilis among pregnant women and the consequent congenital syphilis is now re-emerging in many developing countries. Congenital syphilis is mainly a consequence of the lack of antenatal care (ANC)and control of sexually transmitted infections [5].

Syphilis is a sexually transmitted bacterial infection caused by the spirochaete*Treponema pallidum*. Vertical transmission from mother to fetus can occur during pregnancy. Congenital syphilis infection can result in premature birth, low birth weight, fetal death in-utero, perinatal death and physical malformations. Syphilis in pregnancy is an infection with widespread complications for both the infected woman and her fetus.

Maternal syphilis has been associated with obstetric complications such as:

- Hydramnios
- Abortion
- Preterm delivery
- Fetal complications (fetal syphilis, hydrops, prematurity, fetal distress, and stillbirth)
- Neonatal complications (congenital syphilis, neonatal death, and late sequelae) [6].

Although congenital syphilis has been studied and described for many years, our understanding of the

pathophysiology of maternal transmission of *Treponema pallidum* is still incomplete. Furthermore, the natural history of in utero treponemal infection of the fetus, amnionic fluid, and placenta ispoorly described compared with our knowledge of neonatal and congenital syphilis. These gaps in fundamental concepts of fetal infection and its response to treatment underscore difficulties in our understanding of the optimal therapeutic approach to syphilis in pregnancy [7-8].

Transmission

Syphilis is primarily transmitted from person to person through direct contact with a syphilis ulcer or *chancre* through vaginal, anal or oral intercourse. Chancres occur predominantly on the external genitalia and in the vagina but can also occur in the perianal area or within the rectum. Chancres may also occur on the lips and in the oral cavity. Vertical transmission from an infected mother to the fetus is an important mechanism of infection. Untreated maternal infection can result in adverse pregnancy outcomes, including early fetal loss, stillbirth, prematurity, low birth weight, neonatal and infant death, and congenital disease of the newborn.

Clinical manifestations of congenital syphilis are influenced by;

- Gestational age
- Stage of maternal syphilis
- Maternal treatment
- Immunological response of the fetus [9].

Symptoms

Primary Syphilis

It has an incubation period of 14 days to 3 months. Following infection, a single painless, erythematous papule initially develops, usually on the external genitalia, but occasionally on the mouth, anus or within the rectum. This ulcerates to form a painless "punched out" ulcer or *chancre*. Multiple lesions can occur, particularly in HIV positive patients. Chancres are highly infectious and may be associated with regional lymphadenopathy. Without effective treatment the infection can progress to the secondary stage [10].

Secondary Syphilis

Organisms disseminate from the primary chancre causing symptoms 1-6 months later.

Rash – localised or diffuse mucocutaneousrash, can be macular, papular, pustular or mixed, involving the trunk, limbs, palms of hands or soles of feet. Mucosal ulcers may also occur. Other features may include fever, sore throat, oral ulcers, lymphadenopathy, hepatitis, iritis, arthritis, glomerulonephritis. Signs and symptoms resolve with or without treatment, but without effective treatment, infection will progress to the latent and late stages of disease. Spontaneous resolution of secondary syphilis occurs at 3-12 weeks [11,12].

Latent Infection

Usually asymptomatic. During this period infectivity is low, but up to one-quarter of patients will experience recrudescence of disease.

Tertiary Stage

This stage of disease occurs rarely in developed countries and follows a period of latency of up to 20 years. It is characterised by chronic inflammation, including gummatous syphilis (granulomatous lesions of the skin, mucous membranes, bone or organs), cardiovascular syphilis and neurosyphilis [13-14].

Syphilis in Pregnancy and Neonate

During pregnancy *T.pallidum*can cross the placenta to cause fetal infection, this may occur throughout the course of pregnancy. Spirochaetes are released into the circulation and disseminate to the organs, producing an inflammatory response. Frequency of vertical transmission increases with gestational age whilst the severity of fetal infection decreases with gestational age. Pregnancies complicated by untreated maternal syphilis are at increased risk of adverse outcomes such as intrauterine growth restriction, premature birth, stillbirth, neonatal death and congenital deformities.

Infection can be transmitted to the fetus at any stage of maternal disease. The rate of transmission is 60-100% during primary and secondary syphilis and decreases with later stages of maternal infection; approximately 40% in early latent infection and 8% in late latent infection. Treatment of early maternal syphilis at least 30 days before delivery is the most important factor influencing the risk of congenital infection. 70 - 100% of infants born to untreated mothers will be infected compared to 1% - 2% of those born to women adequately treated during pregnancy [15].

Early Congenital Syphilis: defined as onset of

symptoms before 2 years of age. Clinical manifestations can be varied, however persistent rhinitis (snuffles) is often the earliest presenting symptom occurring in up to 40% of affected neonates. Hepatomegaly, rash, generalised lymphadenopathy, placental and umbilical cord or skeletal abnormalities may also be seen. Skin lesions may contain spirochaetes and can transmit infection. Central Nervous System (CNS) involvement may be symptomatic or asymptomatic. Asymptomatic CNS syphilis is diagnosed by abnormalities of the Cerebral Spinal Fluid(CSF) [16].

Late congenital syphilis: defined as onset of clinical manifestations after 2 years of age. Manifestations are related to persistent inflammation or scarring in affected tissues. Late congenital syphilis occurs in approximately 40% of infants born to women with untreated syphilis in pregnancy. Manifestations include facial deformities, keratitis, sensorineural hearing loss, dental deformities (for example, Hutchinson teeth, mulberry molars), gummas of the skin and mucous membranes, intellectual impairment, hydrocephalus and skeletal deformities ("sabre shins", arthritis) [17].

Clinical Manifestations

Syphilis is caused by the spirochaete*Treponema pallidum*. This organism is transmitted duringsexual activity from a mucocutaneous lesion.The cervical changes, such hyperaemia, eversion, and friability, which occur during pregnancy, may facilitate the entry and lead to spirochaetaemia [18]. T. pallaidum can cross the placenta and cause congenital fetal infection at any time during pregnancy. The manifestatios of congenital syphilis resemble those of adult secondary syphilis, but unlike secondary syphilis frequently there is skeletal involvement such as osteomyelitis, osteochondrosis or periostitis [19].

Placenta in Syphilis

The examination of placenta is often helpful in diagnosis of congenital syphilis and on gross examination it appears large, pale and oedaematous. Microscopically, villi are immature, enlarged with bullous projections and vessels have endovascular and perivascular proliferation. Treponema has been clearly identified in first trimester abortions of women with recent syphilitic infection. The concept in congenital syphilis is that more recent the maternal infection, the more severe the congenital infection. The presence of anti-treponemal IgM antibodies in neonates is diagnostic of congenital syphilis. IgG antibodies are not diagnostic of congenital infection, and may be manifestation of transplacental transmission [19].

The fundamental histological changes of both congenital and acquired syphilis are vasculitis and its consequences, necrosis and fibrosis. Pregnancy has no known effect on the clinical course of syphilis. In acquired infection, after an initial incubation period of 3–90 days, a solitary papule with central ulceration, teeming with spirochetes, erupts at the site of inoculation, which is often found on the genitalia, and less frequently on the rectal and the oral mucosa. This popular lesion is known as the chancre of syphilis and marks the primary stage of the disease. The chancre is accompanied by regional lymphadenopathy in 50% of the cases, and lasts from 4–6 weeks with spontaneous resolution. In about 2–6 weeks after the chancre resolves, systemic manifestations of the disease appear [20].

The systemic manifestations of the disease include low grade fever, headache, generalised lymphadenopathy, symmetrically distributed maculopapular rash found on the palms and the soles, the patchy moth-eaten alopecia seen with follicular scalp lesions, the highly infectious condylomalatum found on the genitalia, mild hepatitis, and nephrotic syndrome. The latent stage of the disease is characterised by reactive serological tests but no clinical manifestations. The latency is arbitrarily subdivided into early (1 year or less from the onset of the infection) and late (more than 1 year) latent stage. In the early latent stage, 25% of the patients will relapse with a secondary syphilitic manifestation whereas the chance for such relapses in the late latent stage is minimal. After years of untreated disease, one third of the adults can develop tertiary syphilis consisting of destructive lesions of the aorta (such as aortic aneurysm, regurgitation, lueticaortitis), central nervous system disorders (such as tabes dorsalis, meningiovascular syphilis, general paresis), skin and skeletal system manifestations (such as gummas). The mother can transmit the infection transplacentally to the fetus or during passage through the birth canal by contact of the newborn with a genital lesion. Breast feeding does not result in the transmission of syphilis, unless an infectious lesion is present on the breast [21].

Until recently, a commonly held but erroneous obstetric principle stated that infection of the fetus does not occur before 18 weeks [22]. Silver and immunofluorescence staining of the fetal tissue, or polymerase chain reaction and rabbit infectivity testing of amniotic fluid showed that *T pallidum* gains access to the fetal compartment as early as 9–10 weeks. Untreated syphilis during pregnancy can

profoundly affect pregnancy outcome, resulting in spontaneous abortion, stillbirth, non-immune hydrops fetalis, intrauterine growth restriction, premature delivery, and perinatal death, as well as serious sequelae in liveborn infected children [23-24].

Oral manifestations of Congenital Syphilis

The orofacial manifestations of congenital syphilis can be split into early and late. Early features include diffuse maculopapular rash, periostitis(frontal bossing of Parrot), and rhinitis. Late features, manifesting at least 24 months after birth, comprise the Hutchinsoniantriad of interstitial keratitis of the cornea, sensorineural hearing loss, and dental anomalies.

Dental Manifestations

The dental anomalies of congenital syphilis only arise in teeth in which calcification occurs during the first year of life, hence typically the permanent incisors and first molars. Of note, the maxillary incisors are more commonly affected than the mandibular ones. The incisors have a screwdriver shape, there being a convergence of the lateral margins towards the incisal edge. In some, there may be notching of the incisal edge, while in others, there may be a depression on the labial surface. The first molar may be bud-shaped and reduced to the size of the adjacent second molar. The normal mesiodistal convexity of the crown may be reduced. Enamel hypoplasia may occur. Yellow discoloration of the skin about the lips can arise soon after birth; the area then becomes increasingly rigid with crack formation and eventual (Parrot's) radial scars—rhagades—of the lips. There may be a loss of the well-circumscribed border of the vermillion.Other, less common orofacial features include atrophicglossitis and a high, narrow palatal vault. Facial neuropathies may rarely occur as can palatal gumma in adulthood [25].

Treatment of Syphilis in Pregnancy

It is important to have a preventive approach before understanding the management, which involves emphasizing the importance of monogamous sexual relationship, along with the use of condoms.

The following recommendations should be considered in the management:

- Screening for other sexually transmitted diseases
- Suspect coexisting syphilis in presence of any other sexually transmitted diseases.
- Counselling about risks of congenital infections
- Specific treatment is to administer specific antibiotics [26].

The treatment for syphilis in pregnancy is identical to that of adults who are not pregnant, except that penicillin is the only agent that is appropriate for use during pregnancy. Tetracyclines are contraindicated in pregnancy because of their effect on fetal bone and tooth development. Erythromycin has inconsistent placental transfer, and treatment failures have been reported [27].

For primary, secondary or early latent syphilis, 2.4 million units of benzathine penicillin G (BPG) is given intramuscularly in one dose [28]. Some experts recommend a second dose of BPG for pregnant women due to the possibility of treatment failures and transmission to the fetus, especially for secondary syphilis [29,30]. For the treatment of late latent syphilis or disease of unknown duration, 2.4 million units of BPG given intramuscularly once weekly for three weeks is recommended. Women with a documented penicillin allergy should undergo desensitization and treatment with penicillin. Individuals with neurosyphilisshould receive 3 to 4 million units of crystalline penicillin G intravenously every 4 h for 10 to 14 days [28].

Individuals infected with the human immunodeficiency virus (HIV) should undergo investigation for neurosyphilisbefore treatment. Following adequate therapy for primary or secondary syphilis, the required monthly follow-up testing should show at least a fourfolddecline in titre three to four months after treatment. If treatment occurs in the latent or late stages or if reinfection occurs, a more gradual decline in titres may be seen, and a low positive titre (1:2,1:4) may persist in approximately 50% of such individuals for two or more years (ie, a serofast reaction). Women in whom titres fail to decline as predicted require investigation and management for neurosyphilis (lumbar puncture for cell count, protein and VDRL), and further therapy.

Discussion

In consideration with the above mentioned manifestations and its effect on the neonates, it is important that preconceptionserological tests for syphilis could represent the key to reduce the incidence of congenital syphilis. Moreover, preconception counselling could play an important role in evaluating the woman and her partner for exposure to sexually transmitted diseases, identifying high risk behaviours and providing health promotion messages and education [31].

All pregnant women should be tested forsyphilis in pregnancy. Women at high risk for acquiring syphilis in pregnancy should beretested at the beginning of the third trimester (28 weeks) and at delivery. HIV testing should be recommended to all pregnant women. HIVtesting is particularly important in women with positive syphilis serology, as is testing for hepatitis B surface antigen, hepatitis Cantibody, chlamydia and gonorrhea. Penicillin is the only antibiotic proven to beeffective in the management of gestational syphilis. Children born to mothers treated witha nonpenicillin regimen should be considered to have been treated inadequately. Syphilis and HIV coinfection is not uncommon. Serocon version may be delayed and clinical presentation atypical in HIV-infected women. Treatment failures for gestational syphilis are more common in this group; treatment of infants should be given consideration regardless of serology and symptomatology [32].

Diagnosis and management of congenital syphilis should be based on maternal history, clinical findings and nontreponemal (VDRL or RPR) and treponemal testing (FTA-ABS and/or MHA-TP). Tests to identify definitively infected infants at birth, such as IgM and DNA detection (polymerase chain reaction), are considered investigational. The persistence of treponemal antibody after 15 to 18 months of age may confirm congenital infection in the asymptomatic child. All children with clinical or serological evidence of congenital syphilis should be treated with penicillin G for 10 to 14 days. Close clinical and serological follow-up of all children potentially exposed to syphilis in utero is required [33].

The major changes in the new recommendations involve increased obstetric involvement in evaluation for signs of fetal syphilis before treatment. Ultrasonographicfetal examination for signs of syphilis is recommended prior to therapy after 20 weeks' gestation. Fetal hepatomegaly, ascites, hydrops, hydramnios, and placental thickening are all sonographic findings that indicate a high risk of fetal syphilis. Fetal treatment failure is higher in this setting, and counseling and management will be improved by fetal ultrasonographic evaluation before treatment. Coordination of care is critical to assure that ultrasonographic examination does not delay needed treatment.

Clearly, the most effective method to reduce congenital syphilis is to reduce the rates of primary, secondary, and latent syphilis in women of reproductive age. However, we must not lose sight of the fact that prenatal syphilis serological testing is an essential component of identifying infected gravidas who need antepartum treatment. Prenatal testing to prevent congenital syphilis must not fall in our priorities as the rates of infectious syphilis in women approach elimination.

References

1. Singhal P, Patel P, Marfatia YS. A case of congenital syphilis with Hutchinson's triad. Indian J Sex Transm Dis, 2011; 32:34-6.
2. Schwalb RA. Hutchinson's incisors in congenital syphilis. Bull Union Cty Dent Soc 1967;16:12-3.
3. Stout FW, Lawson BF. A method for the detection of syphilis in the dental office. S C Dent J, 1970; 28:6-13.
4. Bertram FP. The dentist's role in finding congenital syphilis. J Vener Dis Inf, 1950; 31:191-3.
5. Brighi G, Farneti G, Marangoni A, Tridapalli E, Neri I, Capretti MG, et al. Congenital syphilis like many years ago. Case Rep Infect Dis, 2011; 2011:235059.
6. Nathan L, Bohman VR, Sanchez PJ, Leos NK, Twickler DM, Wendel GD Jr. In utero infection with Treponema pallidum in early pregnancy. Prenat Diagn, 1997; 17:119–23.
7. Nathan L, Twickler DM, Peters MT, Sanchez PJ, Wendel GD Jr. Fetal syphilis: correlation of sonographic findings and rabbit infectivity testing of amniotic fluid. J Ultrasound Med, 1993; 12:97–101.
8. Wendel GD Jr, Sanchez PJ, Peters MT, Harstad TW, Potter LL, Norgard MV. Identification of Treponema pallidum in amniotic fluid and fetal blood from pregnancies complicated by congenital syphilis. ObstetGynecol, 1991; 78:890–5.
9. RaposoVm., Zallen Rd. The Resurgence Of Syphilis: A Case Report Of Oral Cutaneous Secondary Syphilis. J. Colo. Dent. Assoc., 1997; 76:18-9.
10. Siegal Ma. Syphilis AndGonorrhea. Infect. Dis. Dent., 1996; 40:369-83.
11. Junkins-Hopkins J. Multiple Painful Oral Ulcerations. Arch. Otolaryngology-Head Neck Surg., 1995; 137: 833-8.
12. Mani Nj. Secondary Syphilis Initially Diagnosed From Oral Lesions. Oral Surg., 1984; 58:47-50.
13. Kearns G, Pogrel Ma, Honda G. Intraoral Tertiary Syphilis (Gumma) In a Human Immunodeficiency Virus-Positive Man: A Case Report. J. Oral Maxillofac. Surg, 1993; 51:85-8.
14. Aarestrup Fm., Vieira Bj. Oral Manifestation Of Tertiary Syphilis: Case Report. Braz. Dent. J., 1999; 10:117-21.
15. FiumarraNy., Grande Dj., Guinta Jl. Papular Secondary Syphilis Of The Tongue. Oral Surg., Oral Med., Oral Pathol.,1978; 45:540-2.
16. Housego Hons T., Wood Re., Grotepass F., Nortje

Cj. Repair Of Palatal Defect Associated With Late Congenital Syphilis Using A Tongue Flap. J. OralMaxillofac. Surg., 1988; 46:70-3.

17. Stoll Bj. Congenital Syphilis. Evaluation And Management Of Neonates Born To Mothers With Reactive Serologic Tests For Syphilis. Pediatr. Infect. Dis. J., 1994; 13:845-51.
18. Wendel G. Gestational and congenital syphilis. Clin Perinatol, 1988; 15:287–303.
19. Fernando Arias, ShirishDaftari, AmarnathBhide. Perinatal Infectious Diseases Practical guide to high risk pregnancy and delivery: A South Asian perspective. 3rd ed. New Delhi Elsevier; Fetal Infections: p.135-171.
20. Singh AE, Romanowski B. Syphilis: Review with emphasis on clinical, epidemiologic, and some biologic features. ClinMicrobiol Rev, 1999; 12:187-209.
21. Laskaris G. Oral manifestations of infectious diseases. Dent Clin North Am, 1996; 40:395-423.
22. Dippel A. The relationship of congenital syphilis to abortion and miscarriage, and the mechanism of uterine protection.Am J Obstet Gynecol, 1944; 369–79.
23. Harter C, Benirschke K. Fetal syphilis in the first trimester. Am J Obstet Gynecol, 1976; 124:705–11.
24. Nathan L, Bohman V, Sanchez P, et al. In utero infection with Treponema pallidum in early pregnancy. Prenat Diagn, 1997; 17:119–23.
25. Housego T, Wood RE, Grotepass F, Nortje CJ. Repair of a palatal defect associated with late congenital syphilis using a tongue flap. J Oral Maxillofac Surg. 1998; 46:70-3.
26. ShirishDaftari, SudipChakravarti. Manual of Obstetrics. 3rd ed. New Delhi. Elsevier; Perinatal Infectious Diseases; p.164-169.
27. Rolfs RT. Treatment of syphilis, 1993. Clin Infect Dis 1995; 20(Suppl 1):S23-38.
28. Health Canada. Canadian STD Guidelines. Ottawa: Health Canada, 1998:150-9.
29. 1998 Guidelines for the treatment of sexually transmitted diseases. Centers for Disease Control and Prevention. MMWR Morb Mortal Wkly Rep, 1998; 47(RR-1):1-111.
30. Alexander JM, Sheffield JS, Sanchez PJ, Mayfield J, Wendel GD Jr. Efficacy of treatment for syphilis in pregnancy. Obstet Gynecol, 1999; 93:5-8.
31. B.G Patil, AlkaPatil. Intrauterine infections as etiological factors for hearing loss. International Journal of Recent trends in Science and Technology, 2015 April; 14(3):644-649.
32. Sandra R Arnold, E Lee Ford-Jones. Congenital syphilis: A guide to diagnosis and management. Paediatr Child Health, 2000 November/December; 5(8):463-469.
33. George D. Wendel Jr., Jeanne S. Sheffield, Lisa M. Hollier, James B. Hill, Patrick S. Ramsey, Pablo J. Sa´nchez. Treatment of Syphilis in Pregnancy and Prevention of Congenital Syphilis.Clinical Infectious Diseases 2002; 35(Suppl 2):S200–9.