REVIEW

A Review on Congenital Tuberculosis

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ABSTRACT

Background: Congenital tuberculosis is defined as infection acquired to a newborn from infected mother by Mycobacterium tuberculosis bacilli during the intrauterine period or during normal birth. Though tuberculosis infection is very common all over the world, congenital tuberculosis is rare and mortality is 50%. Non-specific symptoms in congenital tuberculosis and difficulties encountered in the diagnosis of tuberculosis in general, make it difficult to reach a final diagnosis so congenital tuberculosis is generally known clinically during the first postnatal month. Maternal tuberculosis is common but congenital tuberculosis is rare and fatal. Also the clinical features are not specific but diagnosis is difficult. So screening of all pregnant ladies can help in early diagnosis and prevention of congenital tuberculosis.

Methods: This article has been produced by analyzing various publications since 1998 till date, and by using search gear, pub med, hinari and google.

Result: Around 350 cases have been reported so far from different part of the world. There is paucity of data from our part of world.

Conclusion: The difficulties in diagnostic and therapeutic conduct of this disease, which are of great interest to public health, points to the need to develop specific protocols.

Key words: Congenital, Review, Tuberculosis
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INTRODUCTION

Congenital tuberculosis is rare despite tuberculosis being a common infection world wide.[1] Three hundred cases were reported in the literature till 1989.[2] Fifty eight cases were reviewed by Abughali et al in 1994[3], and from 2001 to 2005, 18 more cases were reported.[4-10] Tuberculosis (TB) among pregnant women is common, but congenital TB are rare because firstly tuberculosis primarily causes infertility[11] and also secondly placenta forms a protective barrier against the invasion of the fetus by the tuberculous organisms but it has been assumed that the infection acquires in uterus, because of: (i) the age of the infant, (ii) absence of any known contact with an open case of TB, and (iii) generalized dissemination of the disease. The risk of TB in pregnancy has increased owing to recent changes in the epidemiology of the disease, which has led to an increased risk of congenital TB [4, 12]. Although a rare disease, congenital TB should be distinguished from the more frequent acquired neonatal TB, in which the infant is infected after birth by an adult suffering from the disease. Congenital TB may occur as a result of maternal TB when it involves the genital tract or placenta. The signs and symptoms are non-specific; the atypical clinical manifestations of congenital TB and the devastating consequences in absence of early therapy signify the importance of early diagnosis and treatment during the neonatal period.[4,12,13,14]

Infections acquired early in neonatal life also has similar clinical manifestations and treatment. Thus, clinical differentiation of neonatal and congenital tuberculosis is epidemiological.[15]

PATHOPHYSIOLOGY

As described earlier the tubercular bacilli are transmitted transplacentally through the umbilical vein giving to primary localization in liver or lung. It can also be transmitted by aspiration of infected amniotic material either in utero or during passage through birth canal leading to primary infection in lungs or in GIT. Transplacental is usually late in pregnancy with primary lesion in liver leading to characteristic periportal lymphadenopathy. Furthermore, hematogenous spread may lead to lesions in the lung and brain. Caseous lesion in the placenta cause amniotic fluid to be infected. This infected amniotic material aspirated/ ingested will lead to multiple foci in lung and gut resulting in enlarged mesenteric, bronchial or both lymphnodes.[16, 17] Eustachion tube in the newborn is patent and does not collapse. Bacteria can readily access the middle ear via the eustachion tube and spread the disease to middle ear via pharyngeal secretion. This form of disease presents as multiple perforation or total destruction of tympanic membrane.[18] So, it is worthwhile to do histopathological examination of placenta in mother with tuberculosis.

DIAGNOSTIC CRITERIA

Diagnostic criteria for the diagnosis of congenital tuberculosis were laid down by Beitzki in 1935 and subsequently revised by Cantwell in 1994.[19] These are summarized in Table 1.

Table 1: Diagnostic criteria for congenital tuberculosis

A. Beitzki criteria (12, 14)
▪ Isolation of M. tuberculosis from the infant
▪ Demonstration of the primary complex in the liver
▪ In the absence of primary complex in the liver: ❖ Evidence of tuberculosis within days after birth
❖ Absence of contact with a case of tuberculosis after birth
B. Revised criteria by Cantwell (19)
Proven tuberculosis lesions in the infant plus one of the following:
▪ Lesions occurring in the first week of life
▪ A primary hepatic complex
▪ Maternal genital tract or placental tuberculosis

CLINICAL MANIFESTATION

The affected infant is frequently born premature, but signs of disease usually do not appear for several days or weeks. The most common presentation is with respiratory distress, lethargy, poor feeding, fever, irritability, abdominal distension and failure to thrive, seizure. Hepatospleenomegaly and lymphadenopathy are common. Meningitis is uncommon, as is the jaundice. In a small percentage of cases otitis media with or without mastoiditis is the first sign of congenital TB. Obstructive jaundice due to glands in the porta hepatitis may occur and papular or pustular skin lesions may be found in few cases[2,4,6,12,14] some may have progressive liver dysfunction in absence of respiratory symptoms[7] finally, the course is often fulminant, characterized in many cases by dissemination of the infection.[4]

INVESTIGATIONS

Congenital TB is particularly difficult to diagnose. The mothers are often apparently healthy. In one review, 24 of 32 mothers were asymptomatic[3], because the signs and symptoms of tuberculosis in neonates are nonspecific; they are initially attributed to other causes like prematurity, congenital viral infections or sepsis[21, 22] So the diagnostic testing for tuberculosis is necessary.

1. Mantoux test is frequently negative [2,4,12,14] . In the classical study of Hageman et al[23] only 2 of

the 14 infants with congenital TB had positive tuberculin tests. Similarly in another study of 9 infants with congenital TB, only 2 showed the positive reactions (> 10mm).[6]

2. Chest radiography and computed tomography showed the presence of scattered infiltrates, bronchopneumonia, consolidation or periportal hypodensity.[4,10,12]
3. Positive smear and/ or culture results can often be obtained from gastric washings, open liver biopsy, lymph node biopsy, spinal fluid, ear discharge, endotracheal aspirate or bone marrow.[2,4,14]
4. Newer modalities like polymerase chain reaction (PCR) [4,13] and T-SPOT.TB assay are highly beneficial in the diagnosis of congenital TB. The T-SPOT.TB assay is a type of commercially available interferon-gamma (IFN-gamma) released assays (IGRAs) which are based on IFN-gamma released by antigen-specific T-cells. Other types of IGRA are Quantiferon TB Gold and Quantiferon In-Tube tests. T-SPOT.TB assay proved to have greater sensitivity than Tuberculin Skin Tests and also T-SPOT.TB assay have greater specificity than Tuberculin Skin Tests in BCG- vaccinated individuals.[24]
5. Recently phage typing is also used to establish the identity of mycobacteria isolated from mother and the infant.[2,14]
6. Mother's history regarding tuberculosis during pregnancy especially pleural effusion, military or meningeal disease suggesting primary lymphohematogenous spread or history of endometritis. Work up of the mother should include a histological examination of placenta at birth, Montoux test, chest X-ray and endometrial aspiration and curettage.[25-28]

The diagnosis is based on positive smear and/or culture results obtained from gastric washings, liver biopsy, lymph node biopsy, spinal fluid, ear discharge, endotracheal aspirate or bone marrow biopsy and mother's history of tuberculosis in antenatal period.

TREATMENT

Congenital TB is a rare entity, even in human immunodeficiency virus (HIV) endemic populations, and is uniformly fatal if untreated.[4,5] Treatment of the infant should begin as soon as the diagnosis is suspected without waiting for laboratory confirmation, while appropriate specimens should be obtained fast for bacteriological and histological examination.[2,12,14]

Since congenital TB is rare, no therapeutic trials have determined the optimal treatment, however, several regimens have been evaluated and established.[29,30] Treatment regimens should contain at least 2 and preferably 3 drugs to which the organisms are likely to be susceptible.[9,14] Complete recovery has been obtained by combination of isoniazid, rifampin and pyrazinamide for 18 months with intravenous amikacin for initial 2 months.[4] A 6 month course of isoniazid (H), rifampin (R), pyrazinamide (Z) and streptomycin (S) for 2 months and biweekly (R and H) for 4 months has shown good results with a relapse of only 1%, and no deaths from the disease. There are also case reports of successful treatment with HZS, HS and HRZ.[25,28,31] Streptomycin (20-30 mg / kg/ day) can be used in infants but is contraindicated in pregnant women.[19] Currently the accepted mode of treatment is isoniazid (10-15 mg / kg / day), rifampin (10-20 mg / kg / day) and pyrazinamide (15-30 mg / kg / day) and either streptomycin or ethambutol (15-25 mg / kg / day) for first 2 months followed by isoniazid and rifampin for 4 to 10 months.[21,26] Corticosteroids may be given empirically if the baby is very ill.[19,30] Supportive therapy such as oxygen, mechanical ventilator and Extracorporeal membrane oxygenation may be required for respiratory failure.[8]

PROGNOSIS

The prognosis is poor. In the pre-chemotherapy era the reported survival rate was very low (around 50%), but since the advent of chemotherapy, the chances of successful treatment have improved the overall survival. Delay in the diagnosis contributes to the increased mortality.[2,14,30]

PREVENTION

Prevention should be possible through early detection of disease during pregnancy and institution of appropriate therapy.[4,14]

RECOMMENDATIONS

In view of the increasing burden of tuberculosis, chances of congenital TB are also likely to increase. As most of the women are asymptomatic

for the disease during pregnancy, we recommend that screening of all possible pregnant women for tuberculosis should be made a necessary protocol.

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