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Pulmonary Tuberculosis in Children

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Tuberculosis (TB) is the most common cause of infection-related death worldwide. Children represent 5 to 15% of all TB cases around the world and are more frequently infected and more easily affected by the most severe forms of the disease such as meningitis and disseminated form .Here, we reviewed TB in children with impact on the routes of transmission, clinical manifestations, treatment, control, and prophylaxis.

Electronic databases (PubMed, Scopus) were searched from June1995 to May 2014 by using key words (pulmonaryTB,epidemiology,transmission,clinical manifestations,treatment,control, and prophylaxis) .

Pulmonary tuberculosis may manifest in several forms, including endobronchial TB with focal lymphadenopathy, progressive pulmonary disease, pleural involvement, and reactivated pulmonary disease . Symptoms of primary pulmonary disease in the pediatric population are often insignificant. Gastric aspirates are used instead of sputum in children younger than 6 years. BCG vaccination is used in many parts of the world and the major role of vaccination is the prevention of life-threatening illness such as disseminated TB and meningitis in children.Treatment is the same as for adults.

Most people infected with M .tuberculosis do not develop active disease. In healthy individuals, the lifetime risk of developing infection to disease is 5-10%. Reactivation of TB often occurs in older children and adolescent and is more common in patients who acquire TB at age 7 years and older.

Keywords: Children; Prevention; Pulmonary Tuberculosis; Treatment

1. Context

Most children with TB infection develop no signs or symptoms at any time. Sometimes, the beginning of infection is stated by several days of low grade fever and a mild cough. Rarely, the child presents a clinically important disease with high fever, cough, and flul ike symptoms that ameliorate approximately within a week (1-5). The majority of children who develop tuberculosis disease experience pulmonary manifestations, but 25 to 35 % of children have an extra pulmonary (EPTB) presentation. The most common extra pulmonary form of tuberculosis is lymphatic which accounting for about two thirds of all cases of EPTB. The second most common form is meningeal form arising in 13% of children with TB (1, 2). The clinical and physical manifestations of disease tend to be different by the age of onset of disease. Pre-school children and adolescents are more likely to have significant signs or symptoms, whereas school-age children often have clinically silent disease (1, 4-10). Half of young children with radiographically moderate to severe pulmonary TB don't have any symptoms or physical findings and, mainly, are detected by contact tracing of an adult with pulmonary TB. Infants also, are more likely to experience clinical manifestations of TB, maybe due to small airway diameters. Non-productive cough and mild dyspnea are the most common symptoms in this age group. Systemic complaints such as anorexia, fever, and night sweats occur less common. Some infants have difficulty in getting weight and growing up. Some infants and young children with bronchial obstruction show localized wheezing or decreased breath sounds that may be accompanied by tachypnea or respiratory distress (1, 4-9). In pediatric pulmonary tuberculosis, the radiographic hallmark is the relatively large size and importance of lymphadenopathy compared with the less significant size of the parenchymal infiltration. The best specimen for diagnosis of pulmonary TB in a child is the early morning gastric lavage (11, 12). Unfortunately, three gastric aspirates detect M. tuberculosis in less than 50% of cases and a negative culture never excludes the diagnosis of PTB in a child. Fortunately, the need for culture confirmation is usually low. If the child has a positive tuberculin skin test, clinical or radiographic findings suggestive of tuberculosis, and known contact with an smear positive pulmonary tuberculosis, the child should be treated for tuberculosis disease (1, 13-16). Treatment methods are like adults and in any patient with HIV drug susceptibility test should be carried out.

2. Evidence Acquisition

Electronic databases (PubMed, scopus) were searched from June1995 to May 2014 by using key words (pulmonaryTB, epidemiology, transmission, clinical manifestations, treatment, control, and prophylaxis).

3. Results

We found major risk factors, transmission and prevention routes, clinical manifestations, diagnosis methods and treatment as below:

3. 2. Transmission

Tuberculosis is transmitted from an infected person to a child and a susceptible person by airborne particles (droplet nuclei). These are 1–5 microns in diameter. These infectious droplet nuclei are released when persons with pulmonary or laryngeal tuberculosis cough, sneeze, or laugh, Droplet nuclei remain suspended in the air for up to several hours (1, 2, 6-10). Patients with high loads of bacteria in their sputums are more likely to transmit the infection than those with a low numbers of bacteria. Persons who show presence of cavities in the lungs on chest-X rays, or have a positive sputum test and have a cough lasting two to three weeks or more, are more likely to transmit the infection to others (1, 12). Also, patients with laryngyal involvement, those who fail to cover their mouth and nose while coughing or sneezing and those are not on appropriate and inadequate medication can transmit the infection more to susceptible close contacts. Young children with pulmonary and laryngeal tuberculosis are less likely than adults to be infectious (1, 6, 9, 12).

3. 3. Clinical Manifestations

TB in children is a direct consequence of adult TB and is a good marker of current transmission in the community. The two main factors detecting the risk of progression to disease are patient's age and immune status (4-9). Neonates are at higher risk of progression of infection to disease, with higher rate of military TB and meningeal involvement. Children between 5 to 10 years are less likely to develop disease than other age groups, and adolescent patients can present with progressive primary pulmonary tuberculosis or cavitary disease (1, 3, 9). Children with AIDS and TB most frequently present with an atypical presentation. The majority of children with tuberculosis infection develop no signs or symptoms at any time. Occasionally, the initiation of the infection is marked by several days of low grade fever and mild cough. Rarely, the child experiences a clinically significant disease with high fever, cough, malaise, and flulike symptoms that resolve within a week.

3. 4. Diagnosis

A major challenge of pediatric TB is making an accurate diagnosis. Less than 15% of children with TB have a positive sputum smear and mycobacterial culture detects the bacilli in 30%–40% (1, 2, 6). In the absence of bacteriological confirmation, the diagnosis of childhood TB in countries where TB is endemic is based on close contact with an infectious patient, a positive tuberculin skin test, presence of suggestive clinical signs and syptoms, and or abnormalities on a chest-X ray (17-20). Chest radiograph findings may be normal for a significant proportion of children with confirmed pulmonary TB. Collecting an adequate sample for microbiological studies feces with a significant challenge, particularly about children less than 6 years who cannot produce a good sputum specimen (9, 10, 12). The best specimen for diagnosis of pulmonary TB in a child is the early morning gastric lavage which obtained before the child has uparisen and peristalsis has emptied the stomach of the pooled secretions that have been swallowed within night. Unfortunately, less than 15% of children with TB have a positive sputum smear and three gastric aspirates detect M. tuberculosis in less than 50% of cases on culture medium. Bacteriologic confirmation is common in adolescents and in infants and children with extensive parenchymal involvement (14-16). Although, culture on Lowenstein-Jensen medium is considered to be the gold standard, but,liquid culture systems can give more rapid and more sensitive diagnosis of active TB and drug susceptibility. This method is not widely available in poor countries where the TB rate is high (8, 9, 12). Serum-based antibody also is an easy and rapid way for diagnosis, but, none of the currently available serologic tests are sensitive or specific enough for clinical use. Polymerase chain reaction (PCR) has shown variable sensitivity in various studies, and a negative result does not rule out TB. Conversely, a positive test could occur from cross-contamination of specimens when high standards of laboratory biosafety are not observed. Today, PCR is useful for species identification, molecular epidemiology, and rapid detection of drug resistance (1, 12). The tuberculin skin test (TST) is a widely used as a diagnostic test for evaluation of patients who have symptoms of tuberculosis or in those infections with M tuberculosis is suspected. The sensitivity and the specificity of the TST is about 90% .Efforts are making to develop tests based on detection of antigens, such as lipoarabinomannan in urine or serum samples, and detection of interferon-γ production by sensitized mononuclear cells on stimulation by specific M. tuberculosis antigens ESAT-6 and CFP-10 is an alternative to TST (12-18). This test (interferon-γ release assays) has not been detected to have a major advantages over the TST in terms of sensitivity or specificity and is more expensive; although, it does not require a second patient visit, and they reduce the chances of human error in interpretation. New tests such as antigen detection could mainly play a role in detection of TB in HIV-infected or malnourished children, however, they require to further evaluation (12, 18, 19).

3. 5.Treatment

Two treatment categories recommend for the treatment of pulmonary TB in children (1, 3, 8, 9) are as fllows:

1- A 6-month course of isoniazid (INH) and rifampin (RIF), supplemented during the first 2 months with pyrazinamide (PZA). Ethambutol (ETB) or streptomycin (STM) (in children who are too young to be monitored for visual acuity) may need to be included in the initial regimen until the results of drug susceptibility are available.

2-Another treatment option is a 2-month regimen of INH, rifampin, and pyrazinamide daily, followed by 4 months of high dose of INH and rifampin twice a week.

Drug susceptibility is not required if the risk of drug resistance is not hight. Significant risk factors for drug resistatce include; residence in an area with greater than 4% primary resistance to INH, history of previous treatment with anti-TB drugs, history of exposure to a drug-resistant patient, and origin in a country with a high prevalence of drug resistance (2-6). Drug-resistant organisms occur approximately 10-6; however, individual resistance may be different. The resistance to streptomycin is 10-5, INH is 10-6, and rifampin is 10-8. Therefore, chance that an organism is naturally resistant to both INH and rifampin is on the order of 10-14. Some people have a poor adherence to their regimens and it has a major role in treatment failure, so directly observed therapy (DOT) is recommended for treatment of TB. DOT means a responsible person like as health care provider must watch the patient taking the medications. DOTS-plus strategy, is based on finding suitable strategies for treatment of MDR TB (resistant to INH and RIF) and drug susceptibility testing, as well as judicious usage of second-line drugs (9, 10).

3. 6. Prevention

The key method of preventing tuberculosis (TB) is prompt identification and treatment of patients with TB. Other strategies include patient education, treatment of latent infection, and vaccination.

Patient education; Patients should be educated regarding compliance to therapy, drugs side effects, and follow-up care.

Treatment of latent TB infection

The risk of acquisition of TB following primary infection is high in very young children (< 5 y) and in the adolescent population. Thus, patients in these age groups with a positive TST especially when they are in close contact with a smear positive PTB and no other clinical manifestations should receive INH prophylaxis (21, 22). Active TB should be excluded before the initiation of preventive therapy. Adults with a positive TST and no other clinical or radiographic manifestations who are receiving INH therapy have been reported to have 54-88% protection against the development of infection to the disease, whereas children have been shown to have 100% protection (1, 3, 4, 23, 24). When you are faced with MDR-TB (Multiple drug resistance), observation is recommended, because these drugs are not effective for this kind of infection (3, 4, 24-27). Several drugs have been tried in these circumstances, including PZA, fluoroquinolones, and ETB, depending on the susceptibility patterns. For recent contacts of patients with contagious TB (in the last 3 months), INH therapy is indicated even if the TST result is negative. This is especially true for contacts who are infected with HIV or for household contacts younger than 5 years (4-7, 25, 28).Some countries have an especial guidelines for preventin, For example, in Iran all children younger than 6 years with a TST more than 6 mm and a history with a contagious case should receive INH for 6 months if they do not have the disease. Also, all HIV patients and IVDUs with a TST more than 5 mm with a history of close contact with a patient with contagious form should receive INH for 9 months (26).

3.7. Vaccination

The bacille Calmette-Guérin vaccine (BCG) is available for the prevention of disseminated TB. BCG is a live vaccine prepared from attenuated strains of Mycobacterium. bovis. The important role of BCG vaccination is the prevention of serious disease such as disseminated TB and meningitis among children(26-29). BCG vaccine does not prevent infection with M tuberculosis. From birth time to age 2 months, administration of BCG does not require a previous TST. Thereafter, a TST is mandatory before vaccination. Contraindications for the vaccine include immunosuppressed conditions such as primary or secondary immunodeficiency, high dose steroid use and HIV infection(29-31). However, in the countries of the world where the risk of TB is very high, WHO recommends using BCG vaccine in children who have asymptomatic HIV infection.Adverse reactions due to the vaccine include subcutaneous abscess formation and lymphadenopathy. Rare complications, such as osteitis of the long bones and disseminated TB, may necessitate administration of anti-TB therapy, except for PZA because M,bovis has an natural resistance to this drug(31-35).

3.8. Prevention in Especial Situations

3.8.1. Mother has Current Disease but is Noncontagious at Delivery

In this situation, separation of the mother and infant is not necessary, and the mother can breastfeed her baby. Evaluation of the infant includes chest radiography and TST at age 4-6 weeks is recommended. INH should be administered even if the TST result and chest radiography do not suggest TB, because cell-mediated immunity (CMI) is not enough until age 6 months to prevent progressive disease (26, 31-34). According Iranian guid-line, vaccination is recommended in this child and separation of the mother and infant is not necessary and mother can breastfeed her baby.

3.8.2. Mother has Current Disease and is Contagious at Delivery

Separation of the mother and infant is recommended until the mother is noncontagious. The rest of the management is the same as for the mother with current disease but who is noncontagious at delivery. According to guid- line in Iran, separation of the mother and infant is not necessary, and the mother can breastfeed her baby. But, in this situation the child should receive INH for 6 months (26).

4. Conclusions

The results of the present review suggest the utility of the systematic study of household pediatric contacts for early detection and suitable prevention of infection by Mycobacterium.TB. Development in new vaccines, better diagnostics methods, and shorter duration of treatment, can be improved the tuberculosis outcomes in the world.

Authors' Contribution

Maryam Keshtkar Jahromi and Batool Sharifi-Mood wrote the manuscript.Two authors had an equal role in the writing of paper.

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