

Original article

Diagnosis of pediatric tuberculosis using The Indonesian National Consensus for Pediatric Tuberculosis

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ABSTRACT Diagnosing tuberculosis (TB) in children correctly is critical to appropriate treatment. However, diagnosing TB in children may be difficult and can be imprecise. As our national TB control program has not adequately covered TB in children and adult TB cases still in high rank, our national consensus for pediatric population may facilitate TB diagnosed especially in the field. This cross sectional study as part of longitudinal cohort study of epidemiology of *Respiratory Syncytial Virus* (RSV) in Indonesia (still ongoing) was conducted to know whether criteria used in the algorithm in the consensus compatible to suspected TB diagnosis. The study covered 1000 children under five randomly selected in two districts (Cikutra and Ujung Berung Indah) located in West Java. By using algorithm of The Indonesian National Consensus For Pediatric Tuberculosis (INCPT) with history of known or suspected adult source of TB or early reaction of BCG vaccination and certain general clinical symptoms associated TB as entry criteria for a higher index of suspicion, we diagnosed suspected TB in 57 children. We found that, history of known or suspected adult source of TB and certain general clinical symptoms are two main criteria for suspected TB diagnosis. It appeared that Mantoux test gave a smallest contribution to the diagnosis of suspected TB in the field. No other criterium except known or suspected adult source of TB fulfilled for other five children and prophylactic treatment for TB were given. Those children with suspected TB were given oral anti-tuberculosis (OAT) by Directly Observed Treatment Short course (DOTS) done by local trained persons. [Paediatr Indones 2001; 41:185-190]

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TUBERCULOSIS (TB) REMAINS A MAJOR HEALTH PROBLEM in South-East Asian Regions and ranks high in the list of causes of morbidity and mortality. Thirty one percent cases (2 470 000) of 8 million cases of TB estimated in the world in 1990 of which those 1.3 million TB cases and 450 000 deaths annually occurred in children younger than 15 years of age in this region.^{2,3} Even though each year health authorities

reported new TB cases and deaths, however the reports greatly underestimate the magnitude of the TB problem as this disease largely concentrated in the developing countries where the facilities for detecting, diagnosing and reporting disease are inadequate. In fact, many developed countries has reported the increasing tuberculosis in children each year,^{4, 5,6,7,8} whether Indonesia as one of the developing countries has begun to design and focus to control tuberculosis in children. Although childhood TB has a limited influence on the immediate spread and epidemiology of TB, the occurrence TB in children is a sign of ongoing transmission of infection and contributes to a pool from which TB may arise in the future. Furthermore, more serious forms of TB and extra-

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pulmonary spread may lead to high rates morbidity and mortality.^{3,9} It is also known that the diagnosis of TB in children rest largely on the results of the clinical history and examination, tuberculin testing, radiological examination, and contact history, and thus the diagnosis is consequently less reliable than in adults. In most of developing countries include Indonesia, the majority of cases are not diagnosed due to the lack of appropriate X-ray and laboratory facilities, therefore, there had no information on prevalence or predicted incidence of TB disease in children been reported from national health authorities appropriately.¹⁰ For developing countries the diagnosis of TB in children continues to rely on heavily on clinical and epidemiological grounds and has been classified into suspected, probable, and confirmed by World Health Organization (WHO).^{8,11} This national consensus for diagnosing suspected TB in children must focus great effort on children especially to the most vulnerable children 0 - 5 years of age who have case rate 2 to 4 times the rate for children 5-14 years, high rate of mortality¹⁰ and also more severe disease can occur.^{6,10} This proposed algorithm for a child in a higher index of suspicion for TB infection or suspected TB disease by taking history of exposure to known or suspected adult source of TB, history of early reaction after *Bacillus Calmette-Guerin* (BCG) vaccination and certain general clinical symptoms associated with TB.

In order to evaluate for the first time the criteria used in the algorithm of the consensus in making suspected TB diagnosis in communities, we conducted a prospective cross-sectional study in fewer than five children which have been recruited for RSV study.

Methods

Study subjects. This cross-sectional study used standard questions in data collection form. We collected information regarding history of TB exposure to known or suspected adults TB, history of early reaction after BCG vaccination and certain general clinical symptoms associated with TB in the recruited 1000 under five children for RSV cohort study in two districts (Cikutra and Ujung Berung Indah) located in Bandung municipal area (West Java) for determining of suspected TB children. Written informed consents were obtained from parents or

guardians. Only 991 children entered the study and three entry criteria for a high index suspicion then are collected. Because it's often difficult to obtain history of acid fast bacilli positive smear in adults, we defined a history of TB exposure to known or suspected adults if they had been on symptom bloody cough or placed on ant tuberculosis therapy or cared of/treated in lung hospital. History of early reaction (redness) after 3-7 days BCG vaccination and a certain general symptoms associated TB were the second and third criteria being asked, respectively. The certain general clinical symptoms associated TB occur mostly in the children include: failure to weight gain (defined as no adequate weight gain for a period of 3 months) verified in "Road to Health" cards, anorexia, long-lasting fever of unknown etiology, night sweats, cough more than 30 days, or persistent diarrhea were documented by taking a history from parents or caregivers. The specific findings obtained from physical diagnosis by pediatrician and pediatric chest fellow who help the study include: peripheral lymphadenopathy, conjunctivitis phlyctenularis, pleural effusion, and gibbus. For those 62 children fulfilled one of the entry criteria, they were asked to come to perform chest x-ray and tuberculin skin testing at different place and time with fully arrangement. For those children who did not come, repeated home visits were done by *Kader*.

Radiographic studies. Frontal chest radiograph was obtained on all 62 children with history of TB exposure to known or suspected adults or household TB or general clinical symptoms which performed in each different nearest local hospital and reviewed for possible TB by two radiologists who were blinded to any clinical data. When agreement could not be achieved by two radiologists (one of them is a house-staff interested in pediatric radiologist), the absence or presence of radiological features from the house-staff radiologist interpretation regarded. (The interpretation of chest X-ray will be presented in other report).

Tuberculin skin test. Mantoux skin testing 0.1 ml intradermally using 2 TU of tuberculin purified protein derivative (PPD) 23-RT (Statens Serum Institute, Copenhagen) was administered on the right forearm by one nurse who was familiar with the technique from our teaching hospital and read after 48 hours by a pediatric pulmonology house staff (HMN)

and trained general practitioner (HA). A result was regarded positive if diameter transversal induration of ≥ 10 mm read by them.

Suspected TB children were those with two or more algorithm criteria fulfilled, as follows: history of TB exposure to known or suspected adults or household adult TB cases and general/specific clinical symptoms associated with TB or positive tuberculin skin test or chest radiograph interpretation considered TB. Early reaction of BCG vaccination and general/specific clinical symptoms associated with TB or positive tuberculin skin test or chest radiograph interpretation considered TB. General/specific clinical symptoms associated with TB and positive tuberculin skin test or chest radiograph interpretation considered TB. For those children, OAT by DOTS were given or supervised by local trained persons (*Kader*).

Children with a Mantoux test positive or only history of TB exposure to known or suspected adults or household adult TB cases obtained who were asymptomatic and had normal chest radiograph were regarded as infected, but not disease. Oral antituberculosis is given by DOTS to suspected TB children and only INH is given for five children for prophylactic and supervised by *Kader*. At least two months after treatments, all suspected of TB who had negative Mantoux test were repeatedly Mantoux skin testing performed and clinically evaluated for having TB (the study is still ongoing and will be report later).

Results

In this study, the parents or caretakers of 991 children from two districts were interviewed. No parents or caregivers knew about acid-fast bacilli positive sputum or had never been performed the test. History of known or suspected adult source of TB were found in 62 children. Of the 927 (93.5%) children with history of BCG vaccination, of whom 799 (86.2%) vaccinated children verified with BCG scar, no parents or caregivers gave history of early reaction after 3-7 days of vaccination. Most of the children in both districts area have no "Road to Health" cards and most of the children who had, it was filled in incompletely or not et all, therefore we could not find most of the children showing failure to weight gain from the cards filled in except of the five (8.1%) children of the 62 children with history of exposure to

known or suspected adult source of TB. However, 22 (36%) of them were undernourished at the time of assessment. We could not find also history of long-lasting fever, cough more than 30 days, persistent diarrhea in any of them. On physical examination we found only 3 children with lymphadenopathy and they were on closed contact with adult TB. None of the children showed any other specific clinical findings associated with TB.

Of the 62 children with history of exposure to known or suspected adult source of TB, 32 (52%) were boys and 30 (48%) girls. The children's ages ranged from 7 to 52 months with the median age of 18 months. Most of the children (65%) were well nourished and none of them was severely malnourished found by National Center Health Statistic (NCHS). Fifty-one (82%) of the children had BCG vaccination before which carried out during 3 months after birth. Most of the children (60%) of having a diagnose of suspected TB were < 24 months of age and 46 (81%) children had previous BCG vaccination (Table 1).

TABLE 1. CHARACTERISTIC OF CHILDREN WITH DOCUMENTED HISTORY OF EXPOSURE TO KNOWN OR SUSPECTED ADULT TB

Characteristic	Known		Suspected	
	n	%	n	%
Gender				
Male	32	52	29	51
Female	30	48	28	49
Age (months)				
< 12	11	18	8	14
12 - 24	11	11	10	18
36 - 48	11	19	11	19
48 - 60	2	2	2	4
Nutritional status				
well-nourished	40	64.5	35	61
undernourished	22	35.5	22	39
BCG vaccination				
positive	51	82	46	81
negative	11	18	11	19

A chest radiograph was carried out to all of the children (100%) and chest X-ray findings of 32 (52%) children suggestive to the presence of pulmonary TB (PTB).

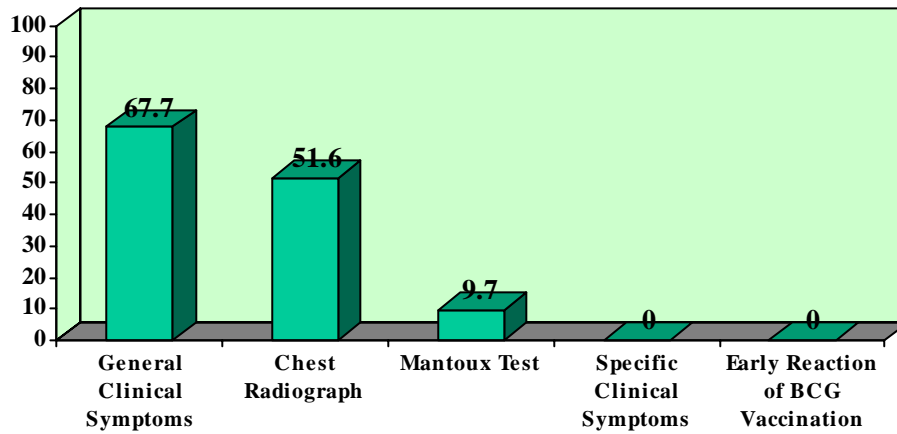


Figure 1. Findings of 62 children with history of exposure to known or suspected adults TB

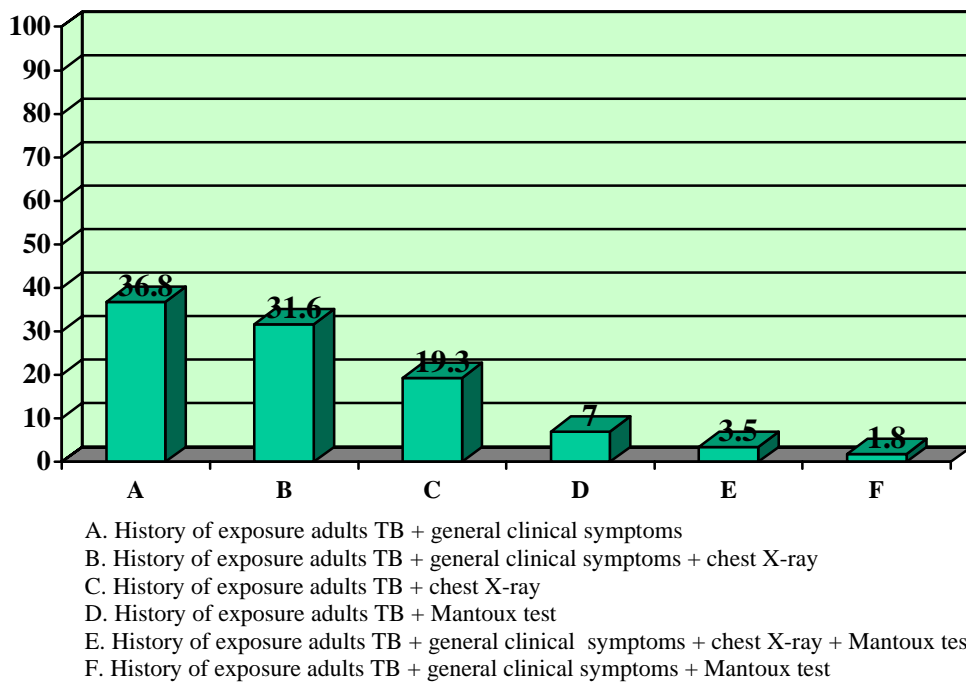


Figure 2. Characteristic Criteria of Children with Suspected TB

Of the 62 children who had a history of exposure of known or suspected adults TB, a Mantoux test was carried out in all of the children (100%), the results read in all of them and the positive induration in the same children reported by the two examiners. Only 6 (9.7 %) had a transverse induration ³ 10 mm and all of them had ³ 15 induration (Figure 1).

Mantoux test positive occurred in each of 3 (50%) well-nourished children as well as undernourished and 4 (67%) of them had also general clinical symptoms. Twenty-one (36.8%) of the 57 children of having suspected TB diagnosed had 2 consensus criteria mostly occurred e.g. history of exposure of known or suspected adults TB and general clinical symptoms. Of the 32

children who showed a presence of pulmonary TB findings on chest X-rays, 19 (33%) children had general clinical symptoms. It was noted that children with history of exposure of known or suspected adults TB and chest X-ray were most likely to occur rather than history of exposure of known or suspected adults TB and Mantoux test. Only 2 (4%) of the children shown to have 4 criteria fulfilled e.g. history of exposure to known or suspected adults TB, general clinical symptoms, chest X-ray as well as Mantoux test (figure 2). Five (8%) of the 62 children had only documented history of exposure to known or suspected adults TB and INH prophylactic chemotherapy was given.

Discussion

It is known that in adult, culture of MTB is the gold standard against which the diagnosis of TB can be determined but this is not for children, even within secondary and tertiary care hospitals. Due to the difficulties and limitations in making the diagnosis by radiological, bacteriological as well as tuberculin skin test, we have tended to rely on too much on two criteria of the algorithm fulfilled to help in making a diagnosis of suspected TB in children. Recently, a study to evaluate the diagnostic value for diagnosing TB in children proposed by The World Health Organization (WHO) was conducted in South Africa prospectively. By using history and certain clinical features e.g. recent weight loss or failure to gain weight, cough or wheezing for > 2 weeks and recent household contact with an adult case of pulmonary TB, it is noted that the simultaneous presence of the three WHO criteria for suspecting TB had a positive predictive value of 63%. No useful value was obtained from the presence of only one or two of the individual criteria and also no cases of TB were identified amongst children with failure to gain weight as the sole criterion of suspecting TB¹².

In this study, 2 TU of PPD-RT 23 (Statens Serum Institute, Copenhagen) used as it was recommended for prevalence studies around the world by WHO is claimed to be *biologically equivalent* to reference standard 5 TU of PPD-S (Siebert's lot 49608)¹³. A positive tuberculin reaction in a young child is indicative of an adjacent case of adults TB. Even though the Mantoux test was technically performed properly and errors in the interpretation of the test and faulty test

materials were likely improbable, most of the children (90.3%) had a negative results. It might imply a real absence of infection or it might occur in apparently healthy children exposed to open TB cases or they were on the incubation period of primary tuberculosis infection¹⁴. It is of interest to note that all of the 51 children vaccinated (82.3%) showed non-response to Mantoux test. They might be have lack for a gene for the major histocompatibility locus HLA-DR3 that diminished responsiveness to tuberculin, probably because of impaired presentation of tubercular antigens by macrophage and other antigen presenting cells (APCs), and may remain persistently tuberculin negative after immunization or infection^{13,14}. It also supported by studies of Ibe at all in children below 4 years that it did not necessarily mean that negative tuberculin response showed no infection with TB¹⁵.

In the diagnosis of childhood pulmonary TB (PTB) the chest X-ray is often the most useful investigation for clinical case definition⁹, however the absence of any abnormality may be misleading. The primary lesion is either too small for recognition on plain film, or obscured by normal structure, especially when good quality radiographs were not performed. Therefore, an apparently normal chest x-rays cannot exclude the presence of PTB.

Primary pulmonary TB is the most common form of the disease to affect infants and children and most of them are asymptomatic, however, it is usually little to suggest the diagnosis unless a family history of TB is obtained. Unlike reported by other study that case contact and skin test are less important as indicator for TB for high prevalence TB countries, and low body weight, prolonged fever and cough being more indicative¹⁶, the present study found that tuberculin skin test or radiographic findings were less likely to found in suspected TB children. In the proposed consensus, we used failure to weight gain in 3 months consecutively as one of general clinical symptoms, but unfortunately many children in this area had not "Road to Health" cards or its filled incompletely, therefore they excluded from the entry of the study when other findings was not found and they might be loss of detection. Although it was not proved bacteriologically, many of the suspected TB children described in this study would not have been diagnosed if they were not screened because they were on contact with known or suspected adults TB. In Beyers's study, it

demonstrated that in an area with a high incidence of TB, 34% of children under the age of 5 years, living in the same household adult TB are diseased, and 14% are infected³.

It may be noted that history of known or suspected adults TB and certain general clinical symptoms associated with TB were most often found in suspected TB children. Mantoux skin testing gave a smallest contribution in diagnosing suspected TB in the community. It is noteworthy to reevaluate further the suspected TB diagnosed we made by observing the children's clinical response after 2 months OAT treatment.

Acknowledgments

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