ISSN 0030-9311

Volume 50 • No. 2 (Supplement) • March 2010

Paediatrica Indonesiana

(The Indonesian Journal of Pediatrics and Perinatal Medicine)

Abstracts of the 4th Annual Scientific Meeting,
Indonesian Pediatric Society,
Medan, Indonesian,
21 - 25 February 2010

Published by:
Indonesian Pediatric Society

Paediatrica Indonesiana

Indonesian Journal of Pediatrics and Perinatal Medicine

Address:
Department of Child Health,
Medical School, University of Indonesia
Jalan Salemba 6, Jakarta 10430, Indonesia
Tel. 62-21-314 7342, Fax. 390 7743

Subscription rate:
Indonesia: Rp 125.000,- per year
All other countries; US $ 60 per year
Single copy: Rp 30.000,- or US $ 10.
(Valid until December 2007)

RISK FACTORS OF TUBERCULOSIS INFECTION IN CHILDREN WITH TUBERCULOSIS CONTACT

Kusdwijono, Vita Diw Wijayanti, Retno Asih Setyoningrum, Landia Setiawati

Division of Respirology
Department of Child Health, Faculty of Medicine
University of Airlangga/dr. Soetomo Hospital
Surabaya

BACKGROUND

Household contact with acid fast bacilli positive adult is the key of tuberculosis (TB) transmission. It also influence by agent, host, and environmental factors that may increase risk for TB infection in children.

OBJECTIVE

To evaluate risk factors of tuberculosis infection in children contact with infectious tuberculosis cases.

METHODS

- Methods: Cross-sectional study
- Sample: Children with tuberculosis
- Setting: Pediatric outpatient clinic, Dr. Soetomo Hospital
- Tool: Multivariate Logistic Regression

The variable of risk factors were age, BCG immunization, nutritional status, high density of people, bacterial load, air sanitation, smoke exposure, and sleep in the same room

RESULTS

Table 1. Risk factors of tuberculosisin children contact with infectious tuberculosis disease

Age (years)					
<5	8	8	0.54	0.02-13.61	0.71
=5	5	10	14.89	0.66-335.11	0.09
BCG Scar	6	12	0.30	0.02-3.89	0.36
Nutritional Status	4	10	7.79	0.53-113.74	0.13
Density of People	6	13	3.96	0.12-128.07	0.44
Bacterial Load	15	14	0.00	0.00	0.99
Air Sanitation	9	13	2.11	0.12-31.24	0.71
Smoke Exposure	5	15	35.51	1.46-858.72	0.03
Sleep in the Same Bedroom	9	16	2.11	0.04-111.87	0.71

There were 15 infection of tuberculosis from 29 children with household contact. 12 were male with median age were 5 years (range 1-14 years). TST response in households of individuals with TB were 18. TST among children who have been recently exposed to an individual with smear positive TB and to examine the influence of various factors on this distribution, given exposure, in a developing country with high BCG vaccination coverage. The prevalence of positive responses to TST in the general population is commonly reported to increase with age. In our study, we showed that the level of infection in children was directly related to the intensity of exposure to the individual with infectious TB. Children who are in contact with individuals with infectious TB are at high risk of developing TB. They also support the importance of contact tracing activities in the control of TB in developing countries associated with early case detection and treatment.

CONCLUSION

The smoke exposure is the significant risk factor for tuberculosis in this population

Keywords: household contact, tuberculin skin test

Buku v no 4

RISK FACTORS OF TUBERCULOSIS INFECTION IN CHILDREN WITH TUBERCULOSIS CONTACT

Kusdwijono, Vita Dwi Wijayanti, Retno Asih Setyoningrum, Landia Setiawati

Division of Respirology
Department of Child Health, Faculty of Medicine
University of Airlangga/dr. Soetomo Hospital
Surabaya

ABSTRACT

Background: Household contact with acid fast bacilli positive adult is the key of tuberculous (TB) transmission. It also influence by agent, host, and environmental factors that may increase risk for TB infection in children.

Objective: To evaluate risk factors of tuberculosis infection in children contact with infectious tuberculosis cases.

Methods: A cross-sectional study of children at Pediatric Outpatient Clinic, dr.Soetomo hospital was done. Tuberculosis infection was confirmed by positive tuberculin skin test using PPD RT 23 2 Tuberculin Unit. The variable of risk factors were age, BCG immunization, nutritional status, high density of people, bacterial load (index case), air sanitation, smoke exposure and sleep in the same room, which were analyzed by multivariate logistic regression.

Results: There were 15 infection of tuberculosis from 29 children with household contact. 12 were male with median age were 5 years (range 1-14 years). The smoke exposure (OR: 35.51; 95% CI: 1.46 – 858.72), age (OR: 14.89; 95% CI:0.66 – 335.11), and nutritional status (OR: 7.79 ; 95% CI:0.53 – 113.74) were risk factors for tuberculous infection in this population. The smoke exposure was the most significant risk factor.

Conclusion: The smoke exposure is the most significant risk factor for tuberculosis infection in this population.

Keywords: household contact, tuberculin skin test, tuberculosis infection

In 1995, the World Health Organization estimated that at least 180 million children under the age of 15 years were infected with *Mycobacterium tuberculosis* worldwide and that nearly 170 000 children died of tuberculosis (TB).[1,2] TB infection and disease among children are much more prevalent in developing countries, where resources for TB control are scarce, than in industrialized countries.[3] However, despite the public health importance of the disease, TB is rarely investigated in children, as the diagnosis is difficult in the young age groups and children are usually not infectious.[4] In addition, contact tracing is rarely done in nonindustrialized countries because of lack of resources, and Isoniazid prophylaxis is not systematically provided to children who are in contact with individuals who have infectious TB.

Most children acquire infection from adults with whom they come in contact in their environment, so the epidemiology of TB in children usually follows that in adults. As infected children represent a large proportion of the pool from which cases will arise in the future, the distribution of TB infection in children can be considered a marker of recent ongoing transmission in the community. This concept has been used in the calculation of the annual risk of TB infection, which is based on the measurement of TB infection repeated tuberculin skin test (TST).[5] The TST has been the classic method used to measure the prevalence of *M tuberculosis* infection in populations and identification of infected individuals.[2] As such, it has been the most widely used immunologic test in the world.[1] Thus, the knowledge of the distribution of TB infection and of the factors that influence it in children are of importance to evaluate the level of ongoing transmission of infection and to help adapt activities within national TB control programs.

Methods

A cross-sectional study of children at pediatric outpatient clinic, Dr.Soetomo hospital. Tuberculosis infection was confirmed by positive tuberculin skin test (TST) using PPD RT 23 2 Tuberculin Unit or patients who had newly detected smear-positive pulmonary TB and were older than 15 years. Pulmonary TB was confirmed by 2 consecutive sputum smears positive for acidfast bacilli and/or positive culture. Induration diameters TST were measured along and across the arm within 48 to 72 hours by trained field workers. For ensuring validity of the TST reading and to reduce intraobserver and interobserver variability, TST reading by each field worker was tested regularly during the course of the study against the same reference reader. Those who departed from standard reference reading were retrained. For analysis purposes, the average of width and length diameters was considered. Various criteria for skin test positivity were explored, and cutoff points of 5 and 10 mm were chosen.

The nutritional status of children was assessed through the use of the weight-for-age and weight-for-height indices. These are expressed as z scores, which represent the distribution in a reference population standardized to a mean of 0 and a standard deviation (SD) of 1. The World Health Organization recommends that 2 SD below the reference median (z = - 2) is the cutoff point for defining abnormally low values.

Households of individuals who had TB were visited at the time of recruitment, and consent was sought from the head of the household to undertake the study. The variable of risk factors were age, BCG immunization, nutritional status, high density of people, bacterial load (index case), air sanitation, smoke exposure and sleep in the same room, which were analyzed by multivariate logistic regression.

Results

Data were collected in the households of 29 individuals with TB contact at Pediatric outpatient clinic Dr. Soetomo hospital, Surabaya between area in The Gambia between March 2008 and October 2009.

There were 15 infection of tuberculosis from 29 children with household contact. 12 were male with median age were 5 years (range 1-14 years). TST responses in households of individuals with TB were 18.

There were 36 subject with BCG imunization and 18 subject had BCG scar. A multivariate model was constructed to control for confounders. The smoke exposure (OR: 35.51; 95% CI: 1.46 – 858.72), age (OR: 14.89; 95% CI:0.66 – 335.11), and nutritional status (OR: 7.79 ; 95% CI:0.53 – 113.74) were risk factors for tuberculous infection in this population. The smoke exposure was the most significant risk factor.

Table 1. The risk factors of tuberculosis in children contact with infectious tuberculosis disease.

Variables	TST positive	TST negative	OR	95% CI	p
Age (years)					
<5	8	8	0.54	0.02-13.61	0.71
≥5	5	10	14.89	0.66-335.11	0.09
BCG Scar	6	12	0.30	0.02-3.89	0.36
Nutritional Status	4	10	7.79	0.53-113.74	0.13
Density of People	6	13	3.96	0.12-128.07	0.44
Bacterial Load	15	14	0.00	0.00	0.99
Air Sanitation	9	13	2.11	0.12-31.24	0.71
Smoke Exposure	5	15	35.51	1.46-858.72	0.03
Sleep in the Same Bedroom	9	16	2.11	0.04-111.87	0.71

Discussion

TST among children who have been recently exposed to an individual with smear positive TB and to examine the influence of various factors on this distribution, given exposure, in a developing country with high BCG vaccination coverage. Within the frame of the main study, we showed earlier that the risk of TST positivity in contacts of individuals with infectious TB was higher. TST responses varied with age, gender, household size, family history of TB, and socioeconomic status.[6] We found

also that, when positive, the TST responses were larger in size in the households of individual with TB than in the households of controls. In the present study, after confirming that recent exposure to an individual with infectious TB was a major factor for TST positivity in children by comparing with control households, we focused on the distribution of TST responses in children within the households of the individuals with TB.

The prevalence of positive responses to TST in the general population is commonly reported to increase with age.[6] In our data set, the main effect of age is observed before 1 year, when the majority of children are TST-negative, after which there is little variation (overlap of CIs), especially when a cutoff point of 10 mm is considered. However, this apparent effect was not confirmed in multivariate analysis after adjusting for household size and proximity to the individual with TB. Similarly, we observed in univariate analysis that female children were more likely to be TST-positive than male children, but this was not confirmed in multivariate analysis, as the effect was probably confounded by the geographic proximity to the individual with TB.

Studies conducted in the 1960s and 1970s showed that household contacts of individual with TB had higher risk of infection than individuals in the general population.[7] In our study, we showed that the level of infection in children was directly related to the intensity of exposure to the individual with infectious TB. As TB is an airborne disease, the risk of an uninfected person's becoming infected is strongly associated with the probability of coming into contact with an individual with infectious TB and the intimacy of that contact.

Poor nutritional status has been reported to decrease TST reactivity in children.[6] In these studies, severe malnutrition was shown to depress immune responsiveness to BCG, although there was some uncertainty about the effect of mild malnutrition. We did not find an association between TST induration and nutritional status, similar to what was reported previously in The Gambia[8]. In our study, however, the proportion of undernourished children was very small among the contacts of individuals with TB, which gave low power to detect an effect.

Vaccination with BCG has been reported to induce cross-reactivity with tuberculin-purified protein derivative, but the degree of tuberculin sensitivity after BCG immunization has been shown to be highly variable, depending on the vaccine strain used, the dosage, the method of administration, the time since vaccination, the age and nutritional status at time of vaccination, and factors known to influence the reaction to TST.[5] TST reactivity in BCG-vaccinated children fades over time but can be boosted in children with repeated skin testing.[3,8] There is no reliable method to distinguish tuberculin reactions caused by vaccination with BCG from those caused by natural mycobacterial infections.[5] In a large data set collected in Malawi, the prevalence of TST positivity was consistently higher over all ages in individuals with a BCG scar than in individuals without a BCG scar.[1] In our data set, however, we did not find a difference in the prevalence of TST positivity among children with and those without a BCG scar for both cutoff points of 5 and 10 mm.

Children who are in contact with individuals with infectious TB are at high risk of developing TB.[1] Despite the former vaccination with BCG, it has been suggested that a positive TST in a child who has close contact with an adult with infectious TB most likely represents infection with *M tuberculosis*, and treatment of this latent infection should be considered, especially if the child is younger than 5 years.[1] This finding is of importance in light of the increasing rates of TB in sub-Saharan Africa, where children who are vaccinated with BCG are exposed to adults with active TB. Tracing of the children who are in contact with individuals with infectious TB has been relatively neglected within TB control programs in developing countries, mainly because of managerial difficulties. Our data show that, in the absence of more specific markers of infection, TST can continue to be used to assess TB infection in children who live in the household of individuals with infectious TB in areas with high BCG coverage. They also support the importance of contact tracing activities in

Scanned by CamScanner

the control of TB in developing countries, associated with early case detection and treatment. In our study, we found the smoke exposure (OR: 35.51; 95% CI: 1.46 – 858.72), age (OR: 14.89; 95% CI:0.66 – 335.11), and nutritional status (OR: 7.79 ; 95% CI:0.53 – 113.74) were risk factors for tuberculous infection in this population. The smoke exposure was the most significant risk factor.

REFERENCES

1. Dolin PJ, Raviglione MC, Kochi A. Global tuberculosis incidence and mortality during 1990–2000. *Bull World Health Organ.* 1994;72:213–20.
2. Raviglione MC, Snider DE, Kochi A. Global epidemiology of tuberculosis. Morbidity and mortality of a world-wide epidemic. *JAMA.* 1995; 273:220–6.
3. Murray CJL, Styblo K, Rouillon A. Tuberculosis in developing countries: burden, intervention and cost. *Bull Int Union Tuberc Lung Dis.*1990;65:6–24
4. Donald PR, Fourie PB, Grange JM. *Tuberculosis in Children.* Pretoria, South Africa: JL Van Shaik Publisher; 1999
5. Bleiker MA, Sutherland I, Styblo K, ten Dam HG, Mislenovic O. Guidelines for estimating the risks of tuberculous infection from tuberculin test results in a representative sample of children. *Bull Int Union Tuberc Lung Dis.* 1989;64:7–12.
6. Lienhardt C, Sillah J, Fielding K, Donkor S, Manneh K, McAdam K. Distribution of tuberculin skin test responses within household of tuberculosis patients and community controls in The Gambia. *Int J Tuberc Lung Dis.* 2001;5(suppl 1):S227
7. Elliott A, Bradley AK, Tulloch S, Greenwood BM. Tuberculin sensitivity in rural Gambian children. *Ann Trop Paediatr.* 1985;5:185–9.
8. Andersen S, Geser A. The distribution of tuberculous infection among households in African communities. *Bull World Health Organ.* 1960;22:39–60.

Scanned by CamScanner