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P-RES-005

Clinical profile and outcome of HIV-TB coinfecting children

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Abstract

Background. Patients with human immunodeficiency virus (HIV) infection are often accompanied by tuberculosis (TB). This co-infection may lead to difficulties in diagnosis and treatment. Outcome is unpredictable and depends on the immunology status.

Objective. To describe the clinical presentation and outcome of children with HIV-TB co-infection.

Methods. A cohort retrospective study was performed using data from medical records of children with HIV-TB co-infection at Respirology Division, Dr. Soetomo Hospital Surabaya from 2009 to 2013. Data of clinical features and nutritional status were recorded. Treatment response was measured among others by improvement in body weight after the completion of anti tuberculosis therapy.

Results. Two hundred and sixty nine patients with HIV infection, fifty one patients with HIV-TB co-infection. Male to female ratio was 1.2:1. Mean age was 60.8 (SD 52.86) months. The clinical presentations were fever (92.16%), cough (86.28%), undernutrition (82.35%), loss of body weight (72.55%), anorexia (41.18%), lymph nodes enlargement (39.22%) and liver enlargement (15.69%). History of contact was found in 56.86% and tuberculin test was positive in 9.80% patients. Most common type of TB was Lung TB with negative smear AFB sputum (90.20%), lymphadenitis TB (7.84%) and miliary TB (1.96%). Weight gain was achieved in 92.00% patients. Other opportunistic infections were pneumonia (68.63%), stomatitis (29.41%), chronic diarrhea (23.53%) and urinary tract infection (11.77%). Mortality was found to be 9.80%.

Conclusion. The most common clinical presentations were fever, cough and undernutrition. With completion of anti tuberculosis therapy, nutritional status improved in the majority of these children.

Keywords: HIV-TB co-infection, clinical profile, outcome

P-RES-006

Tuberculin test in human immunodeficiency virus: is still worth?

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Abstract

Background. Tuberculin test is a test used to check if a person has been infected with tuberculosis (TB) bacteria. This test assessing the delayed type hypersensitivity (DTH) response and modulate host cellular mediated immunity (CMI) responses. Human immunodeficiency virus (HIV) infection leads to low levels of CD4⁺ T cells which result in lost of CMI. The low CMI level may lead in false negative tuberculin test's result.

Objective. To compare the result of tuberculin test in HIV and non HIV patients.

Methods. We conduct a cross-sectional study of pediatrics respirology outpatient clinic using medical record data from 2009 to 2013. The data including gender, age, diagnosis, and tuberculin test. The significancy of difference between the two groups' tuberculin test was analyzed.

Results. We included 163 subjects which 82 are male. Median of age is 4 years (SD 4.39). Fifty one (31.3%) with HIV infection and 112 (68.7%) subjects are non HIV. The diagnosis including lung TB (78.5%), miliary TB (3.7%), meningitis TB (1.8%), scrofuloderma (1.2%), spondylitis TB (4.3%), abdominal TB (0.6%) and lymphadenitis TB (16.6%). Totally, tuberculin test was positive in 73 (44.8%) patients. Range of induration in HIV subjects is 10 to 18 mm [Mean 14.8 (SD 2.95)], and in non-HIV patients is 10 to 24 mm [mean 13.6 mm (SD 3.59)]. Tuberculin test was positive in 9.8% among the HIV subjects and 60.7% among the non HIV subject. There's significant difference between tuberculin test in HIV-Non HIV subjects.

Conclusion. There is significant difference between HIV-Non HIV tuberculin test.

Keywords: tuberculin test, children, human immunodeficiency virus

CLINICAL PROFILE AND OUTCOME OF HIV-TB COINFECTED CHILDREN

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Abstract

Background: Patients with human immunodeficiency virus (HIV) infection are often accompanied by tuberculosis (TB). This co-infection may lead to difficulties in diagnosis and treatment. Outcome is unpredictable and depends on the immunology status.

Objective: To describe the clinical presentation and outcome of children with HIV-TB co-infection.

Methods: A cohort retrospective study was performed using data from medical records of children with HIV-TB co-infection at Respiriology Division, Dr. Soetomo Hospital Surabaya from 2009 to 2013. Data of clinical features and nutritional status were recorded. Treatment response was measured among others by improvement in body weight after the completion of anti tuberculosis therapy.

Result: Two hundred and sixty nine patients with HIV infection, fifty one patients with HIV-TB co-infection. Male to female ratio was 1.2:1. Mean age was 60.8 (SD 52.86) months. The clinical presentations were fever (92.16%), cough (86.28%), undernutrition (82.35%), loss of body weight (72.55%), anorexia (41.18%), lymph nodes enlargement (39.22%) and liver enlargement (15.69%). History of contact was found in 56.86% and tuberculin test was positive in 9.80% patients. Most common type of TB was Lung TB with negative smear AFB sputum (90.20%), lymphadenitis TB (7.84%) and millitary TB (1.96%). Weight gain was achieved in 72.00% patients. Other opportunistic infections were pneumonia (68.63%), stomatitis (29.41%), chronic diarrhea (23.53%) and urinary tract infection (11.77%). Mortality was found to be 9.80%.

Conclusions: The most common clinical presentations were fever, cough and undernutrition. With completion of anti tuberculosis therapy, nutritional status improved in the majority of these children.

Keywords: HIV-TB co-infection, clinical profile, outcome, children.

BACKGROUND

Tuberculosis (TB) is a major cause of death among children with human immune deficiency virus (HIV) infection worldwide, especially in low-income countries.^{1 2 3 4 5}

In 2010, there were 8.8 million (8.5 - 9.2 million) incident cases of TB with 1.1 million (0.9 - 1.2 million) deaths from TB among HIV negative people and an additional 0.35 million (0.32 - 0.39 million) deaths from HIV-associated TB. In 2009, there were almost 10 million orphan children as a result of parental deaths caused by TB. Among the estimated 8.8 million new patients with TB, about 13% were estimated to be HIV-positive, 1.4 million people died of TB, including 990,000 deaths among HIV-negative individuals and 430,000 among people who were HIV-positive (WHO 2011).^{1 2}

The interaction between HIV and TB infections is bidirectional. HIV infected person has 50 - 60% life time risk of developing TB disease, as compared to 10% life time risk in a HIV-negative person. HIV infection increases the risk of both primary and reactivation TB and this risk increases markedly with advancing HIV infection. Due to dysfunctional immune system in HIV infected individual, pathogenesis of TB is altered resulting in varied clinical manifestations. Moreover, the correlation

between CD4 count and occurrence of opportunistic infections, especially TB is obscure in HIV infected children.^{2 4 5}

In resource-limited settings, the diagnosis and treatment of TB in HIV-infected children is very complicated and challenging, resulting in delayed diagnosis.^{2 4 5}

Anti-tuberculosis treatment should be started immediately at diagnosis with a four drug regimen, irrespective of the disease severity. Moreover, tuberculosis disease in an HIV infected child is considered to be a clinical indication for initiation of antiretroviral treatment. The World Health Organization recommends starting antiretroviral treatment in children as soon as anti-tuberculosis treatment is tolerated and within 2- 8 weeks after initiating it. The treatment of choice depends on the child's age and availability of age-appropriate formulations, and potential drug interactions and resistance. Treatment of multidrug resistant tuberculosis in HIV-infected children follows same principles as for HIV uninfected children. There are conflicting results on effectiveness of isoniazid preventive therapy in reducing incidence of tuberculosis disease in children with HIV.⁵

Antiretroviral therapy (ART) has been associated with dramatic reductions in the progression to AIDS and death. Studies in a variety of settings have shown that among HIV infected person rates of TB are significantly lower in those who receive ART and progressively decline with longer duration of ART.²

Data on HIV/TB co-infection in children are still lacking. There are on-going large clinical trials on the prevention and treatment of TB/HIV infection in children that hopefully will help to guide an evidence-based clinical practice in both resource-rich and resource-limited settings.⁵

OBJECTIVE

To describe the clinical presentation and outcome of children with HIV-TB co-infection.

METHOD

A cohort retrospective study was performed using data from medical records of children with HIV-TB co-infection at Respiriology Division, Dr. Soetomo Hospital Surabaya from 2009 to 2013.

The diagnose of TB infection based on history of contact, tuberculin positivity, sputum/gastric lavage, FNAC or biopsy of lymphnodes, for smear microscopy and culture for AFB, imaging studies (chest X-ray, USG abdomen, CT scan), body fluid analysis (CSF, pleural or ascitic fluid) as appropriate.²

Data of clinical features and nutritional status were recorded. Treatment response was measured among others by improvement in body weight (nutrition status) after the completion of anti tuberculosis therapy. Nutritional status was classified using WHO standard growth charts and classification. Outcome was measured with number of children alive and death after completion of treatment or lost for follow up.

RESULT

During the study, two hundred and sixty nine patients with HIV infection, fifty one patients with HIV-TB co-infection. Male to female ratio was 1.2:1. Mean age was 60.8 (SD 52.86) months (figure 1).

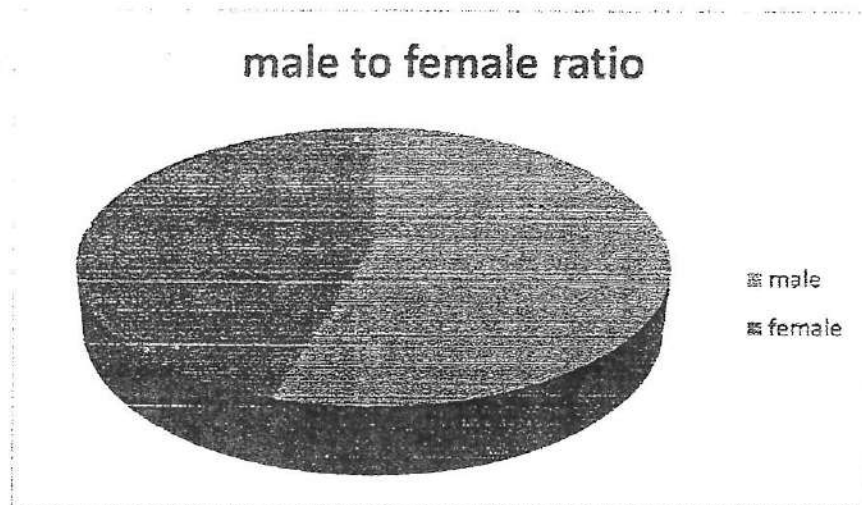


Figure 1. Gender distribution of subjects

The clinical presentations were fever (92.16%), cough (86.28%), undernutrition (82.35%), loss of body weight (72.55%), anorexia (41.18%), lymphnodes enlargement (39.22%) and liver enlargement (15.69%) (table 1). Majority of cases (78.43%) resulted from mother-child transmission and 21.57% resulted from other transmission (circumcision, transfusion or unknown). History of contact was found in 56.86% and tuberculin test was positive in 9.80% patients.

Table 1. Clinical characteristics of subjects

Mean age of presentation (months) (mean \pm SD)	60.8 \pm 52.86
Sex	
- Boys, n (%)	28 (54.90)
- Girls, n (%)	23 (45.10)
Clinical features	
- Fever, n (%)	47 (92.16)
- Cough, n (%)	44 (86.28)
- Undernutrition, n (%)	42 (82.35)
- Loss of body weight, n (%)	37 (72.55)
- Anorexia, n (%)	21 (41.18)
- Lymphnodes enlargement, n (%)	20 (39.22)
- Liver enlargement, n (%)	8 (15.69)
Mode of transmission	
- Mother-child, n (%)	40 (78.43)
- Other, n (%)	11 (21.57)
History of contact, n (%)	29 (56.86)

Positive tuberculin test, n (%)	5 (9.80)
Type of TB	
- Lung TB, negative smear AFB sputum, n (%)	46 (90.20)
- Lymphadenitis TB, n (%)	4 (7.84)
- Miliary TB, n (%)	1 (1.96)
Therapy	
- ARV + anti tuberculosis, n (%)	32 (62.75)
- Anti tuberculosis without ARV, n (%)	10 (19.60)
- Lost for follow up, n (%)	9 (17.65)
Nutritional improvement	
- Severe - moderate malnutrition, n (%)	1 (4.00)
- Severe malnutrition - normal, n (%)	9 (36.00)
- Moderate malnutrition - normal, n (%)	8 (32.00)
- Still normal, n (%)	5 (20.00)
- Still with moderate malnutrition, n (%)	1 (4.00)
- Still with severe malnutrition, n (%)	1 (4.00)
Other opportunistic infections	
- Pneumonia, n (%)	35 (68.63)
- Stomatitis, n (%)	15 (29.42)
- Chronic diarrhea, n (%)	12 (23.53)
- Urinary tract infection, n (%)	6 (11.77)
Outcome	
- Alive, n (%)	37 (72.55)
- Death, n (%)	5 (9.80)
- Lost for follow up, n (%)	9 (17.65)

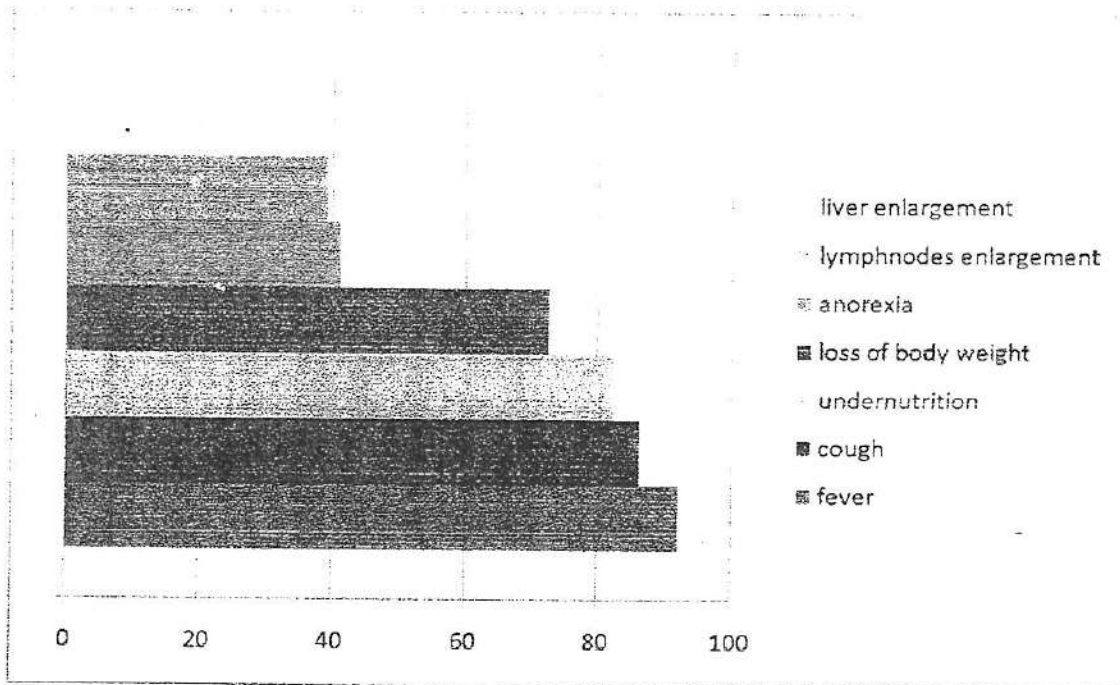


Figure 2. Clinical manifestation of the disease

The most common type of TB was Lung TB with negative smear AFB sputum (90.20%), lymphadenitis TB (7.84%) and milliary TB (1.96%) (figure 2). Majority of patients (62.75%) got complete anti tuberculosis and anti retroviral therapy. Weight gain was achieved in 72.00% patients. Other opportunistic infections were pneumonia (68.63%), stomatitis (29.41%), chronic diarrhea (23.53%) and urinary tract infection (11.77%).

Outcome was measured as number of children alive after completion of ATT. Other outcome being deaths and lost to follow up were also recorded. Mortality was found to be 9.80%, alive was 72.55% and lost for follow up was 17.65%.

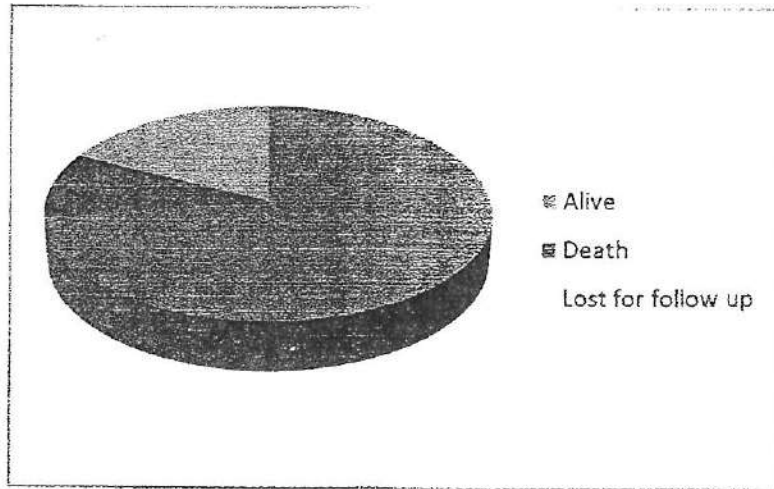


Figure 3. Outcome of the disease

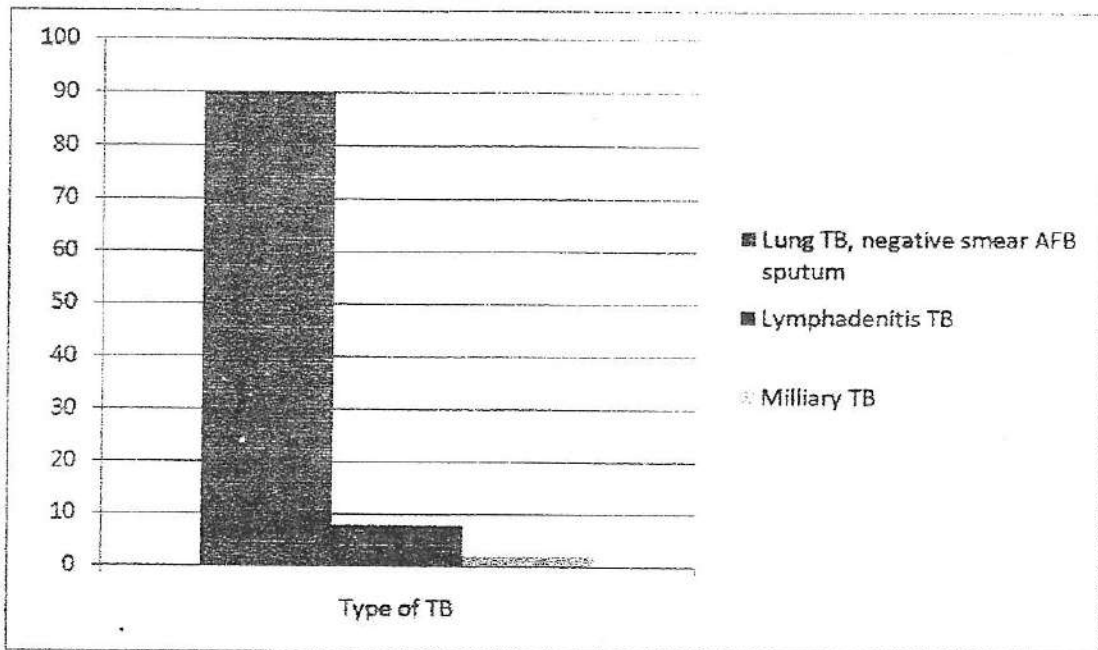


Figure 4. Type of TB

DISCUSSION

In this retrospective study of 269 children with HIV infection who were registered at our center, the prevalence of TB was found to be 18.99%. This was similar to the studies by Agarwal et al from India 2008 with 18.6%, Adhikari et al with 13% in South Africa.²

In this study, 28 cases (54.90%) were males and 23 cases (45.10%) were females, with a Male: Female ratio of 1.2:1. This suggests that males are commonly affected in HIV with TB than females.

WHO guidelines state that diagnosis of TB in an HIV positive child should follow the same approach as for HIV-uninfected children, with taking into account the history of TB contact, clinical features suggestive of TB (such as prolonged cough, poor weight gain or weight loss), positive tuberculin skin test (TST) \geq 5mm considered to be positive in HIV infected individuals, and suggestive chest X-ray signs.⁵

Pulmonary TB is common in HIV-infected children, potentially due to their reduction in immunity, which might help the progression of latent TB infection to active TB.¹ In our study, 90.20% of these co-infected children had pulmonary TB and remaining 9.8% had extrapulmonary TB. The prevalence of pulmonary and extrapulmonary TB was 43.6% and 56.4% respectively in study by Rajshekaran et al, 56% and 44% by Lodha et al, 64% and 36% by Dhurat et al and 73% and 27% by Agarwal et al.²

In our study, 56.86% had history of household contact with adult pulmonary TB. While Kumar et al from West Indies reported history of contact in 79%, Shrestha et al from Nepal, reported 36.6% of their cohort of immuno-competent children having history of contact with adult pulmonary TB.²

Tuberculin test was performed in all children and found to be positive in 9.80% of children. Whereas Kumar et al reported mantoux positivity in 50% of their cohort of 24 co-infected children, Kiwanuka from Uganda reported Mantoux being positive in 32% of their 43 HIV-TB co-infected children. Shrestha et al reported mantoux positivity in 39% of non HIVTB infected children from Nepal.²

Children with TB often fail to gain weight and become symptomatic with features of malnutrition. Treatment response was assessed by change in the nutritional status from baseline to that after completion of ATT. The prevalence of severe malnutrition (40%) was reduced after completion of anti tuberculosis therapy. Similar incidence of 50% of severe malnutrition at the time of diagnosis was reported by Mana et al from Peru.¹ Though several adult studies have shown improvement in nutritional status after completion of treatment, there are no pediatric literatures available.² Severe weight loss and cough can be used as a clinical guide to identify HIV-infected children at risk of co-infection with TB who will require careful observation, further evaluation and intervention.⁴

Outcome as measured by children surviving after completion of therapy was 72.55% in our study. Kumar et al from West Indies, reported survival of 80% among

their cohort of children with HIV-TB co-infection. Shrestha et al in their study of non-HIV but TB infected children reported a survival rate of 73.3%. Madhi SA et al in their South African cohort of hospitalized children with HIV-TB coinfection reported mortality rate of 13.4%.²

The limitation of our study, lack of information on CD4 count of HIV-infected children, which makes it difficult to determine the extent of immune deficiency in the HIV-infected children, and we can't evaluation of treatment response of anti tuberculosis therapy beside from nutritional status.

CONCLUSION

The most common clinical presentations were fever, cough and undernutrition. With completion of anti tuberculosis therapy, nutritional status improved in the majority of these children.

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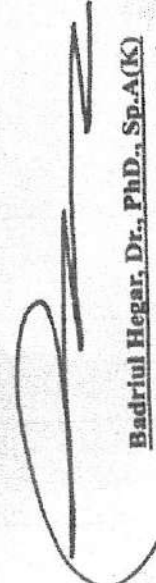
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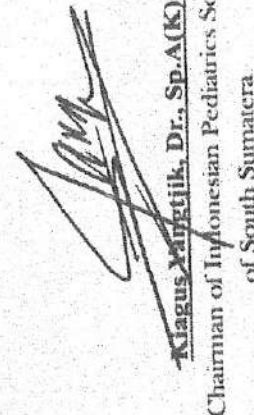
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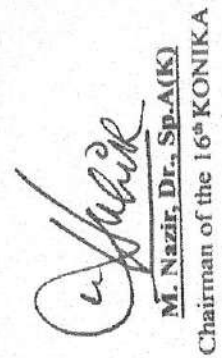
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This program has been accredited by Indonesian Medical Association (IMA/IDI) with maximal credit points of 30 (participant), 1 (speaker), and by Indonesian Pediatrics Society (IPS/IDAI) as category I and V CPD (No. 6754/CPD- I/Apl/2014 and 6755/CPD-V/Apl/2014)
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