

ORIGINAL ARTICLE

Asymptomatic intestinal helminth co-infection among pulmonary tuberculosis patients in urban Surabaya: a preliminary study

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ABSTRACT

BACKGROUND

Pulmonary tuberculosis (TB) is a leading cause of morbidity and mortality, and East Java province is the second largest contributor of co-infection in Indonesia. Asymptomatic helminth infection among pulmonary tuberculosis patients causes another public health problem. Few data relate to helminth infection based on clinical and immunological outcomes of pulmonary TB in highly endemic areas.

METHODS

This study was designed as a preliminary study and aimed to determine helminth co-infection among TB patients with a macroscopic assessment. This cross-sectional study was conducted in June-August 2017.

RESULTS

Among 16 treated active TB patients from TB cohort data of Tanakali Kedinding health center found that 56% were stool smear-positive for *Trichuris trichiura* eggs, but had no clinical symptoms.

CONCLUSION

Whether or not the helminth infection may have an impact on the diagnosis and treatment of active TB remains to be further investigated. Co-infection could be inhibited by the host immune response and improve the prognosis of TB treatment.

Keywords: co-infection, helminthiasis, tuberculosis, urban area

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ABSTRAK

Ko-infeksi asimtomatik helminthiasis pada pasien tuberkulosis paru di kota Surabaya: studi pendahuluan**LATAR BELAKANG**

Penyakit tuberkulosis paru (TB) hingga saat ini masih menjadi penyebab utama tingginya angka morbiditas dan mortalitas, dan propinsi Jawa Timur termasuk penyumbang penderita kedua terbanyak di Indonesia. Hanya sedikit data informasi diketahui terkait infeksi kecacingan yang terjadi pada penderita TB baik secara klinis dan imunologi pada daerah endemis.

METODE

Studi ini di desain sebagai studi awal dan bertujuan untuk menilai ko-infeksi kecacingan diantara penderita TB. Studi potong-lintang ini dilakukan pada bulan Juni-Agustus 2017.

HASIL

Enam belas penderita aktif TB berdasarkan data kohort tuberkulosis Puskesmas Tanakali Kedinding, didapatkan 56%-nya positif kecacingan dengan ditemukannya telur *Trichuris trichiura*.

KESIMPULAN

Walaupun efek dari infeksi kecacingan tidak berdampak terhadap diagnosis dan pengobatan tuberkulosis, akan tetapi sebaiknya penderita yang terdeteksi sebagai tuberkulosis aktif, dilakukan skrining kecacingan terlebih dahulu. Ko-infeksi dapat di hambat oleh respon imun penderita dan meningkatkan prognosis pengobatan tuberkulosis.

Kata kunci: ko-infeksi, helminthiasis, tuberkulosis, perkotaan

INTRODUCTION

Pulmonary tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* that has high morbidity and mortality rates. The infection occurs through the inhalation of droplets containing viable bacteria of persons infected with *Mycobacterium tuberculosis*.⁽¹⁾ Radiographs show that *Mycobacterium tuberculosis* has a predilection for the apex of the lungs but may also cause infections in other organs, which is called extra-pulmonary TB. According to National Health Report data 2016, tuberculosis is still one of the leading causes of high morbidity among all infectious diseases at the health centers and Indonesia was in the third rank among TB burden countries.⁽²⁾

Due to our geographic conditions, especially the population concentrations living in urban and rural areas and engaged in various economic activities, the distributions of some Neglected Tropical Diseases (NTD) are overlapping. In developing countries, people living in slum and squatter areas are usually easily affected with tuberculosis and intestinal helminth infection, especially co-infection with soil-transmitted helminths. It is well-known that intestinal parasitic infections are also one of the neglected tropical infections and one of the most common infections in the world.⁽³⁾ The occurrence of co-infection of TB and intestinal helminthiasis has become one of the major public health problems

in Indonesia. However, there are no current data regarding the co-infection of helminthiasis among TB patients. The majority of the data in Indonesia only refer to single diseases, such as the prevalence rate of pulmonary tuberculosis or the prevalence rate of helminthiasis in Indonesia. Only one study conducted in Bandung, West Java with immunological assessment found 30.5% co-infection of helminths in TB patients compared to the 57.8% found in Brazil.^(4,5)

The present study was designed as a preliminary study and aimed to determine helminthiasis co-infection among TB patients with macroscopic assessment, a conventional technic that could be used in primary health care. The study also aimed to explore and generate information on comprehensive TB treatment and eradication, especially in endemic areas.

METHODS

The study was conducted from June to August 2017 in the catchment area of Tanakali Kedinding Health Centre, Surabaya, East Java, an urban area located next to the Suramadu bridge of Surabaya city. The area is known as an urban slum and squatter area, where the incidence of pulmonary tuberculosis (TB) is the highest of the other areas.

A cross-sectional study was conducted among all subjects who had already been diagnosed with clinical symptoms as a TB patient and had

acid-fast bacilli (BTA) positive sputum smear microscopy at the health center as part of the standard TB treatment program. All of the subjects were registered as an active patient in the TB cohort database and received TB treatment. The study subjects were taken by purposive sampling so that 16 subjects TB active were enrolled in this study.

The subjects' characteristics and risk factor information such as medical history, environmental sanitation, and patient's behavior were collected through interviews using a structured questionnaire, and by observation and home visits. To explore helminth co-infection among pulmonary tuberculosis patients, the study used stool specimens and examined them for the presence of parasites by the microscopic direct smear method. Stool samples were collected from all subjects and processed for the examination of parasites at the Parasitology Laboratory, Faculty of Medicine, Airlangga University. An applicator/toothpick was used to mix one small drop of feces with water on a clean glass slide. A thin smear was made and covered with a coverslip. The area under the coverslip was examined using 10x and 40x objectives.

Data processing was performed by simple descriptive analysis to explain the characteristics, risk factors, and helminth co-infection among TB patients. The study was approved by the Ethics Review Board of the Faculty of Medicine, Airlangga University (No.3853/UN3.1.1/PPd.10/2016), and permission to conduct the study in the community was obtained from the Head of Tanakali Kedinding Health Centre, Surabaya. Informed verbal consent was obtained from each study subject and any information related to the study was kept confidential.

RESULTS

The study involved 35 subjects from the total number listed in the 2016 TB cohort database at Tanakali Kedinding health center. The subjects were selected by purposive sampling based on the inclusion criterion of residing within an 8 km radius around the health center. Only 17 subjects could be visited based on their home address and 16 returned the pot with stool samples to be examined, while one subject could not because of a defecation problem.

Table 1. Laboratory results of TB patients' stool direct smear of Puskesmas Tanakali Kedinding Surabaya

Parameter		n (%)
Stool – direct smear :		
Helminth eggs detected	Positive	9 (56.25)
	Negative	7 (43.75)
Type of parasite	<i>Trichuris trichiura</i>	+

Based on the stool direct smear results 9 out of 16 subjects (56.25%) who suffered from pulmonary tuberculosis were positively co-infected with soil-transmitted helminths (STH), which was *Trichuris trichiura*. The internal factors among subjects were under 60 years, male and only 44% has National Health Insurance (JKN).

Table 2. Characteristics and clinical history of TB patients Tanakali Kedinding Surabaya

Variabels		n (%)
Age	< 60 yr	12 (75)
	≥ 60yr	4 (25)
Sex	Male	9 (56)
	Female	7 (44)
Health insurance	JKN	7 (44)
	none	9 (56)
BCG immunization	Yes	7 (44)
	No	9 (56)
TB in family	Yes	4 (25)
	No	12 (75)
BTA smear - 1	Positive	11 (68.8)
	Negative	5 (31.2)
Length of treatment	< 2 mo	3 (18.8)
	2-6 mo	6 (37.6)
	recurrent	7 (43.6)
BMI	< 18.5 kg/m ²	7 (44)
	18.5-22.9 kg/m ²	9 (56)

Fifty sixth percent (56%) of subjects got BCG while infancy, only 25% has tuberculosis family-related, and 68.8% were positive in the first smear, 43.6% among subjects were recurrent TB treatment and normal nutritional status.

Table 3. Environmental and practices factors

Variabels		n (%)
Environmental score	Good	6 (37.5)
	Poor	10 (62.5)
Health practices	Good	14 (87.5)
	Poor	2 (12.5)

Based on the environmental score which was house observation and sanitation, 62.5% was poor, however for health practices, 87.5% has a good scoring.

DISCUSSION

Subjects with tuberculosis were positively infected with *Trichuris trichiura*, it is also known that infections caused by intestinal parasites do not cause clinical symptoms, thus why the active pulmonary TB subjects never complain about the infestation. The results of this study were similar to those of previous studies on helminth co-infection that have been conducted by in Indonesia, Ethiopia, and Africa, although there are differences in the number of subjects and incidence rate.^(4,6-8) This study supports the statements that have been made by their previous studies, although this preliminary study did not determine the causes and screen immunology indicators.

Based on the internal factors that have been explored, the majority (77%) of TB co-infection subjects were less than 60 years old (range 25 to 56 years) and consisted of an equal number of both genders. Most of the subjects did not have Indonesian National Health Insurance (JKN) card, thus received continued TB treatment only by showing their national identity card (KTP), which means the treatment was covered under Provincial Health Insurance (Jamkesda). To get the appropriate treatment of tuberculosis Directly Observes Treatment Short Course (TB DOTS) program, there have to be no services care access barrier at the health center. Of the total number of TB treatment subjects in Tanakali Kedinding, 44% were on TB recurrent and new cases of TB phase 1 and phase 2 of DOTS program treatment, and 25% cases of intestinal helminths co-infection were found among the recurrent TB treatment subjects. From discussion with them, the patients already knew that all treatment under the DOTS program was covered by the government, which means that the patients do not need to pay for the treatment. However, they should comply with the programmed treatment and take the package of medicine as prescribed by the doctor, and routine control to get continuing medicine and follow-up their treatment compliance by periodical screen of sputum BTA as an indicator of progress therapy. Despite of this, many of the TB patients, in

general, tend to stop treatment prematurely, which is one risk factor become multi-drug resistance of tuberculosis (MDR-TB) and further some cases become develop of extensively drug-resistance tuberculosis (XDR-TB).^(1,2)

Based on the clinical history of the co-infection TB patients, more than half of the subjects (56.2%) never received BCG immunization in childhood. In a study conducted by Elias et al., it is stated that there is the possibility of helminth infection among TB patients due to disruption of the immune response in antigen recognition of *Mycobacterium tuberculosis* due to lack of previous exposure to mycobacteria.^(9,10) A study by Elias et al. also reported that administration of anthelmintics among TB patients who had been vaccinated with BCG, had increases in IFN-gamma and IL-12, compared to subjects not given the anthelmintics.⁽¹¹⁾ However, patients who were not given anthelmintics had increased levels of TGF-beta.⁽¹²⁾ One of TGF-beta functions as a suppressor immune mediator that might block the inflammation process. Usually, helminthiasis infection was chronic and increased the level of TGF-beta expression. This indicates one of the possible causes of the high rate of TB, especially in tropical regions, i.e. a decrease in immunogenicity of the BCG vaccine.⁽¹³⁾ Thus it could be stated that patients who are not vaccinated become more vulnerable. However, the exact mechanism is still unknown, even from the theory we learned that helminth infection-induced T helper-2 and T-regulator, and the responses may contribute to depressed *Mycobacterium tuberculosis* specifically T-cell response.⁽¹⁴⁾ Apart from BCG immunization issues, the result found that apparently, most respondents were in the initial phase of TB treatment (2 months) or under treatment for recurrent tuberculosis. The severity of co-infection depends on the intensity of helminth infestation in the subject's body because the infestation is related to immune response.^(4,15) In the current study, we could not determine the intensity of infestation or severity of infection, due to used only stool direct smears as a screening tool for helminthiasis.

Among those who get treatment as tuberculosis patients, 25% of co-infection has a history of tuberculosis within the family. At the first sputum smear examination, most of the

subjects' sputum result was positive (68.8%), and at the second examination after phase I of treatment, the BTA sputum smear result became negative (68.8%), and the rest (25%) was not yet checked at that time. The anthropometry that we have conducted is based on WHO definition. The results of nutritional status among the co-infection subjects and no co-infection of those who received treatment were underweight to normal. The current situation was supported by the theory that TB patients in the course of the disease to prevent weight loss and ultimately causes a decrease in the nutritional status.⁽¹⁶⁾ Low BMI would increase the severity of tuberculosis five times that of normal BMI.⁽¹⁷⁾ Similarly finding was also reported in Ethiopia.⁽¹⁸⁾ It can be concluded that in TB patients with poor nutritional status, in whom the nutrient adequacy requirements are not fulfilled; the immune system capacity to fight infection is reduced. Furthermore, this makes the TB subjects more prone to secondary infection, such as helminth infection, designated as co-infection.

Soil-transmitted intestinal helminth infestations such as ascariasis, trichuriasis, and hookworm disease, refer to intestinal worms infecting humans that are transmitted from contaminated soil through the fecal-oral route. As stated above, a parasite species found based on smears was *Trichuris trichiura*, similarly known as whipworms. The worm is a multi-cellular organism with a long, flat, or round body. The larvae of whipworms live in the large intestine of humans and can cause intestinal disease. The infection is caused by ingesting eggs when hands

or fingers contaminated with soil with whipworms eggs are put in the mouth or by consuming vegetables or fruits that are not cooked or washed properly. Whipworm infection could be of light or heavy intensity; light infection usually gives no symptoms. Soil-transmitted helminths usually occurs in warm and humid climates with poor hygiene and sanitation, such as in the current location where the environment is a slum and squatter area. Environmental factors such as crowded neighborhoods and houses without adequate ventilation and direct sunlight, lead to easy transmission and recurrent TB among the population. This environmental condition is the one found at Tanakali Kedinding sub-district, Surabaya city. People who live in this area under such conditions are at potential risk not only for helminths contamination but also for pulmonary tuberculosis. In such communities, both helminths and TB infection tend to cluster within households or families.

Referring to the TB patient cohort data in Puskesmas Tanakali Kedinding, we found that 56.25% were infected with soil-transmitted helminth co-infection. In general, the geographical distribution of STH is influenced by factors such as soil conditions, poor sanitation facilities, unhealthy sewage systems, lack of water resources, type of toilet, and socio-demography data.^(14,19,20) Our observed finding, most of the subjects already had a source of clean water and latrines in their houses, but the sewage (fecal waste) disposal system was not explored. It remains unclear whether the cause of co-infection was contamination with the



Figures 1. The geographical distribution of co-infection with helminths and tuberculosis⁽²¹⁾

contaminated soil around the houses or due to unhealthy behavior, it means their behavior was not per clean and healthy living concept (*Perilaku Hidup Sehat dan Bersih*). Because TB co-infection with intestinal helminth is not only due to the environmental factors, but could also refer to unhealthy lifestyle among community members, such as not sufficiently implemented on water, sanitation, and hygiene (WASH) or non-hygienic food handling or not proper food handling and preparation at home or preference of buying food with not adequate sanitation from street vendors at their workplace due to practical habit.

From the below figure we could see the risk of infection and could be used as a reflection on national eradication programmed on tropic infection diseases.

Based on the simplified map made by Salgame according to WHO data showed the geographic distribution of tropical diseases, and Indonesia is shown as one of the countries that have a risk of three kinds of tropical diseases, helminths, tuberculosis, and malaria, or co-infection helminths and tuberculosis. Due to that reason and as stated by Anwar it should be conducted integrated control strategy, to lead reduction of STH at the community level. Further exploration is required to determine the risk factors for disease transmission of helminths among persons with tuberculosis in the endemic area.^(14,21)

One limitation of this study was that it did not evaluate immunological parameters to show the immunological reactions against the intestinal parasitic infestation among the TB subjects.

CONCLUSION

The findings of this study support the assumption that there are positive cases of asymptomatic co-infection of intestinal helminth among pulmonary TB patients, for which we should be on the alert. Because tuberculosis and helminths infection could be overlap acquire infection among the population. The study recommend conducting screening and treatment for STH co-infection among TB patients.

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CONFLICT OF INTEREST

All authors declare no conflicts of interest, and this is study was self-funded by the principal investigator.

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