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Epidemiology of Child Tuberculosis (A Cross-Sectional Study at Pulmonary Health Center Semarang City, Indonesia)

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Abstract. Mycobacterium tuberculosis is an acid-resistant bacterium that caused tuberculosis. The children might suffer tuberculosis by direct transmission of adult smear positive. The analytic observational study with a cross sectional was conducted. Samples were pediatric patients from January 2015 until December 2016. The 344 subject as total sampling were included as samples. Data were obtained through interviews and direct observations then analyzed with Chi-Square method. The results of these study were the majority of subjects were 3 years old (51.7%), the majority were female (55.2%), already immunized BCG (82.6%), and had moderate nutritional status (40.7%). More than half subjects had no contact with adult smear positive (64.5%). Most of subject had house population density ≥ 8m^2 per person (99.4%), the level of humidity 40-70% (99.4%), the presence of ventilation 10% from floor area (75.6%), and all the composition of the floor made from tiles. In contrary, the lighting levels were not qualified <60 lux (99.5%). Most of the subject had family members who smoked inside (61.6%). The education level of the parents majority completed high school (41.9%), relatively had a good knowledge about tuberculosis (98%), and almost respondents were housewives (89.5%) with family income above the minimum wage Semarang (53.4%). The results of Chi-Square test showed that there was a relationship between the gender of the child (OR = 0.445; 95%CI = 0.241-0.821) and the presence of smokers (OR = 2.007; 95%CI = 1.074-3.751). It was suggested to educate the parents about smoker as the risk factor of child tuberculosis.
Keywords: tuberculosis, children, smoker

1. Introduction

Tuberculosis is an infectious disease of the respiratory system caused by *Mycobacterium tuberculosis* to the part of the lung parenchym. Tuberculosis is transmitted through the air (droplet nuclei) [1]. A person diagnosed as a suspect tuberculosis if found on his/her main clinical symptoms such as cough with phlegm for more than three weeks, coughing up blood, shortness of breath and chest pain [2] Tuberculosis (TB) has existed for millennia and remains a major global health problem. In 2015, 6.1 million new TB cases were notified to national authorities and reported to WHO. Notified TB cases increased from 2013–2015, mostly due to a 34% increase in notifications in India. However, globally there was a 4.3 million gap between incident and notified cases, with India, Indonesia and Nigeria accounting for almost half of this gap [3].

Infection typically occurs when a child inhales *Mycobacteria tuberculosis* exhaled by an individual with pulmonary or laryngeal TB. Primary infection due to skin inoculation, ingestion into the gastrointestinal tract or congenital infection due to transplacental transmission occurs very rarely. After

inhalation, a primary reaction often occurs consisting ofa small parenchymal lesion in the lung with regional lymphaden- opathy, often perihilar or mediastinal. Bacilli may then spread throughout the lungs and pleura, which can result in intrathoracic TB [4].

Tuberculosis is arguably one of the major deadly diseases affecting children in developing countries, causing the death of approximately >80,000 children annually, and with over 500,000 new cases each year, reflecting ongoing transmission within communities. At least 1 million children become ill with TB each year. Children represent about 10-11% of all TB cases. Only 5 countries do not yet report to WHO the notification of cases among children [5,6]. There was an increase in the case notification rate of TB among children between 2011 and 2014 the Lagos State TB and Leprosy Control Programme (LSTBLCP) shown that the incidence of pediatric tuberculosis is higher than the number of notifications, particularly in young children [5,6]. *Global Tuberculosis Report* 2013 published by WHO states that among 530,000 cases of tuberculosis in the world, 74,000 cases are children tuberculosis cases [7] In 2015, 210,000 children died of TB, including 40,000 TB deaths among children who were HIV positive. Researchers estimate that 67 million children are infected with TB latent TB) and are therefore at risk of developing disease in the future. Researchers estimate that 25,000 children develop multidrug-resistant TB every year [3]

According to Tuberculosis Recent Update of Indonesia January-December 2012 issue states that the proportion of children tuberculosis in Indonesia is 8.2%. While for the Central Java Province in 2012, the proportion of children tuberculosis is amounted to 11% and for Semarang in 2011 is amounted to 13% of all tuberculosis cases. The Center for Pulmonary Health Semarang is one of health services focuses on pulmonary health. BKPM Semarang also focuses on tuberculosis treatment. According to BKPM Profile in 2012 shows that there is an increasing number of children tuberculosis case in 2011-2013. This number indicates there is an increasing of cases found. The number of cases in 2011 amounted to 3.53%, then by 7% in 2012, and by 11.57% in 2013.

Childhood tuberculosis has been neglected by health programmers and academics, because the cases are few, non-infectious and the perception that effective TB control in adults will prevent TB in children. Childhood tuberculosis is underdiagnosed in many countries with high TB burden [8–10].

Factors that contribute to low case detection among children include inability of children to produce sputum. Even when sputum is produced by a child, cheap diagnostic tests, such as smear microscopy, can only accurately detect 30% of the cases. Other factors include low capability among healthcare staff to diagnose childhood TB, reliance on smear microscopy as the primary method of TB detection, ineffective family-centered contact tracing, paucity of printed workers aid/guidelines, dearth of adequate training on childhood TB screening and diagnosis, and lack of data-capturing tools [11].

Children are more susceptible to developing active TB compared with adults, and acquire the infection mostly from adults within their household, including their parents [12,13]. Lack of relevant data on age-related trends of TB in children. The understanding of the global epidemiology of childhood TB could have been better, and planning of effective control measures easier if relevant data were available [5].

2. Methods

2.1. Study site

The research was conducted at The Center for Pulmonary Health Semarang, Central Java Province, Indonesia.

2.2. Selection subject

For this study, cases of TB are defined in accordance with WHO recommendation. Initial screening criteria used to identify suspected TB cases included low grade fever and weight loss. Additional criteria were cough for more than 3 weeks for pulmonary TB, and localizing signs/symptoms including palpable lymph nodes, headache/vertigo, and backache. Children suspected of having pulmonary TB are encouraged to provide morning sputum for microscopy. Three morning sputum samples are examined for each child. Chest Xray and tuberculin skin test (TST) is carried out by the clinic staff (treating physician)

in those unable to produce sputum and those found to be sputum smear negative on microscopy. TST is performed using five tuberculin units (TU) of tuberculin purified protein derivative (PPD)-S with .5 mm induration as cut off.

2.3. Study design

The analytic observational study with a cross sectional was conducted. Samples were pediatric patients from January 2016 until August 2017. The 344 subject as total sampling were included as samples. Data were obtained through interviews and direct observations then analyzed with Chi-Square method.

2.4. Ethic statement

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors. Ethical approval was obtained from the Committee of Public Health Research Ethics, Diponegoro University (126/EC/FKM/2015). Informed consent was acquired from parent or guardian.

3. Result and discussion

Table 1 shows the distribution incidence of Child Tuberculosis. From this table it can be seen that half of the subject suffered tuberculosis.

Table 1. Distribution Incidence of Child Tuberculosis

Incidence of Child Tuberculosis	Total (f)	Percent (%)
Positive of Child TB	172	50
Negative of Child TB	172	50

After a long period of neglected by health program planner in childhood tuberculosis due to lack of childhood TB cases, difficulty of diagnosis, non-infectious and the belief that effective TB control in adults will prevent TB in children [8,9,14], in this study, we found half of subject suffered from childhood tuberculosis (Table 1). TB in children is increasingly becoming an important cause of global child morbidity and mortality in developing countries. At least 1 million children fall ill with tuberculosis (TB) each year. Children represent about 11% of all TB cases [3,6]. All reflecting ongoing transmission within communities [15]. The estimated proportion of total childhood tuberculosis for each country ranged from 4% to 21% [6]. The burden of childhood TB infection and TB disease is an important indicator of the overall trend of disease and ongoing transmission within the community [15,16]. Estimating the TB burden in the children population, in any level, is important to encourage authorities to facilitate the next process such as new drugs and market appropriate pediatrics formulations [17].

Most of the children who are subject of this study are mostly 0-4 years old at (65.7%) and (55.2%) of them are female. A total of (82.6%) have been immunized with BCG classified as moderate nutritional status as much as (40.7%). It was similar with a result that stated uniform distribution of ages in the household model of exposure led to disease estimates that were 11% higher than the distribution based on adult age and sex notifications [6]. An assumption that the efficacy of BCG vaccination did not wane towards the equator resulted in disease estimates that were 27% lower for all methods of estimating infection [6].

Most children in this study also showed that (64.5%) had no contact history with positive BTA patients and do not have a history of contact with neighbors (79.7%). In contrary with other results that stated children are more susceptible to developing active TB compared with adults, and acquire the infection mostly from adults within their household, including their parents [12,18].

A study showed that 1.8% of children in household contacts of adult TB patients also had TB, higher proportion of TB in female children which showed vulnerability of the female child and considerable role of mother in disease transmission [19,20]. From our result we know that gender of the child were associated with the incidence of childhood tuberculosis (OR=0.445; 95%CI= 0.241-0.821), this in line

with the study conducted by Codlin et al in Pakistan, they found that TB is highly prevalent, translating, into thousands of excess female cases per year [21]. Higher frequency of disease in the females may reflect poor nutritional status of the girl child in making them more vulnerable to the disease [22].In crowded houses, a greater degree of shared airspace increases exposure to *M. tuberculosis,* which can even be increased by limited air movement in closed spaces—hence a greater risk of infection and tuberculosis disease [12,13]. There are many risk factors related to TB like living in the same house with close family members or friends who had active TB is significantly [8.69 confidence interval (CI): 3.00-25.18] associated with TB [23]. Large family size and small house predisposes 9 times a risk to develop LTBI (CI: 3.00-25.28) [24].

In terms of environmental factors (Table 2), (99.4%) of subject have qualified house environment regarding the population density, but the lighting levels are not qualified by (96.5%). Humidity level of house environment is already qualified by (99.4%) and already has qualified ventilation by (75.6%). The whole floor is already plastered or tiled. TB is also more prone to develop where ventilation and sunlight are inadequate because *Mycobacterium* would not easily move away or killed [25,26]. Meanwhile, there are (61.6%) smokers who live with subject under the same roof. Most smokers smoke in the living room (32%). The education level of the parents by (41.9%) completed high school with relatively good knowledge about tuberculosis by (57%) As many as (89.5%) respondents are not working or can be said only as a housewife with family income per month by (63.4%) are above minimum wage. TB adult and childhood TB is prevalent in poor and marginalized population which associated with overcrowding and poor nutrition [12,27].

In this study some variables associated with the incidence of child tuberculocis are child age (*p value* 0,023), sex (*p value* 0,000), nutritional status (*p value* 0,033), contact history with positive BTA patients (*p value* 0,018), and prescence of smokers (*p value* 0,033). Age and sex variations in the prevalence of tuberculosis infection and disease have been reported worldwide, related to biologic mechanisms, socioeconomic and cultural factors may play a role in determining age and sex differences in rates of infection, progression to disease, and treatment outcome [28–30].

While immunization status, history of neighbor contact, population density, lighting level, humidity level, prescence of ventilation, education level, knowledge level, and income level not significantly related with the incidence of child tuberculocis. For more details can be seen in Table 3. Vaccination provides a highly effective strategy to control vaccine-preventable diseases; however, the fact that only a few people develop tuberculosis after *Mycobacterium tuberculosis* infection differentiates tuberculosis from classic vaccine-preventable diseases. The BCG vaccine offers some protection against disseminated forms of tuberculosis in young children (and against leprosy), but does not consistently protect against adult-type tuberculosis [31]. Disseminated BCG disease need careful consideration during genetically modified BCG vaccine development. Additionally, prominent T-cell epitopes are genetically highly conserved, similar to essential housekeeping genes, suggesting that *M tuberculosis* subverts some T-cell-mediated immune response to benefit its own survival and spread. An accurate correlate or biomarker of protection has not yet been identified [32]. The important roles played by innate immune responses and localized (non-circulating) T-cell populations have only recently been described, and these might lead to new discoveries. The diverse range of pathological abnormalities related to the ontogeny of the immune response in children presents opportunities to characterise important immunological mechanisms. Immunohistological studies could also advance understanding of protective immune responses in children with latent *M tuberculosis* infection and provide answers to many unresolved beliefs about latent tuberculosis infection [33,34].

Improvements in the mechanistic understanding of tuberculosis disease and protection are greatly needed, as is a reduction in major policy–practice gaps, since most children in tuberculosis endemic areas are unable to access effective tuberculosis care [35–38].

Table 2. Distribution of House Environment of the Respondents.

Factors Related	Total (f)	Percent (%)
Population Density		
1. Unqualified	2	0.6
2. Qualified	342	99.4
Lighting Level		
1. Unqualified	332	96.5
2. Qualified	12	3.5
Humidity Level		
1. Unqualified	2	0.6
2. Qualified	342	99.4
Presence of Ventilation		
1. Unqualified	84	24.4
2. Qualified	260	75.6
Composition of the Floor		
1. Half or whole is soil	0	0
2. Whole plastered/ tiled	344	100
Presence of Smokers		
1. Present	212	61.6
2. None	132	38.4
Smoking area		
1. No one smokes	164	47.7
2. Terrace	18	5.2
3. Living room	110	32.0
4. Family room	52	15.1

Our study found that present of smoker in home were related to the incidence of tuberculosis (OR 0.498;95%CI=0.320-0.776). The present of smokers in home is an indisputable fact as risk factor of tuberculosis in many studies. Study also proved that family history of smoking related to incidence of TB (OR=2.8, 95% CI:2.3-18.2). Exposure of second-hand smoke increase for both the risk of TB infection and development of active TB disease, among children or adults. Smoking inside home will make their family also exposed. Smoking is also contributing factor for latent infections [odds ratio (OR) 3.20 (1.30-8.20)] [39]. A meta-analysis produced evidence that smoking is a risk factor for TB infection and TB disease [40,41]. TB infection and TB disease are biologically increased by smoking. Smoking causes histological changes in the lower respiratory tract, including peribronchial inflammation, fibrosis, vascular intimal thickening, and destruction of alveoli. This leads to alterations in the epithelial function, such as reduced ciliary activity, decreased clearance of inhaled substances, and abnormal vascular and epithelial permeability, alterations in macrophage number and response [42,43], and decrease in CD4 and CD8 cells that produce interferon gamma and TNF alpha [43].

Table 3. Factors related to the incidence of childhood tuberculosis

Factor Related	Diagnosis of Child Tuberculocis				*p value*	POR	CI (95%)
	f	%	f	%			
Child Age					0.023[a]	1.674	1.093-2.564
a. <3 years old	94	56.6	72	43.4			
b. ≥3 years old	78	43.8	100	56.2			
Sex					0.000[a]	0.445	0.288-0.686
a. Male	60	39.0	94	61.0			
b. Female	112	58.9	78	41,1			
Immunization status					0,118[a]	1,632	0.926-2.876
a. No BCG	24	40.0	36	60.0			
b. BCG	148	52.1	136	47.9			
Nutritional status					0,033[a]	0.602	0.386-0.939
a. Malnutrition	52	41.9	72	58.1			
b. Moderate-good nutrition	120	54.5	100	45.5			
Contact History					0,018[a]	1.757	1.123-2.748
a. Present	72	59.0	50	41.0			
b. None	100	45.0	122	55.0			
History of neighbor contact					0.082[a]	1.662	0.974-2.833
a. Present	42	60.0	28	40.0			
b. None	130	47.4	144	52.6			
Population Density					0.499[b]	0.497	0,447-0.553
a. Unqualified	0	0.0	2	0.0			
b. Qualified	172	50.3	170	100.0			
Lighting Level					0.378[a]	0.488	0.144-1.652
a. Unqualified	168	50.6	164	49.4			
b. Qualified	4	33.3	8	66.7			
Humidity Level					0.499[b]	0.497	0.447-0.553
a. Unqualified	2	100.0	0	0.0			
b. Qualified	170	49.7	172	50.3			
Presence of Ventilation					0.380[a]	0.777	0.474-1.273
a. Unqualified	46	54.8	38	45.2			
b. Qualified	126	48.5	134	51.5			
Presence of Smokers					0.003[a]	0.498	0.320-0.776
a. Present	92	43,4	120	56,6			
b. None	80	60,6	52	39,4			
Smoking area					0.013[a]	0.569	0.371-0.873
a. Terrace/ Living room/ Family room	78	43.3	102	56.7			
b. No one smokes	94	57.3	70	42.7			
Education Level					0.174[a]	1.445	0.887-2.354
a. Completed kindergarten,elementary school, junior high school	50	56.8	38	43.2			
b. Completed high school, diploma/ bachelor/ master	122	47.7	134	52.3			
Knowledge Level							
a. Poor knowledge	78	52.7	70	47.3	0.446[a]	1.209	0.789-1.854
b. Good knowledge	94	48.0	102	52.0			
Income Level					0.057[a]	1.573	1.011-2.448
a. Below minimum wage	72	57.1	54	42.9			
b. Above minimum wage	100	45.9	118	54.1			

[a]*Continuity correction*; [b] *fisher's exact test*

Conclusion

The results of Chi-Square test showed that there was a relationship between the gender of the child (OR = 0.445; 95%CI = 0.241-0.821) and the presence of smokers (OR = 2.007; 95%CI = 1.074-3.751). It was suggested to educate the parents about smoker as the risk factor of child tuberculosis.

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References

[1] Palomino J C, Leão S C and Ritacco V 2007 *Tuberculosis* ed Juan Carlos Palomino, Sylvia Cardoso Leão and Viviana Ritacco (Brazil: Bernd Sebastian Kamps and Patricia Bourcillier)
[2] Basterrechea M, Sancho R, Idígoras P and Temprano Y M 2009 [Characterization of tuberculosis cases in the foreign- and native-born population in Guipúzcoa (Spain) from 2003-2007]. *Gac. Sanit.* **23 Suppl 1** 74–9
[3] World Health Organization 2017 *Global tuberculosis report 2016* (Geneva, Switzerland: World Health Organization)
[4] Morris S K, Demers A-M, Lam R, Pell L G, Giroux R J and Kitai I 2015 Epidemiology and clinical management of tuberculosis in children in Canada. *Paediatr. Child Health* **20** 83–8
[5] Daniel O J, Adejumo O A, Abdur-Razzaq H A and Ebunoluwa J O 2015 Trend of childhood TB case notification in Lagos, Nigeria, 2011–2014 *Int. J. Mycobacteriology* **4** 239–44
[6] Dodd P J, Gardiner E, Coghlan R and Seddon J A 2014 Burden of childhood tuberculosis in 22 high-burden countries: a mathematical modelling study *Lancet Glob. Heal.* **2** e453–9
[7] World Health Organization 2013 *Global Tuberculosis Report 2013* (Geneva, Switzerland)
[8] Lamb G S and Starke J R 2017 Tuberculosis in Infants and Children *Microbiol. Spectr.* **5**
[9] Singh J P N, Mohammed R, Thayyullathil T, Al-Khal A and Al-Suwaidi Z 2016 Childhood tuberculosis in Qatar. *Int. J. mycobacteriology* **5 Suppl 1** S162
[10] World Health Organization 2015 *Childhood tuberculosis* (Geneva, Switzerland: World Health Organization)
[11] Oshi D C, Chukwu J N, Nwafor C C, Meka A O, Madichie N O, Ogbudebe C L, Onyeonoro U U, Ikebudu J N, Ekeke N, Anyim M C, Ukwaja K N and Aguwa E N 2016 Does intensified case finding increase tuberculosis case notification among children in resource-poor settings? A report from Nigeria *Int. J. Mycobacteriology* **5** 44–50
[12] Karim M R, Rahman M A, Mamun S A, Alam M A and Akhter S 2012 Risk factors of childhood tuberculosis: a case control study from rural Bangladesh *WHO South-East Asia J. Public Heal.* **1** 76–84
[13] Zafar M 2014 Prevelence of latent tuberculosis and associated risk factors in children under 5 years of age in Karachi, Pakistan *J. Assoc. Chest Physicians* **2** 16
[14] Marais B J and Pai M 2007 Recent advances in the diagnosis of childhood tuberculosis. *Arch. Dis. Child.* **92** 446–52
[15] Brent A J 2012 Childhood TB Surveillance: Bridging the Knowledge Gap to Inform Policy *J. Trop. Med.* **2012** 1–6
[16] Lestari T, Probandari A, Hurtig A-K, Utarini A, Starke J, Marais B, Pai M, Sakundarno M, Nurjazuli N, Jati S, Sariningdyah R, Purwadi S, Alisjahbana B, Werf M van der, Bachtiar A, Miko T, Machmud R, Besral B, Yudarini P, Mehta F, Chadha V, Basri C, Loprang F, Jitendra R, Nelson L, Wells C, Kesehatan R D, Irawati S, Arias N, Prihatini S, Rintiswati N, Voskens J, Kimmerling M, Teo S, Alfaham M, Watson J, Berman S, Kibel M, Fourie P, Strebel P, Rie A van, Beyers N, Gie R, Kunneke M, Zietsman L, Donald P, Marais B, Gie R, Schaaf H, Hesseling A, Enarson D, Beyers N, Lobato M, Cummings K, Will D, Royce S, Nelson L, Schneider E, Wells C, Moore M,

Harries A, Hargreaves N, Graham S, Mwansambo C, Kazembe P, Broadhead R, Maher D, Salaniponi F, Marais B, Gie R, Schaaf H, Hesseling A, Obihara C, Starke J, Enarson D, Donald P, Beyers N, Smieja M, Marchetti C, Cook D, Smaill F, Aissa K, Madhi F, Ronsin N, Delarocque F, Lecuyer A, Decludt B, Remus N, Abel L, Poirier C, Delacourt C, Sharma S, Sarin R, Khalid U, Singla N, Sharma P, Behera D, Lolekha R, et al 2011 High caseload of childhood tuberculosis in hospitals on Java Island, Indonesia: a cross sectional study *BMC Public Health* **11** 784

[17] Coghlan R, Gardiner E, Amanullah F, Ihekweazu C, Triasih R, Grzemska M and Sismanidis C 2015 Understanding Market Size and Reporting Gaps for Paediatric TB in Indonesia, Nigeria and Pakistan: Supporting Improved Treatment of Childhood TB in the Advent of New Medicines ed S Esposito *PLoS One* **10** e0138323

[18] Frydenberg A R and Graham S M 2009 Toxicity of first-line drugs for treatment of tuberculosis in children: review *Trop. Med. Int. Heal.* **14** 1329–37

[19] Batra S, Ayaz A, Murtaza A, Ahmad S, Hasan R and Pfau R 2012 Childhood tuberculosis in household contacts of newly diagnosed TB patients. *PLoS One* **7** e40880

[20] Ruwende J E T, Sanchez-Padilla E, Maguire H, Carless J, Mandal S and Shingadia D 2011 Recent trends in tuberculosis in children in London *J. Public Health (Bangkok).* **33** 175–81

[21] Codlin A J, Khowaja S, Chen Z, Rahbar M H, Qadeer E, Ara I, McCormick J B, Fisher-Hoch S P and Khan A J 2011 Short report: Gender differences in tuberculosis notification in Pakistan *Am. J. Trop. Med. Hyg.* **85** 514–7

[22] Schaaf H S, Cilliers K, Willemse M, Labadarios D, Kidd M and Donald P R 2012 Nutritional status and its response to treatment of children, with and without HIV infection, hospitalized for the management of tuberculosis. *Paediatr. Int. Child Health* **32** 74–81

[23] Escott S and Newell J 2007 Don't forget the bigger picture ed A Green *J. Health Organ. Manag.* **21** 506–18

[24] Rafiza S, Rampal K G and Tahir A 2011 Prevalence and risk factors of latent tuberculosis infection among health care workers in Malaysia *BMC Infect. Dis.* **11** 19

[25] Kibret K T, Yalew A W, Belaineh B G and Asres M M 2013 Determinant factors associated with occurrence of tuberculosis among adult people living with HIV after antiretroviral treatment initiation in Addis Ababa, Ethiopia: a case control study. *PLoS One* **8** e64488

[26] Bouscaillou J, Evanno J, Prouté M, Inwolé A, Kabran M, N'Guessan T, Djé-Bi S, Sidibé S, Thiam-Niangoin M, Badou R N, Blanchetière P and Luhmann N 2016 Prevalence and factors associated with HIV and tuberculosis in People who use drugs in Abidjan, Ivory Coast *Int. J. Drug Policy*

[27] Boccia D, Hargreaves J, De Stavola B L, Fielding K, Schaap A, Godfrey-Faussett P and Ayles H 2011 The association between household socioeconomic position and prevalent tuberculosis in Zambia: a case-control study. *PLoS One* **6** e20824

[28] Güler M, Ünsal E, Dursun B, AydIn Ö and Capan N 2006 Factors influencing sputum smear and culture conversion time among patients with new case pulmonary tuberculosis *Int. J. Clin. Pract.* **61** 231–5

[29] Mukherjee A, Sarkar A, Saha I and Chowdhury R 2012 Gender differences in notification rates, clinical forms and treatment outcome of tuberculosis patients under the RNTCP *Lung India* **29** 120

[30] PrayGod G, Range N, Faurholt-Jepsen D, Jeremiah K, Faurholt-Jepsen M, Aabye M G, Jensen L, Jensen A V, Grewal H M S, Magnussen P, Changalucha J, Andersen A B and Friis H 2011 Weight, body composition and handgrip strength among pulmonary tuberculosis patients: a matched cross-sectional study in Mwanza, Tanzania. *Trans. R. Soc. Trop. Med. Hyg.* **105** 140–7

[31] McShane H, Jacobs W R, Fine P E, Reed S G, McMurray D N, Behr M, Williams A and Orme I M 2012 BCG: Myths, realities, and the need for alternative vaccine strategies *Tuberculosis* **92** 283–8

[32] Comas I, Chakravartti J, Small P M, Galagan J, Niemann S, Kremer K, Ernst J D and Gagneux S 2010 Human T cell epitopes of Mycobacterium tuberculosis are evolutionarily hyperconserved *Nat. Genet.* **42** 498–503

[33] Mudenda V, Lucas S, Shibemba A, O'Grady J, Bates M, Kapata N, Schwank S, Mwaba P, Atun R, Hoelscher M, Maeurer M and Zumla A 2012 Tuberculosis and Tuberculosis/HIV/AIDS-Associated Mortality in Africa: The Urgent Need to Expand and Invest in Routine and Research Autopsies *J. Infect. Dis.* **205** S340–6

[34] Zumla A, Atun R, Maeurer M, Mwaba P, Ma Z, O'Grady J, Bates M, Dheda K, Hoelscher M and Grange J 2011 Viewpoint: Scientific dogmas, paradoxes and mysteries of latent Mycobacterium tuberculosis infection *Trop. Med. Int. Heal.* **16** 79–83

[35] Wallis R S, Kim P, Cole S, Hanna D, Andrade B B, Maeurer M, Schito M and Zumla A 2013 Tuberculosis biomarkers discovery: developments, needs, and challenges *Lancet Infect. Dis.* **13** 362–72

[36] Bivas-Benita M, Gillard G O, Bar L, White K A, Webby R J, Hovav A and Letvin N L 2012 Airway CD8+ T cells induced by pulmonary DNA immunization mediate protective anti-viral immunity *Mucosal Immunol.* **6**

[37] Ottenhoff T H M 2012 The knowns and unknowns of the immunopathogenesis of tuberculosis [State of the art] *Int. J. Tuberc. Lung Dis.* **16** 1424–32

[38] Donald P R, Marais B J and Barry C E 2010 Age and the epidemiology and pathogenesis of tuberculosis *Lancet* **375** 1852–4

[39] Den Boon S, Van Lill S W P, Borgdorff M W, Verver S, Bateman E D, Lombard C J, Enarson D A and Beyers N 2005 Association between smoking and tuberculosis infection: a population survey in a high tuberculosis incidence area *Thorax* **60** 555–7

[40] Bates M N, RD R, KR S, DC C, S B and R P 2007 Risk of Tuberculosis From Exposure to Tobacco Smoke *Arch. Intern. Med.* **167** 335

[41] Patra J, Bhatia M, Suraweera W, Morris S K, Patra C, Gupta P C and Jha P 2015 Exposure to Second-Hand Smoke and the Risk of Tuberculosis in Children and Adults: A Systematic Review and Meta-Analysis of 18 Observational Studies ed M Pai *PLOS Med.* **12** e1001835

[42] Hodge S, Hodge G, Ahern J, Jersmann H, Holmes M and Reynolds P N 2007 Smoking Alters Alveolar Macrophage Recognition and Phagocytic Ability *Am. J. Respir. Cell Mol. Biol.* **37** 748–55

[43] Shang S, Ordway D, Henao-Tamayo M, Bai X, Oberley-Deegan R, Shanley C, Orme I M, Case S, Minor M, Ackart D, Hascall-Dove L, Ovrutsky A R, Kandasamy P, Voelker D R, Lambert C, Freed B M, Iseman M D, Basaraba R J and Chan E D 2011 Cigarette Smoke Increases Susceptibility to Tuberculosis—Evidence From In Vivo and In Vitro Models *J. Infect. Dis.* **203** 1240–8

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