

Factors associated with tuberculosis cases in Semarang District, Indonesia: case–control study performed in the area where case detection rate was extremely low

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Abstract

Objectives Indonesia is ranked as the 4th highest contributor to tuberculosis (TB) in the world. Semarang District in Central Java displays extremely low case detection rate (CDR), possibly contributing to the local prevalence of TB.

Methods A case–control study was performed to explore the factors that cause such low CDR. We recruited 129 TB cases and 83 controls that visited the same centers and were not diagnosed with TB.

Results The cases had 7.5 ± 2.3 symptoms/person on average, indicating the delay in diagnosis because the controls only displayed 1.0 ± 1.7 . The multiple logistic regression analysis comparing the cases/controls extracted following factors as a risk to have TB: farmer, close contact with TB patients, ignorance of whether Bacillus Calmette–Guérin (BCG) was accepted or no, smoking, low income, a lot of people living in the same room, irregular hand wash before meals, not wash hands after blow, soil floor, and no sunlight and no ventilation in the house.

Conclusions Neither the cases nor the controls knew the symptoms and how to avoid TB infection, which probably

caused the delay in diagnosis. It is difficult to change the current living conditions. Thus, the amendment of the community-based education program of TB seems to be required.

Keywords Tuberculosis · Case detection rate · Risk factors · Indonesia · DOTS

Abbreviations

BCG	Bacillus Calmette–Guérin
CDR	Case detection rate
CI	Confidence interval
DOTS	Directly observed treatment short course
HIV	Human immunodeficiency virus
MA	Monovariate analysis
MDR	Multidrug resistant
MLR	Multiple logistic regression analysis
TB	Tuberculosis

Introduction

Tuberculosis (TB) is one of the biggest problems throughout the world and a leading cause of death and major public health problem [1]. Many people with TB remain poorly diagnosed or are diagnosed only after long delays. The high burden of undiagnosed TB causes much suffering such as economic hardship and sustained transmission [2–4].

According to Global Tuberculosis Report 2012 [5], Indonesia is ranked as the 4th (0.4–0.5 million) highest contributor to the TB world after India (2.0–2.5 million), China (0.9–1.1 million), and South Africa (0.4–0.6

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million). Since 2000, 22 high burden countries account for 82 % of all estimated incident cases [5].

The diagnosis of TB in Indonesia in 2011 is 807 per 100,000 population and that in Central Java 637 per 100,000 population [6]. The TB case detection rate (CDR) of Central Java Province is estimated to be 56.93 % [7], but among its local districts Semarang displays an extremely low CDR, 19.21 % [8]. National target for TB control strategy in Indonesia, according to the strategic plan of the Ministry of Health from 2010 to 2014, is to reduce the TB prevalence to 224 per 100,000 population. Output targets are to (1) increase the CDR of new cases of smear-positive pulmonary TB from 73 to 90 %, (2) reach successful treatment of new cases of smear-positive pulmonary TB to 88 %, (3) increase “the percentage of province with CDR above 70 %” to 50 %, and (4) increase “the percentage of the province with treatment success rate above 85 %” from 80 to 88 % [9].

To achieve the national targets for controlling TB, some strategies seem to be very important: empowerment in the community; early detection and registration of TB patients; improvement of the quality of directly observed treatment short course (DOTS) services; facing the challenges of TB/HIV, multidrug-resistant (MDR-TB) and childhood TB; meet the demands of poor and other vulnerable groups in the society [9]. Domain knowledge is very important in the formation of action. In several developing countries, TB patients are perceived to seek late care or avoid care, due to misunderstanding of popular TB etiologies such as sharing utensils, heavy labor, smoking, bewitchment, and hereditary transmission [10–12]. Thus, it seems very important to know the basic knowledge, attitude, and behavior of the people in such a low CDR region to implement TB programs.

In the present study, differences in the basic knowledge, attitude, and behavior were compared among the TB cases registered in 2012 at the health centers in Semarang District and the controls that visited the same health centers and were diagnosed differently.

Methods

This study was designed to be a case–control study [13] from 2012 January to 2013 October. TB cases (129) were recruited from the cases registered as TB diagnosis at the health centers in Semarang District and 50 % were female. The controls (83) were recruited among those who visited the same health centers and were diagnosed differently, and 52 % were female. The average age of the cases and controls (Mean \pm SD) was 41.2 ± 15.3 and 35.7 ± 11.7 , respectively. This research was approved by the ethical committees of Kanazawa University School of Medicine, Japan, and Diponegoro University School of Medicine, Dr

Kariadi Hospital Semarang, Indonesia, and Semarang State University, Indonesia. All participants approved this research and gave written informed consent.

TB information of the cases

TB cases were sent to the health center from clinics and diagnosed to have TB using physical examination, microscopic examination by Ziehl Neelsen staining, X-ray, etc.

The method of diagnosis, symptoms, and treatment methods were examined. All of them were treated with DOTS properly regardless of having side effects.

Characteristics of the cases and controls

Demographic characteristics such as gender, age, occupation, origin, BCG experience, close contact with TB patients, smoking habit, having pets, and income were examined. The source of TB information (multiple answers) was also examined. Thereafter, differences in living condition and attitudes in daily life were examined.

Knowledge and opinion about TB

The participants were questioned about the symptoms of TB (multiple answers) and the ways to avoid it (multiple answers). Differences in the opinion and attitude against TB between the cases and controls were examined.

Statistical analysis

The difference in the age and numbers of complaint of the cases and controls was estimated using Student's *t* test. The differences in the frequency of answers between the cases and the controls were estimated by Chi square (χ^2) test (monovariate analysis, MA). Multiple logistic regression analysis (MLR) with the cases/controls as the dependent variable was utilized with the independent variables using groups classified by characteristics of the cases and controls. All analyses were performed with SPSS ver. 19 (SAS Institute Inc., Cary, NY). In all analyses, $p < 0.05$ was taken to indicate statistical significance.

Results

The 129 cases included 65 males and 64 females, respectively, and the average age was 41.2 ± 15.3 (Table 1). Although all the cases were registered at the health centers, around 20 % were diagnosed at the different medical facilities (Table 2). Sputum smear was the first choice for diagnosis [1, 14], but 20 cases were diagnosed without any clinical examination. Chest X-ray was utilized for the

Table 1 Demographic characteristics of the cases and control

	Cases		Controls			Cases		Controls	
	N	%	N	%		N	%	N	%
Total	129		83		Smoking				
Gender					No	41	32	34	41
Male	65	50	40	48	No, but family smokes	45	35	28	34
Female	64	50	43	52	Yes	44	34	21	25
Occupation ^a					Pet				
Farmer	101	78	31	37	Yes	67	52	34	41
Others	28	22	52	63	No	62	48	49	59
Education ^a					Income ^a				
Elementary school	38	29	8	10	<100	96	74	38	46
Jr high school	59	46	32	39	100–150	19	15	31	37
High school or higher	32	25	43	52	>150	14	11	14	17
Origin					Source of TB information (multiple answers)				
Rural	106	82	70	84	Broadcast ^b	74	57	64	77
Urban	23	18	13	16	Billboards ^b	10	8	20	24
Have you ever had BCG? ^a					Newspaper ^b	18	14	23	28
Yes	33	26	46	55	Medical ^b	89	69	37	45
No	30	23	21	25	Acquaintance ^b	9	7	24	29
Do not know	66	51	16	19	Teacher ^b	6	5	25	30
Close contact with TB patients ^a									
Yes	18	9	0	0					
No	111	86	83	100					

Average age of the case and control (Mean \pm SD) was 41.2 ± 15.3 and 35.7 ± 11.7 , respectively, and the difference was significant ($p < 0.05$, Students' *t* test)

^a Significant difference in the rate of answers between the case and the control ($p < 0.05$, χ^2 test)

^b For multiple answer questions, the difference in the rate of each source was examined using χ^2 test. The case and control displayed significant differences in all sources ($p < 0.05$)

Table 2 The diagnosis method and symptoms

	N	%
Location of diagnosis		
Health center	101	78
Private clinic	16	13
Others	12	9
Way of diagnosis		
No clinical examination	20	16
Smear alone	39	30
Smear, X-ray	70	54
Symptoms (multiple answers)		
Cough with sputum	125	97
Cough >2w	123	95
Hemoptysis	78	60
Dyspnea	86	67
Chest pain	102	79
Malaise	108	84
Anorexia	108	84
Weight loss	101	78
Sweat at night	77	60
Subfever >1 Mo	72	56

Mantoux test was utilized only in 2 cases. The mean \pm SD of complaints/person was 7.5 ± 2.3 , whereas that of the controls only 1.0 ± 1.7 ($p < 0.05$, Students' *t* test)

diagnosis of more than half of the cases. Long-lasting cough with sputum was the most common symptom that was followed by chest pain, malaise, anorexia, and weight loss. Around two-thirds displayed hemoptysis, dyspnea, sweat at night, and long-lasting subfever at night. The cases had many symptoms, 7.5 ± 2.3 complaints/person on average. These cases were registered; hence, all of them underwent treatment, whether they knew it was under DOTS or not (Table 3). Nine had no supervisors and at least one-fourth had to pay treatment fee, suggesting that they were not under DOTS. More than 85 % of the cases quit taking medicine at 6 months, regardless of the frequency of medication in the first 2 months. Treatment with 4 drugs was most common, but that with 2 drugs was also observed in around 15 % of the cases. Sputum smear was the most common examination during treatment followed by chest X-ray.

The controls were selected from people who visited the same health center and diagnosed as not having TB. We tried to obtain age- and gender-matched controls. We could achieve gender-matched controls, but their age was slightly lower than the cases (Table 1). Around 80 % of the cases were farmers and around 30 % of them had graduated from elementary school alone. More than half of the controls had received BCG, whereas more than half of the cases did not

Table 3 Information related to treatments of the cases

	<i>N</i>	%
Was treatment made under DOTS?		
Yes	80	62
No	14	11
Do not know	35	27
Who was the supervisor? ^a		
Family	86	67
Medical Service	67	52
None	9	7
Was treatment free of charge?		
Yes	80	62
No	33	26
Do not know	16	12
How long was the duration of treatment?		
<6 Mo	7	5
6 Mo	112	87
> 6 Mo	10	8
How frequent do you take medication within the first 2 Mo?		
Everyday	80	62
1x/week	35	27
Longer	14	11
How many kinds of drugs did you take?		
2	19	15
3	34	26
4	70	54
5	6	5
Did you suffer from side effects?		
+	70	54
Which examinations were utilized during treatment? ^b		
Sputum smear	104	81
Chest X-ray	79	61
Sputum culture	11	8.5
Mantoux test	11	8.5
Distance to the health center		
≤5 min	85	66
≤30 min	21	16
Longer	26	18

^a 35 cases were supervised both by family and medical staff^b 76 cases were subjected to more than two examinations

know whether they received BCG or not. Nine percent of the cases experienced close contact with TB patients, but none of the controls did. The income of the cases was significantly lower than that of the controls, and three-fourths of them got less than 100 \$/month. The cases had already been diagnosed, and hence they obtained more TB information from the medical staff than the controls, but they usually did not use other sources (Table 1). When the living conditions were compared, all conditions were significantly different between the cases and the controls

Table 4 Comparison of living conditions of the participants

	Cases		Controls	
	<i>N</i>	%	<i>N</i>	%
Number of persons in the same room ^a				
1	15	12	10	12
2	84	65	72	87
>3	30	23	1	1
House floor ^a				
Soil	35	27	2	2
Plaster	49	38	18	22
Ceramics	45	35	63	76
Location of kitchen ^a				
Outside	51	40	60	72
Inside	78	60	23	28
Fuel for cooking ^a				
Cordwood	52	40	8	10
Gas	77	60	75	90
Window in each room ^a				
Yes	52	40	8	10
No	77	60	75	90
Open windows every day ^a				
Yes	43	33	60	72
No	86	67	23	28
Sunlight into the house ^a				
Yes	66	51	76	92
No	63	49	7	8
Ventilation in every room ^a				
Yes	50	39	75	90
No	79	61	8	10
Humidity in the house ^a				
Humid	84	65	17	20
Not humid	45	35	66	80

^a Significant difference between the cases and the controls ($p < 0.05$, χ^2 test)

(Table 4). “Ceramic floor”, “outside kitchen”, “gas for cooking”, “open windows every day”, “sunlight into the house”, and “ventilation in every room” were more common in the controls, whereas “window in each room” and high “humidity in the house” were common in the cases.

The cases less frequently “washed their hands before eating”, but more frequently “shared their dishes with others” and “drunk from the same glasses/bottles” than the controls (Table 5). They also less frequently “washed their hands after nose blowing” than the controls, whereas no difference was observed in the frequency of whether “they worked when they felt unwell” between these two groups.

To clarify what kinds of physical factors were the most affected differences in the cases and the controls, the MLR was applied (Table 6). The cases/controls were the dependent variables and the groups divided by the above-

mentioned information were used as determinants. The method of obtaining TB information was removed from the determinant, because that from the cases was modified as described above. The obtained risks were “farmers”, “close contact with TB patients”, “whether or not they did not know they received BCG”, “smoking”, and “low

income “100 \$/month”. “High income ”150 \$/month” was also extracted as a risk compared with “middle income 100–150 \$/month”. To “wash hands before eating”, “wash hands after nose blowing” and “not work when unwell” were protective. Among living conditions, “live with more than 3 person in the same room”, “soil floor”; no “sunlight in the house” and no “ventilation in the house” were extracted as risk.

Regardless of many symptoms, the cases did not always display significant differences with the controls regarding what they thought were TB symptoms (Fig. 1). “Long-lasting subfever” alone was significantly greater in the controls.

More than 70 % of both the cases and the controls thought that it was important to “cover mouth/nose when someone sneezed” (Fig. 2). More than half of the controls thought that “avoiding sharing dishes”, “avoiding drinking from the same glass/bottle”, “washing hands after touching items in the public” and “maintaining good nutrition” were the ways to avoid getting TB and the rates were significantly higher than the cases. In fact, 76 % of the controls washed hands before eating and only 35 % of the cases did so (Table 5). Moreover, 76 % (9 + 67) of the cases at least sometimes “shared their dishes” and “drank from the same glass”, which was significantly higher than the controls. On the other hand, 87 % (39 + 48) of the controls at least sometimes “washed hands after blowing nose”. “Vaccination” was also higher in the controls than in the cases (Fig. 2).

Opinions related to the seriousness and shame did not display any significant difference between the cases and the controls (Table 7). Although many of the cases and controls thought TB to be “serious”, they did not always think that TB was “serious at workplaces” and “affected work performance”. Significant difference was not observed in

Table 5 The differences in attitudes between the participants

	Cases		Control	
	N	%	N	%
Do you wash your hands before eating? ^a				
Yes	45	35	63	76
Sometimes	72	56	18	22
No	12	9	2	2
Do you eat from the same dish with others? ^a				
Yes	11	9	8	10
Sometimes	86	67	28	33
No	32	25	47	57
Do you drink from the same glasses/bottles with others? ^a				
Yes	7	5	9	11
Sometimes	92	71	35	42
No	30	23	39	47
Do you wash your hands after blowing nose? ^a				
Yes	25	19	40	48
Sometimes	69	53	32	39
No	35	27	11	13
Do you work when you are unwell?				
Yes	23	18	25	30
Sometimes	78	60	40	48
No	28	22	18	22

^a Significant difference between the cases and the controls ($\rho < 0.05$, χ^2 test)

Table 6 Multiple logistic regression analysis using case/control as the dependent valuable and living status as determinants

	Comparison	Reference	Odds	P	95 % CI	
Source of TB information (multiple answers) was excluded because this information was modified by consultation of the cases to the health center. Among determinants, age class, gender, education, pet, sharing the dishes, drinking from the same bottle/glass, location of kitchen, fuel for cooking, opening the window every day, and humidity in the house were not selected	Occupation	Workers	Farmers	0.05	<0.01	0.00 0.20
		Others	Farmers	0.05	0.01	0.00 0.54
	Close contact with TB patients	No	Yes	0.00	0.02	0.00 0.49
	BCG	Yes	Do not know	0.04	<0.01	0.00 0.32
	Smoking	No	Yes	0.14	0.04	0.01 0.92
	Income (\$/Mo)	100–150	<100	0.05	<0.01	0.00 0.33
		100–150	>150	0.08	0.04	0.01 0.89
	Person/room	1	≥3	0.00	<0.01	0.00 0.35
		2	≥3	0.00	<0.01	0.00 0.27
	Wash hands before eating	Yes	Sometimes	0.06	<0.01	0.01 0.32
	Wash hands after blowing nose	Sometimes	No	0.06	0.01	0.01 0.46
	Work when unwell	No	Yes	0.09	0.02	0.00 0.66
	Floor	Ceramics	Soil	0.06	0.04	0.00 0.90
	Sunlight in the house	Yes	No	0.06	0.02	0.00 0.67
	Ventilation in the house	Yes	No	0.02	<0.01	0.00 0.24

Fig. 1 Differences in the knowledge about TB symptoms between the cases and controls (multiple answers). Asterisk significant differences ($p < 0.05$, χ^2 test and Student's t test)

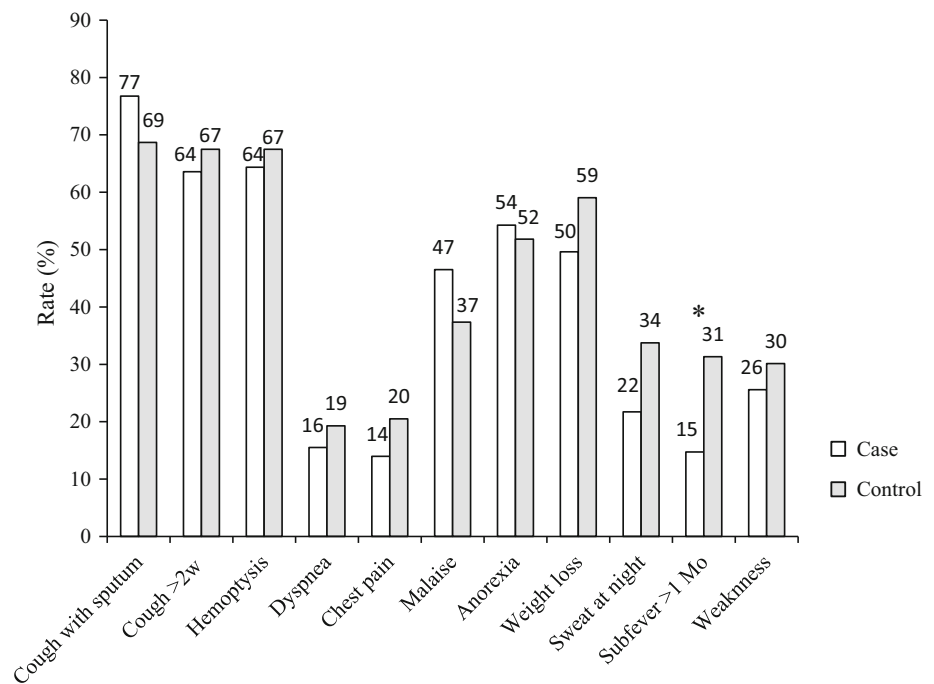
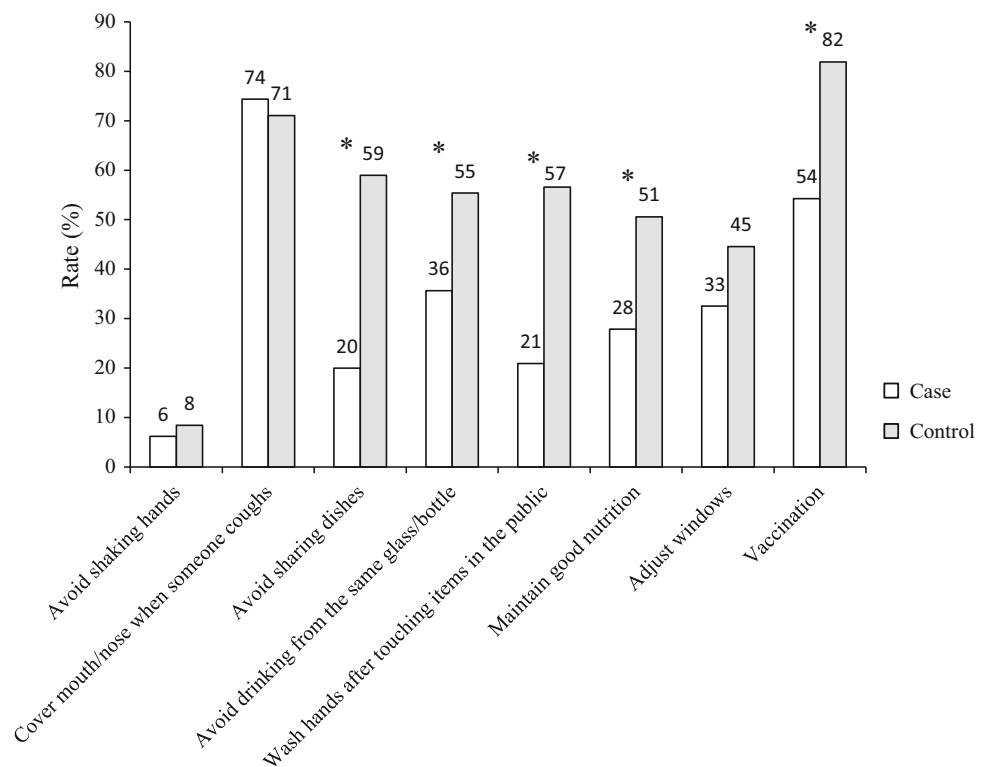


Fig. 2 Differences in the way that the cases and controls thought was good to avoid getting TB. Asterisk significant differences ($p < 0.05$, χ^2 test)



“being ashamed of having TB”, but the cases tended to want to “hide having TB”. Significantly more controls thought “TB affected relationship with others” and “wanted to be isolated”, whereas there was no significant difference in “TB affecting family responsibility” against the controls. Both of the cases and controls usually tried to

be good to TB patients. Around 50 % of the controls believed that “TB treatment was very costly”, but around one-fourth of the cases did not think so. “HIV-positive people’s concern about TB” was significantly higher in the controls than in the cases. Around one-fourth to one-third of the cases and controls believed that TB was hereditary.

Table 7 Differences in the opinion against TB between the cases and controls

	Cases		Controls	
	<i>N</i>	%	<i>N</i>	%
Do you think that TB is serious?				
Yes	91	71	67	81
No	2	2	3	4
Do not know	36	28	15	18
Do you think that TB is serious at workplaces?				
Yes	46	36	34	41
No	14	11	10	12
Do not know	69	53	39	47
Does TB affect your work performance?				
Yes	51	40	43	52
Not always	60	47	29	35
No	18	14	11	13
Do you feel ashamed of having TB?				
Yes	49	38	22	27
No	53	41	35	42
Do not know	27	21	26	31
Do you want to hide having TB? ^a				
Yes	14	11	10	12
Not always	74	57	30	36
No	41	32	43	52
Does TB affect your relationship with others? ^a				
Yes	20	16	36	44
Not always	72	56	35	42
No	37	29	12	14
Does TB affect family responsibilities?				
Yes	58	45	41	49
Not always	53	41	35	42
No	18	14	7	8
Do you want to live isolated due to having TB? ^a				
Yes	5	4	12	14
Not always	43	33	25	30
No	81	63	46	55
How do you feel about a person with TB?				
Desire to help	94	73	59	71
Want to stay away	28	22	20	24
No particular feeling	7	5	4	5
Is TB treatment very costly? ^a				
Yes	32	25	42	51
Not always	44	34	21	25
No	53	41	20	24
Do you think that HIV-positive people should be concerned about TB? ^a				
Yes	23	18	39	47
Not always	79	61	30	36
No	27	21	14	17
Do you think that TB is hereditary				
Yes	30	23	24	29
No	79	61	47	57
Do not know	20	16	12	14

^a Significant difference between the cases and the controls ($p < 0.05$, χ^2 test)

Discussion

In Indonesia, regular health examination is not mandatory [6]. Therefore, after symptoms became apparent, the person visited the clinic where sputum smear was not always available. The cases in the present study displayed 7.5 ± 2.3 complaints/person on average, indicating the delay of diagnosis [15]. Although early diagnosis and initiation of treatment of infectious cases are the best measures to reduce transmission [3, 16, 17], in some countries 20 % of patients were not diagnosed for over 6 months from the onset of symptoms [18]. Even after the symptoms became obvious, it took at least 2 more days for diagnosis, because positive TB was defined as more than 2 positive sputum smears in the smear performed three times within 2 days [14]. Household contacts continued meantime, when patients were with potentially infectious forms proceeding to high prevalence of TB [19, 20]. On the other hand, culture was not common, whereas patients with smear-negative, culture-positive TB were reportedly responsible for TB transmission [21, 22]. Immediate introduction of culture examination is required because, in addition to high sensitivity, it allows determining whether the patient is sensitive to anti-TB drugs and useful for finding extrapulmonary TB [14].

The cases did not always know whether they were under DOTS treatment or not, but all the cases could luckily quit taking medicine regardless of the obvious delay of diagnosis. Around 80 % of the cases were farmers and around 30 % had graduated from elementary school alone; hence, their income was lower than the controls. Low income and low education are reportedly associated with TB infection [4, 23–25]. They also had lost the chance of BCG injection. This occupation was also extracted as a risk by the MLR. However, the MLR extracted high income as a risk as well. Such a result is not always in accordance with several studies [4, 23–25], whereas it is conceivable that people with high income, regardless of their occupation, have more chances to live and/or work at places with a lot of people where a risk of TB transmission is supposed to be high. The number was small, but only cases had a chance of close contact with TB patients. TB contact was absolutely a risk factor for TB transmission [18, 26]. No significant difference was found in the rate of “smoking” by the MA, but the MLR extracted “smoking” as a risk. This is in good accordance with a previous report [23]. It is natural that the “source of TB information” of cases was medical staff, but the cases were not always eager to collect information from other sources compared with the controls. All the items related to living condition were significantly different between the cases and the controls according to the MA. Among them, the MRL extracted “small number of persons in a room”, “ceramic floor”, “sunlight in the

house”, and “ventilation in the house” as protective. The importance of good ventilation has been emphasized elsewhere [3, 23]. Excluding “work when unwell”, their attitudes displayed significant differences between the cases and the controls by the MA. “Share the dish” and “drink from the same glasses/bottles” were not extracted by the MLR. Instead, “work when unwell” was extracted as well as “wash hands before eating” and “wash hands after nose blowing”. These findings may be a reflection that TB is airborne. In general, the cases were not aware of the danger in their attitudes, which was in good accordance with previous reports [10–12].

Both the cases and the controls did not recognize “dyspnea” and “chest pain” as TB symptoms. Significant differences existed, but “long-lasting subfever” was also not considered as TB symptoms. “dyspnea”, “chest pain,” and “long-lasting subfever” were less frequent than “cough with sputum”, “malaise”, and so on, but a number of cases complained of these. Thus, it seems necessary make people aware of TB symptoms [10–12].

TB itself was recognized to be dangerous both by the cases and the controls, but they did not recognize its dangerousness at work places. Many of the cases were farmers; hence, it seems less possible to spread TB than workers. However, TB-positive workers can work and be able to transmit TB to their colleagues. On comparing the rate of both the cases and controls who thought “having TB was a shame”, the rate of “wanted to hide having TB” was less. It seems natural that more controls who did not receive TB treatment believed that TB “affected relationship with others” and wanted to “live isolated in case of TB” than the cases. DOTS performed under the governmental hospitals and health centers were free [9], but some cases visiting private hospitals/clinics had to pay the treatment fee. A higher rate of “HIV-positive people should be concerned about TB” in the control was reflection that they were more eager to collect information than the cases. HIV infection reportedly affected TB infection [27]. However, the number who believed “TB was hereditary” was not different between the two groups.

Some aspects underlying the low coverage CDR are socioeconomic, education/knowledge, and stigma problems [4]. Economic conditions will affect the public in obtaining not only good environmental home conditions, but also an excellent level of education. The level of education in this study was relatively low because many people only finished elementary school where sufficient TB education was impossible. Poor education will cause shortage of knowledge about TB, leading the public into embarrassment and sometimes attitude to hide their disease if they are exposed to TB. Such conditions in some people may cause delay in going to health service [18]. As a result, TB has spread among farmers even when their contact has

not always been intense like workers. It is very difficult to change occupation, income, and housing conditions immediately. Thus, community-based TB education is very important. It may be useful to educate and expose not only public, but also private practitioners to community-based TB programs [9, 28].

Some cases were not dependent on the free DOTS program. To inform about the existence of this program is also good education. Utilization of this program not only reduces multidrug-resistant TB, but also helps reduce out-of-pocket expenses to patients [27]. The number of syndromes of the cases absolutely indicates the delay in diagnosis.

The classic symptoms of TB are fever, cough, and weight loss, but they are non-specific and can be mimicked by other conditions, including malignancy and other pulmonary infections. That is, in an early stage, such syndromes are not always specific to TB. However, importance of these classic lung related with syndromes should be aware of that they are possible signs of initiation of TB expansion [29].

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