Predominant Determinants of Delayed Tuberculosis Sputum Conversion in Indonesia

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Abstract

Context: Sputum conversion in the first 2 months of tuberculosis (TB) treatment is closely related to successful treatment and a decrease in the likelihood of relapse. In 2015, there were 76% high TB burden countries with low rate of TB successful treatment. **Aims:** This study aims to evaluate the correlation between delayed sputum conversion and several determinants including social determinants, smoking, malnutrition, and type II diabetes mellitus (DM). **Settings and Design:** A case–control approach was used to study the potential determinants. A case sample group consisted of smear-positive TB patients with delayed sputum conversion (31 patients) at community health centers in Bandar Lampung, Indonesia. Meanwhile, a control sample group consisted of smear-positive TB patients with sputum conversion (62 patients). **Subjects and Methods:** Primary data consisted of social determinants and smoking, were collected through in-depth interviews. Meanwhile, secondary data consisted of malnutrition, DM, and sputum conversion were obtained from the medical record. **Statistical Analysis Used:** Data were analyzed using Chi-square and multivariate logistic regression. **Results:** Low education (odds ratio [OR]: 5.313; 95% (confidence interval [CI]: 1.711–16.503), low social class (OR: 4.993; 95% CI: 1.430–17.430), smoking (OR: 7.457; 95% CI: 1.757–31.640), and DM (OR: 7.168; 95% CI: 1.746–29.431) influenced delayed sputum conversion. **Conclusions:** TB control programs in high TB burden countries with low rate of TB successful treatment, should be integrate TB treatment education, smoking cessation programs and follow-up treatments for TB patients with DM to improve the probability of sputum conversion and successful treatment.

Keywords: Delayed sputum conversion, diabetes mellitus, smoking, social determinants

INTRODUCTION

Treatment and cure rates are the key indicators of a successful tuberculosis (TB) control program. The successful treatment of infectious TB is essential in preventing the spread of the disease and has an immediate impact on reducing the number of new cases.[1] In 2015, among 30 high TB burden countries, there were 76% countries (including Indonesia), with successful treatment <90%.[2]

Sputum conversion is a widely used indicator to measure early response to TB treatment. A negative sputum conversion after 2 months of treatment indicates that there has been a bacteriological response to the anti-TB treatment. This indicator is closely associated with successful long-term TB treatment as well as increasing cure rates.[3]

The progression of a patient's TB infection, treatment, and sputum conversion can be directly or indirectly influenced by social determinants[4] such as education, occupation, income, and social class. These factors often lead to stratification or discrimination within the community, which can cause a person to be more susceptible to TB.[5] Additional risk factors that are closely related to sputum conversion include smoking, malnutrition, and type II diabetes mellitus (DM).[4,6-8] These conditions contribute to delayed sputum conversion in TB patients.[9]

Bandar Lampung, Indonesia had a high incident rate of TB. (2056 cases in 2016) with a higher than the average number of TB patients with DM, as well as a high percentage of smokers within the general population (31.3%).[10,11] Based

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on the reported data, the city's TB cure rate in 2014 was only 64.3%, far below the national target of 85%. In addition, there was a significant disparity in cure rates. Some community health centers (CHC) reported a 99% cure rate while others achieved <40%.[12] Research has shown that many TB patients in Bandar Lampung, Indonesia, ranked low on an assessment of their social determinants and was also clustered in population areas with characteristics of low social determinants.[13,14]

This research studied the influence of social determinants (education, occupation, income, and social class) as well as smoking, malnutrition, and DM on delayed sputum conversion in Bandar Lampung.

SUBJECTS AND METHODS

A case–control study was performed from June to November 2016. The study focused on 17 CHCs where a large number of smear-positive TB patients with delayed sputum conversion were registered. These 17 CHCs were part of the 30 CHCs in Bandar Lampung that have conducted a directly observed treatment short course TB strategy.

This study surveyed 311 smear-positive TB patients who had received treatment from the 17 CHCs in Bandar Lampung from January to July 2016. A selected number of respondents were divided into a case sample group and a control sample group. The respondents in the case sample group comprised 31 smear-positive TB patients with delayed sputum conversion. The respondents in the control sample group comprised 62 smear-positive TB patients who had achieved sputum conversion after 2 months of treatment. There were twice as many respondents in the control sample group as the case sample group. Both total sampling and simple random sampling were used to select the case and control patient samples. In addition, respondents in the control sample group were matched to respondents in the case sample group in terms of age distribution (<31 years old: 22.5%; 31–40 years old: 13%; 41–50 years old: 22.5%; 51–60 years old: 42%) and sex (female: 50%; male: 50%) to minimize any bias caused by age or sex.

Both independent and dependent variables were studied in this research. Independent variables included: Education (reflecting the respondent's education in terms of the number of years of schooling completed: Low indicated <9 years, and high indicated more than 9 years);[15] occupation (reflecting the respondent's occupation over the past 12 months: Unemployed or employed); income (reflecting the level of the respondent's income: Less than or the same as the Bandar Lampung minimum payment standard or more than the Bandar Lampung minimum payment standard);[16] social class (reflecting the respondent's ownership of productive assets that can provide income: The respondent had no productive assets or had productive assets);[5] smoking (reflecting the respondent's smoking activity through the first 2 months of TB treatment: Yes or no); malnutrition (reflecting the respondent's body mass index that was recorded near the beginning of the TB treatment: Less than or the same as 18.5 or more than 18.5);[17]

and DM (reflecting the respondent's DM status that was recorded near the beginning of the TB treatment: Yes or no). The single dependent variable in the study was delayed sputum conversion (yes or no).

Primary and secondary data were collected for this study. The primary data were obtained through an in-depth interview using a questionnaire and included questions on education, occupation, income, social class, and smoking. The secondary data were collected from the CHCs study and consisted of the identity of the smear-positive TB patient, the patient's body mass index and the patient's DM status. The data were analyzed using Chi-square for the bivariate analysis and logistic regression for the multivariate analysis, the latter of which was then continued by interaction analysis. These analyses were performed to identify any influence between the independent and dependent variables.

This research received ethical approval from the Faculty of Medicine, University of Lampung. Respondents also provided informed consent to be included in this research as participation was voluntary.

RESULTS

As indicated in Table 1, 51.6% of the 93 respondents were categorized as having a low level of education, 37.6% of the respondents had no occupation, 82.8% had an income of less than the minimum salary standard, and 28% had no productive assets. In addition, among the 93 respondents, many had risk factors for delayed sputum conversion: 14% of the respondents had a smoking habit, 51.6% suffered from malnutrition, and 15% suffered from DM.

The results of the Chi-square bivariate analysis are also presented in Table 1. The determinants of education and smoking significantly influenced delayed sputum conversion with an odds ratio (OR) = 4.255 (95% confidence interval [CI]: 1.644–11.015) and an OR = 5.932 (95% CI: 1.656–21.248), respectively. The ORs of >1 indicate that smoking and low levels of education are considerable risk factors for delayed sputum conversion. These results conform with the bivariate descriptive analysis that showed that there were more respondents who smoked and had a low level of education in the case sample group compared to the control sample group. In contrast, the variables of occupation, income, social class, malnutrition, and DM had no influence on delayed sputum conversion.

Table 2 presents the results of the logistic regression for the multivariate analysis after a series of analysis stages. These results have also been through interaction analysis between the education and social class variables. The interaction analysis shows that there is no significant interaction between the variables of education and social class (the *P* value of a moderate variable = 0.994).

As shown in Table 2, the following variables influenced delayed sputum conversion: Low education (OR = 5.313; 95%

Table 1: Cross tabulation of social determinants, smoking, malnutrition, diabetes mellitus, and delayed sputum conversion in Bandar Lampung

Variables	Sputum conversion delay		P	OR (95% CI)
	Yes (%)	No (%)		
Education				
Low	23 (47.9)	25 (52.1)	0.004	4.255 (1.644-11.015)
High	8 (17.7)	37 (82.3)		
Occupation				
No	15 (42.9)	20 (57.1)	0.198	1.969 (0.814-4.761)
Yes	16 (27.6)	42 (72.4)		
Income				
Less than Bandar Lampung minimum payment standard	26 (34.2)	51 (65.8)	1.000	1.122 (0.352-3.570)
More than Bandar Lampung minimum payment standard	5 (31.25)	11 (68.75)		
Social class				
Have no productive assets	12 (46.2)	14 (53.8)	0.165	2.165 (0.849-5.523)
Have productive assets	19 (28.4)	48 (71.6)		
Smoking				
Yes	9 (69.2)	4 (30.8)	0.008	5.932 (1.656-21.248)
Low education	7 (77)	2 (23)		
High education	2 (50)	2 (50)		
No	22 (27.5)	58 (72.5)		
Malnutrition				
Yes	17 (35.4)	31 (64.6)	0.826	1.214 (0.511-2.884)
No	14 (31.1)	31 (60.9)		
DM				
Yes	8 (57.1)	6 (42.9)	0.081	3.246 (1.013-10.402)
Low education	6 (67)	3 (33)		
High education	2 (40)	3 (60)		
No	23 (29.1)	56 (70.9)		

OR: Odds ratio, DM: Diabetes mellitus, CI: Confidence interval

Table 2: The last logistic regression model of social determinants, smoking, malnutrition, diabetes mellitus, and delayed sputum conversion in Bandar Lampung

Variable	B	P	Exp(B)	95% CI
Education	1.670	0.004	5.313	1.711-16.503
Social class	1.608	0.012	4.993	1.430-17.430
Smoking	2.009	0.006	7.457	1.757-31.640
DM	1.970	0.006	7.168	1.746-29.431

DM: Diabetes mellitus, CI: Confidence interval

CI: 1.711–16.503), having no productive assets (OR = 4.993; 95% CI: 1.430–17.430), smoking (OR = 7.457; 95% CI: 1.757–31.640), and DM (OR = 7.168; 95% CI: 1.746–29.431). The OR values indicate that smoking is the most influencing variable. The result analysis also shows that education, social class, smoking, and DM explain 36.9% of delayed sputum conversion variation, while 63.1% of the variances were explained by other variables which were not studied in this research.

DISCUSSION

Bivariate and multivariate analyses strongly indicate that a low level of education significantly influenced the respondents' delayed sputum conversion. This result concurs with previous reviews reporting that a low level of education, either directly or indirectly through other TB risk factors, influences the likelihood of successful TB treatment, particularly delayed sputum conversion.[3] The current result is also in line with reviews concluding that a higher level of education tends to improve career opportunities and working environments. More education will also likely lead to higher income and the accumulation of productive assets, improving a patient's access to health care and increasing the chance of sputum conversion.[18] Based on the bivariate data analysis in Table 1, a low level of education was a predominant characteristic among the respondents in the case sample group. Those same respondents also tended to have a smoking habit. The data analysis revealed that there were about three times as many respondents with a low level of education and smoking activity in the case sample group (77%) compared to the control sample group (23%). This result is in line with research from Morocco that found a high prevalence of smoking was associated with illiteracy and low levels of education.[19]

Respondents in the case sample group with low levels of education also tended to be more likely to suffer from DM compared to respondents with low levels of education in the control sample group. The data analysis shows that

there were two times as many respondents with low levels of education and DM in the case sample group (67%) compared to the control sample group (33%). This result concurs with research reporting that low social determinants such as education are closely related to the incidence of DM.[20] Moreover, as seen in the respondent interviews, the respondents in the case sample group with low levels of education also tended to have inadequate knowledge of TB treatment. This lack of knowledge prompted some respondents to discontinue their anti-TB treatments, leading to delayed sputum conversion.

Smoking has a significant influence on delayed sputum conversion, as shown by both the bivariate and multivariate analyses [Tables 1 and 2]. Similar research in Brazil found that TB patients who smoke are 2.28 times more likely to have a delayed sputum conversion compared to nonsmoking TB patients (95% CI 1.02–5.33).[6] Similar research in Iran found that the cure rate of both nonsmoking TB patients and TB patients who quit smoking after diagnosis was higher compared to the cure rate of smoking TB patients.[21] Davies *et al.* stated that the normal mucociliary clearance of tracheal bronchial secretions and alveolar macrophage function against *Mycobacterium tuberculosis* on TB patients are impaired by smoking behavior. Therefore, it takes longer for smoking TB patients to achieve sputum conversion than nonsmoking TB patients.[22] In the current research, the age of smoking respondents in the case sample group varied from 25 to 45 years old, a range that can be categorized as adult age. The smoking respondents in the case sample group also primarily had a low level of education. This correlation should be highlighted for its relevance to smoking cessation programs for TB patients with delayed sputum conversion, particularly given review results indicating that the chance of successful cessation in young or adult smokers was smaller than that for older smokers.[23] In addition, the research has shown that successful smoking cessation rates among smokers with a low level of education are smaller than in those with a higher level of education.[24]

Multivariate analysis of the current data shows that DM influenced delayed sputum conversion. This result concurs with a review reporting that DM was closely related to poor TB treatment, including delayed sputum conversion.[9,20] Similarly, research conducted in India and Georgia found that TB patients with DM comorbidity have a longer sputum conversion time than patients with only TB. Comorbidity patients also tend to have poorer TB treatment results.[25,26] Anti-TB treatments often impact the pancreas, decreasing insulin levels, and increasing glucose levels, which worsen a patient's DM condition. High glucose levels also provide nutrition for *M. tuberculosis* and make the bacteria resistant to treatment. Therefore, sputum conversion times are longer for TB patients with DM. These patients need a treatment strategy tailored to their specific medical condition; the follow-up is also important.[27] This approach is supported by research from Fiji on TB patients with DM who were closely linked to the health system and

likely to receive follow-up treatment; this factor increased the chance of sputum conversion in the first 2 months.[28]

Multivariate analysis of the current study demonstrates that low social class significantly influenced delayed sputum conversion. This result concurs with a review reporting that the accumulation of productive assets correlated with economic ability and health care access, which in turn led to better health, including sputum conversion.[18] This result also in line with research conducted in India found that TB patients with comorbidities leading to delayed sputum conversion primarily occurred in communities with low social class.[29]

Based on the above results, delayed sputum conversion is closely related to smoking, DM, and certain social determinants, such as education and social class. In addition, respondents with low levels of education tended to have both DM and smoking habits, leading to delayed sputum conversion. To accelerate the sputum conversion rate, TB control program in high burden countries with low successful treatment should be integrate certain program related with the determinants. Regarding TB patients with low levels of education as well as low social class, TB control programs should improve patient knowledge of TB treatment to increase compliance. Research in Vanuatu found that an emphasis on patient education that encouraged treatment adherence improved sputum conversion among delayed sputum converters.[30] In addition, TB control programs should be integrated with programs to encourage patients to stop smoking, especially for TB patients with low levels of education who are young to adult smokers. TB control programs should also include treatment follow-up for TB patients with DM to ensure appropriate TB treatment. An increase in the sputum conversion rate will raise the TB cure rate and decrease the incidence of the disease.

Conflicts of interest

There are no conflicts of interest.

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