HOSTED BY

Available at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/IJMYCO

# Diabetes mellitus and its influence on sputum smear positivity at the 2nd month of treatment among pulmonary tuberculosis patients in Kuala Lumpur, Malaysia: A case control study ☆

*Noorsuzana Mohd Shariff* [a,b,*], *Nazarudin Safian* [b]

[a] *Infectious Disease Cluster, Advanced Medical and Dental Institute, University of Science Malaysia, Pulau Pinang, Malaysia*
[b] *Department of Community Health, National University of Malaysia Medical Center, Jalan Yaacob Latiff, Kuala Lumpur, Malaysia*

ARTICLE INFO

*Article history:*
Received 11 August 2015
Received in revised form
3 September 2015
Accepted 6 September 2015
Available online 1 October 2015

*Keywords:*
Risk factors
Sputum smear nonconversion
Tuberculosis

ABSTRACT

*Objective/background:* Many studies have suggested that sputum smear conversion after 2 months of antituberculosis treatment is an important determinant of treatment success and can be a predictor for relapse. The objective of this study is to determine the factors that influence sputum smear conversion after 2 months of treatment among pulmonary tuberculosis patients receiving treatment in the Institute of Respiratory Medicine in Kuala Lumpur, Malaysia.

*Methods:* A total of 75 cases and 75 controls were interviewed, and their medical records were retrieved in order to extract the information needed. All analyses were conducted using SPSS version 17, and binary logistic regression analysis was used to determine the predictors of sputum smear nonconversion.

*Results:* Results showed that the following factors were associated with sputum smear positivity after 2 months of intensive treatment: diabetes mellitus ($p = .013$, odds ratio [OR] = 2.59, 95% confidence interval [CI] 1.27–5.33), underweight body mass index ($p = .025$, OR = 1.67, 95% CI 0.80–3.49), nonadherent to tuberculosis treatment ($p = .024$, OR = 2.85, 95% CI 1.21–6.74), and previous history of tuberculosis ($p = .043$, OR = 2.53, 95% CI 1.09–5.83). Multivariable analysis identified diabetes mellitus ($p = .003$, OR = 4.01, 95% CI 1.61–9.96) as being independently associated with the risk of persistent sputum smear positivity after 2 months of intensive treatment.

*Conclusion:* Based on the findings, identification of these factors is valuable in strengthening the management and treatment of tuberculosis in Malaysia in the future. This study emphasizes the importance of diabetes screening and integration of diabetic controls among tuberculosis patients in achieving better treatment outcome.



* Corresponding author at: Department of Community Medicine, Universiti Kebangsaan Malaysia Medical Center, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaakob Latiff, 56000 Kuala Lumpur, Malaysia.
E-mail address: suzana_1910@yahoo.com (N.M. Shariff).

Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2015.09.003

## Introduction

An alarming current statistics by the World Health Organization reported that three out of 10 deaths worldwide are due to communicable diseases, which also account for 51% of Years of Life Lost globally [1]. Unlike the successful story of smallpox elimination, it seems that tuberculosis has made its comeback and is becoming a re-emerging global public health problem.

Sputum smear conversion among pulmonary tuberculosis patients was said to be the most important indicator in evaluating the effectiveness of treatment provided to patients and also the infectivity of the disease. In proving this, Holtz et al. [2] carried out a retrospective cohort study on civilian tuberculosis patients with multidrug resistance in Latvia. Through this study, they found that treatment outcomes were statistically significantly worse for patients who did not convert their sputum positivity within 2 months of treatment [2]. This is supported by Dembele et al. [3], who found that the cure rate was higher among patients who were smear-negative at the 2nd month (77.3%) of follow-up. In response to this knowledge, another researcher conducted studies looking into the factors which can influence sputum smear conversion in order to help improve and empower the current treatment practice.

Among other developing countries, Malaysia has been classified by the World Health Organization as an intermediate tuberculosis burden country. Recent statistics by the Disease Control Division of Ministry of Health Malaysia [4] revealed that 17,506 new cases were registered in Malaysia in the year 2008. Out of this big number, 10,441 cases were infectious forms.

Even though the sputum conversion rate at the end of 2 months in Malaysia stayed above the targeted level (>85%), in the year 2008, on average, 7.65% of the infectious tuberculosis patient reported delays in sputum conversion. This increases the tendency of prolonged inactivity of the patient, which later increases the risk of high secondary attack in the community. As a consequence, it increases the national burden due to increased incidence of tuberculosis.

Even though the factors influencing sputum smear conversion have been studied well, however, to the best of our knowledge, there have been no similar studies done in Malaysia. Findings from other international studies might not be applicable to the Malaysian population as our cultural and local practices differ.

Therefore, the aim of this study was to determine the factors that may influence the sputum smear conversion after 2 months of intensive treatment among pulmonary tuberculosis patients. In-depth understanding of factors that may contribute to this phenomenon is crucial to combat poor treatment outcome and further reduce the dynamic transmission of tuberculosis in the community.

## Materials and methods

This study was carried out as an unmatched case–control study within June 2010 to September 2010.

### *Study population*

This study was conducted at the tuberculosis clinic at the Institute of Respiratory Medicine (IPR), which is located at Jalan Pahang, Kuala Lumpur, Malaysia. This institute provides outpatient clinics (2 times/wk; Monday and Thursday) and inpatient services to patient with tuberculosis, as well as patients with other serious respiratory diseases.

The sampling population of this study was all smear-positive pulmonary tuberculosis patients with persistence of positivity after 2 months of intensive treatment who registered at the IPR from December 2009 to June 2010. Purposive sampling was applied in enrolling cases and controls in this study.

Patients were included as a case if they were initially diagnosed of smear-positive pulmonary tuberculosis with clinical and/or bacteriological evidence, tested positive with microscopic sputum smear investigation (at least 2 acid-fast bacilli positive) at the end of the 2nd month of intensive antituberculosis treatment, aged $\geqslant$20 years, able to understand and communicate wisely in Malay language, willing to participate in the study, and had signed the consent form. However, those who were initially diagnosed of smear-positive pulmonary tuberculosis with clinical and/or bacteriological evidence, and tested negative using microscopic sputum smear investigation at the end of the 2nd month of intensive antituberculosis treatment were included as controls for this study.

Those who were not registered with the IPR, diagnosed with another form of tuberculosis such as extra pulmonary tuberculosis, human immunodeficiency virus positive, pregnant women, terminally ill at which restricting them to give full cooperation, did not do their sputum smear examination after 2 months of intensive treatment with doubtful smear results, or, unwilling to participate were excluded from this study.

### *Study instruments*

Data was collected using three instruments: (1) structured self-administered questionnaires; (2) patients' records; and (3) anthropometric measurements. The administered questionnaire was used to assess the participants sociodemographic information, treatment related factors, and their smoking habit. Next, patients' records were used to obtain information regarding laboratory results of sputum smear after 2 months of treatment of each participant, their diabetes status, treatment regime, and adherence to treatment. As for the anthropometric measurement, two scales, namely Seca bellissima 841 digital weighing scale (with 0.1 kg level of accuracy) and Seca bodymeter microtoidse tape (Seca Medizinische Waagen und Messsysteme Vogel & Halke GmbH & Co, Hamburg, Germany) (error of measurement of ±0.1 cm), were used in measuring body weight and height, respectively. Body mass index was calculated based on these two readings.

### *Data collection procedure*

Before the researcher started to collect data from the respondents, cases and controls were met during their follow-up; which is on Monday or Thursday. The researcher approached

the eligible patients nicely and they were given an explanation regarding the study. Nothing was done before the patients signed the consent form. After they agreed, each participant's body weight and height were measured following the standardized technique. Measurements were carried out by the researcher herself. During the measurements, the participant was asked to wear light clothes, no shoes, and to stand straight with both hands at the body side. In order to avoid measurement bias, readings were taken twice and only the average was used. The body mass index was classified according to clinical practice guidelines on the management of obesity, Ministry of Health Malaysia (2004) [5]. Next, the researcher gave a set of questions to be answered by the participants. This was a self-administered questionnaire and each of the patients were given about 10 min to answer all the questions with researcher supervision.

### *Statistical analysis*

Data were entered and analyzed by using the SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA). Data were presented as descriptive statistics either as mean, median, standard deviation, frequencies, or percentages. Differences and associations between categorical variables were analyzed using chi-square test. Student *t* test or Mann–Whitney *U* test (for data which were not normally distributed) were used to compare the differences in means of continuous variables. Multiple logistic regressions with forward stepwise strategy was used in assessing the association between the risk factors (independent variables) and the outcome of sputum smear conversion after 2 months of intensive treatment, statistically adjusted for potential confounding effects of other covariates. A $p$ value <.05 was used as the level of significance.

### *Ethical considerations*

This study was conducted on a voluntary basis whereby every patient has their own right to participate or withdraw from the study. Oral and written information in Bahasa Melayu were provided to all participants prior to obtaining informed oral and written consent. All data were kept confidential for academic purposes only. Also, ethical approval and formal permission was obtained from the Ethical Committee of Universiti Kebangsaan Malaysia, Faculty of Medicine, Kuala Lumpur, Malaysia and the director of IPR, accordingly. This study was also registered with the National Malaysian Research Registry.

## Results

During the study period, a total of 150 smear-positive pulmonary tuberculosis patients were recruited into the study. With ratio of cases to controls was 1:1, and 75 of them were analyzed as cases and the rest were represented as controls. One-hundred and fifty eligible patients were approached during their follow-up and 100% of the patients were willing to participate and give a positive response towards the study.

Among 150 patients recruited in this study, cases were found to be slightly older compared with the controls, with a mean of age 45 ± 11.33 years and 43 ± 14.79 years, respectively. The range of ages was between 20 years and 76 years. More men were seen among the cases (79%) compared with only 67% among controls. In terms of ethnicity, more than half of the respondents were Malay. Furthermore, most of them were married.

On bivariable analysis, it was found that those patients who did not adhere to their treatment had three times higher odds of having sputum smear nonconversion after 2 months of intensive treatment compared with those religiously taking their drugs (odds ratio [OR] = 2.85, 95% confidence interval [CI] 1.21–6.74). Moreover, patients with a history of previous tuberculosis treatment had three times higher odds of having sputum smear nonconversion after 2 months of intensive treatment compared with new cases. However, the other sociodemographic characteristics have no significant influence on sputum smear conversion in this study (Table 1).

With regards to patients' smoking habit, no significant associations were seen between smoking status and sputum smear conversion in this current study (Table 2).

Next, bivariable analysis on the relationship between diabetes mellitus and sputum smear conversion after 2 months of antitreatment revealed an interesting finding. This study showed that diabetes mellitus was significantly associated with delays in sputum smear conversion after the intensive treatment. Patients who are smear-positive pulmonary tuberculosis with the presence of diabetes mellitus had 2.6 times higher odds of having sputum smear nonconversion compared with those without this metabolic deficiency (OR = 2.59, 95% CI 1.27–5.33).

Furthermore, body mass index was shown to be significantly associated with sputum smear nonconversion after 2 months of tuberculosis treatment ($p$ = .025). Being underweight and obese were proven to be a causative factor towards sputum smear nonconversion compared with those with an ideal body weight (OR = 1.67, 95% CI 0.80–3.49 and OR = 1.77, 95% CI 0.39–8.06, respectively; Table 3).

Further analysis using multiple logistic regression was performed to determined factors that are independently associated with sputum smear-positivity after 2 months of intensive treatment. All of the variables that were found to be significant on the bivariable analyses ($p$ < .05) were entered into the multiple logistic regression model using forward stepwise strategy.

The final multiple binary logistic regression model showed that, diabetes mellitus remained to be an independent causative factor of sputum smear nonconversion after 2 months of intensive treatment. Finding showed that, patients with diabetes mellitus were four times more likely to be nonconverted compared with those without diabetes mellitus (OR = 4.00, 95% CI 1.61–9.96). After adjusting for confounders and interactions, adherence to treatment, history of tuberculosis treatment, and body mass index were no longer significantly associated with the 2nd month sputum smear conversion and were excluded from the final prediction model ($p$ > .05) (Table 4).

## Discussion

In this study, the mean age for both patients in the case group and control group was found to be around the middle adult

**Table 1 – Association between sociodemographic characteristics of cases and controls and sputum smear conversion after intensive treatment.**

| Characteristics | Cases ($n = 75$) | | Control ($n = 75$) | | $X^2$[a] | $p$ | Crude OR[b] (95% CI) |
|---|---|---|---|---|---|---|---|
| | $n$ | % | $n$ | % | | | |
| *Sex* | | | | | | | |
| Women | 16 | 21.3 | 25 | 33.0 | 2.72 | .099 | Reference |
| Men | 59 | 78.7 | 50 | 66.7 | | | 1.84 (0.89–3.83) |
| *Marital status* | | | | | | | |
| Single | 21 | 28.0 | 31 | 41.3 | 2.94 | .086 | Reference |
| Married | 54 | 72.0 | 44 | 58.7 | | | 1.81 (0.92–3.58) |
| *Occupation* | | | | | | | |
| Laborer | 33 | 44.0 | 38 | 50.7 | 0.74 | .690 | Reference |
| White-collared | 16 | 21.3 | 13 | 17.3 | | | 1.42 (0.59–3.38) |
| Unemployed | 26 | 34.7 | 24 | 32.0 | | | 1.25 (0.60–2.58) |
| *Ethnicity* | | | | | | | |
| Malay | 40 | 53.3 | 42 | 56.0 | 6.32 | .097 | Reference |
| Chinese | 11 | 14.7 | 20 | 26.7 | | | 0.58 (0.25–1.36) |
| Indian | 14 | 18.7 | 9 | 12.0 | | | 1.63 (0.64–4.19) |
| Other | 10 | 13.3 | 4 | 5.3 | | | 2.63 (0.76–9.05) |
| *Education level* | | | | | | | |
| Primary | 23 | 30.7 | 24 | 32.0 | 2.14 | .343 | 1.59 (0.59–4.36) |
| Secondary | 43 | 57.3 | 36 | 48.0 | | | 1.99 (0.78–5.08) |
| Tertiary | 9 | 12.0 | 15 | 20.0 | | | Refere nce |
| *Adherence to treatment* | | | | | | | |
| Yes | 54 | 72.0 | 66 | 88.0 | 6.00 | .024 | Reference |
| No | 21 | 28.0 | 9 | 12.0 | | | 2.85 (1.21–6.74) |
| *History of TB treatment* | | | | | | | |
| Yes | 21 | 28.0 | 10 | 13.3 | 4.92 | .043 | 2.53 (1.09–5.83) |
| No | 54 | 72.0 | 65 | 86.7 | | | Reference |

*Note:* CI = confidence interval; OR = odds ratio; TB = tuberculosis.
[a] Pearson Chi-Square test was performed.
[b] Univariate binary logistic regression was performed.

**Table 2 – Association between smoking and sputum smear conversion after intensive treatment among cases and control (N = 75).**

| | Cases ($n = 75$) | | Controls ($n = 75$) | | $X^2$[a] | $p$ | Crude OR (95% CI)[b] |
|---|---|---|---|---|---|---|---|
| | $n$ | % | $n$ | % | | | |
| *Smoking* | | | | | | | |
| Current smokers | 40 | 53.3 | 35 | 46.7 | 1.42 | .493 | 1.46 (0.73–2.92) |
| Former smokers | 10 | 13.3 | 8 | 10.7 | | | 1.60 (0.55–4.65) |
| Nonsmokers | 25 | 33.3 | 32 | 42.7 | | | Reference |
| *No. of cigarette/d ($n = 75$)* | | | | | | | |
| ⩽ 10 | 13 | 32.5 | 16 | 45.7 | 1.43 | .488 | Reference |
| 11–20 | 18 | 45.0 | 12 | 34.3 | | | 1.85 (0.66–5.19) |
| >20 | 9 | 22.5 | 7 | 20.0 | | | 1.58 (0.46–5.41) |
| *Pack y ($n = 75$)* | | | | | | | |
| ⩽ 10 | 13 | 32.5 | 12 | 34.3 | .03 | .985 | Reference |
| 11–20 | 8 | 20.0 | 7 | 20.0 | | | 1.06 (0.29–3.80) |
| >20 | 19 | 47.5 | 16 | 45.7 | | | 1.09 (0.39–3.07) |

*Note:* CI = confidence interval; OR = odds ratio; y = year.
[a] Pearson Chi-Square was performed.
[b] Univariate binary logistic regression was performed.

age, i.e., 40–45 years. Patients enrolled in this study were found to be older compared with other prior studies conducted in Saudi Arabia. Singla et al. [6], in their study to predict persistent of sputum smear-positivity among Saudi Arabian pulmonary tuberculosis patients 2 months after treatment, showed that the mean age of their patients was

**Table 3 – Association between diabetes mellitus, body mass index, and sputum smear conversion after 2 months of treatment among cases and controls (*N* = 150).**

| | Cases (*n* = 75) | | Controls (*n* = 75) | | $X^2$ | *p* | Crude OR[c] (95% CI) |
|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | | | |
| *Diabetes status*[a] | | | | | | | |
| Diabetic | 31 | 41.3 | 6 | 21.3 | 6.97 | .013 | 2.59 (1.27–5.33) |
| Nondiabetic | 44 | 58.7 | 59 | 78.7 | | | Reference |
| *Body mass index*[b] | | | | | | | |
| Underweight | 33 | 44.0 | 21 | 28.0 | 9.24 | .025 | 1.67 (0.80–3.49) |
| Ideal weight | 31 | 41.3 | 33 | 44.0 | | | Reference |
| Overweight | 6 | 8.0 | 18 | 24.0 | | | 0.36 (0.13–1.01) |
| Obese | 55 | 6.7 | 33 | 4.0 | | | 1.77 (0.39–8.06) |

*Note:* CI = confidence interval; OR = odds ratio.
[a] Pearson Chi-Square test was performed.
[b] Fisher's exact test was performed.
[c] Univariate binary logistic regression was perfomed.

**Table 4 – Multiple binary logistic regression model of factors influencing sputum smear conversion after 2 months of treatment (*N* = 150).**

| Factors | B | S.E | Wald | *p* | Adjusted OR (95% CI) |
|---|---|---|---|---|---|
| Diabetes mellitus | 1.39 | 0.46 | 8.94 | .003* | 4.01 (1.61–9.96) |
| Body mass index | | | 7.51 | .057 | |
| Underweight | 0.60 | 0.42 | 2.05 | .152 | 1.83 (0.80–4.18) |
| Overweight | −1.10 | 0.58 | 3.64 | .056 | 0.33 (0.10–1.03) |
| Obese | −0.19 | 0.85 | 0.05 | .820 | 0.83 (0.16–4.33) |

*Note:* CI = confidence interval; OR = odds ratio; S.E = standard error.
* $p < .05$.

37.9 ± 33.3 years. Patients with persistent positivity were found to be slightly older compared with patients in the control group [6]. This pattern is paralleled with another study which showed that old age and those older than 60 years were at a higher risk of sputum smear delay [7].

No significant association was seen between sex and sputum smear conversion at the end of intensive antituberculosis treatment. This finding was coherent with the study by Pajankar et al. [8] in 2008. However, many other studies have suggested an association between sex and outcome of sputum smear conversion after the intensive phase. As an example, Banu Rekha et al. [9] and Singla et al. [10], in their study among pulmonary tuberculosis patients showed that being male was associated with a lack of sputum smear conversion at the end of the intensive phase. Most commonly, the explanations given by other researchers to explain the reason why men were more likely to experience a delay in sputum smear conversion after the intensive treatment compared with women were related to smoking and alcohol consumption.

With statistical analysis, this recent study showed no significant association between other sociodemographic determinants such as marital status, level of education, occupation, and monthly income with the sputum smear conversion after intensive phase. This finding was in agreement with another comparative cross-sectional study done by Kassam et al. [11], which showed that no significant difference in cure rates were seen between patients with high and low incomes. However, some of these determinants were found to be more frequent among those who were not sputum smear converted compared with the controls. For instance, we observed that patients engaged in a white collared occupation were more likely to be nonconverted compared with those who were laborers. This recent finding contradicts an earlier study done 9 years ago in Uganda. That study showed that subsistence farmers were 4.63-fold more likely to have retreatment tuberculosis compared with unemployed patients [12].

This recent study showed no statistically significant association between smoking and sputum smear conversion at the end of the intensive treatment. This study suggests that smokers and nonsmokers converted with almost the same rate to a negative sputum status. The finding was supported by the two other prior studies [13,14]. However, a study by Metanat et al. [15] suggested a different finding, saying that there was a significant delay in sputum smear conversion time between smokers and nonsmokers, which is contrary to the present study.

Next, the results of this study showed that patients with diabetes mellitus were three times more likely to have sputum smear nonconversion at the end of intensive treatment compared with those without this metabolic deficiency. This positive association was increased up to four times after controlling for other risk factors in the multivariable analysis. Findings of this study are in-line with four other different studies conducted among pulmonary tuberculosis patients in Indonesia, China, Saudi Arabia, and India. All of these

studies agree that diabetes has a significant impact on the patients' sputum smear conversion after 2 months of tuberculosis treatment [16–19]. However, the finding of this recent study is in contrary with another case control study which showed no significant effect of diabetes on the sputum smear positivity after 2 months of treatment [20]. In explaining this, we have to look into the pathophysiology of diabetes and its relation to general body function. Bashar et al. [21] provides us with the answer by suggesting that diabetic patients have some degree of impaired gastrointestinal drug absorption, even in the absence of clinical gastroparesis. Not only that, the hyperglycaemic state may additionally interfere with achieving adequate tissue levels of the medications, or interfere with alveolar macrophage or CD4+ cell function [21].

At the end of the study, we found that pulmonary tuberculosis patients who were underweight or obese were two times more likely to be nonconverted compared with those with an ideal body mass index. This finding was in agreement with another international study conducted by Khan et al. [22]. These group of researchers provided a more clear direction regarding body mass index and tuberculosis outcome by showing that those pulmonary tuberculosis patients who had >5% weight gain during the intensive phase of therapy had a lower relapse risk compared with those who gained ⩽5% [22].

The possible explanation would be that tuberculosis has a well-known negative effect on patients nutritional status by affecting dietary intake due to loss of appetite, poor absorption of nutrients from the intestine, and increase uptake of nutrients by specific target tissue due to the increase of body metabolism. Moreover, severe malnutrition has a profound effect on cell-mediated immunity [23].

Our study showed that patients with poor adherence to antituberculosis treatment during the intensive treatment were three times more likely to experience sputum nonconversion compared with those who religiously taking their drugs. This finding was in parallel to the result obtained by Thomas et al. [24], which suggested that patients who took treatment irregularly were 2.6 times more likely to have relapse than those who were adherent [24]. Similarly, in other setting, Burman et al. [25] showed that noncompliant patients had 9.9 times more risk of poor outcomes from the initial course of therapy more often than compliant patients.

Another treatment related factor observed in this recent study was the association between previous history of tuberculosis treatment and sputum smear conversion after the intensive treatment. In this study, significant association between the two factors was observed. Patients with previous history of tuberculosis treatment were found to be three times more likely to have sputum smear nonconversion compared with those without previous exposure to tuberculosis. This finding was supported by Singla et al. [6] and Fortun et al. [26] who projected that factors significantly related to a delay in smear conversion to negative were previous administration of antituberculosis drugs (therapy or prophylaxis).

This is possibly due to a previous infection which may induce the presence of initial cavitations and increase the extent of residual lesions of the lung. Cavitations have been shown to be significantly associated with prolonged time-to-smear conversion among pulmonary tuberculosis treatment [7]. However, Telzak et al. [27] disagrees with this finding by showing that no prior history of tuberculosis was the factor independently associated with an increased number of days for both smear and culture conversion.

Despite all the encouraging findings found in this recent study, there are several limitations that were faced by the researcher during the study process, such as a small number of samples, effect of study location, and the efficacy of documentation in the patients' registry. These limitations should be considered wisely before an interpretation of the study findings could be made.

In conclusion, sputum smear conversion after the intensive antituberculosis treatment was found to be significantly related to diabetes in this study. Therefore, it is hoped that the results of this study will be utilized to improve the planning and implementation of tuberculosis treatment by overcoming the problems regarding delay in sputum smear conversion. Patients should be consulted on healthy eating and the importance of diabetic control. Future research in this area should proceed with a cohort study focusing on a bigger diversity of other factors such as radiological, microbiological, and genetic contributions.

## Conflicts of interest

We have no conflict of interest to declare.

## Acknowledgments

We would like to thank the Director of Institute of Respiratory Medicine, Kuala Lumpur and all the tuberculosis clinic staffs for their permission, great cooperation, and support to conduct this study. A very sincere appreciation also goes to all the pulmonary tuberculosis patients who participated in this study. We would also like to thank the ethic committee of Universiti Kebangsaan Malaysia for the research funding.

## REFERENCES

[1] World Health Organization, Global Tuberculosis Control 2009, Epidemiology Strategy Financing, WHO Press, Switzerland, 2009.
[2] T.H. Holtz, M. Sternberg, S. Kammerer, et al, Time to sputum culture conversion in multidrug-resistant tuberculosis: predictors and relationship to treatment outcome, Ann. Intern. Med. 144 (2006) 650–659.
[3] S.M. Dembele, H.Z. Ouedraogo, A. Combary, et al, Conversion rate at two-month follow-up of smear-positive patients in Burkina Faso, Int. J. Tuberc. Lung Dis. 11 (2007) 1339–1344. Available from: <http://www.ingentaconnect.com/content/iuatld/ijtld/2007/00000011/00000012/art00013?token=00531b3625585a97f3d275c277b42573a67547d6634252c6e7645592f653b2a2d3a7c4e7247700b998c>.
[4] Ministry of Health Malaysia, Health Facts, 2008. Available from: <http://vlib.moh.gov.my/cms/documentstorage/com.tms.cms.document.Document_4adad34b-c0a81049-13ce5ad0-53e20a3e/2008.pdf>.
[5] Ministry of Health Malaysia, Clinical Practice Guidelines on Management of Obesity, 2004.

[6] R. Singla, M.M. Osman, N. Khan, Factors predicting persistent sputum smear positivity among pulmonary tuberculosis patients 2 months after treatment, Int. J. Tuberc. Lung Dis. 7 (2003) 58–64.
[7] M. Guler, E. Unsal, B. Dursun, et al, Factors influencing sputum smear and culture conversion time among patients with new case pulmonary tuberculosis, Int. J. Clin. Pract. 61 (2007) 231–235.
[8] S. Pajankar, R. Khandekar, M.A.A. Amri, et al, Factors influencing sputum smear conversion at one and two months of tuberculosis treatment, Oman Med. J. 23 (2008) 263–268.
[9] V.V. Banu Rekha, R. Balasubramanian, S. Swaminathan, Sputum conversion at the end of intensive phase of Category-1 regimen in the treatment of pulmonary tuberculosis patients with diabetes mellitus or HIV infection: an analysis of risk factors, Indian J. Med. Res. 126 (2007) 452–458.
[10] R. Singla, N. Khan, N. Al-Sharif, et al, Influence of diabetes on manifestations and treatment outcome of pulmonary TB patients, Int. J. Tuberc. Lung Dis. 10 (2006) 74–79.
[11] N. Kassam, A. Fanning, J.R. Cruz, et al, Outcome of tuberculosis treatment: a comparison between Alberta and Nicaragua, Can. J. Infect. Dis. 11 (2000) 85–88.
[12] N. Anyama, S. Sseguya, A. Okwera, et al, The challenge of re-treatment pulmonary tuberculosis at two teaching and referral hospitals in Uganda, Afr. Health Sci. 7 (2007) 136–142.
[13] A.T. Abal, B. Jayakrishnan, S. Parwer, et al, Effect of cigarette smoking on sputum smear conversion in adults with active pulmonary tuberculosis, Respir. Med. 99 (2005) 415–420.
[14] C.C. Leung, T.H. Lam, W.M. Chan, et al, Diabetic control and risk of tuberculosis: a cohort study, Am. J. Epidemiol. 167 (2003) 1486–1494.
[15] M. Metanat, B.S. Mood, M. Parsi, et al, Effect of cigarette smoking on sputum smear conversion time among adult new pulmonary tuberculosis patients: a study from Iran Southeast, Iran. J. Clin. Infect. Dis. 5 (2010) 14–17.
[16] B. Alisjahbana, E. Sahiratmadja, E.J. Nelwan, et al, The effect of type 2 diabetes mellitus on the presentation and treatment response of pulmonary tuberculosis, Clin. Infect. Dis. 45 (2007) 428–435.
[17] F. Mi, S. Tan, L. Liang, et al, Diabetes mellitus and tuberculosis: pattern of tuberculosis, two-month smear conversion and treatment outcomes in Guangzhou, China, Trop. Med. Int. Health 18 (2013) 1379–1385.
[18] A.A. Viswanathan, N.C. Gawde, Effect of type II diabetes mellitus on treatment outcomes of tuberculosis, Lung India 31 (2014) 244–248.
[19] L.A. Chaudhry, E.B. Essa, S. Al-Solaiman, et al, Prevalence of diabetes type-2 & pulmonary tuberculosis among Filipino and treatment outcomes: a surveillance study in the Eastern Saudi Arabia, Int. J. Mycobacteriol. 1 (2012) 106–109.
[20] R. Singla, S.K. Bharty, U.A. Gupta, et al, Sputum smear positivity at two months in previously untreated pulmonary tuberculosis patients, Int. J. Mycobacteriol. 2 (2013) 199–205.
[21] M. Bashar, P. Alcabes, W.N. Rom, et al, Increased incidence of multidrug-resistant tuberculosis in diabetic patients on the Belleue Chest service, 1987–1997, Chest 120 (2001) 1514–1519.
[22] A. Khan, T.R. Sterling, R. Reves, et al, Lack of weight gain and relapse risk in a large tuberculosis treatment trial, Am. J. Respir. Crit. Care Med. 174 (2006) 344–348.
[23] N. Kennedy, A. Ramsay, L. Uiso, et al, Nutritional status and weight gain in patients with pulmonary tuberculosis in Tanzania, Trans. R. Soc. Trop. Med. Hyg. 90 (1996) 162–166.
[24] A. Thomas, P.G. Gopi, V. Chandrasekaran, et al, Predictors of relapse among pulmonary tuberculosis patients treated in a DOTS programme in South India, Int. J. Tuberc. Lung Dis. 9 (2005) 556–561.
[25] W.J. Burman, D.L. Cohn, C.A. Rietmeijer, et al, Noncompliance with directly observe therapy for tuberculosis: epidemiology and effect on the outcome of treatment, Chest 111 (1997) 1168–1173.
[26] J. Fortun, P.M. Davila, A. Molina, et al, Sputum conversion among patients with pulmonary tuberculosis: are there implications for removal of respiratory isolation?, J Antimicrob. Chemother. 59 (2007) 794–798.
[27] E.E. Telzak, B.A. Fazal, C.L. Pollard, et al, Factors influencing time to sputum conversion among patients with smear positive pulmonary tuberculosis, Clin. Infect. Dis. 25 (1997) 666–670.