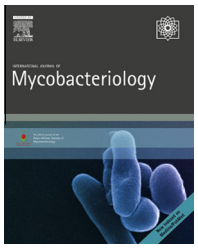
International Journal of Mycobacteriology 5 (2016) 51–58

HOSTED BY

Available at www.sciencedirect.com

ScienceDirect

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



Previous treatment, sputum-smear nonconversion, and suburban living: The risk factors of multidrug-resistant tuberculosis among Malaysians

Noorsuzana Mohd Shariff [a,b,*], *Shamsul Azhar Shah* [a], *Fadzilah Kamaludin* [c]

[a] *Community Health Department, Universiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur, Malaysia*
[b] *Advanced Medical and Dental Institute, Universiti Sains Malaysia, Pulau Pinang, Malaysia*
[c] *Office of Deputy Director General of Health Malaysia, Ministry of Health Malaysia, Putrajaya, Malaysia*

ARTICLE INFO

Article history:
Received 10 October 2015
Received in revised form
9 November 2015
Accepted 12 November 2015
Available online 28 November 2015

Keywords:
Multidrug resistant
Risk factors
Tuberculosis

ABSTRACT

The number of multidrug-resistant tuberculosis patients is increasing each year in many countries all around the globe. Malaysia has no exception in facing this burdensome health problem. We aimed to investigate the factors that contribute to the occurrence of multidrug-resistant tuberculosis among Malaysian tuberculosis patients. An unmatched case-control study was conducted among tuberculosis patients who received antituberculosis treatments from April 2013 until April 2014. Cases are those diagnosed as pulmonary tuberculosis patients clinically, radiologically, and/or bacteriologically, and who were confirmed to be resistant to both isoniazid and rifampicin through drug-sensitivity testing. On the other hand, pulmonary tuberculosis patients who were sensitive to all first-line antituberculosis drugs and were treated during the same time period served as controls. A total of 150 tuberculosis patients were studied, of which the susceptible cases were 120. Factors found to be significantly associated with the occurrence of multidrug-resistant tuberculosis are being Indian or Chinese (odds ratio 3.17, 95% confidence interval 1.04–9.68; and odds ratio 6.23, 95% confidence interval 2.24–17.35, respectively), unmarried (odds ratio 2.58, 95% confidence interval 1.09–6.09), living in suburban areas (odds ratio 2.58, 95% confidence interval 1.08–6.19), are noncompliant (odds ratio 4.50, 95% confidence interval 1.71–11.82), were treated previously (odds ratio 8.91, 95% confidence interval 3.66–21.67), and showed positive sputum smears at the 2nd (odds ratio 7.00, 95% confidence interval 2.46–19.89) and 6th months of treatment (odds ratio 17.96, 95% confidence interval 3.51–91.99). Living in suburban areas, positive sputum smears in the 2nd month of treatment, and was treated previously are factors that independently contribute to the occurrence of multidrug-resistant tuberculosis. Those with positive smears in the second month of treatment, have a history of previous treatment, and live in suburban areas are found to have a higher probability of becoming multidrug resistant. The results presented here may facilitate improvements in the screening and detection process of drug-resistant patients in Malaysia in the future.

* Corresponding author at: Department of Community Medicine, Universiti Kebangsaan Malaysia Medical Centre, Faculty of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaakob Latiff, 56000 Kuala Lumpur, Malaysia.
E-mail address: suzana_1910@yahoo.com (N. Mohd Shariff).
Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2015.11.001

Introduction

Tuberculosis (TB) is a disease that has long brought harm to many people in the world, and until now, the formula or recipe to eliminate the disease is still vague and has yet to be found [1]. Recently, the world does not only have to face higher numbers of new TB cases each year, but another challenge arises in the form of multidrug-resistant TB (MDR-TB). This new development can shake the efforts done in tackling and managing this disease. By definition, a TB patient is classified as MDR-TB if he or she shows resistance to two most potent anti-TB drugs, namely, isoniazid and rifampicin, with or without resistance to other first-line drugs [2]. According to a recent report, an estimated 3.6% of new TB cases and 20.2% of those previously treated patients are MDR-TB globally in year 2012 [2].

Even though Malaysia is classified as an intermediate TB-burden country and a low MDR-TB burden (0.3–1.3% of all culture-positive TB patients were detected MDR-TB) by the World Health Organization [3], yet we are surrounded by countries with higher burdens of TB and high prevalence of MDR-TB, for example, Myanmar and Indonesia. In year 2013, an estimated 22% and 13% of all TB patients in Myanmar and Indonesia were detected and notified to be MDR-TB, respectively [2]. The influxes of foreign workers from these countries, TB/human immunodeficiency virus (HIV) coepidemic, and poor treatment to some extent are believed to contribute to an increase in the incidence of TB and the emergence of drug-resistant cases in Malaysia. Consequently, TB has become the top leading cause of death among other communicable diseases in Malaysia for 8 consecutive years since 2006 until 2013 [4,5]. Even more alarming, since 2013, we are seeing confirmed cases of extensively drug-resistant TB being detected and started treatment in Malaysia [2]. This rare type of multidrug-resistant patients (who are not only resistant to isoniazid and rifampicin, but also to fluoroquinolones and at least one injectable second-line anti-TB drugs) brings more challenges in tackling TB in Malaysia. However, fortunately until now, no cases of totally drug-resistant TB were reported in Malaysia.

In response to these data, several studies had been carried out by previous researchers in some states in Malaysia to try to look into the epidemiology of the disease, reasons for patients defaulting treatment, evaluation of TB treatment outcomes, as well as the prevalence of drug-resistant-TB cases in Malaysia [6–8]. However, to the best of the authors' knowledge, far too little attention has been paid to the cause of patients' resistance to the two most potent anti-TB drugs in Malaysia. Therefore, this present study aimed to determine the factors that influence the occurrence of MDR-TB among Malaysian TB patients. This study is expected to assist treatment providers in Malaysia in designing the preventive approach and in the detection of drug-resistant cases, tailored to local circumstances. Previous international studies have demonstrated a significant association between several risk factors, such as history of previous TB treatment, HIV positive, diabetes, smoking, treatment noncompliant, and alcoholism, and MDR-TB [9–11].

Methods

Ethical considerations

This study has received ethical approval from the Malaysian Research & Ethics Committee, Ministry of Health Malaysia, and is registered under the National Medical Research Registry (NMRR-12-1218-12850). In addition, this study also received approval from the Secretariat of Medical Research & Innovation, Universiti Kebangsaan Malaysia Medical Centre. Clear explanations had been given to each participant at the beginning of the study, and simultaneously, an informed consent was obtained. Participants were recruited on a voluntary basis.

Study population and design

This recent study was carried out at the Institute of Respiratory Medicine located in Jalan Pahang, Kuala Lumpur, Malaysia. This government tertiary hospital was formerly known as the National Tuberculosis Centre. We conducted an unmatched case-control study among TB patients who received anti-TB treatments from April 2013 until April 2014 at this health institute. Cases were purposively selected among those who are clinically, radiologically, and/or bacteriologically diagnosed as pulmonary TB patients; aged 18 years old and above; have local citizenship; and were confirmed to be resistant to both isoniazid and rifampicin through drug-sensitivity testing. On the other hand, pulmonary TB patients who fulfilled the mentioned criteria and were treated during the same time period, but sensitive to all first-line anti-TB drugs were randomly selected as controls.

Data collection

Data were obtained from both the patients' medical records and a set of pretested self-administered questionnaires. The patients' medical records were reviewed to obtain information, such as age at diagnosis, gender, home address, type of TB, drug and sensitivity test results, diabetic status, HIV status, and sputum-smear status at three intervals (at diagnosis, 2nd month, and 6th month). On the other hand, the questionnaire was used to obtain information regarding their marital status, occupation, ethnicity, education level, history of imprisonment, exposure to other TB cases, adherence to treatment, smoking history, alcohol intake, history of drug abuse, and house characteristics. Household crowding was categorized according to the definition of person per bedroom. A household is classified as crowded if more than two persons stay in the same bedroom [12]. The classification of patients' area of living, either urban or suburban, was carried out by referring to the standardized definition by the Department of Statistics Malaysia based on the Population and Housing Census of 2010 [13]. The level of nicotine dependency was measured using the Malay version of the Fagerstrom test for nicotine dependence adapted from a previous study [14]. A *passive smoker* is defined as someone who is reported to be regularly aware of seeing and smelling, or