Geographical Factors in Diagnostic Delay among Multidrug Resistant Tuberculosis Patients

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Abstract

Background: Diagnostic delay is a factor that can increase the high burden of multi-drug resistant tuberculosis (MDR-TB). Xpert Mycobacterium tuberculosis/Rifampicin known as Xpert is a rapid diagnostic test to detect MDR-TB. Diagnostic delay defined the duration between a positive result of Acid Fast Bacilli (AFB) smear and positive result of MDR-TB by Xpert examination. This study aimed to compare the analysis of the geographical factors in the diagnostic delay of MDR-TB patients at Dr. Hasan Sadikin General Hospital as the top referral hospital in West Java Indonesia.

Methods: This study was conducted in the period July–December 2016 using cross sectional design. A total of 152 MDR-TB patient data were collected from medical records of MDR-TB patients registered in MDR-TB clinic at Dr. Hasan Sadikin General Hospital in the period 2015–2016. The socio-demographic characteristics were collected and analyzed descriptively The diagnostic delay among MDR-TB patients was analyzed by Mann Whitney test.

Results: Diagnostic delay of MDR-TB patients was 15 days in median, with a minimal and maximal delay of 2–140 days. There was a significant difference of diagnostic delay between patients from Bandung with a median of 9(2-135) days and patients from outside of Bandung with a median of 18(2-140) days, with $p<0.01$.

Conclusions: MDR-TB patients from outside Bandung have a longer diagnostic delay than patient from Bandung . A further expansion of using Xpert as a rapid diagnostic test for MDR-TB patient is needed.

Keywords: Diagnostic delay, multi-drug resistant tuberculosis, Xpert

Introduction

Indonesia is one of the high burden countries of tuberculosis cases in the world.[1] High burden of TB were added by the existence of multidrug resistant tuberculosis (MDR-TB) and the TB-HIV coinfection.[1,2] Multidrug Resistant Tuberculosis cases is still increasing. In 2015, there were 3507 MDR-TB suspect, 504 exposed and 377 cured.[3] Due to the increasing and development of MDR-TB effective diagnostic tools are needed to diagnose MDR-TB. Nucleic acid amplification testing (NAAT) is a diagnostic method for TB that enables specific and sensitive identification of mutation of Mycobacterium tuberculosis (MTB) gene that correlate with drug resistance.[1,4] Rapid test Xpert MTB/RIF also known as Xpert is one of the examples of rapid diagnostic tools that has been recommended by the World Health Organization (WHO) in 2010.[1,2,5]

The MDR-TB diagnostic in Indonesia is detected by a conventional method and rapid test. Early examinations have used acid fast bacilli (AFB), then used a conventional method such as culture with Lowenstein Jensen (LJ) solid media and Mycobacterium Growth Indicator Tube (MGIT) liquid media and examination with Drug Susceptibility Test (DST) however, this procedure needs more time than a rapid test such as Xpert or Line Probe Assay (a method to examine a sensitivity of rifampicin and isoniazid).[2] Based on WHO guidelines about the implementation of Xpert shows that Xpert has a high accuracy that can diagnose 99% with BTA positive patient and 80% with BTA negative patient, Xpert also can detect a complex MTB DNA and rpoB genes mutation directly from sputum sample

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less than two hours, therefore this method is recommend as a rapid test to diagnose drug resistant tuberculosis by WHO.[2,6] A study about the implementation of Xpert in three Indonesian districts, showed that the use of rapid test Xpert quickly detects drug resistant tuberculosis and can lower the diagnostic delay from a mean of 75 days becomes 1 day with $p<0.001$.[5]

Furthermore, factors associated with diagnostic delay are the centralized management of health care and poor health care seeking.[7] A study from China showed that more than half of the number of patients have a diagnostic delay of 30 days, the influencing factors are poor knowledge about MDR-TB, low socio-economic conditions, also lack of access to the health care facility and close contact with MDR-TB patients.[8,9] This study aimed to analyzed the geographical factors in the diagnostic delay of MDR-TB patients at Dr. Hasan Sadikin General Hospital as the top referral hospital in West Java Indonesia.

Methods

This study was a cross sectional study conducted in the period July–December 2016 using medical records of MDR-TB patients registered in the MDR-TB clinic at Dr. Hasan Sadikin General Hospital Bandung in the period 2015–2016. Data were collected after permission was approved by the Health Research Ethics Committee Faculty of Medicine, Universitas Padjadjaran with ethical number 508/UN6.C1.3.2/KPEK/PN/2016.

The inclusion criteria were complete medical records of the MDR-TB patients aged ≥ 18 years old. The exclusion criteria were the incomplete or missing medical records of patients. The sample collection used total sampling. A total of 152 medical records were included in the final analysis (Figure 1).

The variables in this study were the socio-demographic characteristics of the patient (age, gender, residence, occupation, and income) and diagnostic delay. The patient's residence was divided into 2 locations, namely Bandung City (as the capital city of West Java and the location of Dr. Hasan Sadikin General hospital), and Outside Bandung City. Diagnostic delay in this study is defined as the duration between positive acid fast bacilli (AFB) result and positive rifampicin resistant in Xpert examination.

Furthermore, data analysis was performed using a computer program. The categorical data consisting of gender, residence, and occupation, were analyzed by descriptive statistics and presented by number and percentage. The numerical data consisted of age and diagnostic delay. Age was presented by the mean and

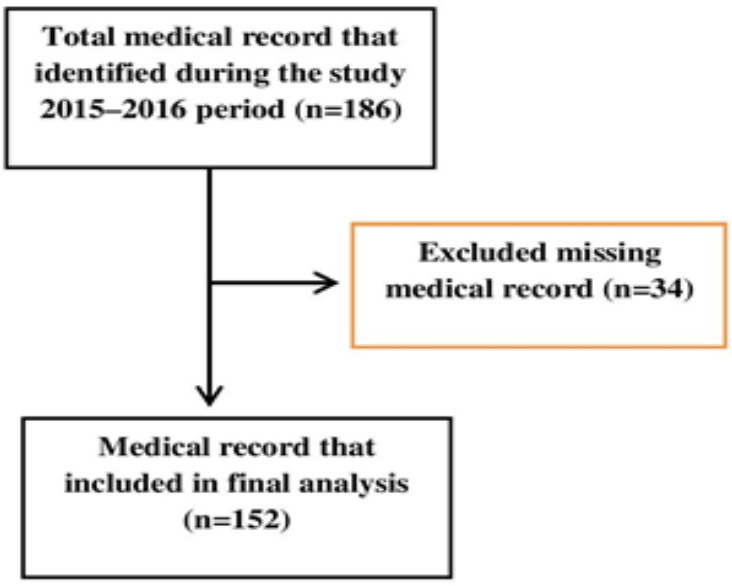

Figure 1 Flow Diagram of Subject Inclusion in the Study

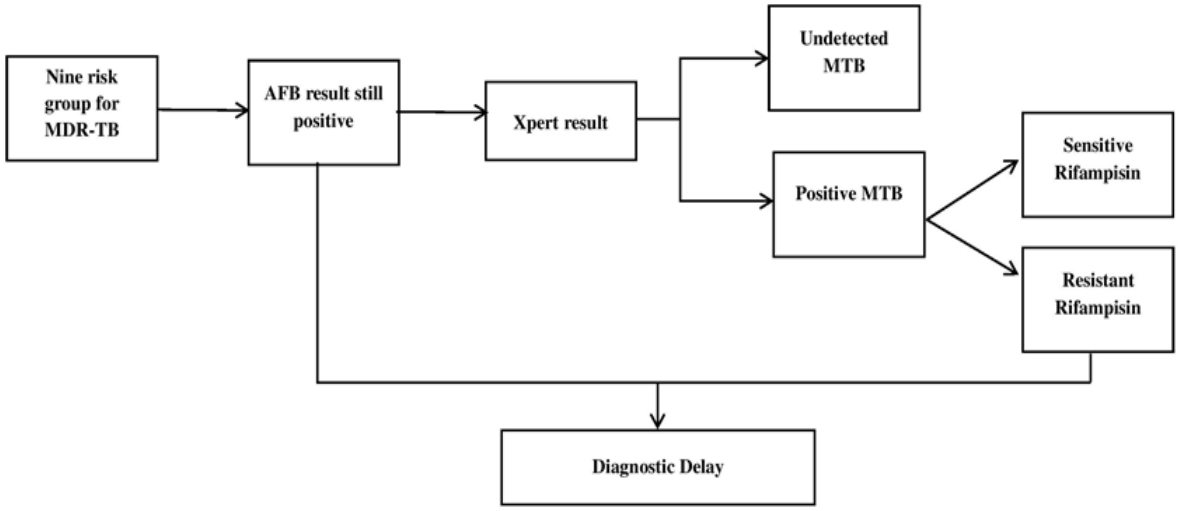

Figure 2 Diagnostic Delay

standard deviation. Diagnostic delay was presented by median and minimal-maximal. The analyzes began from determining the data normality with Kolmogorov Smirnov test, and Mann Whitney test was used to compare the diagnostic delay of MDR-TB patients who came from Bandung and Outside Bandung city with 95% Confidence Interval (CI). For the statistical test, $p<0.05$ was regarded as statistically significant.

Results

Out of 152 patients, most of the participants were male , and the majority of patients's

Table 1 Socio-demographic Characteristic of MDR-TB Patient

Characteristic	n(%)
Gender	
Male	90(59.2)
Female	62(40.8)
Age (mean, standard deviation)	(39.4; 12.75)
Residentce	
Bandung city	32(21.1)
Outside Bandung city	120(78.9)
Occupation	
Unemployed	5(3.3)
House wife	29(19.1)
Employee	12(7.9)
Laborer	14(9.2)
Student	8(5.3)
Entrepreneur	20(13.2)
Government Servant	5(3.3)
Unknown	59(38.8)

Table 2 Duration of Diagnostic Delay

Duration of diagnostic delay	median(min-max)	p-value*
Total	15 (2-140)	0.001
Bandung city	9 (2-135)	
Outside Bandung city	18 (2-140)	

Note: *Mann Whitney test

residence were in Bandung city (Table 1).

This study showed that there was a statistical significance of diagnostic delay between patients from Bandung with a median delay of 9 days and outside Bandung city with a median delay of 18 days with p<0.01 with the total median diagnostic delay of 18 days with minimal and maximal range of 2 to 140 days. While the diagnostic delay of patients from outside Bandung was longer than from Bandung city (Table 2).

Discussion

In this study, the majority of study participants were male respondents. This result is similar with a study from Zhang et al.[10] in China, which stated that male participants have higher proportion of risk than female participants. This study also supported the study conducted by Mekonnen et al.[11], most of the study participants are male (64.5%). This finding is due to the environmental exposure by drug resistant tuberculosis strain.[10] The study from Elmi et al.[12] showed that male has a higher risk to MDR-TB due to alcohol abuse, drug abuse dependency by intravenous injection, or status of imprisonment that male often do than female. In contrary, a study conducted by Nair SA et al.[13] showed, male and female have the same risk for drug resistant tuberculosis. In this study, age of the majority was 39.4 years old, this finding shows the same results as the study in India, however is different with the study by Ullah et al.[14] in Pakistan, which reveals that 10-25 year-olds are at risk to developed MDR-TB due to poor compliance for people in that age group are busy in school or at work. Poor treatment of compliance has a bad influence to the outcome because it will increase the transmission of drug resistant bacterial strain.[15]

Furthermore, in occupation, housewife has a high proportion of risk. This might be due to close contacts among family members who had MDR-TB, because the transmission of tuberculosis could occur by person to person through infectious droplets. This was also influenced by the infectious degree and environment conditions. This finding was similar with the study conducted by Mulu et al.[9] which stated that the second majority of occupation is housewife (24.2%) after farmer (25.5%).

Moreover, the total diagnostic delay in this study showed that patients with drug resistant tuberculosis have a median diagnostic delay of 15 days with the minimal and maximal range of 2 to 140 days. The median diagnostic delay in this study was lower than the study conducted by Li et al.[8] in China, where the diagnostic delay is defined as the duration between onset of symptom until true diagnosis, which reaches 30 days of delay. In another study by Zhang et al.[10] the diagnostic delay is defined as the results of sputum smear and drug susceptibility test (DST), that reach 102 days of delay. The diagnostic delay occurs due to the poor capacity of the laboratory to detect drug resistance.[10]

In Indonesia, laboratories with a diagnostic facility to detect drug resistant tuberculosis still increase. Until June 2015, there were 41 Xpert, certified culture laboratories and certified DST laboratories spread among the provinces, however, although they were spread in all provinces, the diagnostic delay still occurs.[3] In this study, the diagnostic delay of patients from outside Bandung reached 18 days in the median, this number was longer than the diagnostic delay of patients from Bandung which reached 9 days in the median with p<0.01. This finding was similar with the meta-analysis study from Li et al.[8] in China that patients in rural areas have a higher susceptibility to develop MDR-TB than patients in the city. This is due to the poor access to health facilities, lack of transportation to reach health facilities, and lack of laboratories with tools to diagnose MDR-TB.[7,8]

The limitation of this study was, this study did not measure the diagnostic delay received from the laboratory and the patient's delay as those factors could influence the total diagnostic delay.

In conclusion, this study finds that the diagnostic delay of patients from outside

Bandung is longer than of patients from Bandung city. It needs every endeavor to increase an early diagnostic in suspected drug resistant tuberculosis patients in the primary health care, hospital or other health care facility, and one of them is through extension of using Xpert in Indonesia as rapid diagnostic tools for MDR-TB.

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