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Associated Factors for Positive CXR Among TB High Risk Group Screening in Kedah

Abstract **—**Screening for Tuberculosis (TB) using Chest X-Rays (CXR) among high-risk individuals is essential to help reach the End TB Strategy goal in reduction of 90% in TB incidence by 2035. Even though Ministry of Health Malaysia has made screening compulsory, the number of cases detected is not encouraging. Therefore, it is essential to identify factors contributing to positive screening that would improve case detection. High-risk groups are individuals that are compulsory to be screened using chest x-ray, regardless of presence or absence of TB symptoms. A cross sectional study was done in 2016 involving individuals belonging to TB high-risk groups who underwent screening in Kedah, Malaysia. Data was obtained from the TB information system (TBIS) 104 A, an information system used for TB screening monitoring and chest x-ray report of the selected individuals. It involved 1417 individuals who were randomly selected from various health facilities in six districts of Kedah. Among all 1417 study samples, 1036 (73.1%) individuals were asymptomatic. Among the asymptomatic individuals, only 91 (8.8%) had positive CXR findings. Smokers were found to have almost 3 times the odds of having positive CXR findings compared to non-smokers [Adjusted OR (95% CI): 2.71 (1.03, 7.15), p-value<0.05] when gender and age are controlled. The elderly age group had almost three times the odds of having positive CXR findings compared to the younger age group [adjusted OR (95% CI): 2.85 (1.83, 4.43), p-value <0.05]. Males had almost twice the odds of having positive chest x-ray compared to females [adjusted OR (95%CI): 1.7 (1.08, 2.09), p-value <0.05]. As a conclusion, smokers were important group of individuals that must be prioritised during high risk group TB screening, especially among males and elderly smokers.

Keywords **—Tuberculosis, screening, chest x-ray, high risk group, smoker**

1 INTRODUCTION

Tuberculosis (TB) remains a major health threat worldwide, with an estimated 10.4 million incidence of new TB cases in 2015 [1]. It has contributed to the top 10 causes of death worldwide in 2015 and was responsible for more deaths than HIV and Malaria [1]. Malaysia is a country with Intermediate burden of TB due to the incidence less than 100/100,000 population. The latest notification rate for Tuberculosis (all forms) in Malaysia was 79.44/100,000 population in 2015 [2], while in Kedah, it was lower at 61.73/100,000 [3]. Despite measures done to detect cases, there is still a slow increase in the notification rate for the past 10 years in Malaysia and Kedah. This is worrisome as these individuals left untreated in the society and have potential to spread the infection. The control of TB required an exponential increase of case detection [4]. However, it did not happen as such. For and individual to show symptoms of TB, it takes a very long time, up to 15 years from the day he or she is infected [5] . By the time they seek treatment, they may have already spread the bacterial via coughing. Thus, detecting them during the asymptomatic phase is crucial [6]. Strategies must be strengthened to increase case detection. By focusing TB screening and detection among high-risk individuals and providing prompt treatment, TB spread can be reduced [7]. High-risk individuals are commonly among the marginalised people who have difficult healthcare access, such as the elderlies, immigrants, drug abusers, and prisoners. People with chronic airway diseases, exposed to occupational hazard predisposing to TB infection such as healthcare worker and miners are also at risk [8].

There was a huge gap between estimated TB incidences and case detection by World Health Organisation (WHO). Globally, there were gap of 2.4 million of undetected TB, and similar

situation also occur in Malaysia, where there were estimated of 20/100,000 population had TB but not diagnosed [9]. Notification rate for TB (all forms) in Malaysia for the year 2015 was 79.44/100,000 population while WHO estimated 104/100,000 population in 2014 [3]. This indicates that Malaysia is still not aggressive enough in detecting new cases. Sputum smear microscopy is the main method used in case detection. However, this method it is unreliable among asymptomatic individuals due to low bacterial load, making them undetectable [10]. Therefore, Chest X-Ray (CXR) has been selected by Ministry of Health (MOH) Malaysia as the screening tool for high-risk population [11]. This study aimed to identify which high-risk group and what are the major factors associated with positive CXR finding.

1.1 Materials and Methods

This was a cross sectional study using the TB information system (TBIS) 104 A, a screening registry for high risk groups for TB and the chest x-ray report from health facilities in Kedah. It was approved by both the Human Research Ethics Committees (HREC) (USM/JEPeM/16120597) and the Medical Research & Ethics Committee (MREC), Ministry of Health Malaysia (NMRR-16-2704-33659 [IIR]). Duration of the study was from December 2016 to March 2017 and was conducted in TB Unit, Kedah State Health Department, Radiology unit Hospital Sultanah Bahiyah Alor Setar, along with other government hospitals and health clinics selected.

The reference population were high-risk group for TB population from all districts in Kedah and the source population were all people who were screened using CXR for TB. Inclusion criteria include individuals screened by CXR, individuals with complete information, and CXR reporting done by radiologist. Screening done by Mantoux test or sputum test without CXR were excluded.

The sampling method used was stratified multi-stage random sampling [12]. Out of the 11 districts in Kedah, with total of 9 Hospitals and 58 Health clinic, six districts were randomly selected, stratified by hospitals and health clinics. The district chosen were Kubang Pasu, Kota Setar, Kuala Muda, Kulim, Pendang and Langkawi. Three hospitals and 11 health clinics were randomly selected.

Within the selected facilities, the samples were chosen randomly and proportionately. An online proforma was designed to assist in the data collection using Microsoft Forms. “Positive CXR” defined in this study were any CXR findings with at least one of the features of either active pulmonary TB (PTB) or old pulmonary TB according to the template of X-Ray reporting for TB screening by Salwati [13]. Features suggestive of active PTB include; upper lobe consolidation/cavities, reticulonodular opacities, milliary nodules, pleural effusion, nodules (tuberculoma) and hilar / mediastinal nodes. Features suggestive of old PTB were; calcified nodules, pleural thickening/calcification, fibrosis/traction bronchiectasis, bullae and tapped lung/chronic collapse.

The factors studied were symptoms, age, sex, nationality, ethnicity, and the risk groups which consist of patients with End Stage Renal Failure (ESRF), diabetes, smokers, institutionalised person, contacts with TB patient during first visit, and substance abusers.

1.2 Results

1.21 Socio demography

In this study, most of the people involved were middle age. The mean (SD) of age is 49.19 (18.2) years. Table 1 shows that based on age group classification, adult 15 to 64 years old were the highest portion, 1113 (78.5%) followed by elderly above 65 years old, 304 (21.5 %). Both children 15-18 and adult 18-64 years old were group together as ‘adult’ because the definition of adult TB is individuals more than 15 years old. There was no significant difference between sex, with male accounting for 726 people (51.2%) and female 881 (48.8%). Most of the population were Malay 1024 (72.3%) followed by Indian 139 (10.7%), Chinese 122 (9.3%), foreigners 119 (8.4%) and other races 13 (1.0%). Large proportion of the population were asymptomatic, 1036 (73.1%).

From the 1417 sample obtained, only 200 (14.1%) of the CXR had positive finding. This study will focus more on asymptomatic patient because this group are important in High Risk Group TB Screening.

Table 1: Sociodemographic Characteristics

Variable		n	(%)
Age group			
	<65	1113	78.5
	>65	304	21.5
Sex			
	Female	691	(48.8)
	Male	726	(51.2)
Ethnicity			
	Malay	1024	(78.8)
	Indian	139	(10.7)
	Chinese	122	(9.3)
	Foreigners	119	(8.4)
	Others	13	(1.0)
Symptoms			
	Asymptomatic	1036	(73.1)
	Symptomatic	361	(26.9)

1.22 Proportion of positive chest x-ray (CXR) among asymptomatic individuals

Among all 1036 individuals who were asymptomatic, only 91 (8.8%) had positive CXR. The proportion of positive CXR among asymptomatic people who were screened were divided into few groups, as showed in table 2 below.

Table 2: Positive chest x-ray (CXR) among asymptomatic high-risk group individuals

Variable	Positive chest x-ray n (%)	Total
Gender		
Male	56 (11.1%)	506
Female	35 (6.6%)	530
Age Group		
>65	51 (14.4%)	354
<65	40 (5.8%)	682
High Risk Group		
Elderly	51(14.4%)	354
HIV	1 (25.0%)	4
Smoker	6 (20.6%)	29
ESRF	3 (20.0%)	15
Substance Abuse	2 (13.3%)	15
Diabetes	57 (13.3 %)	538
Institutionalized	5 (7.2 %)	69
Close Contact	14 (4.4 %)	316
COAD	0 (0%)	6
Overall	91 (8.8%)	1036

Table 2 shows the results after removal of symptomatic patient and reanalysis. Based on age group, the elderly (>65) had highest proportion (14.4%) followed by adults (<65), 5.8 %. The male subjects accounted for bigger proportion than female, with 11.6 % compared to 6.6%. Among high-risk group individuals, HIV has highest proportion of positive CXR (25%) followed by smokers (20.7%), End Stage Renal Failure (ESRF) (20%), people with substance abuse (13.3%), diabetics (10.6%), institutionalised person (7.2%), and close contacts during the first visit (4.4%).

1.23 Associated factors for positive chest x-ray among asymptomatic high-risk group individuals

All factors studied were analysed using simple logistic regression. The variables that were significant in this univariable analysis were elderly, sex, smokers, diabetes and close contacts as shown in Table 3. Identification of independent association between the variables were analysed using multiple logistic regression. Variables with p-value of <0.25 were selected. Forward and backward LR was applied and for final enter method, variables that was included were age group, sex and smokers. There was no interaction found among the three variables and the model was fit.

In multivariable analysis, smokers were found to have almost 3 times odds of having positive CXR compared to non-smokers [Adjusted OR (95% CI): 2.71 (1.03, 7.15), p-value<0.05] when gender and age are controlled. The elderly age group had almost three times odds of having positive CXR compared to the younger age group [adjusted OR (95% CI): 2.85 (1.83, 4.43), p-value <0.05], and males had almost twice the odds of having positive chest x-ray compared to females [adjusted OR (95%CI) : 1.7 (1.08, 2.09), p-value <0.05] (Table 3).

2 DISCUSSION

One of the challenges for TB control in Malaysia is early case detection in the community. Like other intermediate burden countries, Malaysia's TB population are mainly concentrated among the high-risk groups, who are usually asymptomatic. However, the incidence of sputum test with negative Acid-Fast Bacilli (AFB) smear, but positive sputum culture for Mycobacterium tuberculosis is high [8]. Therefore, systematic CXR screening is a good tool apart from conventional sputum smear microscopy.

Table 3: Associated factor of positive CXR among asymptomatic high-risk individuals (N= 1036)

	Simple Logistic Regression			Multiple Logistic Regression		
	B	Crude OR (95% CI)	P-value	B	Adjusted OR (95%CI)	P-Value
Age Group						
<65		1.00			1.00	
>65	0.99	2.7 (1.74, 4.17)	<0.05	1.04	2.85 (1.83, 4.43)	<0.05
Sex						
Female		1.00			1.00	
Male	0.56	1.76 (1.13, 3.73)	<0.05	0.53	1.70 (1.08, 2.09)	<0.05
Nationality						
Malaysian		1.00				
Non-Malaysian	-1.36	0.87 (0.34, 2.23)	0.77			
HIV						
No		1.00				
Yes	1.25	3.48 (0.35,33.8)	0.28			
Smoker						
No		1.00			1.00	
Yes	1.04	2.83 (1.12,7.14)	<0.05	1.00	2.71 (1.03, 7.15)	<0.05
ESRF						
No		1.00				
Yes	0.97	2.65 (0.73,9.57)	0.13			
Substance Abuse						
No		1.00				
Yes	0.47	1.61 (0.35,7.25)	0.38			
Diabetes						
No		1.00				
Yes	0.48	1.61 (1.03,2.52)	<0.05			
Institutionalised						
No		1.00				
Yes	-0.22	0.80 (1.31,2.04)	0.64			
Close Contact						
No		1.00				
Yes	-0.94	0.38 (0.21,0.69)	<0.05			

Hosmer and Lameshow goodness of fit test not significant; p-value of 0.246; Classification table showed 86% correctly classified; Receiver Operating Characteristics (ROC) curve was 0.733

Since the implementation of systematic screening using CXR among the high-risk group in Malaysia's government hospitals and health clinics in 2014, it has become an added value for TB screening, on top of the regular symptomatic screening implemented earlier on. However, the yield of positive CXR finding was low [14]. CXR is also costly and unavailable in some clinics in rural areas. These factors have reduced the justification to continue this program and demotivates healthcare personnel in fully implementing it. Majority of individuals screened were asymptomatic, therefore, by concentrating on the factors associated with positive CXR findings among the asymptomatic individuals, prioritization can be done, and resources can be allocated adequately, leading to more case detection. Improvement in the x-ray facility is also needed in order to improve case detection through good quality radiograph. Digital x-ray machine produces more superior image quality than conventional x-ray and the digital image dan be adjusted. Transferring the image from radiographer to radiologist is also easy because it does not need x-ray film anymore. With the good image quality, better judgement can be made by the radiologist in interpreting the radiograph. Thus, upgrading to digital x-ray machine is necessary. Continuous training is also needed for the radiologist and medical officers in interpreting CXR.

In this study, diabetes was found to be the highest risk group screened, because they were immunocompromised and were prioritized by the healthcare personnel, but the yield is proven to be lower than other groups. This study also found that Hba1c reading was not significantly associated with positive results among diabetic patients. Therefore, reprioritization should be done.

Malaysia HIV control program have long established that for any individuals diagnosed as HIV, they must be screened for TB and vice versa [15], but there was no specific TB screening program among smokers. In this study, smokers had high percentage of having positive CXR (20%) compare to other risk groups, except HIV (25%). When other confounders were controlled, smoking was also found to be a significant predictor for positive CXR findings. This is not surprising as smoking is a known risk factor to get TB and abnormal chest x-ray finding [16-18]. Smoking can cause lung injury and can trigger chronic inflammation in the lungs. It can become the precursor of idiopathic pulmonary fibrosis that will cause abnormalities in the lung seen with CXR [19]. It can disrupt the muco-ciliary function of the lung and predispose smokers towards lung infections.

In this study smoking habit was also adopted by other high-risk groups, such people with substance abuse, HIV and Chronic Obstructive Airway Disease (Table 2). This was also supported by other studies, making it more important [20, 21]. However, this study only identifies individuals who had CXR suggestive of

TB. Whether they are confirmed to have active TB is not known

3 CONCLUSION

This study has narrowed the high-risk group that needs to be prioritised for screening, with smokers found to be an important risk-group to be targeted, especially among males and elderly smoker. It is highly recommended that the current Ministry of Health (MOH) Malaysia programs that involve smokers, such as quit smoking clinic and smoker identified during routine health and dental screenings, do a routine chest x-ray for their clients.

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