PREVALENCE AND ASSOCIATED FACTOR FOR POSITIVE CHEST X-RAY DURING TUBERCULOSIS SCREENING AMONG HIGH RISK GROUPS IN KEDAH

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By

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LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
CCRC	Cure and Care Centre
COAD	Chronic Obstructive Airway Disease
DM	Diabetes Mellitus
DOTS	Directly Observed Treatment, short course
ESRF	End Stage Renal Failure
HIV	Human Immunodeficiency Virus
HRG	High Risk Group
JKNK	Jabatan Kesihatan Negeri Kedah
KKM	Kementerian Kesihatan Malaysia
NHMS	National Health and Morbidity Survey
OR	Odds Ratio
RM	Ringgit Malaysia
ROC	Receiver Operating Characteristic
SD	Standard Deviation
TNF	Tumour Necrosis Factor
UN	United Nation
USM	Univeristi Sains Malaysia
WHO	World Health Organisation

LIST OF SYMBOLS

<	Less Then
>	More then
=	Equal to
≤	Less than equal to
≥	More than equal to
□	Alpha
B	Beta
%	Percentage
Δ	Precision/Delta
&	And

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ABSTRAK

PREVALENS DAN FAKTOR-FAKTOR BERKAITAN DENGAN PENEMUAN X-RAY POSITIF SEMASA SARINGAN TUBERKULOSIS DALAM KALANGAN GOLONGAN BERISIKO TINGGI DI KEDAH 2016

Latar Belakang: Program pemeriksaan tuberkulosis (TB) dalam kalangan kumpulan risiko tinggi menggunakan sinar-x dada telah dilaksanakan oleh Kementerian Kesihatan Malaysia tetapi kadar pengesanan kes tidak menggalakkan. Langkah mengenalpasti faktor-faktor yang menyumbang kepada pemeriksaan sinar-x yang positif adalah penting supaya kes-kes positif TB tidak akan tercicir dan dapat membantu menghalang rangkaian penularan TB dalam masyarakat.

Kaedah Kajian*:* Kajian keratan rentas telah dijalankan ke atas pesakit-pesakit yang disaring semasa saringan golongan berisiko tinggi di Negeri Kedah. Pesakit-pesakit yang terlibat adalah daripada senarai yang telah dimasukkan di dalam Sistem Maklumat Tibi (TBIS) 104 A yang merupakan sistem pemberitahuan bagi saringan ini. Kajian ini melibatkan 1417 orang yang melibatkan fasiliti yang telah dipilih secara rawak, daripada enam buah daerah yang juga dipilih secara rawak. Analisa regresi lojistik mudah dan analisa lojistik pelbagai digunakan untuk mengenalpasti faktor-faktor yang dikaitkan dengan keputusan x-ray dada yang positif dengan mengambil kira nilai p <0.05 dalam model akhir

Keputusan*:* Dalam kajian ini kebanyakan pesakit adalah pada usia lewat dewasa. Min (SD) bagi umur ialah 49.19 (18.2) tahun. Pembahagian antara Lelaki dan perempuan adalah 51.2% dan 48.8%. Majoriti adalah warganegara Malaysia, yang terdiri daripada 72.3% Melayu, 9.8% India, 8.6% Cina dan 0.9% lain-lain. Prevalens x-ray dada positif terdiri daripada beberapa kumpulan. Dalam kumpulan umur,

warga emas mempunyai prevalens yang paling tinggi, diikuti dewasa dan kanak-kanak. Lelaki lebih ramai berbanding perempuan dan jika mengikut kumpulan etnik, Cina merupakan kumpulan yang mempunyai prevalens tertinggi bagi x-ray dada positif. Individu yang mempunyai gejala mempunyai prevalens yang tinggi jika dibandingkan dengan yang tiada gejala. Dalam kalangan golongan berisiko tinggi, merokok merupakan kumpulan yang mempunyai prevalens tertinggi diikuti HIV/penyalahgunaan substan, penyakit buah pinggang/penyakit paru-paru kronik, lain-lain, institusi, kencing manis dan kontak. Selepas pelarasan faktor penyebab, faktor penentu yang signifikan bagi x-ray dada positif ialah umur, AOR (95% CI) 1.03 (1.01-1.04), gejala AOR (95% CI) 3.8 (2.72-5.50), institusi AOR (95% CI) 2.1 (1.09-4.25 dan HIV/Penyalahgunaan substan AOR (95% CI) 3.6 (1.35-10.0)

***Kesimpulan**:* Penemuan x-ray dada positif semasa saringan golongan berisiko tinggi TB dipengaruhi oleh faktor seperti pertambahan umur, dan gejala-gejala TB. Antara dua belas golongan berisiko yang telah dikaji, dua kumpulan risiko telah dikenalpasti sebagai kumpulan penting yang perlu diberikan priority iaitu institusi and HIV/Penyalahgunaan substan. Oleh yang demikian, ini akan mempermudahkan saringan ini supaya dijalankan dengan lebih efisyen

KATA KUNCI:

tuberkulosis, golongan berisiko tinggi dan faktor perkaitan, x-ray dada positif.

ABSTRACT

PREVALENCE AND ASSOCIATED FACTOR FOR POSITIVE CHEST X-RAY DURING TB SCREENING AMONG HIGH RISK GROUPS IN KEDAH 2016

Background: Tuberculosis screening program among high risk groups using chest x-ray have been implemented by Ministry of health Malaysia but the case detection are not encouraging. More prioritization is needed to identify factors that contribute to a chest x-ray screening positive so that the positive cases would not be missed and may help in halting the chain of transmission of TB in the society.

Methodology: This was a cross sectional study involving patients who were screened during TB screening for high risk groups in Kedah in 2016. The patients involved were from the list that has been included in the TB information system (TBIS) 104 A which is a notification system for this screening. The study involved 1417 people involving facilities which were randomly selected from six regions that were also selected randomly. Data analysis was conducted using SPSS version 22 for descriptive and inferential analysis. Simple logistic regression analysis and multiple logistic analysis was used to identify factors associated with chest x-ray result at *p*-value of <0.05 in the final model

Results: In this study, most of the people involved were at their late adulthood. The mean (SD) of age was 49.19 (18.2) years. Male accounts for 726 people (51.2%). Majority of the sample population were Malaysian 1298 (91.6%) which comprise of Malay 1024 (72.3%) followed by Indian 139 (9.8%), Chinese 122 (8.6%) and other

races 13 (0.9. Majority of the sample population were asymptomatic 1036 (73.1%). Diabetes were the largest proportion of risk group screened 638 (45.0 %), followed by contact 334 (23.6%), 'others unspecified' 204 (14.4%), institutionalised 124 (8.8), clients of quit smoking clinic 57 (4.0%), End Stage Renal Failure/Chronic Obstructive Airway Disease 33 (2.3%) and lastly HIV/Substance abuse 27 (1.9%). Prevalence of positive x-ray was divided into few groups. In age group, elderly has highest prevalence followed by adult and children. According to gender, male has higher prevalence than female. If according to ethnicity, Chinese has highest prevalence of positive chest x-ray among all ethnic. Symptomatic people have higher prevalence if compared to asymptomatic. Among high risk group individual, smoking has highest prevalence of positive chest x-ray (28%) followed by HIV/Substance abuse (25.9%), ESRF/COAD (24.2%), 'Other unspecified' (21%), Institutionalized (16.9%), Diabetes (12.6%) and Contacts (7.1%). After other cofounders were adjusted, the important risk factors are age AOR (95% CI) 1.03 (1.01-1.04), symptoms AOR (95% CI) 3.8 (2.72-5.50), institutionalised AOR (95% CI) 2.1 (1.09-4.25) and HIV/Substance abuse, AOR (95% CI) 3.6 (1.35-10.0).

***Conclusion**:* The discovery of positive chest x-ray during screening for high risk groups affected by factors such as age, and symptoms of TB. Among the twelve-risk factors that have been studied, two risk factors have been identified as an important factor that should be given priority which are institutionalized and HIV/Substance abuse. Consequently, this will facilitate the screening to be carried out more efficiently

KEYWORDS:

tuberculosis, high risk groups and associated factors, positive chest x-ray

CHAPTER 1

INTRODUCTION

1.1 Introduction

1.1.1 Tuberculosis in Malaysia

TB is still a major health threat to world and Malaysia. There were estimated 10.4 million new (incident) TB cases worldwide (WHO, 2016). It contributed to the top 10 causes of death worldwide in 2015, and was responsible for more deaths than HIV and malaria (WHO, 2016). Our country is known as an Intermediate Burden of Tuberculosis due to the incidence rate that was less than 100/100,000 population. The latest notification rate for Tuberculosis (all Form) in Malaysia was 79.44/100,000 population in 2015 (Figure 1.1), while in Kedah TB notification rate (all form) at the same year (Figure 1.2) was lower at 61.73/100,000 (MOH, 2016)

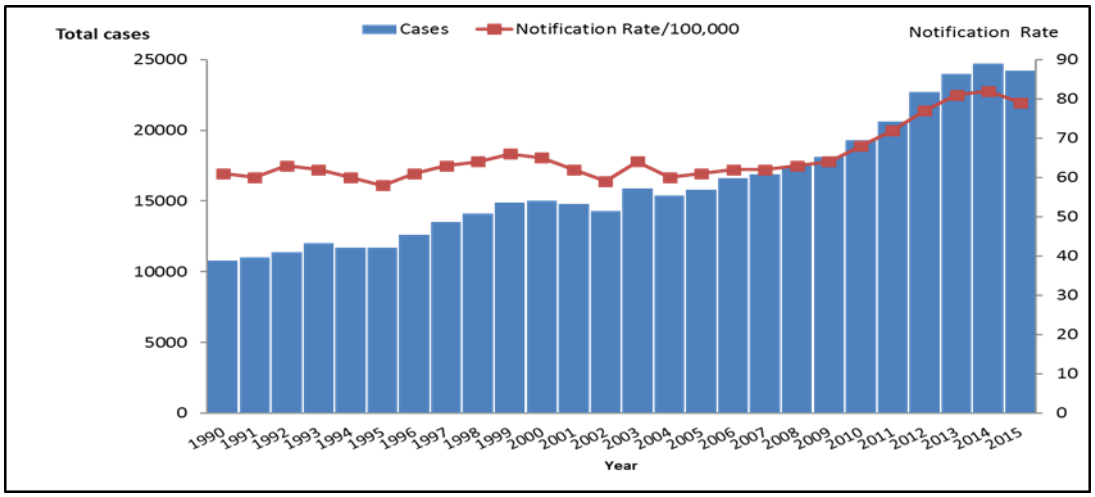

Figure 1.1: TB Notification Rate (All Case), Malaysia (1990-2015), Adapted from Kedah State Health Department Annual Report 2015

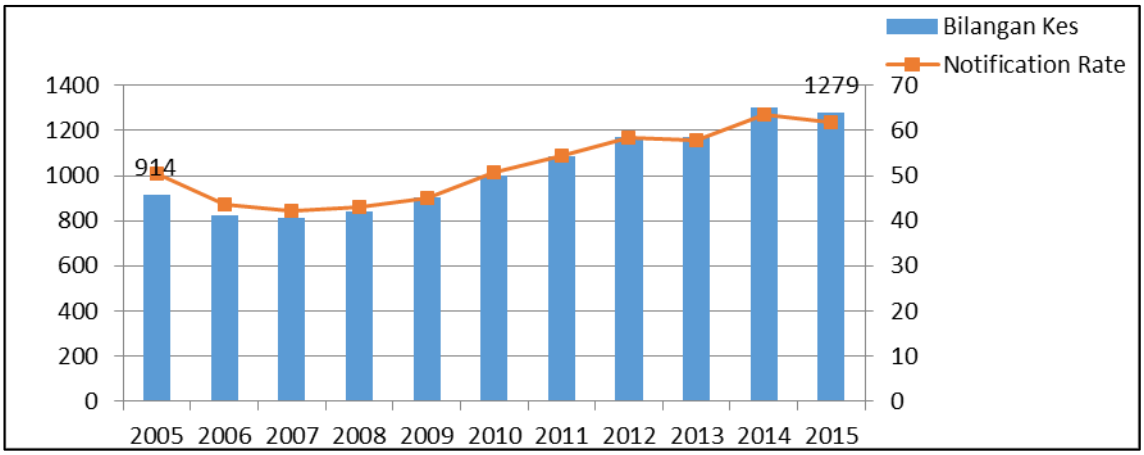

Figure 1.2: TB Notification Rate (All Case), Kedah (2005-2015), (Adapted from Kedah State Health Department Annual Report 2015)

1.1.2 The importance of screening for case detection

If we look at the trend of cases in Figure 1and Figure 2, we can see that despite a lot of measures done to detect cases, there was still a slow increase of notification rate for the past 10 years for both in Kedah and Malaysia. This is worrying because it means that the untreated patient still lingers in the society and will transmit to others who are susceptible to the disease. To better control this disease, the notification rate should have increased exponentially for the past 10 years but after we have treated most of the patients, the transmission rate would have gone down. We can take example from HIV/AIDS control program that concentrated on screening program during early 90's (MOH, 2011; MOH, 2016). The reported cases of HIV increased dramatically from 1988 and peaked in 2002, and then the rate declined slowly after (Figure 1.3).

Every year TB sector, MOH came out with the target number for case detection rate (CDR) calculation, which is the estimated number of new patient that should be detected in that year that becomes the denominator for CDR calculation. The

numerator will be the actual case detected in that year. The target case detection rate (CDR) was 95% and is one of the indicator that hardly achieved by all of states in Malaysia except Johor which have exceeded 95% target in 2015. Ideally, the number of new cases detected should exceed the number of estimated cases, but that's never happen. For detection of cases, we are too dependent on symptomatic individual who seek for treatment in hospital (MOH, 2016). As we already know, for TB to exert the full-blown symptoms, it must reach certain amount of tubercle bacilli in the patient's lung and by the time the patient came to seek healthcare, he has already coughed out tubercle bacilli and spread it to the society. What we should do is to further expand our detection of cases towards asymptomatic or people who are having less symptoms as well. Therefore, something must be done to further strengthen the strategy to increase case detection. Part of the solution is, to concentrate TB screening in high risk individuals followed by prompt treatment in reducing the spread of TB in the country (WHO, 2013a).

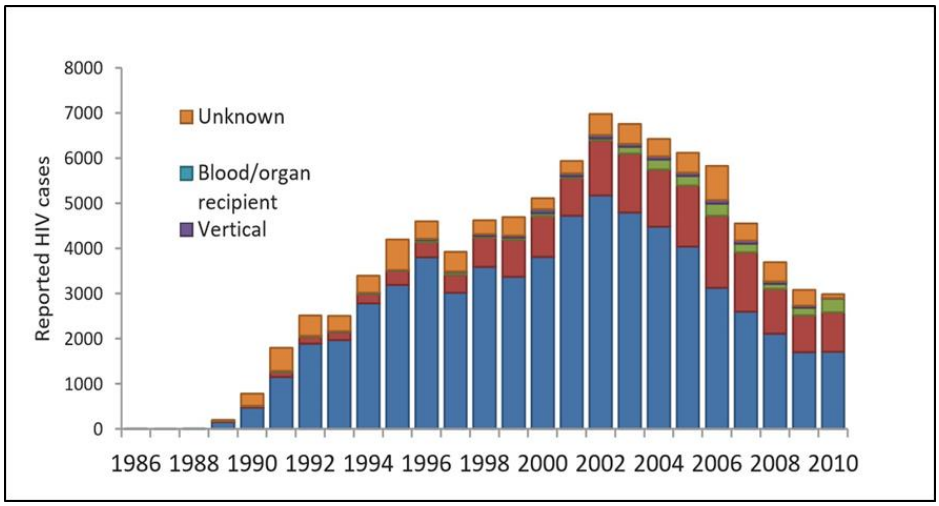

Figure 1.1: Reported HIV Cases per Transmission Mode, Malaysia 1988-2010, Adapted from National Strategic Plan for AIDS, MOH 2016)

1.1.3 High Risk Groups

For intermediate burden country like Malaysia, TB may only concentrate on a specific group of people, that we called high risk group or populations. Usually they do not seek for treatment because they don't recognize the symptoms or they have no symptom at all because being in immunocompromise state. They are also belongs to a group of people who usually have difficult access to healthcare such as elderly, immigrant, drug abuser, prisoner, and people who are having underlying disease such as COPD or people who are exposed to occupational hazard that predispose to TB infection such as healthcare worker and miners (WHO, 2013a). They are those a group of people who are marginalized and being neglected by society and family, especially elderly, HIV, institutionalized and substance abuser (WHO, 2013a)

1.1.4 Increasing number of high risk population

In recent years, there was substantial Increase in number of high risk population in Malaysia. Particularly in Kedah, the rate was alarming. These include an increased number of people who involved in substance abuse (new & old case) which was 19,532 in 2011 and increased to 26,668 in 2015. Kedah is also have highest prevalence of new cases of substance abuse in Malaysia (Agensi Antidadah Kebangsaan, 2016). There was an increased number of diabetic case in Malaysia including Kedah (Institut Kesihatan Umum, 2016). In 2005 there were 13,000 patients on dialysis in Malaysia and the number have reached 20,000 by 2008 (Hooi, 2006). We also can see there was shifting of population towards elderly population and there was influx of immigrants from high burden country to Malaysia

1.1.5 Huge incidence gap

There was huge gap between estimated TB incidences by the WHO and Malaysia. Notification rate for TB (all form) in Malaysia for the year 2015 was 79.44/100,000 population while WHO estimates was at 104/100,000 population in 2014 (TB & Leprosy Sector, 2016). With the gap of 2.4 million of undetected TB patients, it means that we are not aggressive enough in detecting new cases. There were few limitations as highlighted by the WHO which include limitation of sputum smear microscopy (WHO, 2013b). Sputum smear microscopy was unreliable in asymptomatic patients because bacterial load for them was very low and cannot be detected (Nobuyuki, 2013). Those in high risk group are often asymptomatic as they will not seek treatment and even if they have symptoms, it is unlikely for them to seek for treatment until they develop severe complication (Nobuyuki, 2013). Sputum smear microscopy is also time consuming for both patient and clinician especially to the former since it requires many steps. Therefore, chest x-ray has been selected by MOH Malaysia as the screening tool for the high-risk group population.

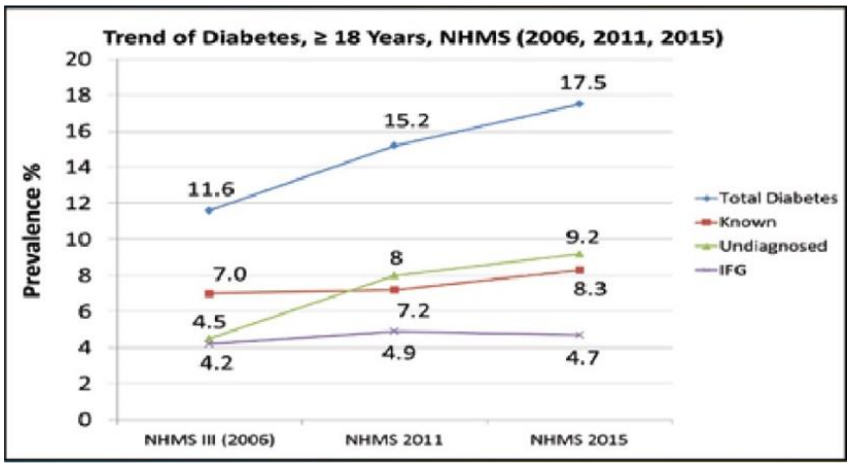

Figure 1.4: Trend of Diabetes, from NHMS 2006, 2011 & 2015 shows increasing trend of Diabetes prevalence among adults, adapted from National Health Morbidity Survey Factsheet, 2015

1.1.6 Chest X-ray as a screening tool

The advantages of chest x-ray are relatively easier, not time consuming and will be able to detect more sputum AFB negative but culture positive patient (Nobuyuki, 2013). There were also few disadvantages which are poor detection outcome (Miller et al., 1998) and the yield is too low and not economical (Gottridge, 1989). Recently in Kedah, since screening for high risk group of TB started in 2014, the yield was around 4% (MOH, 2016). There were few issues highlighted in which one of it is improper chest x-ray selection among high risk group who were screened. There were also no proper assessment and risk prioritization where clinicians just screened everybody who are at risk.

WHO has developed guidelines on screening for active TB. It suggests that screening, if done in the right way and targeting the right people, may reduce suffering and death (WHO, 2013a). Active case detection using chest x-ray is one of the recommended tools for TB screening by WHO and has been adapted by MOH. Historically in 1974, after reviewing the results of several decades of TB screening, the ninth report by WHO's Expert Committee on TB recommended that indiscriminate TB case-finding using miniature mass radiography should be abandoned due to its inefficiency (WHO, 2013a). This is supported by studies done in early 90s that found out chest x-ray are of value in 0% to 1.3% (Gottridge, 1989).

After a decade, WHO have looked back towards chest x-ray for TB screening and found out that its useful only if the TB prevalence among the target population is high (Nobuyuki, 2013). Other studies also found out that targeted screening using x-ray is an effective tool for the early detection of active TB in hard-to-reach populations (Story, 2012). Therefore, chest x-ray that specifically targeting high-risk

groups was useful in the early detection of active disease (Fuentes, 2014). As mentioned earlier, the high-risk group are usually immunocompromised as they did not have profound symptoms. Therefore, high risk group screening that has been adapted by MOH is to screen all high risk group individual, including all symptomatic and asymptomatic individual (TB & Leprosy Sector, 2016a; WHO, 2013a).

Prevalence of chest x-ray positive among high risk groups in other countries with a low incidence of TB is almost like in Malaysia. In a study done in Spain, they found out of 3654 x-rays done among high risk groups, 227 (6.21 %) were positive (Fuentes, 2014). Similar finding also reported by (Miller et al., 1998) in Routine Emergency Department Chest Radiograph done in high risk group of TB in New Jersey, United States, 2% had chest radiographic findings considered to be meaningful for further investigation to confirm diagnosis of TB.

Previous studies found few associated factors that influence positive chest X-rays. (Boon, 2006) reported that TB patients with HIV are more likely have positive radiographic findings which are atypical. Other study conclude that the older the patient in a high risk group, the more chest x-ray positivity seen, as reported by Miller et al. (1998). This mean that the radiographic changes was significantly higher if the patient is older. However, there were also findings in studies that shows no significant different between chest x-ray finding for those among high risk group or not, as reported by Bacakogˇlu (2001) who conclude that diabetes does not affect radiological features of pulmonary infiltrates and diabetic patients had a higher prevalence of typical x-ray presentations but no significant difference compared with non-diabetics (Paquette et al., 2014)

1.2 Problem Statement and Rationale of study

TB incidence is still high in Malaysia and still increasing. There was a huge detection gap between our true incidence and WHO estimated incidence particularly among high risk group. Chest X-Ray is an effective tool, but have poor yield and it's not being used effectively. Therefore, screening must be very selective to detect more cases. We want to identify which group among the high-risk individuals who are more likely to have positive chest X-Ray and possible contributing factors as well.

This study aimed to identify which are the higher risk group and what are the major factors that have higher odds of positive chest x-ray finding. By obtaining the information we will be able recognize which group we must prioritize for chest x-ray screening. Hopefully with this study, we can detect more TB cases and with more case detected, we will able to break the chain of transmission in the society and will benefit our country as a whole

1.3 Research questions

1. What is the prevalence of positive chest x-ray among high risk groups in Kedah?

2. What are the associated factors of positive chest x-ray among high risk groups?

1.4 Objectives

1.4.1 General objective

To study the prevalence and associated factors of positive chest x-ray in high risk group for tuberculosis (TB) in Kedah

1.4.2 Specific objectives

1. To determine the prevalence of positive chest x-ray for TB screening among high risk group in Kedah.

2. To describe the socio demographic factors (age, sex, and ethnicity) and clinical characteristics (symptoms, co-morbidities) of high risk group for TB in Kedah.

3. To identify the associated factors of positive chest x-ray in high risk group of high risk group for TB in Kedah.

1.5 Hypotheses

There are significant association between symptoms, co-morbidities and socio demographic factors (age, sex, and ethnicity) and the positivity of chest x-ray among high risk groups in Kedah.

CHAPTER 2

LITERATURE REVIEW

The search for literature review was done with subscribed USM online tools such as Science Direct, Springer Link, JAMA, Scopus, OVID and ProQuest. Outsource search engines were also used which include PubMed and Google Scholar. Few of the references also manually searched in Online MOH Archive and from the library in Kedah State Health Department. Based on literature review, the risk factors of chest x-ray positivity have been identified and the relevant risk factors for Malaysia have been selected for this study.

2.1 Socio-demographic factor for chest x-ray positivity

2.1.1 Age

Many studies have found that the risk of getting TB increased by increasing age (MOH, 2012a; WHO, 2016) However not many studies were done to evaluate chest x-ray positivity towards TB-meaningful finding. But there are many studies done to evaluate chest x-ray screening towards positive TB either by sputum smear microscopy or GENE X-Pert (Casas *et al*., 2013)

Bacakoğlu (2001) did a retrospective cohort study among diabetics and non-diabetics who acquire TB. They found that diabetics have lower mean age compared to non-diabetics to have abnormal X-Ray. Age is important even within a risk group itself, where a study done among TB contact in children by Khalilzadeh *et al*. (2003) reveal

that the risk for positive radiological findings were higher in 10-14 years old compared to 5-9 years old.

There was a study done by Goetsch *et al.* (2012) in Germany, who screened homeless and illicit drug users for TB using chest x-ray and proceed to sputum microscopy to see if there were positive x-ray finding. The study concluded that age was the only variable to be associated with the risk of smear positive TB for both risk group. Different risk group also has difference in age for the manifestation of positive chest x-ray. Another study done among high risk individual in Spain by Goetsch *et al*. (2012) stated that drug users became smear positive TB at a younger age compared to homeless people. Age is also an important predictor of positive chest x-ray, even among low risk individual. As reported by Yeshurun *et al*. (1996) during compulsory screening of approximately 5000 Israeli Defence Force, they found out that abnormal findings were influenced by age. Another study done using routine chest x-ray among 481 asymptomatic high risk groups individual (drugs, alcohol abuse and emergency psychiatric illness) that attended the emergency department in New Jersey in 6-month period, also stated that the patient with positive radiographic changes was significantly older (Miller *et al*., 1998). As a conclusion, age is an important factor in determining positivity of chest x-ray, even among high risk and non-high risk population and within the particular high risk group itself.

2.1.2 Sex

Male gender is known to have higher risk in getting pulmonary TB (MOH, 2012a; WHO, 2016). The male to female ratio was 15:10, based on a study done in Kedah, Malaysia (Ismail, 2004). Similar findings also was found in a Cambodian prevalence

study involving 37,417 individuals by Mao *et al*. (2014) where there were 15.1:10 ratio of males to females among smear positive TB cases and, 14.8:10 ratio of males to females for smear-negative, culture-positive TB.

A similar picture is seen in chest x-ray from a cross sectional study done in Uganda involving 863 symptomatic from outpatient department, which showed significant gender difference with x-ray was suggestive of TB in 66.5% of males and in 44.8% of female ($p<0.001$). For confirmed Pulmonary TB patients, males have higher odds of having abnormal chest x-ray (OR 5.0, 95% CI: 3.29, 7.57, $p <0.001$) (Boum *et al*., 2014).

However, Zhang *et al*. (2015) reported that there were no differences in sex for positive chest x-ray during TB screening using chest x-ray involving 8418 elderly that was classified in high risk individuals (symptomatic, close contact and diabetes). In other study done in emergency department by (Miller *et al*., 1998) mentioned earlier, also found that there was no significant difference in sex for positivity of chest radiograph among the risk groups.

Fuentes (2014) also found that gender is not a significant factor for positive TB in screening for active TB in high-risk groups done in Spain. In another study done among diabetic TB patients, there was also no significant difference in gender for TB among diabetics and when compared with non-diabetics, the gender difference is also insignificant (Tatar *et al*., 2009).

2.1.3 Nationality

There are studies that looked into positive chest x-ray and relation with nationality in screening programs for immigrants and refugees. Pulmonary TB accounts for 22.4%

of disease detected by FOMEMA sdn bhd in 1998 and 1999 using chest radiographs (Leong, 2006). In an active case finding among high risk group individual using chest x-ray in Spain, they reported that the prevalence of TB detected during screening in immigrants were significantly higher compared to poor people, drug user, foreigners >2 years and native born (Fuentes, 2014).

In regards to confirmed case of pulmonary TB, foreigners are at higher risk, when compared to Malaysian (Nissapatorn *et al*., 2007). This is particularly true for those who are from high burden countries such as Indonesia, Philippine and Myanmar. The finding is similar in other countries as well such as United States, where the incidence rate of TB in foreign-born were higher than U.S citizen (Talbot *et al*., 2000). Another study also in Unites States also found that refugees in their first year of arrival has highest incidence rate of TB compared to other foreign-born residents (Lobato, 2008). This situation is almost like in Kedah because there was sudden influx of Rohingya ethnic immigrants from Myanmar who arrived in the end of 2015, in which majority of them still resides in Belantik Immigration Detention Depot and some of them have already been released to designated villages all over Kedah with UNHCR identification card. In Malaysia, 12.3% of notified TB cases in 2015 were among the immigrant population (MOH, 2016). In Sabah, immigrants contributed more than 24% of the newly detected TB cases (Dony *et al*., 2004) and the figures became larger due to huge influx of immigrants to Sabah in recent years. We are surrounded by high TB burden country and most of immigrants that came to Malaysia are from these countries. Therefore, it is important to know the impact of nationality on TB screening program in our country.

From an evaluation done in Selangor, incidence rate for all forms of TB according to nationality were 126.7/ 100,000 population for foreigners, compared to overall incidence rate for Selangor for 2001, at 43.1/ 100,000 population (Venugopalan, 2004). However, even though foreigners might have higher risk to get TB infection, most of them present as symptomatic patient, rather than from screening, such as by FOMEMA. This is supported by a study in Netherland by Verver *et al*. (2001) who found that foreigners who undergone TB screening using chest x-ray were less likely to have positive sputum smear microscopy.

2.1.4 Ethnicity

In a screening for pulmonary TB using mobile digital chest radiography done in London, Unite Kingdom, revealed that there was no significant difference in chest x-ray positivity among white, black african, black caribbean, south asian and others (Story, 2012). Similar finding also found during Chest x-ray screening for TB done in a Hong Kong prison, revealed that there was no significant different in yield of CXR screening among Chinese and other races (Leung et al., 2005).

In Malaysia, chest x-ray positivity among different ethnicity is unclear because it was barely discussed in the studies that have been done. However, pertaining to differences among ethnicity in active TB, one study done in Selangor clearly described the difference of incidence rates among all Malaysian ethnics, which are indian: 41.6/ 100,000 population, Malays: 39.7/ 100,000 population, chinese: 29.3/ 100,000 population and others: 24.8/ 100,000 (Venugopalan, 2004).

2.2 Symptoms

The availability of TB symptoms also plays a major role in chest x-ray positivity, as reported in previous study that sensitivity of chest x-ray can be up to 100% when combined with presence of symptoms (Hoog, 2012; Joshi, 2012).

Cavitary lung disease is a common presentation and they typically present with prolonged cough, associating fever and/or night sweats and weight loss. This cavitation is easily detected by trained personnel through chest x-ray (Heemskerk, 2015). Chest x-ray when combined with symptoms screening, will increase the number of TB detected (Churchyard *et al*., 2010).

2.3 High Risk Group for TB

2.3.1 Person with Human Immunodeficiency Virus

Person with Human Immunodeficiency virus (HIV) infection is a known risk factor for TB, as stated in a study that people with HIV are prone to get TB, due to their immune-compromised state (Baughman, 1999). In terms of chest x-ray finding, most of HIV patient have normal chest x-ray, as reported by Akinbami *et al.* (2012). In a prevalence survey done in Georgia, United States by Hoog (2012), they concluded that chest x-ray abnormality for HIV infected person was lower compared to HIV uninfected person. Furthermore, for the HIV infected individual, the chest x-ray finding of ‘any abnormality’ can yield more smear or culture positive cases, compared to chest x-ray with ‘only pulmonary or pleural abnormality’. It means that

HIV infected person often presents with atypical chest x-ray finding that does not confine to lung parenchyma alone.

Similar finding was reported by Aderaye *et al*. (2004) in a study involving TB patient from outpatient department in Ethiopia, in which they found that chest x-ray findings for a HIV infected person who was diagnosed to have TB were mostly atypical and can be normal or with minimal changes. Similar findings also reported by Palmieri *et al.* (2002b) in a study done among HIV patient in Italy. Elliott *et al*. (1990) also mentioned that TB patient who are HIV positive are more likely to be sputum smear negative and less likely to show classical upper lobe involvement and cavitation. As a conclusion, HIV is a risk to acquire TB infection, but it's the other way around for chest x-ray finding.

2.3.2 Diabetes Mellitus

Diabetes is a known risk factor for TB, as mentioned by several studies. From a retrospective cohort study in Korea using nationwide database of 331, 601 patients, higher incidence of TB was found among patient with diabetes and most of them was likely to be diagnosed in the first year of diagnosis (Heo *et al*., 2015). It is consistent with Jabbar *et al*. (2006) who reported in a study involving adults with diabetes in Pakistan, which stated that patient with diabetes mellitus are ten times more common to have TB, compared to those without diabetes.

Regarding the chest x-ray finding, a study done in Turkey by Bacakogˇlu, (2001), found that the clinical and radiological presentation of TB among diabetics is insignificant. Al-Wabel *et al*. (1997) also reported similar findings where chest x-ray involvement including cavitary disease was again similar between diabetics and non-

diabetics. However, if we compare the findings of the x-ray, non-diabetic patient usually presents with upper lobe involvement and cavitation, but diabetic patients often presents with lower lobe involvement. A comparative study done by Perez-Guzman *et al*. (2001) in Mexico, compared 192 TB patients with underlying diabetes mellitus with 130 TB patients without diabetes, found that the chest x-ray was mostly atypical. They also noted that the presentation was mostly lower lung lesion and its frequency increased by age.

2.3.3 Smokers

Smokers were known to impose higher risk of developing TB. A cross-sectional study done in Spain, involving 13,038 from their TB registry found smokers have 1.5 odds of having pulmonary TB compared to non-smokers (Altet-Gomez *et al*., 2005). Other study also reported similar findings, where smokers were significantly associated with TB, especially among younger population (Oh *et al*., 2016). Similar finding also mentioned by Leung *et al*., 2003 in a study involving 851 patients from Hong Kong's TB registry.

In terms of chest x-ray finding, smokers were also prone to get abnormal chest x-ray. In a study done by Altet-Gomez *et al*. (2005) that mentioned earlier, they also found that TB who smoke have 1.9 odds to develop cavity lesions in their x-ray finding, compared to non-smokers.

2.3.4 Institutionalised individuals

Institutionalised individuals are defined by persons living in an institution, which in this study, are imprisoned, inmates of immigration detention centre and old folk's home. These groups of people cannot control the condition which they live and are

prone to get many diseases, mainly airborne disease like TB. People in institutions pose higher risk than the normal population, evidenced by a study by Southern *et al*. (1999) in London, where they screened homeless people at 35 shelters, and found a high prevalence of TB, which were 17.2 per 1000 person screened, more than the normal population. This is because they were living in a crowded place and confined space, where the ventilation is poor.

The rates are even higher among prisoners, where in 1992, the reported incidence rate among prisoners in U.S was 156.2/100,000 compared to 10.4/100,000 for the normal population (Valway *et al.*, 1994). It also was reported a ten times higher risk to have TB, compared to the normal population (Puisis *et al*., 1996; Valway *et al*., 1994). The finding was similar to a cohort study by Story (2012) among TB patient in London, where the study reported highest prevalence of TB were among the homeless (788/100,000 population), followed by drug users (345/100,000 population) and prisoners (208/100,000). They were significantly higher, compared with overall prevalence which was 27.1/10,000 population. In a screening using chest x-ray for TB in a Hong Kong prison by Leung *et al.* (2005), among the risk groups included in the study, the yield for positive TB was highest, which are 1.23% for prisoners, followed by 0.98% for contacts and 0.32% for HIV infected individuals.

Regarding chest x-ray positivity among prisoners, Leung *et al*. (2005) found that prisoner have higher yield of positive chest x-ray which was 6.51 %, compared with other mass x-ray screening involving low risk population, which ranged from one to four percent (Gottridge, 1989; WHO, 2013b).

2.3.5 End Stage Renal Failure

If we compare findings of the National Health Morbidity Survey (NHMS) in 2006 and 2015 (Institut Kesihatan Umum, 2016), we can see that the prevalence of diabetes in Malaysia is increasing and diabetic renal disease account for 80% of all dialysis patient. Renal failure patients are known to have higher risk to get TB, because they are immuncompromised (Nantha, 2014). They also have higher risk of TB reactivation, and also faced with the risk of transmission during dialysis (Lee *et al.*, 2010). Shajahan *et al*. (2016) also reported similar findings whereby renal impairment can predispose patient to TB.

2.3.6 Chronic Obstructive Pulmonary Disease

Having the diseases, Chronic Obstructive Pulmonary Disease (COPD) is listed as one of the associated factor of TB, according to Malaysia Clinical Practice Guideline (CPG) (MOH, 2012a). They are also prone to require long term use of steroids. Therefore, this makes them more vulnerable to get TB infection (Shajahan *et al.*, 2016). Other studies also find similar findings as well, such as from a population based study involving 115, 867 COPD patients from Swedish hospitals by Inghammar *et al*. (2010), the odds of having TB was three times more than the normal population.

From x-ray screenings involving 546 COPD patients in United Kingdom, 13% of all x-ray done among COPD patients have TB features, most of them are old PTB (Wallace *et al*., 2009). This also have larger yield compared with other mass x-ray screening involving low risk population, which ranged from one to four percent (Gottridge, 1989; WHO, 2013b).

2.3.7 Contact with TB patient

Contacts have higher risk to be infected by TB, either via household or social contact (MOH, 2012a). The contacts were also being followed up until 18 month just to make sure they did not get infected TB, because as we already know, the incubation period of TB can be more than one year. From a study done in United Kingdom by Underwood *et al*. (2003a), where they compared the yield of TB in between 643 contacts of active TB with 322 immigrants being screened. They found the yield for contact screening was significantly higher, 7.7% and 3.3 % respectively. This is because contact screening is done among the group of family members and neighbourhood that already have higher risk to get TB.

Kilicaslan *et al*. (2009) also mentioned similar findings in the study involving 6188 household contacts for 1570 index cases in Istanbul, where the incidence rate of active TB was higher than normal population, especially for those who are in the 15-34 age group. For latent TB, Moran-Mendoza *et al*. (2010) concluded in his study that household contact has highest odd of getting latent TB.

2.3.8 Substance abuse

Substance abuse is a known risk factor to get TB (MOH, 2012a). It has been mentioned in previous study that it is an important risk group among other risk group. In a study done by Story (2012), who screened high risk group individual for TB, substance abuse has higher odds of getting TB, when compared to homeless and people who live in shelters. This was because they also have other risk factors, such as improper housing, being poor, malnourished, has HIV and other co morbidities as

well. For example, a study in Russia mentioned that HIV infection is primarily related to intravenous drug use (Fleming *et al*., 2006).

2.4 Conceptual framework

The conceptual framework below explains the factors included in the study. Those factors influence the positivity of the chest x-ray are symptoms of the patient, whether symptomatic or asymptomatic and the types of symptoms experienced by the patient. The socio demographic factors studied are age, gender, race and nationality. The high-risk groups that included in the study are the risk group defined by MOH to be included for x-ray screening. The groups are end stage renal failure, chronic obstructive airway disease, diabetes, smoker, institutionalised people, contact of TB patient, HIV patient, and substance abuse. Rheumatoid arthritis and anti-TNF is not included because since the directive is still new, many hospitals did not have adequate data.

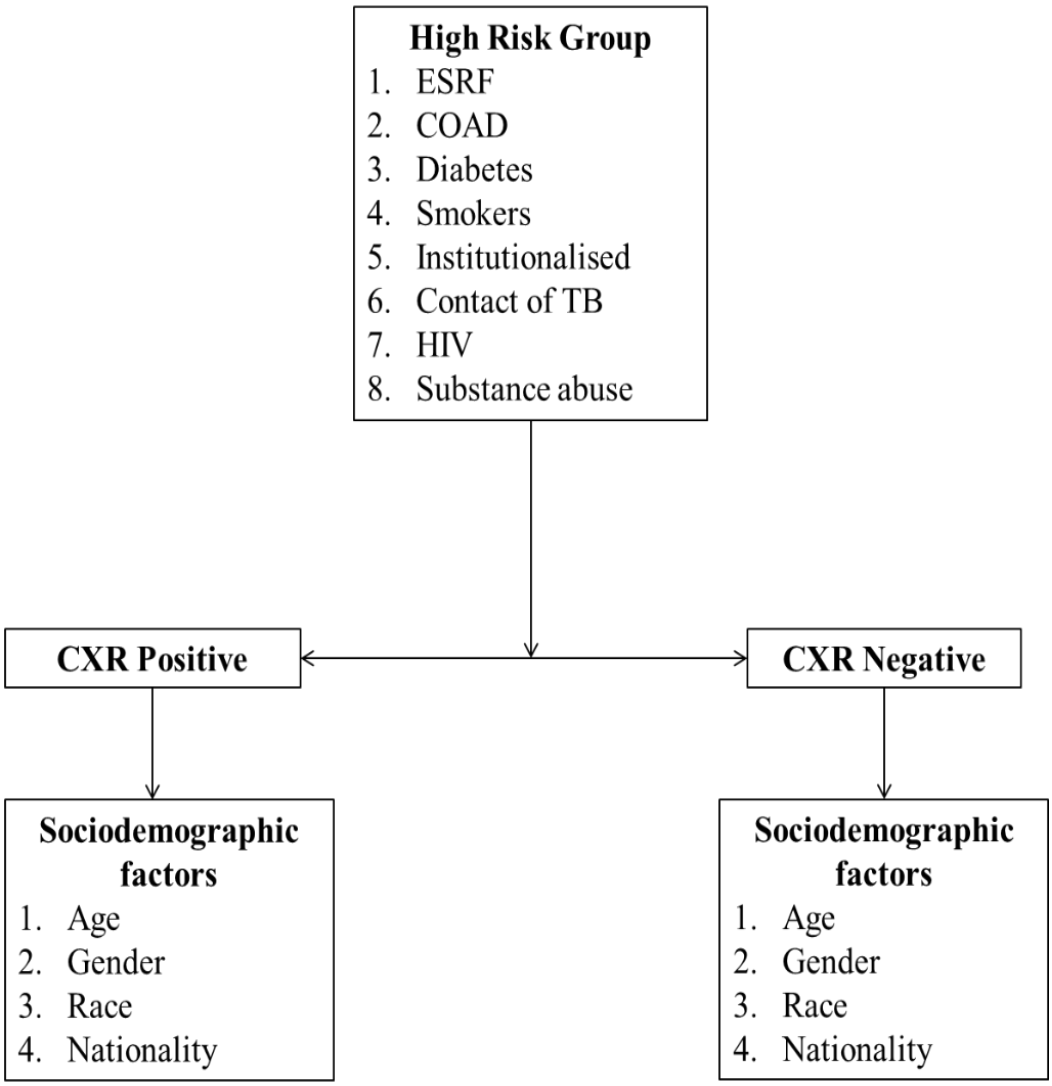

Figure 2.1: Conceptual framework

CHAPTER 3

METHODOLOGY

3.1. Study design

This was a cross sectional study using the screening registry for high risk groups of TB patient retrieved from TBIS 104 A and the chest x-ray reporting report from the facilities of Kedah.

3.2 Study duration

This study was done from December 2016 to March 2017.

3.3 Study location

This study was conducted in TB Unit, Kedah State Health Department, Radiology unit Hospital Sultanah Bahiyah Alor Setar, along with other Hospitals and Health Clinics which are selected in the study. State of Kedah is the northern state of Malaysia beside Perlis. It borders to Thailand and Perlis from the north, Penang and Perak from south and Kelantan from the east. The widths are 250,000 km squares, almost equivalence to Kelantan state. It consists of 11 districts which are:

1. Langkawi Island
2. Kubang Pasu
3. Padang Terap

4. Kota Setar
5. Pendang
6. Sik
7. Baling
8. Kuala Muda
9. Yan
10. Kulim
11. Bandar Bharu

Figure 3.1: Map of Kedah