FACTORS INFLUENCING AND SPATIAL DISTRIBUTION OF TUBERCULOSIS MORTALITY IN KELANTAN FROM 2013 TO 2014

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by

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LIST OF ABBREVIATIONS

AFB	Acid-Fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
ART	Anti-Retroviral Therapy
BCG	Bacillus Calmette Guerin
CDC	Centre for Disease Control
CI	Confidence Interval
CPG	Clinical Practice Guideline
CXR	Chest X-Ray
DOTs	Direct Observe Treatment short-course
GIS	Geographical Information System
HAART	Highly Active Anti-retroviral Therapy
HIV	Human Immunodeficiency Virus
IGRA	Interferon-Gamma Release Assay
MDR-TB	Multidrug-Resistant Tuberculosis
MOH	Ministry of Health
MTB	Mycobacterium tuberculosis
NCD	Non-communicable Disease
NTM	Nontuberculous Mycobacterium
NTP	Nation Tuberculosis(Control) Program
OR	Odds Ratio
PS	Power and Sample

PTB	Pulmonary Tuberculosis
SAT	Self-Administration Treatment
SD	Standard Deviation
SE	Standard Error
TB	Tuberculosis
TST	Tuberculin Skin Test
VR	Vital Registration
WHO	World Health Organization

LIST OF SYMBOLS

α	Parameter estimate
β	Parameter estimate/ coefficient
n	Number of observation
%	Percentage
Δ	Precision
p	P-value
Z	Z distribution
df	Degree of freedom

FAKTOR YANG MEMPENGARUHI DAN TABURAN RUANGAN KEMATIAN HASIL KES TUBERKULOSIS DI KELANTAN DARI 2013 HINGGA 2014

ABSTRAK

Tuberkulosis (TB) adalah penyakit berjangkit yang kerap berlaku dan merupakan salah satu beban kesihatan awam kepada Kementerian Kesihatan. Kajian ini adalah untuk menentukan faktor-faktor yang dikaitkan dengan kematian di kalangan kes TB. Di Malaysia masih menjadi satu cabaran yang besar kepada kesihatan awam terutama kadar rawatan yang tidak berjaya meningkat setiap tahun. Untuk menentukan taburan spatial dan faktor-faktor yang dikaitkan dengan kematian dalam kalangan kes-kes TB. Satu kajian keratan lintang telah dijalankan. Semua data kes TB yang memenuhi kriteria dari semua Pejabat Kesihatan Daerah di Kelantan dari tahun 2013 hingga tahun 2014 telah dikumpulkan untuk menentukan hasil rawatan TB. Data dianalisis dengan menggunakan perisian ArcGIS versi 10.1 dan IBM SPSS versi 22.0. Semua data koordinat; longitud dan latitud untuk kes-kes TB dan fasiliti kesihatan dari Garmin GPSmap 60CSx dipindahkan ke MS excel 2010. Jarak Euclidean antara kes-kes TB dan fasiliti kesihatan diukur berdasarkan jarak Euclidean dan disimpan dalam fail yang sama. Kemudian data tersebut diimport ke dalam ArcMap 10.1 sebagai lapisan data shapefile. Lapisan data yang mempunyai koordinat pada peta disimpan ke dalam format fail JPEG. Regresi logistik ringkas dan logistik berganda telah digunakan untuk membentangkan faktor-faktor berkaitan yang menyumbang kepada kematian kes TB. Sebanyak 1645 kes TB dari tahun 2013 hingga 2014 telah direkodkan, di mana kadar kematian kes adalah 13.1%. Majoriti kes TB adalah lelaki 65.0%, min (SD) umur berusia 48.7 (18.05) tahun dan bilangan kes paling tinggi terletak di Kota Bharu (25.1%). Kira-kira 25% adalah

pesakit dengan keputusan kultur kahak positif, 12% adalah pesakit dengan HIV positif dan sembilan peratus ketidakpatuhan dengan rawatan DOTs sambungan. Kes TB juga telah diplot berdasarkan jarak Euclidean menggunakan ArcMap 10.1 dalam peta Kelantan dan dapatannya adalah 32% kes TB terletak dalam jarak melebihi 10 kilometer (km) dari kemudahan kesihatan. Semi-variogram menunjukan tiada perkaitan jarak Euclidean antara pesakit dengan pesakit yang lain. Ini mencadangkan tiada perkaitan untuk autokorelasi ruang. Dapatan kajian ini menunjukkan bahawa kes yang lebih berumur (OR=1.05, 95%C.I=1.03, 1.08), kultur kahak positif (OR=2.11, 95%CI=1.15, 3.89), HIV positif (OR=20.50, 95%CI=9.10, 46.20), ketidakpatuhan rawatan DOTs sambungan (OR=24.17, 95% CI=11.84, 49.35) dan jarak antara kes TB dengan fasiliti kesihatan melebihi 10 km (OR=2.54, 95% CI=1.39, 4.64) dikaitkan dengan kematian yang signifikan dalam kalangan kes TB. Kesimpulannya, kes yang lebih berumur, kultur kahak positif, HIV positif, ketidakpatuhan dengan rawatan DOTs sambungan dan jarak yang jauh dari kemudahan kesihatan adalah berisiko tinggi untuk kematian di kalangan kes-kes TB.

FACTORS INFLUENCING AND SPATIAL DISTRIBUTION OF TUBERCULOSIS MORTALITY IN KELANTAN FROM 2013 TO 2014

ABSTRACT

Tuberculosis (TB) is a common communicable disease and one of the public health burdens to the Ministry of Health. This study was to determine the factors associated with mortality among tuberculosis cases. In Malaysia it is still major challenge to public health especially unsuccessful treatment rate increases by year. To determine the spatial distributions and factors associated of mortality among TB cases. A cross-sectional study was conducted. All eligible TB cases data from all District Office in Kelantan from year 2013 to year 2014 were collected to determine the outcome of the TB treatment. Data were analyzed using software ArcGIS 10.1 and IBM SPSS version 22.0. All coordinate data; longitude and latitude both of TB cases and health facilities from Garmin GPSmap 60CSx were transferred into MS excel 2010. Euclidean distances between TB cases and health facilities were measure based on Euclidean distances and saved in same file. Then the data were imported into ArcMap 10.1 as a shapefile data layer. The data layers with the coordinate on a map were saved into JPEG file format. Simple and multiple logistic regressions were applied to present the associated factors that contributed to the mortality of TB cases. A total of 1645 of TB cases from year 2013 to 2014 were recorded in which the mortality of cases were 13.1%. Majority TB cases were male 65.0%, mean (SD) age was 48.7 (18.05) years old and highest number of cases located in Kota Bharu (25.1%). Approximately, 25% were sputum culture positive, 12% HIV positive and nine percent was noncompliance with DOTs maintenance treatment. TB cases also was plotted based on Euclidean distance used ArcMap 10.1 on Kelantan

map and the result were 32% of TB cases were located more than 10 km from health facilities. Semi-variogram shows that there is not significant Euclidean distance between cases with another case. Euclidean distance had suggested no relationship with spatial autocorrelation. Result shows that cases with older age (OR=1.05, 95%C.I=1.03, 1.08), sputum culture positive (OR=2.11, 95%CI=1.15, 3.89), HIV positive (OR=20.50, 95%CI=9.10, 46.20), non-compliance to DOTs maintenance treatment (OR=24.17, 95% CI=11.84, 49.35) and distance more than 10 km (OR=2.54, 95%CI=1.39, 4.64) were significantly associated with mortality among TB cases. In conclusion, those with older age, sputum culture and HIV positive, noncompliance with DOTs maintenance treatment and far away from health facilities are posing higher chance of mortality among TB cases.

CHAPTER 1

INTRODUCTION

1.1 Pulmonary Tuberculosis

Tuberculosis (TB) is an infectious diseases caused by *Mycobacterium Tuberculosis (MTB),* transmitted from an infected person through fine respiratory droplets. TB is spread from one person to another person. Whenever an infected person cough, sneeze or spit, they propel the TB germs into the air (CDC, 2011b).

Patients with active pulmonary tuberculosis (PTB) typically presents with productive cough for two weeks or more, hemoptysis, loss of appetite, weight loss and fever, and less common symptoms such as night sweating chest pain, dyspnea and voice hoarseness (CPG, 2002).

A microbiology diagnosis of PTB is carried out by examining sputum smears and sputum cultures from clinical specimens based on the detection of acid fast bacilli (AFB). Patients who were suspected of having infectious PTB should submit at least two sputum specimens for the microscopic test in a quality-assured laboratory.

According to WHO (2010), at least one sputum specimen should be collected in the early morning because the sputum has the highest yield. These techniques are an important guideline modality of current investigations but lack aim sensitivity or are time consuming. Hence, Nucleic Acid Amplification Tests for the detection of MTB are useful tools for a rapid diagnosis of PTB.

With regards to radiograph imaging modalities of PTB diagnoses, chest radiography remains the primary imaging modality for PTB cases. The chest x-ray

(CXR) features of severity grading is based on the expansion involvement of the lungs; minimal, moderate and advance (CPG, 2002).

Figure 1.1 Minimal lesion

Slight lesions without cavity, small parts confined to one or both lungs. Not exceeding the upper zone of total extended.

Figure 1.2 Moderate lesion

Dense and confluent lesions not exceeding total volume in one lung. Disseminated lesion slight to moderate density in one or both lungs not exceeding the volume of one lung. The total diameter of cavity must not exceed 4 cm.

Figure 1.3 Advanced Severe lesion

More extensive than moderately advanced of Lesion.

Source: Ministry of Health. Control and Management of Tuberculosis (2nd Edition), Putrajaya Ministry of Health; 2002

Figure 1 .1 -1.3 Grading of severity in CXR features of PTB as followed:

Tuberculin skin test (TST) or Mantoux test is a screening tool for TB that has been utilized for a long time. TST comes with advantages such as they are cheap and easily performed. However, the interpretation of result is challenging because sometimes, patients do not return or delay returning and it will possibly yield no result or it might be an inaccurate one. The reading of induration is prone to subjective errors. However, it is the preferred test among children of less than five years of age. False positive results of TST may be caused by *Nontuberculous Mycobacteria* (NTM) infection or previous Bacillus Calmette Guerin (BCG) vaccination. False negative results can be seen in patients who have immunocompromised system. Extensive TB pulmonary or military TB can also depress the immunity which will lead to a paradoxically negative TST (CPG, 2002).

Besides, Interferon-Gamma Release Assays (IGRAs) which is the whole-blood test in the diagnosis of MTB are more expensive screening test compared to TST. The advantages of IGRAs include the results which can be available faster with no subjective errors in reading by subsequent test and BCG vaccination. However, this expensive test is not preferred to children less than 5 years of age, and a person who has lately been exposed to *M.tuberculosis* and immunocompromised (CDC, 2011a).

A systematic review on the cost-effectiveness of screening tools supports the use of IGRAs in screening high risk groups. The expensive cost of the IGRAs compared to the TST is compensated by saving the cost through targeting more of CXRs and offering of chemoprevention. The cost-effectiveness strategy is the two-step strategy whereby a positive TST is followed by IGRAs (Nienhaus *et al.*, 2011).

TB treatment should be both able to cure and reduce risk of transmission. Hence TB is an airborne infectious disease. A standardized TB treatment regimen is the most important control of PTB. Appropriate regimens, duration of treatment as well as adherence are required to achieve cure, prevent mortality and morbidity, reduce transmission of tuberculosis and prevent the emergence of MDR-TB (CPG, 2012).

The duration of TB treatment regimen for new case is six-month regimen consisting of two phases which are intensive phase and maintenance phase. Intensive phase is first two months from the day patients started TB regimen with daily dosages 2EHRZ (Ethambutol (E), Isoniazid (H), Rifampicin (R), Pyrazinamide (Z)) and followed by maintenance phase for next four months with daily dosages 4HR is recommended for newly-diagnosed PTB (CPG, 2002).

However, the interruption of TB treatment includes those patients treated as new cases of missed treatment for more than one month. If the smear or culture positive result indicate failure again, relapse or return after default treatment regimen is expected (CPG, 2002). The WHO recommended a retreatment regimen which consists of first-line drugs 2HRZES/1HRZE/5HRE if country-specific data present low or medium levels of MDR-TB in TB patients or if such data is not available. Drug sensitivity test (DST) must be done, once the results become available the drug regimen will be adjusted for patient appropriately (WHO, 2010).

When the interruption of TB treatment during intensive phase occurs with patients delaying the next treatment after the last visit of more than 14 days, patients need to restart TB regimen from the beginning. If patients delay within 14 days, patients will continue from the last dosages of their treatment. However, if the interruption was more

than or less than 14 days, the intensive phase of interruptions should be given the total number of planned dosage (CPG, 2012).

On the other hand, the interruption treatment occurred during maintenance phase which was after receiving 80% of the total planned doses, treatment may be stopped if sputum AFB smear was negative at initial presentation. If sputum AFB smears was positive, the treatment will be continued. Besides that, if patient received less than 80% of total planned doses with interruption lapse more than two months, they need to restart treatment from the beginning. However, if interruption lapse is less than two months, they need to continue treatment from the last date it stopped to complete full course of treatment (CPG, 2012).

Complications during Pulmonary TB treatment commonly occur in the lower and middle lobes especially in adults. Lobar or segmental atelectasis seen in children less than two years of age, involving the anterior segment of the upper lobe or the medial segment of the middle lobe. The organism may remain quiescent within this nodule, serving as a possible source of reactivation. The effusion is often sole manifestation except in infants which is usually unilateral, which may result in pleural thickening and calcification (Burrill *et al.*, 2007).

1.2 Geographical Information System (GIS)

Geographical information system (GIS) is a system for management, analysis and display of geographic information to represent a series of datasets. GIS is unique geographical database, based on structured database to describe the world in geographic design with certain features which were represented as polygons. GIS dataset provides a geographic

representation of some aspects in the world include ordered collection of sets of pints, line, and polygons, terrains and other surfaces in survey datasets.

In addition, ArcGIS software work with many data formats that supported data sources such as Excel files (.xls) and shapefiles (.shp) used in this study. GIS datasets include traditional tabular attributes that represent the geographic objects. Tables can be linked to the geographic objects by selected fields.

ArcGIS includes a set of map data layers that describe these boundaries with the levels of geography including countries, administrative areas, postal codes and others. ArcMap is the central application used in ArcGIS to display and explore GIS datasets in study area, where we assign symbols to create map layouts. ArcMap is also the application to create and edit datasets represents geographic information as a collection of layers and other elements in a map. Commonly, map elements include data frame containing map layers, a scale bar, north arrow, title, descriptive text, a symbol legend and other information

1.3 Burden of TB in Malaysia

TB is still one of the globally deadliest communicable diseases and ranks as the second leading cause of death from an infectious disease worldwide after HIV (WHO, 2014). TB mortality rate globally fell by an estimated 45% between years 1990 to 2013 and there was estimated; 9.0 million people developed TB and 1.5 million died from the disease in year 2013(WHO, 2014).

TB remains a significant health issue for Malaysia and most other developing countries in the past few years. Malaysia has been reporting an increasing number of

cases ranging from one to five percent annually. In 2009, 18,102 new cases were registered through the surveillance system which demonstrated the differences between states across the country. Six states had notification rates above the national rate of 63.9 per 100,000 which included Sabah, Kuala Lumpur, Kelantan, Sarawak, Terengganu and Pulau Pinang (Ministry of Health Malaysia, 2009).

The prevalence of TB varied geographically, which was considerably higher in urban compared to rural areas (WHO, 2014). Nowadays, TB infection in Malaysia recorded a decline by two percent in 2015 with 24,220 compared to 24,711 in the year 2014. However, Health Minister Datuk Seri Dr. S. Subramaniam said the total number of TB deaths was found increased by 5.8%, from 1,603 deaths in 2014 to 1,696 deaths in 2015 (Bernama, 2016).

Several factors were listed as they have been associated with TB mortality. Demographic factors, diabetic, HIV (Mohd *et al.*, 2011), non-compliance of DOTs (Naing *et al.*, 2001) and age and underweight (Birlie *et al.*, 2015) were associated with TB mortality. These factors were applied in spatial analysis in the mapping of TB mortality.

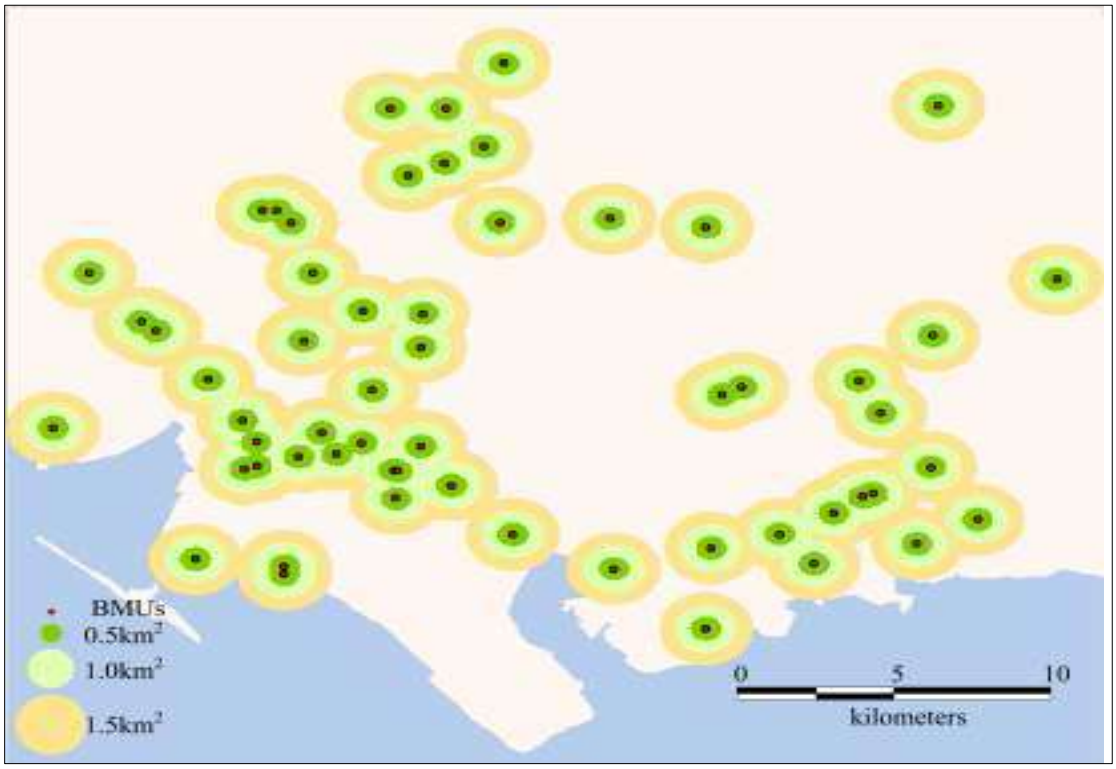
1.4 Direct Observed Treatment short-course (DOTs)

Intermittent drug regimen was designed for administration under Directly Observed Therapy (DOT). It has the potential to improve adherence to treatment. A standardized short-course TB treatment regimen of six months under DOTs by a trained supervisor was administrated to make sure patient takes medication (CPG, 2002). These trained supervisors include health personnel and ordinary trained persons. However, if this

regimen is not administered under DOT, it may lead to treatment failure, relapse and acquired drug resistance.

WHO recommends daily doses throughout the courses of anti TB treatment for new PTB cases. However, a daily intensive phase followed by thrice weekly maintenance phase is an option which provided that each dose is directly observed and patient has improved clinically. A maintenance phase with twice weekly dosage is not recommended since missing one dose means the patient receives only half the total dose for that week (WHO, 2010).

Location of health care is an important factor related to DOTs implementation. Its location can be allocated by GPS device. Accessibility of the health cares to the patients can be monitored by ring buffer GIS technique in the spatial analysis. Miandad *et al.* (2014) had shown accessible measurement which depicts the centers fall in 0.5 km radius area, and this accessibility revealed the location of health centers which were not planned to provide optimum services to population located under 1 km radius in cluster as shown in figure 1.4.



Legend

- BMUs
- 0.5 km radius area
- 1.0 km radius area
- 1.5 km radius area

Figure 1.4 Analysis of accessibility to BMUs

1.5 Rational of study

TB is major issued for the world wide health care includes our country Malaysia. For the past few years, the prevalence and mortality among TB cases increase rapidly except for year 2015 prevalence of TB in Malaysia was shown reducing the number in case notification. This study may help the Malaysia Ministry of Health (MOH) through the finding of outcome treatment of TB mortality. The finding of this study may provide information for the treatment strategy reduces the mortality. Furthermore, the finding from this study may also help MOH to improve effectiveness of DOTs in initial treatment and maintenance treatment through this study based on districts in Kelantan.

1.6 Research Question

i. Were there significant associations between socio-demographics factors (age, genders, and races) and TB cases?

ii. Were there significant associations between clinical characteristics factors (diabetic, smoking, BCG scar, sputum smear, sputum culture, chest x-ray, status HIV, DOTs intensive, DOTs maintenance treatment and distance) and TB cases?

iii. Were there significant associated factors (gender, race, sputum smear, sputum culture, status HIV, DOTs intensive, DOTs maintenance treatment and distance) between spatial areas of TB cases?

1.7 Research objective

1.7.1 General Objective

To study the spatial distribution and outcome of Tuberculosis (TB) cases in Kelantan.

1.7.2 Specific objectives

i. To determine the mortality among TB cases in Kelantan.

ii. To determine the spatial distribution of TB cases in Kelantan.

iii. To determine factors (age, gender, race, diabetic, smoking, BCG scar, chest x-ray, sputum smear, sputum culture, status HIV, DOTs intensive, DOTs maintenance treatment and distance) associated with TB mortality among TB cases in Kelantan.

1.8 Research hypothesis

i. There were significant associations between socio-demographics and of TB cases?

ii. There were significant associations between clinical characteristics and of TB cases?

iii. There were significant associations between spatial areas and of TB cases?

CHAPTER 2

LITERATURE REVIEW

2.1 Epidemiology of Tuberculosis

According to WHO, new notification cases of TB have been falling for several years and fell at a rate of 2.2% between 2010 and 2011 with the TB mortality rate has decreased to 41% since 1990. TB is also one of the top killers of women, with 300 000 deaths among HIV negative women and 200 000 deaths among HIV positive women in 2011 (WHO, 2012).

Press statement on 15 January 2014 reported that TB is fast rising as a non-communicable disease (NCD) with the higher death rate compare to dengue. Deputy Health Minister Datuk Seri Dr. Hilmi Yahya had stated recently that foreigners contributed to the sudden surge of TB cases in Malaysia and Health Ministry Director of Disease Control Division, Dr. Chong Chee Keong also reported that there has been a steady increase of TB cases from 2007 to 2011 with the notification rate of 72 cases per 100,000 population in 2011 to 78.8 cases per 100,000 population in 2012. The mortality rate due to TB is between 5.3 and 5.8 deaths for every 100,000 population as shown in Table 2.1 (Malaymail Online, 2014).

Table 2.1 Breakdown TB cases and death according to states in Malaysia from Year 2007-2012

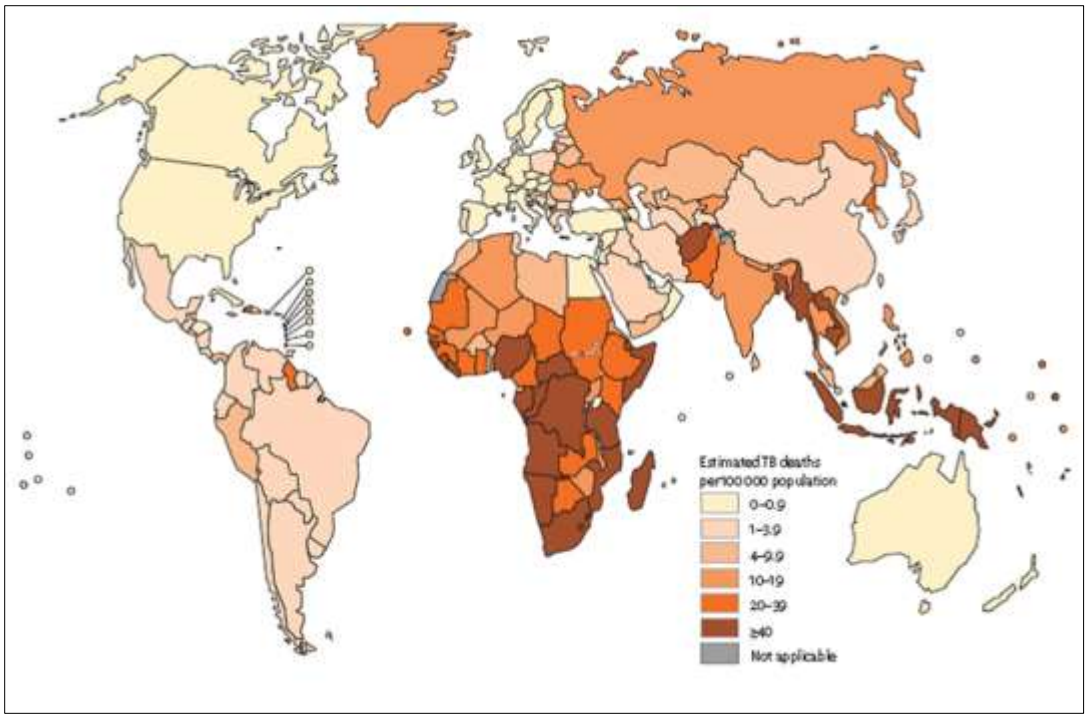
	2007		2008		2009		2010		2011		2012	
STATE	**CASES**	**DEATHS**	**CASES**	**DEATHS**	**CASES**	**DEATHS**	**CASES**	**DEATHS**	**CASES**	**DEATHS**	**CASES**	**DEATHS**
Perlis	112	13	129	12	119	18	121	18	141	18	185	13
Kedah	812	63	843	61	903	78	1000	101	1084	85	1174	100
Penang	880	98	943	127	1039	150	1062	148	1126	128	1245	117
Perak	1210	181	1160	152	1250	179	1389	151	1309	159	1554	190
Selangor	2484	84	2374	87	2342	100	2829	111	3242	216	3560	108
WPKL/ Putrajaya	1253	22	1387	47	1429	57	1455	33	1907	83	1906	64
N.Sembilan	395	35	506	44	408	41	426	35	449	35	480	16
Malacca	349	58	337	48	339	54	395	32	511	48	546	55
Johor	1591	188	1700	189	1855	180	2058	134	2038	151	2046	182
Pahang	723	116	779	109	838	130	806	107	788	132	890	112
Terengganu	661	107	730	125	762	125	664	108	667	81	733	114
Kelantan	**1265**	**289**	**1354**	**295**	**1324**	**205**	**1333**	**232**	**1448**	**232**	**1436**	**140**
Labuan	45	3	67	3	66	2	80	3	106	1	99	1
Sabah	3433	164	3376	140	3515	179	3728	233	3794	188	4426	245
Sarawak	1705	83	1821	93	1913	84	1991	111	2056	87	2430	63
Total	**16,918**	**1,506**	**17,506**	**1,532**	**18,102**	**1,582**	**19,337**	**1,557**	**20,666**	**1,644**	**22,710**	**1,520**

Source: Malaymail Online on 15January 2014

TB cases in Hospital Kota Bharu found that 58 patients died in 1999. A majority of them died (74%) without completing the 6-month regimen, six patients (10.3%) were diagnosed as having disseminated milliary TB; one patient was reported as having toxoplasmosis and cryptococcal infections while the rest were due to TB disease who had not completed the treatment, or from other causes which not stated in the patient records (Naing *et al.*, 2001).

2.2 Mortality of TB patients

Globally, according to WHO report for TB deaths among HIV negative averaged 16 cases per 100,000 population, meanwhile when included TB deaths among HIV-positive, the average were 21 cases per 100,000 population in 2014. However, these might vary for Western Europe and African regions as well as five higher burden countries; Afghanistan, Bangladesh, Cambodia, Indonesia and Myanmar, where there are developed countries in Western Europe; Canada, the United States of America, Australia and New Zealand, TB patients mortality rate are less than one per 100,000 population and for most of African region as well as five high burden countries more than 40 died per 100,000 population (WHO, 2015).



Source: WHO (2015)

Figure 2.1 Estimated TB mortality rates excluding TB deaths among HIV-positive 2014

Figure 2.1 were adapted from WHO report in 2015, these figures showed the globally estimated TB mortality rates which exclude death among TB/HIV. The study in China in 2010, showed the mortality rates due to PTB were higher among those who living in western and rural areas (Zhang *et al.*, 2012).

However, Nájera-Ortiz *et al.* (2008) studied in Los Altos, a region Chiapas in Mexican states found high rates among PTB, results of home visits follow-up patients located 78 (18%) already died, these 40 cases were associated with PTB but 33 (83%) died without receiving any medical treatment.

In Malaysia, TB mortality in Sabah had declined since 1995 to 2001 had 14 deaths per 100,000 population in 1985 compared to 7 deaths per 100,000 population in year 2001 (Dony *et al.*, 2004). However, a study done in Kota Bharu found the mortality rate of PTB patients was 6.8 per 100,000 populations living in urban area was 59.3% (Mohd *et al.*, 2011). In addition, Abdul Rasam *et al.* (2016) studied local

TB cases at Section U19, Shah Alam to define potential high-risk areas revealed that the majority of hot spot areas are close to urban cities such as Damansara, Petaling Jaya, and Kuala Lumpur.

2.3 ArcGIS software

The ArcGIS software is a commercial mapping software which was difference with open source because ArcGIS more user-friendly with high-powered and versatile commercial mapping software. ArcGIS does not only offer intuitive and easy-to-use interfaces but also useful, built-in geospatial tools. Besides that, the spatial analysis is equipped with spatial technologies designed to quickly perform everything from network analysis, land-use analysis and others. This commercial mapping software makes the analysis as simple as possible.

In addition, it is an excellent technical support because GIS was distributed by professional and well-established companies, commercial mapping software which typically includes superb technical support, ranging from extensive FAQ sections to email assistance, to over-the-phone inquiries. ArcGIS software process involves a great number of spatial analysis and geoprocessing capabilities typically do its own terms. This forces us to work within the confines of the software, stifling technical own plugins and workarounds. Then, scalability issues make GIS applications development easy with built-in app-builder features and comes with some scalability concerns.

Open source mapping software such as MapServer, PostGIS, QGIS, SAGA GIS and others open sources GIS software was well-functioned for GIS application development. Open source mapping software does not possess app-builders, allows for cheap, personalized, and specific application development. This software allows

developers to tailor their apps to meet exact specifications, while costing nothing of the software licensing fees.

On the other hand, open source mapping software allows developers to have absolute license over the apps they create. There are no strict software standards to keep developers confined from doing exactly what they want to do. While many commercial GIS software apps are only made for Windows operating systems, open source GIS software works with Windows, Mac, Linux, and others.

The choice of open source or commercial GIS mapping software depends on the project. The commercial GIS software is more user-friendly, and excels in the areas of spatial analysis, data manipulation, and data management. Open source GIS software is better-suited for situations in which more freedom and customization is needed. Though open source technology is free, we must still have to invest in GIS developers and analysts to get the technology working right. Good applications using open source GIS tools include custom GIS app development and web mapping.

2.4 Projection of coordinates systems in GIS

Coordinate system is also known as map projections that was designed for spatial data. There are two types of projection of coordinate systems which were geographic and projected. A spherical coordinate system such as latitude-longitude refers to geographic coordinate systems. Geographic coordinate system (GCS) uses a three-dimensional spherical surface to define locations on Earth. GCS includes an angular unit of measurement, a prime meridian, and a datum based on a spheroid. The spheroid defines the size and shape of the Earth model, while the datum connects the spheroid to the Earth's surface. A point is referenced by its longitude and the latitude

values are angles measured from the earth's center to a point on the earth's surface. The angles are often measured in degrees.

Projected coordinate system (PCS) is defined on a flat with two-dimensional surface. PCS has constant lengths, angles, and areas across the two dimensions. PCS is always based on GCS, sphere or spheroid includes a map projection, a set of projection parameters that customize the map projection for a particular location, and a linear unit of measure. Each map projection has a set of parameters that must be defined. The parameters specify the origin and customize a projection for the area of interest. Angular parameters use the GCS units, while linear parameters use the PCS units.

There are many types of map projection such as Cassini, Mercator, Transverse Mercator, Universal Transverse Mercator (UTM) and others. This study used Kertau (RSO) projection and UTM zone 48N (Transverse Mercator). This projection is suitable for Malaysia with the origin of the projection easting 194,617 and northing 442,639 in zone 48N (Department of Survey and Mapping Malaysia, 2009).

Kelantan is a state located in the north of Malaysia, with the capital city of Kota Bharu. The latitude of Kelantan, Malaysia is 187243 and the longitude is 652238 (Department of Survey and Mapping Malaysia, 2009).

2.5 Factors associated with mortality of TB cases

2.5.1 Gender

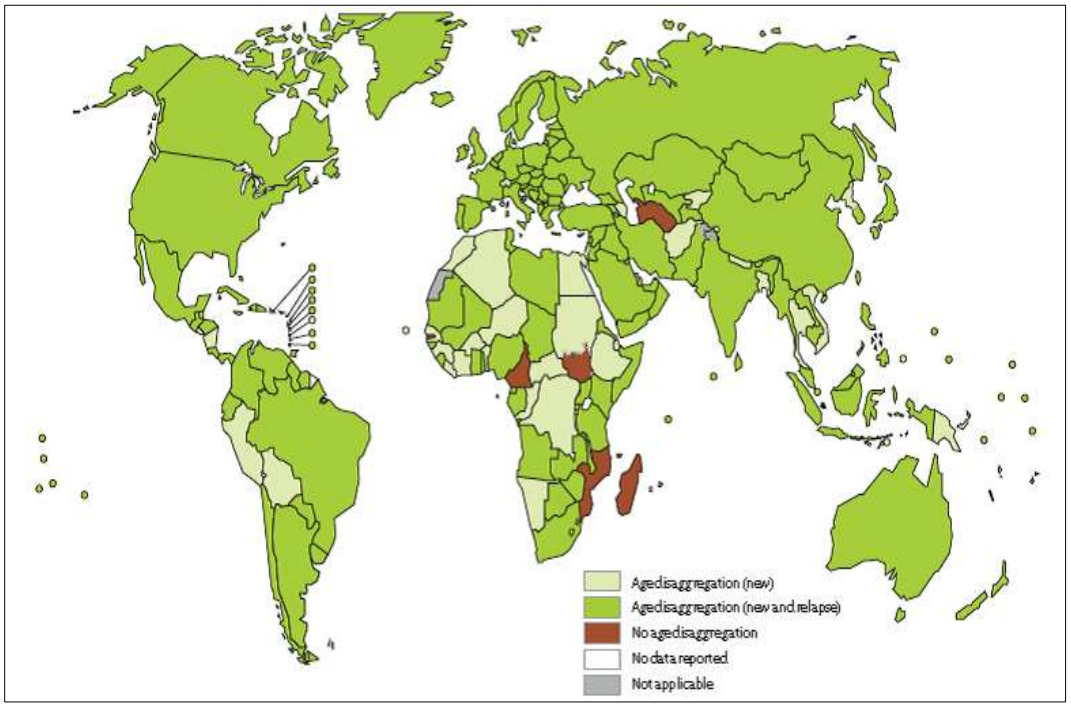
In the year 2011, the World Health Organization reported that TB is one of the top killers among women with 300 000 deaths among HIV negative women and 200 000 deaths among HIV positive women (WHO, 2012). About 60% of TB cases and death occurs among men but it was also comparatively high among women (WHO, 2014).

A study in China had found that the mortality due to TB were higher in males (70.5%) compared to females (29.5%) (Zhang *et al.*, 2012). Low *et al.* (2009) reported that mortality among TB cases in Singapore was higher in males with 80.3% compared to female which was only 19.7%.

A previous study found that TB among Malaysians and foreigners occurred commonly in men than female in both groups but there was no statistical difference between both groups ($p>0.05$) (Nissapatorn *et al.*, 2007). However, Ariffin *et al.* (2015) found that a majority of TB cases in Gombak district were men (63.2%).

2.5.2 Age

Figure 2.2 shows that the estimates of TB incidence and TB mortality were disaggregated by age and gender. Specifically, estimates are shown for men which are age defined as males aged older than 15 years compared with women which is defined as female age younger than 15 years (WHO, 2015).



Source :WHO (2015)

Figure 2.2 New and relapse TB case notifications disaggregated by age, 2014

A study from Isfahan Province from 2006 to 2011 reported that mortality in people aged over 65 had a higher risk of death (Shahrezaei *et al.*, 2015). The incidence and prevalence of TB varies in different age groups and majority of patients aged 21 to 60 years age group (69.5%) (MoH, 2012).

An audit of TB deaths which was done among 54 TB patients in Penang hospital found that about 48% who died were aged under 50 years (Hooi and Goh, 1995). However, Atif *et al.* (2014) reported that the mean age of TB cases was 55 years old approximately.

2.5.3 Race

In the United States, the risk of TB is associated with racial or ethnic minority which was higher among US born blacks, hispanics and Native Americans than whites. The risk of TB was done between racial or ethnic, evaluated by the lowest and highest quartile which had shown the risk concentrating in the lowest quartile (Cantwell *et al.*, 1998).

Nissapatorn *et al.* (2005), found that the TB cases were higher in Malay (58.1%). Ibrahim (2010) did a study on TB patients who were admitted to University of Malaya Medical Centre (UMMC) year 2000-2007; and found Malays contributed the most cases, (43%), followed by Chinese (22%), Indians (17%) and foreigners (18%).

2.5.4 BCG Scar

Bacillus Calmette-Guerin (BCG) is a vaccine for TB disease widely used in many countries with high prevalence of TB to prevent childhood tuberculous meningitis and miliary disease. Many foreign-born persons have been BCG-vaccinated.

A study in American Indians and Alaskan Natives showed that the total number of TB cases were 102 culture confirmed (n=27 in the BCG group and n=63 in the placebo group). The case rate from 1948 to 1998 studied found that the BCG group was 66 cases per 100,000 population years and placebo group was 138 cases per 100,000 population years were diagnosed with TB (Aronson *et al.*, 2004).

Children with a BCG scar and positive tuberculin skin test-reaction had substantially lower mortality during follow-up and TB infection was not likely a confounder of results because their estimates were not affected by excluding children with household contact with a TB case (Roth *et al.*, 2006).

In Malaysia, BCG vaccine has been widely administered for more than eighty years and it mimics the natural immune response to infection. BCG vaccine is given to all newborns and vaccination for children with no scar is done at entry or earlier at primary school (CPG, 2002). However, BCG vaccine cannot be given to persons who are immunosuppressed or who are likely to become immunocompromised. BCG also cannot be given during pregnancy (CDC, 2011b).

2.5.5 History of Smoking

A study in India found that TB death was higher ever among smoker (61%) in Chennai urban India (Gajalakshmi *et al.*, 2003). The finding from other studies, the male who smoked was associated with increased TB incident from 2001 to 2005 (Jee *et. al.*, 2009).

Asrul M. *et al.* (2013) reported that 79.6% cases with TB/HIV co-infection were smokers. On the other hand, Dujaili *et al.* (2011) reported that these 12.0% TB cases who had smoked died and it was associated with dying of TB infection in Penang.

2.5.6 Comorbidity

Comorbidity presents simultaneously in a patient who had one or more other diseases that influence risk of TB mortality. A few comorbidity were include in this study which were diabetic history, smoking history, HIV infection, positive; sputum smear and sputum culture, CXR finding and compliance with DOTs treatment.

2.5.6 (a) History of Diabetes

A study by Alisjahbana et al. (2006) found that Diabetes Mellitus (DM) was common in patients with TB and the study reported that 13.2% were diabetics. In addition, Dooley *et al.* (2009) did a study on the impact of DM with TB outcome treatment and found that 14% of TB patients in Maryland had DM. They also reported that those patients with DM had two times odds of death compared to patients without DM.

Liew *et al.* (2015) revealed that 15.4% of TB cases registered under Malaysia Nation Tuberculosis Surveillance Registry were diabetics and 12.1% of them died during TB treatment. Compared to other study, they found both group TB diabetic and TB non diabetic had no difference in the radiological finding with opacity or cavity of the upper lobe involvement being 89% and 91% in TB diabetic and non-diabetic group. TB diabetic showed to have more treatment success (Nissapatorn *et al.*, 2005).

2.5.6 (b) HIV Status

A study in New York City found the mortality from TB cases was high even among patients without multidrug resistance who were not known to be infected with HIV and most HIV positive patients with delayed therapy died (Pablos-Méndez *et al.*, 1996).

For rural area studies, it was found that the Saharan in Africa's deaths were attributed to TB after three months, and very few HIV negative subjects died but progressively more people with HIV died. This was mainly due to the high mortality rate in all patients in their study, but particularly the relatively higher death rate in the HIV negative group (Kelly *et al.,* 1999).

This was similar to a study on the impact of mortality among TB/HIV cases by Connolly *et al.* (1998) who demonstrated that mortality rates were high among HIV positive case which was 2.4 times higher compared to HIV negative, and 1.4 times higher compared to those with unknown HIV status.

2.5.6 (c) Sputum Smear Test

WHO (2014) reported that from 144 PTB cases that were processed; 107 were smear-positive and 37 were smear-negative or culture- positive. Balabanova *et al.* (2006) who did a study in Samara, Russia reported that a majority (97.7%) of smear-positive new cases converted the sputum finding at end of the intensive phase treatment. However, 3.6 % smear positive cases had died compared to 11.3% cases of smear-negative.

The other study, in Hlabisa district of a rural South Africa reported that the mortality rate among those who was diagnosed with TB had increased in year 1991/92 from 9.2% to 13.4% in 1995; from the cases of mortality among smear-positive case, it had increased from 4.4% to 10.3% respectively (Connolly *et al.*, 1998).

In Sabah, a proportion of sputum smear positive cases in four districts which is Kota Belud, Kunak, Persiangan and Lahad Datu reported that sputum smear negative (50%) was more than sputum smear positive (Dony *et al.,* 2004). A study in Penang

showed that the findings on treatment outcome of PTB patients with smear positive indicated that the treatment success rate was 67.26% which was lower than WHO targets (Atif *et al.*, 2014).

2.5.6 (d) Sputum Culture Test

A previous study by Chan *et al*. (2004) found that from 162 subjects who were sufficient to evaluate outcome, 137 sputum culture (85%) were converted to negative (initial favorable response) compared to 25 (15%) failed conversion to negative (microbiologic failure) and 43 other patients had insufficient sputum samples. The sputum culture results among PTB cases were 27.4% of patients. However, about 55% were done but results were pending (Ariffin *et al*., 2015).

2.5.6 (e) Chest X-ray (CXR) Finding

Chest X-ray is one diagnoses of TB,and CXR often reveals lesion in apical and posterior segments of upper lobes. The lesion in active PTB usually has little or no fibrosis or calcification (CPG, 2002). WHO (2014) reported that a total of 107 smear-positive TB cases were also positive in chest X-ray finding 94 (88%) and a total of 144 bacteriologically confirmed cases, 128 (89%) had a positive chest X-ray.

A study in Nairobi, Kenya found the sensitivity and specificity of CXR score among smear-negative TB suspects were 80% and 67% respectively using chest CXR as a screening tool in all suspects; sensitivity and specificity of the score for TB or no TB was 92%, respectively 63% (van Cleeff *et al.*, 2005). A study at urban, TB clinic in Nashville, Tennessee, USA reported that nine percent had normal CXRs among patient who were HIV infected and six percent of them from non HIV-infected had normal CXRs (Pepper *et al.*, 2008).