EPIDEMIOLOGICAL AND AWARENESS STUDY OF TUBERCULOSIS IN BATU PAHAT, JOHOR, MALAYSIA

SHUAIBU BABAJI SANUSI

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Faculty of Science, Technology and Human Development
Universiti Tun Hussein Onn Malaysia

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DEDICATION

This thesis is first and foremost dedicated to Almighty Allah for seeing me through. Then to my parents Alhaji Sanusi B. Mohammad and Hajiya Binta Sanusi for their unwavering support, advice, encouragement and prayers which guided me towards this achievement, I am very proud of them and may Almighty Allah (S.W.T) reward them abundantly. The thesis is also dedicated to my siblings, uncles and aunties for their prayers and support.

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ABSTRACT

Tuberculosis (TB) remains one of the serious infectious diseases and has been characterized worldwide as an epidemic by World Health Organization (WHO). TB is still a public health problem in Malaysia. Baseline information on the disease situation is one of the prerequisites for the development of appropriate control measures. The cornerstone in proper management of TB patients is ensuring high awareness in communities about TB. Thus the current research is directed to investigate the epidemiology of TB, determined the level of public awareness of TB and some factors that are responsible for the emergence of TB. Retrospective method was used for collecting epidemiological data from the Batu Pahat chest clinic. All registered TB patients (total of 1213 patients) from 2008 to 2013 in Batu Pahat Chest Clinic were included in the study. On the other hand, the awareness study was carried out by the use of questionnaires. A two-stage cluster sampling method was used. 600 respondents were targeted which form the study sample. However, 498 questionnaires were returned. Descriptive data analysis was employed to describe the results in frequency and percentage distribution. It was discovered that there was an annually increase in TB incidence with pulmonary TB the most common infection in Batu Pahat. Almost all (92.7%) the TB cases were new. On the other hand, majority (87.0%) of respondents have heard about TB. Common symptoms identified by respondents were coughing for over 2 weeks (51.8%), hemoptysis (49.2%) and difficulty in breathing (50.2%). Smoking cigarette (74.3%), living with individual having chronic cough (71.5%) and HIV/AIDS (65.7%) were the common risk factors of TB identified by respondents. Most of the respondents (83.5%) were aware of the existence of TB drugs. However, the standard DOTs treatment duration of 6-9 months was identified by few (12.4%) respondents. This research provided information regarding TB status in Batu Pahat. The level of awareness among Batu Pahat general public about TB is fairly good. Meanwhile, more need to be done especially on diabetes as the risk factors of TB and treatment duration.

ABSTRAK

Tuberkulosis (TB) atau batuk kering merupakan satu daripada penyakit berjangkit yang paling serius sedunia dan nyatakan sebagai wabak oleh Pertubuhan Kesihatan Sedunia (WHO). TB kekal menjadi masalah penyakit umum di Malaysia. Maklumat asas tentang keadaan penyakit ini merupakan salah satu prasyarat untuk membangun kan langkah-langkah kawalan yang sesuai. Hal utama dalam pengurusan pesakit TB adalah bagi memastikan kesedaran yang tinggi wujud di kalangan komuniti tentang tibi. Oleh itu, penyelidikan ini telah di jalan untuk mengkaji epidemiologi TB, menentukan tahap kesedaran awam tentang TB dan beberapa faktor yang menjadi penyebab kemunculan TB. Kaedah retrospektif digunakan untuk mengumpul maklumat epidemiologi daripada Klinik Dada Batu Pahat. Kesemua pesakit TB berdaftar (berjumlah 1,213 pesakit) dari tahun 2008 hingga 2013 di Klinik Dada Batu Pahat terlibat dalam kajian ini. Selain itu, kajian tahap kesedaran dijalankan menggunakan kaedah soal selidik. A dua peringkat kaedah persampelan kelompok telah digunakan. Seramai 600 responden sasaran menjadi sampel untuk menjawab persoalan kajian. Bagaimanapun, hanya 498 soal selidik dikembalikan. Analisis data diskriptif digunakan untuk menggambarkan keputusan dalam bentuk kekerapan dan taburan peratus. Didapati peningkatan tahunan bagi insiden TB dengan tibi paru-paru merupakan jangkitan yang paling biasa di Batu Pahat. Hampir semua (92.7%) kes tibi adalah baru. Didapati, majoriti (86.9%) responden mengetahui akan TB. Tanda-tanda biasa yang dikenalpasti oleh responden adalah batuk melebihi dua minggu (51.8%), hemoptesis (49.2%) dan kesukaran bernafas (50.2%). Merokok (74.3%), tinggal bersama individu mempunyai batuk kronik (71.5%) dan HIV/AIDS (65.7%) merupakan faktor risiko utama tibi yang dikenalpasti oleh responden. Kebanyakan responden (83.5%) tahu akan kewujudan ubat TB. Walau bagaimanapun, piawai rawatan DOT dalam tempoh 6-9 bulan dikenalpasti oleh beberapa (12.4%) responden. Penyelidikan ini memberi maklumat berhubung status tibi di Batu Pahat. Tahap kesedaran masyarakat umum di Batu Pahat tentang tibi adalah memuaskan.

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CHAPTER 1

INTRODUCTION

1.1   Background of the research

Tuberculosis (TB) remains one of the most serious infectious diseases both in terms of disease burden and resistance to conventional antibiotic therapy and has been characterized worldwide as an epidemic by World Health Organization (WHO) (Aldwell *et al.,* 2005; Dou *et al.,* 2008; Nissapatorn *et al.,* 2005). TB is endemic in all countries in the world and it kills more people today than any other bacterial disease (Hunter *et al.,* 2006).

It is estimated that one third of the world population i.e. around 2 billion people are latently infected with TB. Around 10% of TB infected persons become sick with active disease, and this high level of latent infection is a suggestion of long-term co-existence of human host and bacterial pathogen (Besharat, 2009; Thomas *et al.,* 2007; Hershkovitz *et al.,* 2008). WHO declared TB in 1993 as a global public health emergency (Rennie, Pai, & Selvadurai, 2011; Abdallah & Ali, 2012), and it is the only disease that has been ever declared as global emergency by WHO (Palomino, 2009).

TB is one of the most important infectious causes of morbidity and mortality among adults (Nissapatorn *et al.,* 2003; Liao *et al.,* 2012). It causes more adult deaths in the world than any other communicable disease in developing countries where 95% of all TB cases occur (Itah & Udofia, 1997). Between 8 to 9 million people develop the disease (Atif *et al.,* 2012; Piuri, Jacobs, & Hatfull, 2009), and approximately 2 million die from TB annually (Nissapatorn *et al.,* 2003; Rennie *et*

al., 2011). With the emergence of drug resistance and the HIV/AIDS epidemic, TB is making a resurgence all over the world (Thomas *et al.,* 2007). In 1995, it was estimated that 8.8 million cases of TB occurred worldwide, 5.5 million (95%) of them in developing countries of Asia, Africa 1.5 million, the Middle East 745,000 and Latin America 600,000. Almost 3 million deaths from TB occurred in 1995, 98% of them in developing countries (Jetan *et al.,* 2010). It is miserably true that 75% of TB cases in developing countries engage adults in the most productive age group, 15-50 years (Itah & Udofia, 1997). The worldwide burden of TB mainly lies in the 22 high prevalence countries and about 50% of prevalence occurs in 5 countries of South East Asia (Liao *et al.,* 2012), namely; India, Indonesia, Bangladesh, Thailand and Myanmar (Tasnim, Rahman & Hoque, 2012).

Around early 1940s and 1950s, TB was the number one cause of death in Malaysia, TB patients were admitted to many sanatoria in various parts of the country and were always managed by surgical means. Chemotherapy of TB became available only in the late 1950s. Malaysian government launched its National TB Control Program (NTP) in 1961 when realized its seriousness (Jetan *et al.,* 2010). Despite control and preventive measures taken, TB is still a public health problem in Malaysia (Rafiza, Rampal & Tahir, 2011). TB was the second most common notifiable communicable disease in Malaysia in 2001 (Jetan *et al., 2010).* Apart from being a deadly disease, TB is also an expensive disease which can give a great economic problem to the country. The TB drugs cost constituted the highest proportion of the cost to the public services (31.7%) while the cost to the patient constitutes 80% of the total treatments cost (Nor *et al.,* 2011).

The re-emergence of this predicament can be attributed to the high influx of foreign workers from high TB burden neighbouring countries such as India and China into the community (Rafiza *et al.,* 2011) and this become one of the reasons why TB could be called "a disease without borders" in Malaysia (Nissapatorn *et al.,* 2003). The immigrant workers, particularly those from high TB burden neighbouring countries constitute about 10% of TB notified cases in Malaysia (Jetan *et al.,* 2010). In Sabah, East Malaysia, immigrants contributed more than 24% of the newly detected TB cases (Nissapatorn *et al.,* 2003).

1.2   Problems

Despite full implementation of Direct Observation Therapy short-course (DOTs) programme and accessibility to TB drugs, the number of TB patients in Batu Pahat chest clinic progressively increased every year.

Baseline information on the disease situation is one of the prerequisites for the development of appropriate control measures. Batu Pahat is an endemic area of TB and no previous study has documented the epidemiology of the disease.

The cornerstone in proper management of TB patients is ensuring high awareness in communities about health in general and pulmonary TB. To the best of our knowledge very few studies have been conducted on assessing public awareness of TB in Malaysia. Thus, the current research directed to investigate the epidemiology of TB, the level of public awareness of TB with regard to clinical symptoms, related risk factors, treatment and attitude have been determined and some factors that are responsible for the emergence of TB have also been discussed.

1.3   Research Questions

1. How is the epidemiology of TB in Batu Pahat, Johor?
2. What is the level of knowledge and awareness of TB infection in Batu Pahat district, Johor?
3. What are the main factors of the emergence of TB cases in Batu Pahat district, Johor?

1.4   Aim and Objective

TB incidence remains endemic in the country. Due the emergence of TB cases among population living in the border of neighbouring countries, Batu Pahat is seen as one of the areas at risk for TB incidence. Therefore, this study aims to investigate the pattern of TB incidence using reconnaissance and direct visit to health

institutions responsible for getting clearer picture focusing in Batu Pahat region. The main objectives of this project are;

1.   To investigate the epidemiology of TB in Batu Pahat, Johor.

2.   To determine the knowledge and level of awareness (of the symptom, risk factors, and Treatment) of TB infection in Batu Pahat district, Johor.

3.   To identify the main factors of the emergence of TB cases that may exist in Batu Pahat district, Johor.

These studies consist of the following part; epidemiological study and awareness survey study. The epidemiological study was carried out at the chest clinic Batu Pahat by reviewing the patient's medical records and extracting some information such as: socio-demographic profiles, TB incidence cases, type of TB, TB case category, clinical presentation, co-morbidity and breaking down of TB patients by district.

The awareness study was carried out by the used of questionnaires, where the questionnaires were administered to the Batu Pahat general public. It consists of the questions on; demographic profile, awareness, knowledge and attitude of the respondents about TB risk factors, TB clinical symptoms, TB treatment and the attitude when any of the symptoms is suspected. Factors that are responsible for emergence of TB were discussed based on the result of both epidemiological and awareness studies.

1.5   Scope of the study

The scope is restricted to matters arising from epidemiology and awareness of TB in Batu Pahat. Three sub-districts were selected in the case study area. These sub-districts were Sri Gading, Simpang Kanan and Peserai. Preliminary study showed that TB incidence is increasing annually. The motivating factor is that no study was carried out on TB in Batu Pahat. The study investigated the epidemiology of TB and determined the level of awareness of TB in Batu Pahat. The study used secondary data from Batu Pahat Chest Clinic for the investigation of epidemiology of TB whilst, for the level of awareness, questionnaires were utilized. The targeted respondents were general public.

1.6   Significance of the research

Particularly in developing countries, epidemiological surveys are expensive and faced with so many constraints. In this study, extracting epidemiological data from hospital based records is well utilized which is less expensive source. Epidemiological studies are more essential for local policy makers concerning TB control, as vulnerable groups are usually highlighted. This study is well applicable in this respect (Abdallah & Ali, 2012). Epidemiological study of TB in each area causes an increase in knowledge and create a room for the successful implementation of a national TB control programme (Moulana *et al.,* 2005; Roy & Chauhan, 2003). Likewise, public awareness of TB plays a significant role in disease control. Lack of awareness of TB along with delay in early detection and inadequate health service resources has been associated with low TB detection rates and the interruption of TB treatment (Koay, 2004; Lu *et al.,* 2010). In contrast, enhanced public awareness of TB could prop up patient detection, early diagnosis and treatment completion. Because public awareness of TB has a significant impact on TB control, the Global Plan to Stop TB 2006–2015 and the Stop TB Strategy launched by the World Health Organization (WHO) positioned advocacy, communication and social mobilization (ACSM) as important components in TB control programmes (Lu *et al.,* 2010).

Delayed presentation is considered as a basis for growing burden of TB in developing countries. Making diagnosis and treatment of TB universally available and accessible is one of the objectives of 'Stop TB' programme. People can only access these services if they are aware of the symptoms of disease, seek early care, and adhere to treatment. More so, early diagnosis and adherence to treatment may decrease emergence of drug resistant strains (Gilani & Khurram, 2009). Knowledge and awareness regarding various aspects of TB among masses is very important to address this problem (Das *et al.,* 2012).

The international society has adopted early case detection and treatment of infectious cases as the main strategy to reduce pulmonary TB infection. To enhance case detection and promote treatment completion, it is important to advise suspected sufferers to seek medical help early. Increasing knowledge about TB could help in achieving this goal; raising TB awareness among the general public should therefore be a main concern for TB control programmes (Lu *et al.,* 2010). Many international

studies have reported poor knowledge, attitudes and practices about TB (Mushtaq *et al.,* 2011).

CHAPTER 2

LITERATURE REVIEW

This chapter emphasized on the related information on TB causative agent (*Mycobacteruim tuberculosis),* epidemiological study of TB, awareness study of TB and Batu Pahat itself. The sub-headings below give a brief review of the literatures.

2.1 History of TB

TB is an ancient disease, it has plagued humankind throughout known history and human prehistory. It can be hypothesize that the genus *Mycobacterium* was originated more than 150 million years ago (Daniel, 2006). Progenitor of *M. tuberculosis* was present in East Africa as early as 3 million years ago, and might have already affected early hominids (Gutierrez *et al.,* 2005; Daniel, 2006; Ahmad, 2011). TB was present in Egypt during the reign of the pharaohs, evidence of spinal and rib lesions pathognomonic of TB have been identified in mummies from that period (Chernick, 2004).

The earliest evidence of TB in human and animals was provided by bone finds chiefly fragments of vertebrae – showing the gibbus typical of tuberculous Pott's disease. The oldest examples of spinal TB, in form of fossil bones, date back to about 8000 BC (Herzog, 1998).

TB was well known in old Greece, then it was called phthisis, Hippocrates clearly recognized TB and also understood its clinical manifestation. ''Phthisis makes its attacks mainly between the age of eighteen and thirty-five,'' he wrote in his aphorisms, clearly recognizing the preference of young adults for active TB

(Daniel, 2006). English speaking people called it consumption, and later the "Captain of all the Men of Death," and "The Great White Plague." The enlarged cervical lymph nodes were called "Scrofula" or "The King's Evil" (Dodor, 2009).

Some few people, suspected the contagious nature of TB. Spain and Italy, for example, had policy to prevent its spread as early as 1699. Patients affected were strictly isolated, and when they died, their bedding and the doors to their rooms were burned and their rooms were re-plastered (Dodor, 2009).

In 1790, Benjamin Marten first suggested that TB is infectious in nature, who attributed the disease to ''some certain species of animalcula.'' French military surgeon Jean-Antoine Villemin demonstrated the infectious nature of TB in 1865 convincingly when he inoculated a rabbit with ''a small amount of purulent liquid from a tuberculous cavity'' removed at autopsy from an individual who died of TB, it was generally discredited at that time (Daniel, 2006; Dodor, 2009).

This history changed dramatically on March 24, 1882, when a German physician and microbiologist Hermann Heinrich Robert Koch made his reasonably famous presentation, Die Aetiologie der Tuberculose, to the Berlin Physiological Society after he was able to identify and isolate the causative organism *M. tuberculosis* (Daniel, 2006; Dodor, 2009; Cole *et al.,* 1998). As early as 1886, Antonin Marfan recommended the existence of acquired immunity to TB. Albert Calmette and Camille Gue´rin in 1908 borrowed Pasteur's technique to create a vaccine against TB. After serendipitously knowing that growth in ox bile diminished the virulence of *M. bovis*, Calmette and Gue´rin carefully performed 230 serial passages of a single isolate of the organism, sufficient for it to lose its ability to cause progressive fatal TB in a variety of animals: guinea pigs, rabbits, cows, horses, monkeys, and chimpanzees. These bacteriologists called their vaccine Bacille Bilie´ (from bile) Calmette et Gue´ rin, which was shortened to Bacille Calmette Gue´ rin, and then to its household name, BCG (Murray, 2004; Dodor, 2009).

Benjamin Weill-Halle and Raymond Turpin were the first people to use this vaccine in 1921, particularly in children at high risk of infection, and soon became popular throughout the rest of Europe (Herzog, 1998). Following the initial success, it is use all over the world. WHO in 1940s, started promoting mass vaccination with BCG in its campaign to control TB (Dodor, 2009). The medications that were used in the treatment of other diseases were also tried on TB. For example, cod liver oil,

prescribed for rheumatism was later given for TB in the late eighteenth century (Dodor, 2009). In the absence of effective drugs, other measures were tried, such as advising patients to move to warmer climates. A movement towards high altitude, where the air was believed to be helpful, began in 1859 with establishment of a sanatorium for TB patients by a German physician, Herman Brehmer (Dodor, 2009). Later, surgical resection (removal) of the affected parts of the lung became the predominant observe in most parts of the world (Dodor, 2009).

The discovery of para-amino salicylic acid (PAS) by Jorgen Lehmann in 1943 and of thiosemicarbazone by Gerhard Domagk during wartime Germany and culminating in 1945 yielded the first therapeutic agents with efficacy in the treatment of TB (Daniel, 2006; Murray, 2004). In 1943 Albert Schatz, Elizabeth Bugie, and Selman Waksman reported the isolation of streptomycin from soil fungus and showed it to be active against the tubercle bacilli in vitro, leading to its administration for the first time to a human patient on November 20, 1944, the first antibiotic and first bactericidal agent effective against *M. tuberculosis* (Daniel, 2006; Dodor, 2009; Murray, 2004). Within a few months it had been used with dramatic results to treat a young woman with TB (Daniel, 2006).

Isoniazid followed in 1952, the first oral mycobactericidal (Daniel, 2006; Dodor, 2009). For nearly 15 years, "triple therapy" remained the standard treatment for all forms of TB. Not only did sanatoriums closed, but also therapeutic mainstays such as pneumothorax and pneumoperitoneum became outdated, and surgical measures such as thoracoplasty and the surgeons who did them vanished. Finally, the availability of rifampin in the mid-1960s and the rejuvenation of pyrazinamide, an older agent that had been suspended owing to its toxicity, allowed the development of current "short-course" antiTB chemotherapy (Murray, 2004).

2.2 Classification of *M. tuberculosis*

According to Cole *et al.* (1998), the taxonomic classification for *M. tuberculosis* is as follows:

Kingdom: Bacteria
 Phylum: Actinobacteria

Class: Actinobacteria

Order: Actinomycetales

Suborder: Corynebacterineae

Family: Mycobacteriaceae

Genus: *Mycobacterium*

Species: *tuberculosis*

M. tuberculosis comes from the genus *Mycobacterium*, which is composed of approximately 100 recognized and proposed species. The most familiar of the species are *M. tuberculosis* and *M. leprae* (leprosy). It belongs to a group of closely related bacterial species termed the *Mycobacterium tuberculosis* complex. It has the following members that include *M. africanum*, *M. bovis* (Dassie's bacillus), *M. caprae*, *M. microti*, *M. mungi*, *M. orygis* and *M. pinnipedii*. This group may also include the *M. canettii* clade. (Cole *et al.,* 1998; Hershkovitz *et al.,* 2008; Talip *et al.,* 2013).

Nowadays the common cause of human TB is *M. tuberculosis. M. bovis* has a wider host range and is the major cause of TB in other animal species. Although in the years before the widespread of milk pasteurization, the cattle- infecting species *M. bovis* was the common cause of human TB. It is estimated that in the pre-antibiotic era *M. bovis* was responsible for about 6% of TB deaths in humans (Hershkovitz *et al.,* 2008; Nester *et al.,* 2009).

The recognized members of the *M. tuberculosis* complex are all clonal in their spread. The main human infecting species are classified into seven oligotypes: type 1 include the East African-Indian (EAI) and some Manu (Indian) strains; type 2 is the Beijing group; type 3 consists of the Central Asian (CAS) strains; type 4 include Ghana and Haarlem (H/T), Latin America-Mediterranean (LAM) and X strains; types 5 and 6 correspond to *M. africanum* and are observed mostly and at very high frequency in West Africa. A seventh type was isolated from the Horn of Africa (Cole *et al.,* 1998).

Other species of this complex belong to a number of oligotypes and do not usually infect humans. Type 2 and 3 are more related to each other closely than the other types. Types 5 and 6 are most closely aligned with the species normally not infectious to humans. Type 3 is divided into two clades: CAS-Kili (found in Tanzania) and CAS-Delhi (found in India and Saudi Arabia) (Cole *et al.,* 1998).

2.3   Morphology of *M. tuberculosis*

M. tuberculosis is a slightly curved or straight, thin, non-motile rod-shaped bacilli that grows in sinuous masses or strands called cords; the rods are 2-4 micrometers in length and 0.2-0.5 um in width (Todar, 2008; Lapierre, 2011; Talaro & Chess, 2012). Unlike other pathogens, it produces no toxins, fimbriae, capsule or enzymes that contribute it infectiousness. Most strains contain complex waxes and a cord factor that contribute to virulence by preventing the by bacterium from being destroyed by lysosomes of macrophages (Talaro & Chess, 2012; Willey, Sherwood & Woolverton, 2011).

The cell wall of this bacterium differs substantially from that of gram-positive and gram-negative bacteria in that it contains several unique lipid and glycolipid. Around 60% of the dry weights of the *M. tuberculosis* cell wall consist of lipids, a much higher percentage than that in most other bacteria. This lipid content imparts the characteristic of acid fastness and is responsible for its resistance to drying and disinfectants, and its pathogenicity (Nester *et al.,* 2009; Talaro & Chess, 2012).

The cell wall also has lipoarabinomannan, trehalose dimycolate, and phthiocerol dimycocerosate in addition to mycolic acid. These compounds are directly toxic to eukaryotic cells and generate a hydrophobic barrier around the bacterium that facilitates resistance and impermeability to antimicrobial agents. And also protects against the killing by acid and alkaline compounds, osmotic lysis and lysozymes (Willey *et al.,* 2011).

2.4   Cultural characteristics of *M. tuberculosis*

M. tuberculosis is an obligate aerobe and it grows very slow with a generation time of 15-20 hours, which is extremely slow compared to the growth of other bacteria, that have division times measured in minutes (*Escherichia coli* can divide roughly every 20 minutes) a physiological feature that may contribute to its virulence (Cole *et al.,* 1998; Cowan, 2009). If a Gram stain is performed on this bacterium, it stains very weakly Gram-positive or not at all (cells referred to as "ghosts"); hence Ziehl-Neelsen staining, or acid-fast staining, is used.

Two media are used to grow this bacterium; Middlebrook's medium which is an agar based medium and Lowenstein-Jensen medium which is an egg based medium. It produces colonies that are small and buff coloured when grown on either medium. Both the two media contain inhibitors to keep contaminants from out-growing the bacterium. It takes a period of 4-6 weeks to get visual colonies on either type of media (Cole *et al.,* 1998; Todar, 2008; Lapierre, 2011).

2.5   Transmission of TB

TB can be transmitted in the following ways: inhalation (most common), ingestion, through breaks in skin (rare), intercourse (rare) and intra-partum (rare) (Lapierre, 2011). It is a communicable disease and patients with pulmonary TB are the most important source of infection. It is spread mostly through the airborne particles. When infectious people cough, sneeze, talk, laugh or spit, droplets nuclei containing *M. tuberculosis* are sprayed into the air. Infection is initiated by inhalation of droplet nuclei, which are particles of 1–5 μm in diameter containing *M. tuberculosis*, expectorated by patients with active pulmonary TB, typically when the patient coughs (Ahmad, 2011; Talip *et al.,* 2013; Desalu *et al.,* 2013).

People nearby may inhale the bacteria and become infected. The tubercle bacilli are extremely resistant to drying and can survive for 6-8 months in dried sputum. Ten (10) or fewer organisms inhaled are not enough to cause infection (Black, 2008; Desalu *et al.,* 2013). The infectiousness of the person depends on several factors such as the infectiousness of the source case, the closeness of contact, the bacillary load inhaled, and the immune status of the potential host (Ahmad, 2011; Talaro & Chess, 2012; Talip *et al.,* 2013). An individual can be infected by *M. tuberculosis* for several years without becoming sick or spreading the organism to other people. But if the immune system is weakened by immunosuppressive disease like HIV infection, diabetes mellitus, malignancy, chronic kidney disease, extremes of ages, and immunosuppressive agent, latent TB infection can develop into active TB disease. If such person with active disease is left untreated, he or she will infect on the average between 10 and 15 people every year (Desalu *et al.,* 2013)

TB infection means that *M. tuberculosis* is in the body, but the immune system is keeping the bacteria under control. The immune system does this by

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