PRE INTENSIVE PHASE HEALTH RELATED QUALITY OF LIFE (HRQOL) AMONG PATIENTS WITH ACTIVE TUBERCULOSIS IN KUALA TERENGGANU:

ITS ASSOCIATED FACTORS AND COMPARISON WITH POST INTENSIVE PHASE .

DR NORHAFIZATUL AIDA BT AMIR KHALID

Dissertation Submitted In Partial Fulfillment Of The Requirement For The Degree Of Master Of Medicine (Internal Medicine)

UNIVERSITI SAINS MALAYSIA

2015

ACKNOWLEDGEMENT

Bissmillahirahmanirrahim

Alhamdullilah, praise to Allah s.w.t the most merciful and the most gracious, for His blessings and guidance that helped me throughout the process of completing the study and writing of this dissertation.

I wish to express my deepest appreciation to my supervisor Dr.Alwi Muhd Besari and my supervisors Dr Norhaya Mohd Razali and Dr Termizy Hassan Mashat for the support, advices and supervision in completing this dissertation.

An appreciation also goes to to Prof Syed Hatim, Dr Siti Azrin and Cik Nur Sulwana from the Biostatistic Department for their guidance on the statistical aspects.

To my beloved mother and mother in law (P Arpahbt Othman) (Che Rahimas bt Che Man), my beloved husband (Encik Mohd Faizal), 2 kids (Maryam and Fatimah) and siblings, thank you very much for your everlasting prayers. With your continuous encouragement, I regain my confidence and strength to win all the challenges.

Last but not least, I would like to dedicate this masterpiece to all my true friends who loyally stood beside me during my happiness and hardships.

Norhafizatul Aida bt Amir Khalid

TABLE OF CONTENT

Chapter 3 : Methodology

LIST OF TABLE

LIST OF FIGURES **PAGES**

ABBREVIATIONS

ADA	Adenosine Deaminase
AFB	Acid fast Bacilli
BP	Bodily pain
DM	Diabetes mellitus
DOT	Directly observed therapy
DOTS	Directly observed therapy, short course
EHRZ	Ethambutol, isoniazid, rifampicin, pyrazinamide
EQA	External quality assurance (EQA) system
EPTB	Extra pulmonary Tuberculosis
GH	General health
HIV	Human Immunodeficiency Virus
HR	Isoniazid, rifampicin
HRQOL	Health Related Quality Of Life
KK	Klinik Kesihatan
MCS	Mental component summary
MDRTB	Multi Drugs Resistant Tuberculosis
MH	Mental health

NAAT	Nucleic Acid Amplification Test
PCS	Physical component summary
PF	Physical functioning
PR1	Pusat Rawatan 1
PTB	Pulmonary Tuberculosis
RCT	Randomised Control Trial
RE	Role partiticipation with emotional health problems (role-emotional)
RP	Role participitaion with physical health problems (role-physical)
SF	Social functioning
SF36V2	Short form 36 version 2
TB	Tuberculosis
VT	Vitality
WHO	World Health Organization

ABSTRAK (BAHASA MELAYU)

Latarbelakang

Tuberculosis merupakan penyakit berjangkit yang kronik yang menjangkiti satu pertiga penduduk dunia. Tuberculosis bukan sahaja memberi kesan terhadap fizikal kepada pesakit tetapi juga kepada kualiti hidup pesakit berkenaan. Pelbagai factor yang boleh mengurangkan kualiti hidup pengidap tuberculosis. Objektif kajian ini adalah untuk menentukan kualiti hidup berkaitan kesihatan pengidap tuberculosis pada awal rawatan dan pada pengakhiran rawatan intensif serta faktor-faktor yang mempengaruhi kualiti hidup pada permulaan rawatan.

Metodologi

Satu kajian‘cross-sectional’ propektif dibuat pada September 2014 sehingga March 2015melibatkan 60 responden, 35 daripadanya adalah pesakit tuberculosis pulmonary, 18 pesakit merupakan pesakit tuberculosis extrapulmonary and selebihn yang mengidap kedua-duanya. Pesakit yang layak akan diberi soalansoalselidik SF36v2 yang dijawab sendiri pada permulaan dan pengakhiran fasa intensif. Markah kualiti hidup dibahagikan kepada lapan domain. Kesihatan dan komponen terkumpul fizikal dan mental. Perbezaan antara markah permulaan dan pengakhiran rawatan intensif diukur mengunakan ‘paired t test’ dan ‘multi linear regression’untuk faktor yang mempengaruhi markah kualiti hidup.

Keputusan

Markah kualiti hidup meningkat untuk kesemua lapan domain dan komponen keseluruhan fizikaldan mental pada pengakhiran fasaintensif. Markah purata PCS pada permulaan rawatan adalah 39.2 (SD±10.19) p <0.005, pada pengakhiran fasa intensif 49.1(SD±9.03) dan purata perbezaan -9.89.Manakala, markah purata bagi MCS pada permulaan rawatan, pengaakiran fasa intensif dan purata perbezaan adalah 42.00(SD±10.77), 50.24(SD±8.79) dan 8.20. Bilangan symptom dan pesakit HIV merupakan prediktif yang membezakan markah untuk PCS pada permulaan rawatan. Manakala menjadi pesakit HIV merupakan faktor yang memberi kesan negatif kepada markah MCS pada permulaan rawatan tuberkulosis.

Kesimpulan

Hasil kajian ini telah membuktikan kualiti hidup berkaitan kesihatan meningkat selepas rawatan intensif serta bilangan symptom pada masa diagnose serta pesakit HIV adalah faktor yang mengurangkan markah PCS.Manakala markah MCS lebih rendah untuk pesakit HIV berbanding pesakit lain.

ABSTRACT (ENGLISH)

Background

Tuberculosis is a chronic infectious disease that has infected one third of the world population. Tuberculosis not only gives an impact physically but also affects the quality of life. The quality of life in tuberculosis patients diminish by multiple factors. The objective of this study is to determine the health related quality of life in active tuberculosis patients at the beginning and at the end of the intensive treatment and the associated factors of quality of life at the beginning of the treatment.

Methodology

This is a cross-sectional prospective study done between September 2014 until March 2015 involving 60 tuberculosis patients in which 35 of them were infected with pulmonary tuberculosis, 18 patients were infected with extrapulmonary tuberculosis and 7 patients had both pulmonary and extrapulmonary Tuberculosis. All eligible patients were asked to complete a self-administered SF36v2 questionnaire at the diagnosis and at the end of the intensive phase treatment of tuberculosis. The quality of life score were scored into eight health domains, physical and mental component summary. The difference of the quality of life score at the beginning and at the end of the intensive phase was assessed using paired t-test and multiple linear regression to assess the associated factors for the quality of life score.

Result

The quality of life score significantly improved all eight domains as well as the physical and mental component summary at the end of the intensive phase. For the PCS, the mean score at the beginning of treatment was 39.2(SD±10.19), at the end of intensive phase was 49.1 (SD±9.03) and the mean difference was -9.89. While for the mean MCS scores at the start of the treatment, after the intensive phase and the mean difference were 42.00(SD±10.77), 50.24(SD±8.79) and 8.20, respectively. The number of symptoms at the diagnosis and being HIV infected patients were the predictive difference in PCS score at the beginning of the treatment of anti-tuberculosis. Being HIV infected patients were the factors that negatively affect the MCS score at the beginning of treatment.

Conclusion

This study showed that the HQOL improved with intensive phase of treatment. The number of symptoms at the diagnosis and being HIV patients were the associated factors that lower the physical component summary score(PCS). Similarly, the mental component summary score(MCS) was lower in HIV patients than non HIV patients.

ABSTRACT

PRE INTENSIVE PHASE HEALTH RELATED QUALITY OF LIFE (HRQOL) AMONG PATIENTS WITH ACTIVE TUBERCULOSIS IN HOSPITAL SULTANAH NUR ZAHIRAH, KUALA TERENGGANU:

ITS ASSOCIATED FACTORS AND COMPARISON WITH POST INTENSIVE PHASE .

DrNorhafizatul Aida binti Amir Khalid

MMed Internal Medicine

Department of Internal Medicine

School of Medical Sciences, UniversitiSains Malaysia

Health Campus, 16150 Kelantan, Malaysia

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DrAlwiMuhdBesari(Supervisor)

DR NorhayaMohdRazali (Co-supervisor)

DrTermizy bin Hassan Mahsat(Co- supervisor)

CHAPTER ONE

INTRODUCTION

1.1 Introduction of Tuberculosis

Tuberculosis is an infectious disease caused by the *Mycobacterium tuberculosis (M. tuberculosis*bacteria*)*. Tuberculosis typically attacks the lungs 90% of the overall cases, as well as affecting other parts of the body, such as lymph nodes, bones, brain and others. It is spread through the air when people who have an active TB infection cough, sneeze, or otherwise transmit their saliva through the air.

The classical symptom of pulmonary tuberculosis fever, cough with or without hemoptysis and loss of weight. The cough usually lasted more than 2 weeks(Miller *et al.*, 2000). Patients with extra pulmonary tuberculosis usually presented depend on the organ involvement. For example, patient with lymphadenitis tuberculosis usually presented with lumps at neck and patient with TB meningitis may come with headache and constuitional symptoms then may progress to coma.

The diagnosis confirmed by isolating *Myobacterium tuberculoisis* from the clinical sample namely from the body fluid, sputum or tissue such as lymph nodes and bones. Few imaging modalities also may help to assist the diagnosis.

Treatment for tuberculosis is difficult and requires the administration of multiple antibiotics over a long period of time. Pulmonary tuberculosis treatment period for non HIV patient is 6 months which consist of 2 months of intensive phase and another 4 months for maintenance phase (Malaysia, 2002).

Tuberculosis is a chronic infectious disease which causes devastating symptoms and requires long course of treatment, that certainly will cause negative impacts to the patient either physically as well as social and mental wellbeing.

1.2History of tuberculosis

Throughout history, tuberculosis was called by various names and terms, including consumption, phthisis, scrofula, Pott's disease, and the White Plague. During the 18^{th} and 19^{th} centuries, tuberculosis already reached its epidemic proportion in Europe and North America and earned the sobriquet, "Captain Among these Men of Death"(Daniel, 2006). *Mycobacterium tuberculosis*, or Koch's bacillus was revealed as organism for tuberculosis in 1882 by Robert Koch, a Prussian physician. Heutilized a new staining method to sputum of tuberculosis and found the pathogen. He also developed tuberculin, a purified protein derivative of the bacteria, which proved to be an ineffective means of immunization. In 1908, Charles Mantoux found it was an effective intradermic test for diagnosing tuberculosis.

The treatment for tuberculosis initially began with surgical intervention including the pneumothorax or plombage technique—collapsing an infected lung to "rest" it and allow the lesions to heal. The first antibiotic against *M. tuberculosis*wasdiscovered by Albert Schatz, Elizabeth Bugie, and Selman Waksmanin in 1944, then isoniazid in 1952 followed by rifampicin in 1970s.

1.3 Epidemiology of Tuberculosis

1.3.1 Epidemiology of Tuberculosis Worldwide

Tuberculosis infected about one third of the world population (estimated about 2 billion people). According to the World Health Organization (WHO), in 2013,estimated 9 million individuals developed TB and 1.5 million died(Organization, 2013).This increment was also compounded by the HIV pandemic, complacency, neglect towards the disease and international movement(CPG, 2012).In 2013, there were estimated 360,000 deaths among people who were HIV-positive(Organization, 2013).

1.3.2 Epidemiology of Tuberculosis in Asia

Half of tuberculosis cases came from most populous countries of Asia which are Bangladesh, China, India, Indonesia, and Pakistan(Dye, 2006).One-third of the world's

burden of tuberculosis (TB), or about 4.9 million prevalent cases, is found in the World Health Organization (WHO) South-East Asia Region(Nair *et al.*, 2010).

1.3.3 Epidemiology of Tuberculosis in Malaysia

In Malaysia, the number of tuberculosis patients increase throughout the year according to CDC Department 2011. The number of new TB cases in the country has increased from 15,000 in 2005 to 22,710 cases in 2012**.** While PTB was the most common form of TB in Malaysia, extrapulmonary TB (EPTB) still posed a threat. In 2011, the number of cases for PTB was 16363 (85%) while for extrapulmonary was 2888 (15%)(CPG, 2012).

1.3.4 Epidemiology of Tuberculosis in Terengganu

According to CDC Department the number of cases increased from 661 (2007) to 733 cases (2012). While the number of death also increased throughout the years with 114 cases in 2012.

1.4 Definition and Classification of Tuberculosis

Tuberculosis is an infectious disease caused by the *Mycobacterium tuberculosis (M. tuberculosis) bacteria*. Tuberculosis commonly involves the lung and it is called Pulmonary Tuberculosis (PTB). Tuberculosis may also affect other organs such as lymph nodes, bones, spine, eyes, brain and many more other organs known as extrapulmonary tuberculosis (EPTB).

1.5 Etiology of Tuberculosis

Tuberculosis is caused by *Mycobacterium tuberculosis*, a small, aerobic nonmotile bacillus. It has unique clinical characteristics in which it is a high lipid content pathogen.This pathogen was first identified and described by Robert Koch in 1882 and he received a Nobel Prize in 1905 for this discovery.

1.6 Risk Factors for Tuberculosis

There are a few important groups of people who have a high risk to get infected. People who live with the infected people namely in close contact, which is the household contacts have higher risk than people with nonhousehold contact(Moran-Mendoza *et al.*, 2010). The immunocompromised people are also included in the high risk group, such as Diabetes mellitus (Jeon and Murray, 2008), Human Immunodeficiency Virus infection (Lienhardt *et al.*, 2005), Chronic obstructive pulmonary disease, End-stage renal disease, malignancy, malnutrition and use of immunosuppresant drugs in rheumatoid arthritis i.e. TNF blockers. Substance abusers and cigarette smokers are also included in the high risk group to be infected by tuberculosis.(Moran-Mendoza *et al.*, 2010); (Lienhardt *et al.*, 2005)

1.7 Pathogenesis of tuberculosis

a. Transmission of tuberculosis

TB is transmitted via aerosol droplets of 0.5 to 5.0 micrometers in diameter whenever infected people cough, sneeze, speak, sing or spit. When the pathogen reaches the pulmonary alveoli, it will invade and relipcate within endosomes of alveolar macrophages. Phagocytosis occurred to eliminate the pathogen (Kumar et al.,2007).

b. The immune response

M tuberculosis has a thick, wavy mycolic acid capsule that protects it from the toxic substance. The bacilli will destroy the macrophages by activating the T lymphocytes and their lymphokines, whereby the activation is the essence of cell-mediated immunity. This immunity also has a detrimental component, called delayed-type hypersensitivity. This component causes caseous necrosis of host tissues(Dannenberg, 1989). Nitric oxide (NO) plays an important role in killing*Mycobacterium tuberculosis* by mononuclear phagocytes, in which found in the urine odel of tuberculosis. Genetic disruption for inducible NO synthase in mouse, is associated with a significant higher risk of disseminationand mortality for tuberculosis infection(Chan *et al.*, 2001). Cytokines such as tumor necrosis factor- α and interleukin 1- β , mycobacterial cell wall components such as lipoarabinomannan and 19 kD lipoprotein, along with the T-cell–derived interferon-γ ,also induce NO expression(Chan *et al.*, 2001).

c. The pathology caused by tuberculosis to the body

The primary site of infection in the lung is known as “Ghon focus", usually located either in the upper part of the lower lobe, or the lower part of the upper lobe(Kumar et al.,2007).Tuberculosis of the lung may also spread from the blood stream or hematogenous transmission whereby it is transmitted from distant sites such as peripheral lymph nodes, the kidneys, the brain, and the bones(Kumar et al., 2007). It is typically located at the upper part of the lung known as Simon focus.

1.8 Diagnosis

Active tuberculosis is diagnosed by clinical presentation as mentioned in the introduction of tuberculosis (sub topic 1.1), supported by imaging and laboratory tests. The diagnosis however is confirmed by isolating *Mycobacterium tuberculosis* from the clinical samples.(CPG, 2012).

1.8.1 Diagnosis of Pulmonary Tuberculosis (PTB)

a. Imaging

Chest radiograph remainsthe primary modality in PTB. It has higher sensitivity and specificity for TB when read by trained readers and detection improved by 1.23 fold (Abubakar *et al.*, 2010). Consolidation with cavitation is the hallmark of adult-type PTB.

Computerised tomography (CT) is useful in cases with high clinical suspicion of TB with normal CXR. It is able to demonstrate endobronchial lesion, lymphadenopathy and pleural complication. High resolution CT has high sensitivity, specificity and positive predictive value of 84%, 97% and 98% respectively(Yeh *et al.*, 2010).

Magnetic Resonance Imaging (MRI) may be considered in pregnant women or children. MRI has better soft tissue characteristics especially for pleural and lymph node assessment; however it is limited by the cost and accessibility.

b. Laboratory

All patients suspected to have PTB should send their sputum specimens for microscopic examination in a quality-assured laboratory for at least two sputum. (CPG, 2012). At least one early morning specimen should be obtained, as this time has the highest yield for sputum collection. Microscopic examination of sputum using conventional light microscopy in diagnosing PTB however has low sensitivity (20-60%)(Steingart *et al.*, 2006).

The newer method, light emitting diode-based fluorescence microscopy (LED FM) has benefit over the conventional FM. It is cheaper, has lower maintenance requirement and do not need a dark room. The sensitivity and specificity for LED FM on pulmonary specimens were 78.3% and 92% respectively(Shenai *et al.*, 2011).

The newer tool for rapid diagnosis of TB is the Nucleic Acid Amplification Tests (NAAT). NAAT provide rapid results within 24-28 hours and also can detect the presence of Mycobacterium weeks earlier than culture(Control and Prevention, 2009). This test has positive predictive values (PPV) of more than 95% with AFB smear positive specimens and able to confirm the presence of Mycobacterium in AFB negative, culture positive 50-80%(Menzies *et al.*, 2009).

Another new test rapid in diagnosing tuberculosis and also detection of rifampicin resistance is Xpert MTB/RIF assay. From a meta-analysis study, this test has

sensitivity and specificity of 90.4% and 98.4% respectively in PTB. While for the rifampicin resistance, the sensitivity was 94% and specificity was 97%. The accuracy of Xpert MTB/RIF assay is higher in smear-positive and sensitive of diagnosing PTB in adults. The assay has pooled sensitivity of 80% and specificity of 86% in diagnosing EPTB(Chang *et al.*, 2012).

Line probe assay is useful in detecting rifampicin ad isoniazid resistance. The pooled sensitivity and specificity for LPA rifampicin resistance demonstrates an excellent accuracy of 98.1% and 98.7% respectively. Whilst for isoniazid resistance, the pooled sensitivity and specificity was 88.7% and 99.2% (Ling *et al.*, 2008)

1.8.2 Diagnosis of Extrapulmonary Tuberculosis (EPTB)

a. Imaging

Ultrasound is useful to demonstrate effusion and to guide for diagnostic tapping for pleural TB. CT and MRI imaging have great values to diagnose musculoskeletal TB. The tools are useful in demonstrating a small focus of bone infection as well as the extent of the disease. MRI is preferred in diagnosing tuberculous spondylitis. (Engin *et al.*, 2000).

In diagnosing TB involving the central nervous system, CT and MRI are very useful. CT is able to demonstrate hydrocephalus as complication of TB involves brain parenchyma and also enhancement of the basal cisterns, whilst MRIbetter demonstrates the involvement of the spinalcord and cranial nerves(Engin *et al.*, 2000).The imaging

modalities for abdominal TB are US, CT and barium studies with diagnostic yields 83% for barium meal follow through, 80% for CT and 77% for US (Khan *et al.*, 2006).

b. Laboratory

EPTB have a lower bacterial load problem in sample collection compared to PTB. In order to support or confirm the diagnosis, samples for *Mycobacterium tuberculosis* culture need to be obtained from the affected sites such as cerebrospinal fluid (CSF), pleural fluid, fine needle aspiration (FNA) and/or biopsy from lymph node, pleura, intestines, skin and any other infected sites. The presence of caseating granulomas, or granulomas with Langerhan's giant cells on histologyor cytology of the specimen is highly suggestive of tuberculosis but they are not specific(CPG, 2012).

In a meta-analysis by Liang QL et al., the measurement of Adenosine Deaminase (ADA) level in pleural effusion is useful for the diagnosistuberculous pleurisy with high sensitivity and specificity for diagnosis. In clinical suspected tuberculous lymphadenitis, combining cytology with microbiology(smear and culture) increases diagnostic yield from 67% to 91% (Asimacopoulos *et al.*, 2010).

1.9 Management

A standardized and appropriate treatment regime is most crucial in TB control. Appropriate transmission and prevent emergence of MDRTB.

Based on well-designed randomized controlled trial (RCT) for many years, treatment regime for newly diagnosed PTB patient is six-month regimen consisting of two months of daily EHRZ* (2EHRZ) followed by four months of daily HR* (4HR) (Fox *et al.*, 1999).

In a systemic review done in 2009 by Menzies D et al. showed significant worse outcome with shorter rifampicin treatment regime(Menzies *et al.*, 2009). Rifampicin should be used for the whole treatment regime including maintenance. The optimal duration of treatment for PTB smear positive is at least six months(CPG, 2012).There is lack of evidence for treatment duration for EPTB, therefore it has been conflicting recommendation. The recommendation by WHO are, all EPTB should contain 6 months of rifampicin based regime of treatment except TB meningitis is 9 -12 months whereas bone and joint TB is 9 months. (Organization, 2010).

In 1995, WHO launched the Direct Observed Therapy, Short course (DOTS), whereby this strategy combines drug treatment with political commitment to ensure adherence. DOT increased completion rate compared to self-administered therapy as showed by a study

done by Anuwatnonthakate A et al(OR=3.3, 95% CI 2.4 to 4.5)(Anuwatnonthakate *et al.*, 2008).

The practice of DOT Malaysia was reported to be 93-100% according to Sistem Maklumat Tibi Kementerian Kesihatan Malaysia.

A part from treating a person with active infection with antibiotics, the aim of TB management is to control TB infection. The preventivemeasures include screening of TB contact, screening TB for high risk group andpreventive measures for health care workers. Regarding TB contact, Index TB patients include both smear positive and negative cases.Contact has higher risk to acquire all type of TB than non contact(Morrison *et al.*, 2008).

With regards to the preventive measures to control tuberculosis and isolation of tuberculosis patients, the aim of isolation of tuberculosis patient is to control nosocromial tuberculosis infection transmissions beyond the resources of low-income countries(Harries *et al.*, 1997).

1.10 Introduction to health related quality of life

WHO defined health as a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity (WHO, 1948). Apart from the physical symptoms, the patient also faces several mental and social problems that have a great impact on the wellbeing and quality of life of the patient. Health-related quality of life (HRQOL) is a multi-dimensional concept that includes domains related to the physical, mental, emotional and social functioning (Khanna and Tsevat, 2007). HRQOL assessment is a relatively new index for health measurement. It is what patients perceived about their health. The conventional clinical and investigation assessment was unable to quantify the impairment of quality of life in a patient. Therefore a framed question of HRQL score need to be done to assess the patient's perception of improvement (Dhingra and Rajpal, 2005).

Patients living with a chronic disease such as tuberculosis, the impact is often encompassing, affecting patients life physically as well as their social, economic and physiological wellbeing (Rajeswari *et al.*, 2005).

A systemic review study measuring health related quality of life in tuberculosis which was done in Canada by Na Guo, Fawziah Marra and Carlo A Marra (2009) revealed that there was no established specific instrument to measure quality of life in tuberculosis patients. Despite the overall study which showed improvement of quality of life with the treatment, the score was still low in tuberculosis patients even after the completion of treatment as compared to the general population (Guo *et al.*, 2009).

A study conducted in Yemen 2009 showed that the HRQOL score of pulmonary and extra pulmonary tuberculosis patients improved significantly at the end of first month of follow up and at the end of the intensive phase (Othman *et al.*, 2011).

A study using DR-12 scale done in New Delhi showed a significant difference between scores in the pulmonary and extrapulmonary cases in both symptoms and total HRQOL scores. In terms of sputum smear, sputum negative showed a higher symptom score. HRQOL scores also showed a negative correlation with sputum grading at 0 week, 4 weeks and 8 weeks for all three scores, symptom, socio-physiological and exercise adaptation and total score (Dhingra and Rajpal, 2005).

The other study which compared tuberculosis patients with the normal population showed that tuberculosis patients had significantly lower mean scores for overall quality of life score. The physical domain was the worst effected domain followed by the psychological domain (Dhuria *et al.*, 2008).

Tuberculosis also causes social implications such as stigma which was revealed by a few studies. It continues even after completed treatment and bacteriologically cured (Chamla, 2004; Rajeswari *et al.*, 2005; Dhuria *et al.*, 2008).

HRQOL assessment in TB research is relatively new. In a systemic review regarding measurement tools for HRQOL in tuberculosis patients, the most frequently used HRQOL instrument is SF-36 currently. 6 out of 12 studies reviewed to have used SF-36 as HRQOL assessment tool. SF-36 appeared to be a valid and reliable tool to be used in TB (Guo *et al.*, 2009).

A study conducted in USA by using a focus group to assess HRQOL of tuberculosis patients revealed that more specific aspects of life were affected such as isolation, as patients diagnosed with tuberculosis were admitted to the isolation ward and social support, unanticipated effects on sexual functioning and financial wellbeing (Hansel *et al.*, 2004).

Sararaks et al (2005) reported that the psychometric properties of SF36 Malay version was acceptable. The internal consistency revealed Cronbach's αs of more than 0.07 for all items except for SF. This study was based based on multi centre study on the asthmatic and population based study(Sararaks *et al.*, 2005).

The factor that influence the quality of life in tuberculosis patients are socioeconomic status including exposure to second hand smoker and low perceived social support, in addition to clinical factors. (Masumoto *et al.*, 2013). While other study done in Pakistan

showed that women enjoyed better quality of life compared to men and rural patients have better HRQOL score compared to the urban patients. Other factors that affect the HRQOL are disease severity, use of drugs and death threats. (Masood *et al.*, 2012). A study done in Wuhan, China in 2003 found a significant association between the SF36 and age, WBC count and number of symptoms, whereas sex and Haemoglobin were the associated factors after treatment (Chamla, 2004).

1.10 STUDY BACKGROUND AND RATIONALE

Tuberculosis is a chronic debilitating disease. It remains the leading cause of morbidity and mortality worldwide especially in resource limited settings. In Malaysia as well as in Terengganu, it is as challenging and consuming as ever before. However, there are only one study done in Penang which examined the impact of health-related quality of life (HRQOL) among tuberculosis patients, especially in relations to factors influencing it (Atif *et al.*, 2014).

The purpose of this study is to determine the health-related quality of life in active tuberculosis patientsin Hospital Sultanah Nur Zahirah, Kuala Terengganu as well as factors that influence their quality of life. This study is an extension of Penang study in which only included newly diagnosed smear positive patients. This is the only HRQOL study in Malaysia included all active tuberculosis patients.

When treating physical impairment in tuberculosis patients, the impact of the disease on the patient's quality of life is often not being considered. Recently, there are emerging interests in health related quality of life especially the impact of chronic diseasesincluding tuberculosis. In this area, the consideration was on what patients perceive regarding their disease and their health. Furthermore this is important for patients adherence and curative (Marra *et al.*, 2004). Moreover further insight into the factors whichare associated with lower quality of life among patients with active TB would enable further steps to be taken to improve the patient's quality of life in the future, thus improving the overall outcome.

CHAPTER TWO

OBJECTIVE

2.1 GENERAL OBJECTIVE

To assess the health related quality of life of active tuberculosispatients in Kuala Terengganu at the beginning and at the end of the intensive treatments and factors influencing their quality of life.

2.2 SPECIFIC OBJECTIVE

i. To comparethe quality of life score of active tuberculosis patientsat the beginning of treatment and at the end of the intensive phase.

ii. To determine the associated factors of quality of life score in active tuberculosis patients at the beginning of treatment.

2.3 RESEARCH QUESTIONS

i. Are there any differencein score of health related quality of life in active tuberculosis patients at the beginning of treatment and at the end of the intensive phase?

ii. What are the associated factors that influence health related quality of life among active tuberculosis patients in Kuala Terengganu?

2.4 RESEARCH HYPOTHESIS

i. The score of health related quality of life score in active pulmonary tuberculosis patientswere lower at the beginning of treatment as compared with the end of the intensive phase.

ii. The associated factors that influenced the score of health related quality of life are gender, age, region and number of symptoms.

CHAPTER THREE

METHODOLOGY

3.1 STUDY DESIGN

For Objective 1 the study design is Prospective cohort and for objective 2 is cross sectional study

3.2 STUDY DURATION

September 2014 until March 2015

3.3 REFERENCE POPULATION

All active tuberculosis patients in Kuala Terengganu

3.2 SOURCE POPULATION

Tuberculosis patients who were registered under Chest Clinic Hospital Sultanah Nur Zahirah, Kuala Terengganu during the study period

3.5 STUDY AREA

Chest Clinic Hospital Sultanah Nur Zahirah, Kuala Terengganu

3.6 SAMPLING FRAME

New tuberculosis registration at Chest Clinic Hospital Sultanah Nur Zahirah, Kuala Terengganu**.**

3.7 STUDY POPULATION

All new active tuberculosis patients who were registered under Chest Clinic Hospital Sultanah Nur Zahirah, Kuala Terengganu.

3.7.1 INCLUSION CRITERIA

All active tuberculosis patients who were registered and has completed the intensive phase under chest Clinic Hospital Sultanah Nur Zahirah, Kuala Terengganu

3.7.2 EXCLUSION CRITERIA

Illiterate patients

3.8.1 SAMPLING METHOD

Universal sampling

All eligible sampling frame within the study period who fulfill the inclusion and exclusion criteria were included in the study in view of limited study subject.

3.9 MEASURING TOOLS

Malay version SF-36 questionnaire. The questionnaire also included the demographic and socioeconomic characteristics of patients. The permission for the use of translated Malay version of SF-36v2® was obtained from the Quality Metric Inc. The questionnaire consist of eight health domains and total of 36 items. Table 3.1 shows the domain and items of SF36. The scoring scale for this questionnaire was using Quality Metric's QM Certified Scoring software.

Domain	No of Item
Physical Functioning (PF)	10
Role-Physical (RP)	4
Bodily Pain (BP)	2
General Health (GH)	5
Vitality (VT)	4
Social Functioning (SF)	2
Role Emotional (RE)	3
Mental Health (MH)	5
Reported Health Transition	1
Total	36

Sararaks et al (2005) reported that the psychometric properties of SF36 Malay version was acceptable. The internal consistency revealed Cronbach's αs of more than 0.07 for all items except for SF. This study was based based on multi centre study on the asthmatic and population based study(Sararaks *et al.*, 2005)

Table3.1 : The domain and items for SF36v2.

3.10DATA COLLECTION

Active tuberculosis patients were identified from chest clinic's registration book during the study period. All eligible subject that fulfill inclusion and exclusion criteria informed consent were obtained and they were given Malay version SF36v2 questionnaire at the baseline and after completed intensive phase. At the baseline they were also given socioeconomic, demographic and clinical data form. The study subjects took about 10-15 minutes to complete the questionnaire. Attempts were made to trace patient at the primary care when the enrolled patients did not visit clinic after completed intensive phase. Enrolled patient who were unable to participate in this study at the end of intensive phase (eg; defaulter, transferred out) were not asked to complete questionnaire.

3.11ETHICAL APPROVAL

This study granted an ethical approval for implementation by Jawatankuasa Etika penyelidikkan Manuasia Universiti Sains Malaysia (JEPeM-USM) with the study protocol code **USM/JEPeM/1405170.** The ethical clearance is valid from January 2015 until December 2015. The approval letter is attached in the Supplementary (sub topic 10.2).This study also registered under National Medical Research Registry (**NMRR-12-1448-14180).**