RANDOMISED CONTROLLED TRIAL ON EFFECTIVENESS OF MOTIVATIONAL INTERVIEWING IN DIABETES AND TUBERCULOSIS EDUCATION WITHIN DIRECTLY OBSERVED THERAPY (MID-DOT) INTERVENTION ON TUBERCULOSIS TREATMENT OUTCOMES AMONG PULMONARY TUBERCULOSIS PATIENTS WITH DIABETES IN KELANTAN

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LIST OF ABBREVIATIONS

AFB	Acid fast bacilli
AIDS	Acquired immune deficiency syndrome
AOR	Adjusted odds ratio
DOTS	Directly Observed Treatment, Short-course
EPTB	Extra pulmonary tuberculosis
HAART	Highly Active Antiretroviral Therapy
HIV	Human immunodeficiency virus
MDRTB	Multi-drug resistant tuberculosis
XDRTB	Extensive drug resistant tuberculosis
MREC	Medical Research Ethic Committee
OR	Odds ratio
PTB	Pulmonary tuberculosis
ROC	Receiver Operating Characteristic
SD	Standard deviation
SPSS	Statistical Package for The Social Science
TB	Tuberculosis
TB/DM	Tuberculosis and diabetes mellitus
TBIS	Tuberculosis Information System
USD	United States Dollar
RM	Ringgit Malaysia
WHO	World Health Organisation
MI	Motivational Interviewing

ABSTRAK

KAJIAN KAWALAN RAWAK TERHADAP KEBERKESANAN INTERVENSI 'MOTIVATIONAL INTERVIEWING IN DIABETES AND TUBERCULOSIS EDUCATION WITHIN DIRECTLY OBSERVED THERAPY (MID-DOT)' TERHADAP KEJAYAAN HASIL RAWATAN BAGI PESAKIT TUBERKULOSIS PARU-PARU YANG MENGHIDAP DIABETES DI KELANTAN

Insiden tuberkulosis (TB) di kalangan pesakit diabetes mellitus (DM) di Malaysia semakin pesat. Ketidakpatuhan terhadap strategi rawatan merupakan salah satu halangan dalam mencapai hasil rawatan TB yang berjaya dan kawalan glisemik yang baik. Motivational Interviewing (MI) telah digunakan dalam mempromosikan penjagaan kendiri di kalangan pesakit diabetes dan terbukti mampu meransang motivasi dalaman pesakit untuk berubah. Tujuan kajian ini adalah untuk menilai keberkesanan intervensi MID-DOT terhadap hasil rawatan TB, kawalan glisemik dan aktiviti penjagaan kendiri di kalangan pesakit TB yang mempunyai diabetes. Sepuluh daerah di Kelantan telah dirawakkan secara berkelompok ke intervensi (5 daerah dengan 15 pusat rawatan TB) dan kumpulan kawalan (5 daerah dengan 12 pusat rawatan TB). 50 Pesakit TB/DM direkrut dalam kumpulan intervensi untuk menerima program intervensi MID-DOT (pendidikan kendiri penjagaan diabetes and tuberkulosis diberikan kepada pesakit setiap minggu selama 6 bulan di mana setiap sesi adalah selama 30 minit yang disampaikan oleh jururawat TB dalam program DOT) manakala 47 pesakit dalam kumpulan kawalan menerima pendidikan kesihatan standard. Hasil kajian yang utama adalah kejayaan hasil rawatan selepas menjalani 6 bulan tempoh rawatan TB. Hasil sekunder adalah perubahan tahap HbA1C dan skor

penjagaan diri diabetes pada peringkat awal, bulan ke-3 intervensi dan bulan ke-6 tempoh intervensi diberikan. Analisis utama bergantung kepada 'Intention to treat' menggunakan 'Repeated Measure analysis of variance (RM Anova)'. Kejayaan hasil rawatan adalah 94% (sembuh 76%, sempurna rawatan 18%) untuk kumpulan intervensi berbanding 72.3% (sembuh 53.2%, sempurna rawatan 19.1%) untuk kumpulan kawalan dengan [risiko relatif (RR) 1.29; 95%CI 1.56-22.67]. Terdapat perbezaan dalam mean HbA1c di antara kumpulan intervensi and kumpulan kawalan pada bulan ke enam tempoh intervensi [F(1,58)=16.48, *p*-value<0.001]. Perbezaan mean HbA1c (penurunan) dalam tempoh 6 bulan adalah signifikan bagi kumpulan intervensi (0.79, 95% CI;0.58-0.99) tetapi tidak signifikan bagi kumpulan kawalan (0.03, 95%CI; -0.25,0.30). Pada masa yang sama, terdapat perbezaan dalam mean DSCA di antara kumpulan intervensi and kumpulan kawalan [F(1,89)=43.51,*p*-value<0.001]. Perbezaan mean DSCA dalam tempoh 6 bulan (penambahan) bagi kumpulan intervensi adalah lebih tinggi (-8.59, 95%CI;-9.98,-7.18) berbanding kumpulan kawalan (-0.68,95%CI;-2.06,0.71). Intervensi MID-DOT yang disampaikan oleh jururawat TB semasa DOT sebagai tambahan kepada pendidikan kesihatan rutin adalah efektif dalam meningkatkan kejayaan hasil rawatan TB serta mencapai pengendalian glisemik yang baik dan amalan penjagaan diri diabetes. Strategi TB dan DM yang inovatif ini sangat disyorkan untuk ditingkatkan ke seluruh negara untuk mengurangkan beban penyakit TB dan diabetes.

KATA-KATA KUNCI

Tuberkulosis, diabetes, hasil rawatan tuberkulosis, temuduga bermotivasi

ABSTRACT

RANDOMISED CONTROLLED TRIAL ON EFFECTIVENESS OF MOTIVATIONAL INTERVIEWING IN DIABETES AND TUBERCULOSIS EDUCATION WITHIN DIRECTLY OBSERVED THERAPY (MID-DOT) INTERVENTION ON TUBERCULOSIS TREATMENT OUTCOMES AMONG PULMONARY TUBERCULOSIS PATIENTS WITH DIABETES IN KELANTAN

Incidence of tuberculosis (TB) patients with diabetes mellitus (DM) patients in Malaysia is rising rapidly. Non-adherence to treatment strategies has been noted as one of the barriers in achieving successful TB treatment outcome and good glycaemic control. Motivational Interviewing (MI) has been use in promoting diabetes self-care among diabetic patients and proven to stimulate patients' internal motivation to change. the aim of this study was to evaluate the effectiveness of motivational interviewing in diabetes and tuberculosis education within directly observed therapy (MID-DOT) intervention on TB treatment outcomes, glycaemic control and diabetes self-care activities among TB patients with diabetes. Ten districts in Kelantan, a northeastern-state in Malaysia, were cluster-randomized into intervention (5 districts with 15 TB treatment centres) and control group (5 districts with 12 TB treatment centres). Fifty pulmonary tuberculosis patients with diabetes were recruited in the intervention group to receive the MID-DOT intervention program (24 sessions of 30 minutes each comprising face to face diabetes self-care and TB education using MI approach every week for 6 months which were delivered by the TB nurses within DOT program), while 47 patients in the control group received standard health education. The primary endpoint was the proportion of patients achieving successful TB treatment outcome after 6-month TB treatment course. Secondary endpoints were the changes of glycosylated haemoglobin (HbA1c) level and diabetes self-care score at

baseline, 3rd month and 6th month of intervention period. Primary analysis relied on intention to treat using Repeated Measures Analysis of Variances (RM Anova). Successful TB treatment outcome was 94% (cured 76%, completed treatment 18%) for the intervention group versus 72.3% (cured 53.2%, completed treatment 19.1%) for the control group with [Relative risk (RR): 1.29, (95% CI 1.56, 22.67)]. A significance difference of mean HbA1c seen between intervention and control group at six months of intervention [F(1,58)=16.48, *p*-value<0.001]. There was a significant reduction of HbA1c of three-time points for intervention group while for the control group, no significant reduction was observed. Meanwhile, a significance difference was also seen in mean diabetes self care activities (DSCA) score between intervention and control group [F(1,89) =43.51, *p*-value<0.001]. The mean difference of DSCA over time was significantly higher in the intervention group (-8.59, 95%CI; -9.98, -7.18) compared to control group (-0.68, 95%CI;-2.06,0.71). MID-DOT intervention delivered by TB nurses during DOT session as an adjunct to the standard health education was shown to be effective in increasing successful TB treatment outcomes as well as achieving good glycaemic control and diabetes self-care practices. This innovative dual diseases strategies is highly recommended to be scaled up to nationwide to reduce TB and DM burden in the country.

KEYWORDS

Tuberculosis, diabetes, TB treatment outcomes, motivational interviewing

CHAPTER ONE

INTRODUCTION

1.1 The double burden of Tuberculosis and Diabetes Mellitus

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* that spreads from person to person through the air (Zumla *et al.*, 2013). It has the potential to affect any part of the body and typically affects the lungs (pulmonary TB) (Golden and Vikram, 2005). A bacteriologically confirmed TB case is determined when a biological specimen is found to be positive by smear microscopy, culture, or WHO-approved rapid diagnostics test. A clinically diagnosed TB case is defined as case which does not fulfil the criteria for bacteriological confirmation, but rather has been diagnosed as active TB by a clinician or other medical practitioner who has decided to give the patient a full-course TB treatment (WHO, 2013).

The major goals for TB treatment include curing the individual patient and minimize the transmission of *Mycobacterium tuberculosis* to others in the community. Effective treatment of TB requires adherence to a minimum of six-month treatment with multiple TB drugs. To improve adherence and cure rates, Directly Observed Therapy (DOT) is recommended for the treatment of TB (Bass *et al.*, 1994). DOT is a method in which patients are observed and documented ingesting each dose of anti-TB medications by a trained health personnel. It forms the cornerstone of the patient-centred approach recommended by the World Health Organization (WHO) for treatment of TB to maximize the likelihood of completion of therapy and help patients adhere to therapy (WHO, 2003b).

WHO declared the TB a global public health emergency in 1993. Since then, it has intensified efforts to control the disease worldwide (WHO, 1994). Despite these efforts, the disease continues to spread, with an estimated 10 million people suffered from TB every year (WHO, 2015). In 2016, 6.3 million new cases of TB were reported (up from 6.1 million in 2015), equivalent to 61% of the estimated incidence of 10.4 million. The latest treatment outcome data show a global treatment success rate of 83%, similar to recent years. In Malaysia, by the end of 2016, 25 739 people had been diagnosed with TB (92 in 100 000 population); the latest treatment success rate was 78% (WHO, 2017).

TB is curable but if left untreated, it can be fatal (Zumla *et al.*, 2013). Broader influences on the TB epidemic includes patient adherence to TB treatment, and the complex interaction between other diseases, poverty, racism, socioeconomic policy, migration, social stigma, gender, and culture. There is consensus among the scientists that health providers and poorly managed health care services have largely attributed to poor adherence of TB patient, while TB comorbidities such as HIV and diabetes contribute to the rise (Addington, 1979).

Diabetes is known to be a risk factor for TB (Stevenson *et al.*, 2007). During the last twenty years, the prevalence of diabetes has increased dramatically in many part of the world and the disease is now a worldwide public health problem. The total number of people with diabetes worldwide is projected to rise from 425 million in 2017 to 629 million in 2045. About 79% live in low and middle-income countries. In Malaysia, at the end of 2017 approximately 3.5 million of adults 20-79 years had been diagnosed

with diabetes (IDF, 2015). However, the prevalence may actually be higher (17.5%) according to National Health Morbidity Survey (NHMS) 2015 (NHMS, 2015).

With the advent of diabetes, there has been dramatic resurgences of TB, as both diseases are linked at rates of 10-30% (Zheng *et al.*, 2017). A few studies have found that diabetes weakens a person's immune system and so increases the risk of developing TB. Recent evidence has shown that the relative odds of developing TB are higher in diabetics than non-diabetics, with odds ratios (OR) ranging from 2.44-8.33 (Alisjahbana *et al.*, 2007; Atif *et al.*, 2014; Jeon and Murray, 2008; Kapur and Harries, 2013). A meta-analysis showed that the risk of death during TB treatment (RR1.89, 95%CI; 1.52-2.36) and relapse following treatment (RR 3.89, 95%CI; 2.43-6.23) were both higher in TB patients with diabetes compared to those without diabetes. The combine outcomes of TB treatment failure and death were also higher (RR 1.69, 95% CI;1.36-2.12) (Baker *et al.*, 2011).

The clinical management of dual diseases is complex. Good glycaemic control which may improve the TB treatment outcomes requires the pharmacological and non-pharmacological efforts from both patients and health care providers (Riza *et al.*, 2014). The therapeutic regimens of TB and diabetes medications recommended by WHO have been shown to be highly effective, but non-adherence to treatment calls for attention (Fox *et al.*, 1999).

1.2 Problem Statements

In TB/DM management, non-adherence to treatment strategies has been identified as one of the barriers in achieving successful TB treatment outcome and good glycaemic control (Addington, 1979; Agarwal *et al.*, 2016; Brown and Bussell, 2011). Adherence declined due to lack of motivation. Appropriates style of counselling, repetitive education session and person delivered the health education has been recognised as major factors that may influenced patients' motivation to make a behaviour change (Barlow *et al.*, 2002). However, the current practice always used traditional counselling approach (show and tell) that often forced, taught, and instructed the patients to change without notice conflicts within the patient to be obstacles for them to change. The patients receiving these methods often report they feel depressed, uncomfortable, powerless, so not motivated to be responsible for their own health (Miller and Rollnick, 2012).

The task of giving diabetes self-care education in TB/DM management are usually given to nutritionists and diabetes educators who only see patients within three to six months durations in diabetes clinic. Ideally, this task should have been delivered repetitively especially during six months of TB treatment (Tan and Magarey, 2008). However, to refer a patient with active TB to a diabetic educator in a separate diabetes clinic for a regular/daily counselling is not an appealing option, both from the patients' and infectious control points of view. Patients may refuse a daily referral during their TB treatment due to stigma. Diabetes clinics may be equipped for TB infection control. There will be a risk of TB cross-transmission to other diabetic patients and healthcare workers if TB patients with diabetes are sent for daily diabetes counselling at diabetic clinics (Riza *et al.*, 2014).

In the current Malaysian context, although TB staff engage daily with patients during DOT, no reinforcement or proper diabetes self-care education is given. A sense of responsibility is lacking as staff have not been trained as diabetes educators. Besides, there is no current educational materials or guidelines specifically addressing the TB and diabetes education to be used by TB staff. Although many diabetes education materials and module available in healthcare setting, the complexity of materials provided may led patients struggle to understand the self-care points of information of their chronic conditions, written medication and translating the knowledge received into the daily practice (Albright *et al.*, 1996; Tan and Magarey, 2008).

In the Pacific Islands region, extensive educational materials have been developed by novel Hawaiian TB-DM study for TB patients with diabetes (Pyan, 2016). However, there are substantial differences in the educational, socioeconomic, and cultural backgrounds of TB patients with diabetes in Malaysia as compared to the Hawaiian patients. Hence, adoption of related TB and diabetes materials from foreign countries to educate TB patients with diabetes in Malaysia is not feasible or practical.

1.3 Research gap

Motivational Interviewing (MI) has been used in smoking cessation and promoting medication adherence among TB patients (Louwagie *et al.*, 2014). However, to the best of the researcher's knowledge, no diabetes self-care education trials using MI approach have been conducted in a population of TB patients with diabetes, which effectiveness may differ because dually infected TB patients may be severely ill or have negative outcome.

Studies relating to glycaemic control among TB patients with diabetes have been relatively scanty, and evidence of a causal association between glycaemic control and TB treatment outcomes remain limited. Methodologies in previous studies have not adequately explained the causal relationship between proper glycaemic control and successful TB treatment outcomes. Many evidence come from studies that conducted retrospectively with no baseline data of HbA1C so that the temporal relationship and causal pathway cannot be assessed (Chiang *et al.*, 2015; Deng *et al.*, 2016; Ruslami *et al.*, 2010; Urquhart, 1996). The interventional studies among the TB population concerning glycaemic control of diabetes are more focused on drug regimes. Therefore, evidence from the field regarding non-pharmacological strategies is lacking.

Recent studies concluded that the strategies in controlling glucose and how tightly glucose control influences the TB treatment outcomes among TB patients with diabetes should be determined. Randomised controlled trials comparing TB treatment outcomes, diabetes complication rates and haemoglobin A1C levels in people who receive diabetes-specific interventions, in addition to standard TB care to those who receive standard TB care, would greatly contribute to building an evidence base for a clearer standard (Deng *et al.*, 2016; Jeon *et al.*, 2012).

1.4 Justification of study

A well-structured coordinating mechanism is necessary to adequately respond to the growing concern of TB and diabetes comorbidity. Cooperation between diabetes and TB services will maximize the efficient use of resources. The current practices on diabetes and TB education to TB patients with diabetes should be enhance and need improvement. Appropriate education materials, repetitive education from both TB and diabetes team, and improvement in counselling for delivering diabetes self-care advices are strongly needed during the six months of TB treatment to achieve good glycaemic control.

Motivational Interviewing (MI) has been used by dietician and diabetes educator in promoting diabetes self-care among diabetic patients and proven to stimulate patients' internal motivation to change. The greater demands for TB nurses with no background training as diabetic educator justifies the need of development of MID-DOT training module in this study. The training module will help professional or other health care practitioners conduct a consistent and effective training for TB staff intended to help them in creating a focus, repetitive and structured TB and DM education during DOT. Such a module can serve as reference material in every TB centre in Malaysia to guide TB staff in positive counselling practice. Culturally appropriate educational materials may be developed to enhance patients-staff communication during educational sessions.

Operational research will be conducted to assist in delivering TB and diabetes self-care education at TB clinic by trained TB nurses during patient visits for daily intake of TB drug (Directly Observed Therapy) during the six months of the TB treatment courses. This TB and diabetes self-care education will be delivered using MI style, which follows the standardized intervention module (MID-DOT training module) and educational materials principally developed for this study.

This study will address the research gap on alternative strategies for management TB patients with diabetes. The findings will delineate some important aspects on the effect of innovative intervention using standardised module and educational materials on TB treatment success through lifestyle modification, glucose monitoring, and medication adherence. It also contributes to the body of literature in the field of association between diabetes, glycaemic control and TB treatment success and help researchers to have a deeper understanding and to clarify the temporal relationship or causal pathway between glycaemic control and TB treatment success.

This study will also increase stakeholder attention to and awareness of the benefits of implementing shared responsibilities between diabetes and TB teams in delivering health education concerning both diseases, especially during 6 months of TB treatment. This study is intended to facilitate more powerful integration programs that can enhance the current strategies among local health authorities. Future researchers may use this research as a guide to methodology for conducting operational research in the TB and diabetes field.

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1.5 Research questions

This study addresses the following research questions:

1. Does the MID-DOT intervention program effective in increasing successful TB treatment outcome among pulmonary TB patients with type 2 diabetes in Kelantan.
2. Does the MID-DOT intervention program effective in achieving good glycemic control during TB treatment among pulmonary TB patients with type 2 diabetes in Kelantan.
3. Does the MID-DOT intervention program effective in achieving good diabetes self-care practices during TB treatment among pulmonary TB patients with type 2 diabetes in Kelantan.

1.6 Objectives

1.6.1 General Objectives

To evaluate the effectiveness of MID-DOT intervention on successful TB treatment outcome including glycaemic control and diabetes self-care practices among pulmonary TB patients with type 2 diabetes in Kelantan.

1.6.2 Specific Objectives

1. To compare the successful of TB treatment outcome between MID-DOT intervention group and usual care group for among pulmonary TB patients with type 2 diabetes in Kelantan.

2. To compare mean HbA1c level over time between MID-DOT intervention group and usual care group among pulmonary TB patients with type 2 diabetes in Kelantan.
3. To compare mean diabetes self-care activities score over time between MID-DOT intervention group and usual care group among pulmonary TB patients with type 2 diabetes in Kelantan.

1.7 Hypothesis

1. The MID-DOT intervention program is effective in increasing successful TB treatment outcome in comparing to standard health education among pulmonary TB patients with type 2 diabetes mellitus in Kelantan.
2. The MID-DOT intervention program is effective in achieving good glycemic control (reduction in HbA1c level) in comparing to standard health education among pulmonary TB patients with type 2 diabetes mellitus in Kelantan.
3. The MID-DOT intervention program is effective in achieving good diabetes self-care practices (improvement of score) in comparing to standard health education among pulmonary TB patients with type 2 diabetes mellitus in Kelantan.

CHAPTER TWO

LITERATURE REVIEW

2.1 Understanding Tuberculosis and Diabetes

TB has been described with the terms “consumption”, “white plague” and "phthisis" throughout the history (Dubos and Dubos, 1952). The *Mycobacterium tuberculosis* bacteria was discovered in early 1900, but the signs and symptoms of TB have been observed as far back as 2400 B.C. Over the past century, there has been a dramatic increase in TB rates, despite the availability of advance screening, diagnostics, and pharmacological treatment (Metcalf, 1991). Overall, a relatively small proportion (5–15%) of the estimated people infected with *Mycobacterium tuberculosis* will develop TB disease during their lifetime. However, the probability of developing TB disease is much higher among people infected with HIV, and also higher among people affected by risk factors such as under-nutrition, diabetes, smoking and alcohol consumption (Zumla *et al.*, 2013).

Based on WHO surveillance data, an estimated 10.4 million people were infected with TB in 2016. 90% were adults, 35% were female, 10% were people living with HIV and 56% were in five countries: China, Indonesia, India, the Philippines, and Pakistan. There were an estimated 1.3 million TB deaths among HIV-negative people (down from 1.7 million in 2000) and an additional 374 000 deaths among HIV-positive people. About 600 000 new cases were resistance to rifampicin (RRTB), the most effective first-line drug, 490 000 of which had multidrug-resistant TB (MDR-TB). In Malaysia, 26 000 TB cases were notified in 2016, reflecting a notification rate of 92

per 100,000 populations with a reported 1414 TB deaths (excluding TB-HIV mortality), giving rise to 4.9 TB deaths per 100,000 populations (WHO, 2017).

TB is also a costly disease which has a terrible economic impact. Approximately 75% to 80% of TB cases are in the economically productive age group. The economic impact of TB comes from the large direct and indirect costs incurred by the patients, suffered because of loss of income following the inability to work and premature deaths. Lengthier treatment, often in hospitals, substantially increases health care costs and economic burdens on families and society. Studies in some developing countries found that the average cost for treatment of susceptible TB was in the range of USD 276-154 and USD 1,000-10,000 for MDR-TB. The cost of treating a single case of MDR-TB or XDR-TB can be thousands of times more expensive than treating drug-sensitive TB (Kang *et al.*, 2006; Laurence *et al.*, 2015; Schnippel *et al.*, 2013). A local study in Penang showed that the cost of treating TB per patient was RM 3482.30. The cost of anti-TB drugs constituted the highest proportion of the cost to the public services (31.7%), while the cost to the patient constitutes 80% of the total costs of treatment (Elamin *et al.*, 2008).

TB treatment outcomes after 6 months of full course of TB regimens are categorised as cured, completed treatment, interrupted treatment, failed treatment and died. In 1993, the WHO introduced surveillance of TB treatment outcomes to evaluate the impact of TB control programs. Treatment success rate, consisting of cured and completed treatment, is an important indicator of national TB control programs, with the set target of 85% (WHO, 2003b). In 2000, the worldwide rate of TB treatment success was 82% in DOTS areas, but only 67% in non-DOTS. Therefore, DOT is a

proven adherence strategy to reduce the development of drug resistance, treatment failure, or relapse after the end of TB treatment. Good case management, which includes establishing a relationship with the patient and addressing barriers to adherence, facilitates successful DOT (Alwood *et al.*, 1994; Chaulk *et al.*, 1995; Walley *et al.*, 2001; Zwarenstein *et al.*, 1998).

The TB treatment success rate in Malaysia declined from 78% in 2000 to 48% in 2006 but increased back after 2007. However, the TB treatment success rate has not reached the 85% target rate set by the WHO. The National Strategic Plan to Control TB 2011-2015 was implemented to strengthen and enhance all activities to reduce burden of TB disease and increase the TB success rate in the country (MOH, 2012). However, due to natural history and complexity of TB disease, treating TB in immunosuppressed groups such as diabetes mellitus (DM) and chronic renal failure (CRF) becomes a major challenge in reducing TB burden. Among several risk factors for TB, which include malnutrition, alcoholism, HIV/AIDS and silicosis, diabetes has only recently been appreciated as the number of TB patients with diabetes is higher than the number of patients with TB-HIV co-infection around the world (Aravindalochanan *et al.*, 2012; Dooley and Chaisson, 2009; Ottmani *et al.*, 2010; Ruslami *et al.*, 2010).

As type 2 diabetes increases globally, it is even more likely to adversely affect TB care and control as the prevalence of diabetes are expected to rise dramatically in the resource-poor areas where TB thrives. An estimate of 450 million people had diabetes worldwide and this number is anticipated to reach 630 million people by 2040 (IDF, 2015). Eighty per cent of them live in low and middle-income countries in the developing world, where active TB is prevalent. Six of the 10 countries that projected

to have the greatest numbers of people living with diabetes by 2035 (China, India, Brazil, Indonesia, Pakistan and Russian Federation) are also classified as high TB-burden countries (WHO, 2016).

With the increased number of diabetes patients among low-resource health care systems, TB and diabetes comorbidity will inevitably increase as 10-30% of TB cases estimated to be attributable to diabetes (Balakrishnan *et al.*, 2012; Chang *et al.*, 2011; Stevenson *et al.*, 2007). Recent studies elsewhere and Malaysia demonstrated the prevalence of diabetes among TB patients is ranging from 13 to 36% (Alisjahbana *et al.*, 2007; Atif *et al.*, 2014; Bacakoğlu *et al.*, 2001; Balakrishnan *et al.*, 2012; Delgado-Sanchez *et al.*, 2015; Gil-Santana *et al.*, 2016; Hemming *et al.*, 2011). These prevalence vary according to the setting possibly attributable to difference in background prevalence of diabetes between populations and methods of screening and diagnosing diabetes (Workneh *et al.*, 2017). Studies all over the world also constantly reported strong association between diabetes and development of active TB. A systematic review of the literatures identified 13 quantitative, age adjusted, observational studies in North America, Russia, UK, Korea, Mexico, Taiwan and India found that diabetes was associated with an increased risk of TB; across three cohort studies, the pooled relative risk of TB associated with diabetes was 3.1, while in case-control studies the odds ratios of TB ranged from 1.16 to 7.83 (Jeon and Murray, 2008).

Diabetes has certain characteristics that may make diabetes patients more prone to TB and suffer worse TB treatment outcomes (Zheng *et al.*, 2017). These characteristics are probably a result of internal factors (e.g. low immune system) and external factors (e.g. poor glycaemic control). Diabetes patient has evidence of immunosuppression

like impaired cell-mediated immunity, micronutrient deficiency, pulmonary micro angiopathy and renal insufficiency, all of which predispose TB patient with diabetes to have 3 times higher risk to develop TB, 2 times higher risk of remaining culture positive, 4 times higher risk of relapse after completed treatment, and 5 times higher risk of death during TB treatment, as compared to those without diabetes (Baker *et al.*, 2011; Jeon and Murray, 2008; Stevenson *et al.*, 2007).

The Diab-Care Asia project, a cross sectional survey of 24,317 diabetic patients from Bangladesh, China, India, Indonesia, Malaysia, Philippines, Singapore, South Korea, Sri Lanka, Taiwan, Thailand and Vietnam found that almost 60% of patients had values of HbA1C exceeding 8% (Chuang *et al.*, 2002). This poor glycaemic control may contribute to the burden of TB incidence worldwide, threaten the TB control and overwhelm the capacity of healthcare systems in low and middle-income countries around the world (Bailey *et al.*, 2016). This also will in turn hamper WHO's target to scale down global TB incidence by 90%, or less than 10 cases per 100,000 population, in 2035 and will further impede the world's long-term vision of eliminating TB as a public health concern by reducing TB rates to less than 1 case per million people by 2050 (WHO, 2015).

Recognizing this double burden, the WHO and the International Union Against Tuberculosis and Lung Disease (The Union) have developed a collaborative framework that can help countries mount a response. This framework set out the principle of 'bidirectional screening'; screen TB patients for diabetes and in context where TB is common, screen people with diabetes for TB (WHO, 2011). The Union and the World Diabetes Foundation co-hosted the first Global Summit on the looming

co-epidemic of diabetes and TB in Bali in November 2015. Bringing together government representativeness, civil society group and other stakeholders from the global health community, the convention culminated with the signing of the Bali Declaration, a unified agreement to act. Key actions include the implementation of the "Collaborative Framework", supporting the training of health personnel, increasing public awareness about both diseases through repetitive education, internal advocacy in national and international forums and update, elimination of stigma around TB and diabetes, supporting policymaking and research activities, and coordinated management in diabetes and TB for good glycaemic control among TB patients with diabetes.

Although several strategies and frameworks address diabetes, achieving optimum glycaemic control is hard in diabetes patient. This is dependent on the quality health care system, financial affordability, patients' behaviour, self-empowerment, and the natural history of both disease. The underlying TB may complicate the glucose control in diabetes patient. TB is curable, but the infection increases body catabolism and raises blood sugar, making diabetes more difficult to manage. Rifampicin (one of the key drugs in any anti-TB regimen) may itself have hyperglycaemic effects that threaten glycaemic control (Riza *et al.*, 2014).

Additionally, type 2 diabetes is a lifestyle disease with the glycaemic control influenced by multiple risk factors such as imbalance dietary intake, low physical activity, smoking, and alcohol intake. Recently, researcher have shown adherence to lifestyle modification is helpful in achieving good glycaemic control instead of prolonged the treatment regimen (Riza *et al.*, 2014). To improve the patients'

adherence to treatment strategies, health personnel play a crucial role in improving patient's knowledge, self-care and internal motivation. Their competency in delivering advice, style of counselling, their frequent meets with the patients might influence patient's interest to make a sustain behavioural changes (Ottmani *et al.*, 2010).

2.2 Perspectives on patient adherence

2.2.1 Definition and context

Adherence is defined as the extent to which a person's behaviour taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider (Urquhart, 1996). Adherence differs from compliance in the sense that adherence requires the patient's decision support and agreement to the provider's recommendations (Horne *et al.*, 2005). Patients should be actively collaborated with health care providers in their own care and that good rapport and communication between patient and health care providers is necessary for an effective practice. Adherence always refers to non-communicable diseases such as hypertension and diabetes; however, infectious disease such as HIV and TB require similar levels of attention and care as many other chronic non-communicable diseases due to their chronic nature (McNabb, 1997).

In terms of TB control, adherence to treatment may be defined as the extent to which the patient's history of therapeutic TB drug-taking coincides with the recommended and prescribed treatment (Munro *et al.*, 2007). In TB patients with diabetes, adherence may extent to their behaviour on following diet and other lifestyle changes. The adherence may be measured using either outcome-oriented or process-oriented

definitions. Outcome oriented definitions use the end-result of treatment, e.g. completed and cure rate, as the indicator of success. The process oriented definition makes use of intermediate variables such as pill counts to measure adherence and appointment-keeping as well as their diabetes self-care activities (Urquhart, 1996) . Ideally, adherence to TB treatment should be measured in terms of both quantity and timing of the medication taken by the patient. This approach is always practical at the individual level, but a more pragmatic approach is needed at the population level. Thus, the success of treatment, that is, the sum of the patients who are cured and those who have completed treatment under the directly observed therapy, short course (DOTS) strategy, is a pragmatic proxy serving as an indicator of treatment adherence (Urquhart, 1992).

2.2.2 Factors that influence adherence to treatment

Previous studies have reported that patients' sociodemographic characteristics, their relationship with health care providers and the regimens offered have been associated with adherence to TB treatment (Sumartojo, 1993). The barriers to a good adherence to TB treatment can be classified as shown below.

A. Economic and structural factors

Those afflicted by TB are typically homeless, poor, and/or unemployed. These groups are hard to reach as they may have unstable living circumstances and lack effective social support networks. This creates an unfavourable environment for ensuring adherence to treatment (Liefooghe *et al.*, 1995).

B. Patient-related factors

Age, gender and ethnicity have been linked to treatment adherence in many countries (Diwan and Thorson, 1999; Farmer, 1996; Hudelson, 1996). Self-belief in the efficacy of TB drugs and knowledge about TB will influence whether or not a patient chooses to complete treatment (Dick and Lombard, 1997).

C. Supportive relationships between the health provider and the patient

Patient satisfaction with the "significant" health care has been shown to be an important determinant of adherence (Lewin *et al.*, 2001; Steyn *et al.*, 1997), but good and empathic relationships are difficult to forge in situations in which health providers are overworked, untrained, unsupported in their tasks, or inadequately supervised, common scenarios in countries with a high TB burden (Steyn *et al.*, 1997).

D. Pattern of health care delivery

Factors related to the organization of clinical services, including availability of expertise, links with patient support systems, and flexibility in the hours of operation, also affect adherence to treatment. Many ambulatory health care settings responsible for the control of TB are organized to provide care for patients with acute illnesses, and staff may therefore lack the skills required to develop long-term management plans with patients. Consequently, the patient's role in self-management is not facilitated and follow-up (WHO, 2003a).

2.2.3 Type of adherence strategies

Numerous measures and strategies have been introduced in various settings to improve patient adherence to treatment. These strategies vary according to whom or what they are targeting for change. Certain strategies target patients directly while aiming to influence adherence indirectly by targeting other actors or factors for change. They may target patients, health providers, the relationship between health providers and their patients, the treatment, patients' social contexts or the health system for change (Hunt and Arar, 2001; Kidd and Altman, 2000; Sbarbaro, 1979; Vermeire *et al.*, 2001). In TB context, the interventions for improving adherence rates may be classified into the following categories:

1. Staff supervision and motivation: management process and training aimed at improving the way in which providers care for patients.
2. Defaulter action: the action to be taken when a patient fails to keep a pre-arranged appointment.
3. Prompts: routine reminders for patients to keep pre-arranged appointments.
4. Health education: provision of information about TB and the need to attend treatment.
5. Incentives and reimbursements: money or cash in kind to reimburse the expenses of attending the treatment centre, or to improve the attractiveness of visiting the treatment centre.
6. Contracts: agreements (written or verbal) to return for an appointment or course of treatment.

7. Peer assistance: people from the same social group helping someone with tuberculosis to return to the health centre by prompting or accompanying him or her.
8. Directly observed therapy (DOT): an identified, trained and supervised agent (health worker, community volunteer or family member) directly monitors patients swallowing their anti-TB drugs (WHO, 2003a).

2.3 Directly Observed Therapy

Directly observed therapy (DOT) was first developed by Wallace Fox in the 1950s with the concept of "entirely supervised administration of medicines". DOT was first adopted in TB drug trials in Madras (India) and Hong Kong as early as the 1960s and is now widely recommended for the measures to promote adherence to TB treatment (Bayer and Wilkinson, 1995; WHO, 2003b). DOT has always meant much more than "supervised swallowing". Projects in countries with a high prevalence of TB have shown that removing the socioeconomic barriers to DOT faced by patients increases both adherence and cure rates (Farmer, 1996; Olle-Goig and Alvarez, 2001). In countries where the prevalence of TB is low, such as the United States, DOT programmes are complex but highly cost-effective and have several components, including social support, housing, food tokens and legal measures (Chaulk *et al.*, 1995).

Since 1991, WHO has promoted the strategy of "directly observed therapy, short course" (now known as the DOTS strategy). "DOTS" is the brand name for a comprehensive technical and management strategy consisting of the following five elements: political commitment; case detection using sputum microscopy among persons seeking care for prolonged cough; standardized short courses of chemotherapy under proper case-management conditions including DOT; regular drug supply; and a standardized recording and reporting system that allows assessment of individual patients as well as of overall programme performance (WHO, 2002).

2.4 Patients education and adherence to TB treatment

2.4.1 Patient education

Patient education has been defined as a deliberate process of influencing patient behaviour and producing the changes in knowledge, attitudes, and practices necessary to maintain or improve health. The aim of patient education is to implement it as a holistic process with the goal of changing the behaviour of the patient and his or her family to improve and benefit their own health. Patient education is an assignment that all health care workers are responsible (Lorig, 1996).

Patients not following professional health advice is a worldwide challenge for health care (Haynes *et al.*, 2008). A growing number of drugs have been shown to significantly improve health if taken as recommended, but according to the WHO, only about 50% of professional health advice is actually taken up by patients (WHO, 2002). Other authors have estimated that the proportion of patients that do not follow doctors' orders ranges from 20% to 80% (Haynes *et al.*, 2008). Poor adherence behaviour has

a wide-ranging impact. From a public health perspective, it often adds to the burden of disease and the pool of infection.

In TB context, non-adherence to drug treatment for tuberculosis has the potential to impact negatively on both the individual patient and on the broader health of the community. It is therefore important to evaluate which interventions are effective in supporting adherence and completion of tuberculosis drug treatment regimen. In diabetics, poor adherence causes poor glycaemic control and increase risk of diabetes complication. This also increases the financial burden placed on public health services and wastes (Haynes *et al.*, 2008).

For health providers it is a source of major frustration and can consume a great deal of time and energy (Vermeire *et al.*, 2001). It also impacts negatively on patients' health and perhaps also their well-being, particularly patients with long-term illnesses (Cleemput *et al.*, 2002). From a research point of view, poor adherence makes clinical trials more difficult and costly to administer and the trial results become less meaningful (van Hoorn *et al.*, 2016).

2.4.2 Patient centred approach

A patient-centred approach has been proposed as a way of enhancing the quality and outcomes of interactions between health providers and patients. According to a systematic review Lewin *et al.* (2001) most interventions to promote a PCA have been directed at primary care physicians in community or hospital outpatient settings. This review also found that patient-centred interventions may have a positive impact on the quality of clinical consultations and patients' satisfaction. Although not confirmed in

the systematic review, some have suggested that there is evidence of a relationship between effective provider-patient communication and improved health outcomes (Stewart, 1995). Thus, the link between improved provider-patient communication and treatment adherence is not entirely clear.

Little is known about the feasibility of implementing a PCA with nurses in busy primary health care facilities in developing country contexts or about how this type of approach is received by health providers and patients in these contexts. The results of one study that explored this in the context of family planning services in Egypt indicate that this type of approach can be feasible, acceptable and associated with better health outcomes in a less developed country setting (Abdel-Tawab and Roter, 2002).

2.4.2.1 Motivational Interviewing (MI)

Motivational interviewing(MI) is defined as "a directive, client-centred counselling style for eliciting behaviour change by helping clients to explore and resolve ambivalence" (Miller and Rollnick, 2012). It is an evidence based, collaborative, guided approach to health behaviour change. In contrast to traditional approaches of behaviour change, MI embodies respect for the patient. It fosters collaboration between the health care provider and patient, demonstrates compassion, and emphasizes the patients' personal autonomy while building self-efficacy (Markland *et al.*, 2005; Rubak *et al.*, 2005). Express empathy through active listening, roll with resistance, avoid arguing with the patient, resolve the patients' ambivalence and support self-efficacy by emphasizing the autonomy are the spirit and principle of MI.