ASSESSMENT OF PHARMACIST INITIATED MEDICATION THERAPY MANAGEMENT PROGRAM IN IMPROVING DISEASE RELATED KNOWLEDGE, MEDICATION ADHERENCE AND HEALTH RELATED QUALITY OF LIFE AMONG TYPE 2 DIABETIC PATIENTS IN SARGODHA, PAKISTAN

By

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LIST OF ABBREVIATIONS

Abbreviation	Terms
ADA	American Diabetes Association
BMI	Body Mass Index
BP	Blood Pressure
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
DSME	Diabetes Self-Management Education
DRPs	Drug Related Problems
FBS	Fasting Blood Sugar
HDL-C	High Density Lipoprotein Cholesterol
HbA1c	Glycated Hemoglobin
HRQoL	Health Related Quality of Life
LDL-C	Low-Density Lipoprotein Cholesterol
MTM	Medication Therapy Management
MTR	Medication Therapy Review
MAPs	Medication Related Action Plan
MDKT	Michigan Diabetes Knowledge Test
MMAS	Morisky Medication Adherence Scale
MDKT-U	Michigan Diabetes Knowledge Test Urdu Version
MMAS-U	Morisky Medication Adherence Scale Urdu Version
TC	Total Cholesterol
TG	Triglyceride
T2DM	Type 2 Diabetes Mellitus
WHO	World Health Organization

PENILAIAN FARMASI DIMULAKAN UBAT PROGRAM PENGURUSAN TERAPI DALAM MENINGKATKAN PENYAKIT BERKAITAN ILMU, PEMATUHAN UBAT DAN KESIHATAN BERKAITAN KUALITI HIDUP DI KALANGAN TYPE 2 PESAKIT DIABETES DI SARGODHA, PAKISTAN

ABSTRAK

Ubat Program Pengurusan Terapi adalah satu perkhidmatan inovatif, ahli farmasi yang diterajui dan menyampaikan yang bercadang untuk menyelesaikan masalah terapi dadah, meningkatkan pendidikan pesakit dan meningkatkan pematuhan kepada regimen terapeutik. Oleh itu, Kajian ini bertujuan untuk menilai kesan ahli farmasi dimulakan Ubat Program Pengurusan Terapi mengenai diabetes berkaitan pengetahuan, pematuhan ubat, kawalan glisemik dan Kesihatan Berkaitan Kualiti Hidup pencapaian antara Jenis 2 pesakit Diabetes Mellitus di Sargodha, Pakistan. Ini adalah satu kajian tiga kali ganda di mana analisis pra-campur tangan diabetes pesakit pengetahuan yang berkaitan, pematuhan ubat, kawalan glisemik dan status semasa Kesihatan Berkaitan Kualiti Hidup telah dijalankan dengan menggunakan alat pra-disahkan. Tiga ratus sembilan puluh dua jenis 2 pesakit Diabetes Mellitus telah dimasukkan untuk meneroka atas objektif yang dinyatakan. Fasa penilaian pra-campur tangan mendedahkan bahawa peserta kajian mempunyai purata pengetahuan diabetes berkaitan (8.02 ± 2.58 daripada 14), pematuhan ubat rendah (4.43 ± 1.78 daripada 8), kawalan glisemik miskin (9.44 ± 1.58) dan Kesihatan Berkaitan Kualiti Hidup (0,4715 ± 0,336 dan 64,77 ± 6,57). maka lain pengetahuan dan pematuhan ubat, sederhana korelasi yang signifikan ($r < 0.3$, $p < 0.05$) diperhatikan di kalangan semua pemboleh ubah bersandar. Analisis pra-campur tangan diikuti

dengan rawak peserta kajian dan pelaksanaan campur tangan pendidikan oleh ahli farmasi. Data yang post campur tangan telah disediakan dari 161 mata pelajaran kumpulan campur tangan dan 164 peserta dalam kumpulan kawalan. Diabetes pengetahuan yang berkaitan, pematuhan ubat dan Kesihatan Berkaitan Kualiti skor Life dikaitkan dengan ketara ($p < 0.001$) apabila kumpulan campur tangan dan kumpulan kawalan dibandingkan pada akhir campur tangan. Terdapat peningkatan dalam skor diabetes berkaitan pengetahuan (10.55 ± 2.56), skor pematuhan ubat (5.24 ± 1.48) dan Kesihatan Berkaitan Kualiti Hidup ($0,6115 \pm 0,286$ dan $68,37 \pm 14,094$) di kalangan peserta kumpulan campur tangan. min HbA1c bermakna dikurangkan kepada 8.97 ± 1.362. Tambahan pula, perbezaan yang signifikan ($p < 0.05$) juga diperhatikan di antara sebelum dan kumpulan intra pasca (lengan intervensi) juga dilaporkan. Kesimpulannya, kajian ini menunjukkan bahawa ahli farmasi dimulakan Ubat Program Pengurusan Terapi memberi kesan positif kepada hasil terapeutik dipilih. Oleh itu, peranan ahli farmasi dalam pendidikan pengurusan diri pesakit mesti diiktiraf sebagai sebahagian penting dalam sistem penjagaan kesihatan dan mesti dipupuk untuk menggalakkan konsep kualiti penjagaan.

ASSESSMENT OF PHARMACIST INITIATED MEDICATION THERAPY MANAGEMENT PROGRAM IN IMPROVING DISEASE RELATED KNOWLEDGE, MEDICATION ADHERENCE AND HEALTH RELATED QUALITY OF LIFE AMONG TYPE 2 DIABETIC PATIENTS IN SARGODHA, PAKISTAN

ABSTRACT

The Medication Therapy Management Program is an innovative, pharmacist-led and delivered service that intends to resolve drug therapy problems, enhance patient education and improve adherence to the therapeutic regimen. The present study was therefore aimed to assess the impact of pharmacist initiated Medication Therapy Management Program on diabetes related knowledge, medication adherence, glycemic control and Health Related Quality of Life outcomes among Type 2 Diabetes Mellitus patients in Sargodha, Pakistan. This was a three phase study whereby a pre-intervention analysis of patients' diabetes related knowledge, medication adherence, glycemic control and present status of Health Related Quality of Life was undertaken by using pre-validated tools. Three hundred and ninety two Type 2 Diabetes Mellitus patients were included to explore above stated objectives. The pre-intervention assessment phase revealed that study participants had average diabetes related knowledge (8.02±2.58 out of 14), low medication adherence (4.43±1.78 out of 8), poor glycemic control (9.44±1.58) and Health Related Quality of Life (0.4715±0.336 and 64.77±6.57). Other than knowledge and medication adherence, moderate significant correlations ($r<0.3$, $p<0.05$) were observed among all dependent variables. The pre-intervention analysis was followed by randomization of

the study participants and implementation of the educational intervention by the pharmacist. The post intervention data were available from 161 subjects of intervention group and 164 participants in the control group. Diabetes related knowledge, medication adherence and Health Related Quality of Life scores were significantly associated ($p<0.001$) when intervention group and control group were compared at the end of the intervention. There was an increase in diabetes related knowledge score (10.55±2.56), medication adherence score (5.24±1.48) and Health Related Quality of Life (0.6115±0.286 and 68.37±14.094) among the participants of intervention group. The mean HbA1c mean reduced to 8.97±1.362. Furthermore, a significant difference ($p<0.05$) was also observed between the pre- and post- intra group (interventional arm) was also reported. In conclusion, the present research demonstrated that pharmacist initiated Medication Therapy Management Program had a positive impact on selected therapeutic outcomes. Therefore, the role of pharmacists in patient self-management education must be recognized as an integral part of the health care system and must be promoted to promote the concept of quality of care.

CHAPTER 1

INTRODUCTION

1.1 Background of the study

Since its earliest description several thousand years ago, Type II Diabetes mellitus (T2DM) has remained a chronic and progressive disease (Montenero, 2000). Over a period of decades, although the ability of diagnosis and treatment of diseases has significantly improved, the disease profile of the world has also altered at a frightening rate (Centers for Disease Control Prevention, 2006). Chronic diseases which include cardiovascular diseases, stroke, cancers, chronic respiratory diseases, diabetes and mental disorders are now accounted for 47% of the global burden of diseases and 60% of all deaths worldwide (World Health Organization, 2003).

Within this context, T2DM is a serious concern with an increasing prevalence around the globe (Tabish, 2007). T2DM is a complicated and overwhelming condition-affecting people of all ages and ethnic groups. In 2003, 194 million of the population had T2DM and almost three-quarters of them were living in the developing world (Narayan et al., 2006). The increasing number of people with type 2 diabetes is a worldwide concern, but the major part of this numerical increase will occur in developing countries. The increase in prevalence of diabetes in developing countries is projected to be 170% compared to 42% in developed countries. (Wild, Roglic, Green, Sicree, & King, 2004). Furthermore, almost 1 million casualties were reported each year because of T2DM and two-thirds of these were reported from the developing countries (World Health Organization, 2002). Population growth, ageing issues, dietary changes, urbanization, increased prevalence of obesity and poor

physical inactivity were the major factors towards an increased incidence of T2DM (Hu, 2011). By 2025, it was anticipated that this figure will be expanded by 72%; 333 million new cases will be reported and the prevalence will be increased to double fold in the Middle East, North Africa, South Asia and Sub-Saharan African regions (World Health Organization, 2002). In line to what is reported, the prevalence of T2DM and its adverse effects were more noticeable in South Asia when contrasted with the other area of the world (Ghaffar, Reddy, & Singhi, 2004). In South Asia, large number of individuals live on or below the poverty line and have lack of access to health care facilities. There are no national welfare plans and provision of medical coverage for the poor people (Khowaja, Khuwaja, & Cosgrove, 2007). The poor people cannot bear to pay for health care facilities, therefore, the individuals are diagnosed belatedly resulting in acute and chronic complications (Danaei et al., 2011).

1.2 Overview of Pakistan's health care system

National public health is a recent innovation in Pakistan. National health planning began with the Second Five-Year Plan (1960-65) and continued through the Eighth Five-Year Plan (1993- 98). In addition to public- and private-sector biomedicine, there are indigenous forms of treatments. Some manufactured remedies are also available in certain pharmacies. Homeopathy is also taught and practiced in Pakistan. Prophetic healing is based largely according to the teaching of the Prophet pertaining to hygiene and moral and physical health, and simple treatments are used, such as honey, a few herbs, and prayers. Some religious conservatives argue that reliance on anything but prayers suggests lack of faith, while others point out that the Prophet

remarked that ‘Allah has provided cure for every disease other than death and old age’ (CIA, 2005;WHO, 2007).

1.3 Structure and health services in Pakistan

The Ministry of Health is responsible for all matters concerning national planning and coordination in the field of health. The Drugs Control Organization is a subsidiary of Ministry of Health. It facilitates local pharmaceutical units and drug importers in registration and licensing and making their participation possible in various events organized the world over (MOH, 2008).

Under the Pakistani constitution, the federal government is responsible for planning and formulating national health policies and provincial governments for its implementation. The private sectors serve nearly 70% of the population, whereas public sector comprises more than 10,000 health facilities ranging from Basic Health Units (BHUs) to tertiary referral centers. BHU covers around 10,000 people, whereas a larger Rural Health Center (RHCs) covers around 30000-450000 people. In Pakistan Primary Health Center (PHC) units comprises both BHUs and RHCs. The Tehsil Headquarters Hospital (THQ) covers the population at sub-district level whereas District Headquarters Hospital (DHQ) serves at district level as its name suggests (Ghaffar *et al.,* 1999). Health system of any country is mainly based on the human resources available. As in case of Pakistan, there is a lack of clear long-term vision for human resource development and the Ministry of Health, both at federal and provincial levels do not have a unit responsible for such an important health system function. The health information system is fragmented. Each vertical program has more or less its own information system and none covers the private health sector.

There is no organized system of disease surveillance and there is limited capacity to use information for decisions. The overall capacity to undertake health policy and system research is deficient (WHO, 2007).

As the population is growing and there are issues of poor housing, lack of exercise, pollution, improper diet and the lack of health education, diseases are rampant. The health care system in Pakistan has been confronted with problems of inequity, scarcity of resources, inefficient and untrained human resources, gender insensitivity and structural mismanagement (Babar, 2006). Pakistan is facing a very precarious economic situation and there is a need of innovative health reforms (Islam, 2002). Political instability caused frequent changes in the government, thus resulting corresponding changes of health policy. Till now, health policies have not been given enough time for proper implementation in the country (Khan & Heuvel, 2007). The low priority given to the health sector by the military regimes has resulted in a persistent contrast between reasonable economic growth and government expenditure on health (MOF., 2009).

1.4 Role of pharmacists in different sectors in Pakistan

It has been estimated that around 8102 pharmacists are present in Pakistan, 2836 work in public sector, 5023 in private setting while 243 pharmacists in total private non-profit organizations (WHO, 2007). Approximately 55% are engaged in production of pharmaceuticals, 15% in the federal and provincial drug control and hospital pharmacy setup, 15% in the sales and marketing of pharmaceuticals, 10 % in community pharmacy, 5% in teaching and research. Pharmacy education is mainly focused on the industrial need, as a result, at present; a large number of pharmacists in

Pakistan are involved with the pharmaceutical industry. Although the world over, the role of pharmacists is recognized in community pharmacies, hospitals and drug regulatory authorities but the health care system of Pakistan has yet to recognize this role (Babar, 2007).

1.5 Diabetes in Pakistan

Pakistan is a South-Asian country with a population of approximately 150 million (69% of the population are rural, over an area of 800,000 km^2). Pakistan is a low-income country with limited resources (Baig et al., 2013). Pakistan was placed amongst the top ten nations of the world with the highest number of individuals with T2DM in 2004 and was anticipated that an expected 14.5 million people of Pakistan will have T2DM by the year 2025 (Sarah, Gojka, Anders, Richard, & Hilary, 2004). T2DM affects both high and low-income group; 12% of individuals above 25 years of age suffer from T2DM and 10% people have impaired glucose tolerance (IGT), which is expected to increase more swiftly in the future (Hakeem & Fawwad, 2010; Shera et al., 1995). Recently, it was reported that there were approximately 6.6 million Pakistani adults with T2DM in 2012 (Kalra, Peyrot, & Skovlund, 2013). In Pakistan, prevalence of newly diagnosed diabetes was 5.1% in male and 6.8% in female in urban areas and 5.0% in men and 4.8% in women in rural regions (Aziz, Hossain, & Siddiqui, 2009).

Even though, T2DM has reached epidemic proportions worldwide, the number of affected individuals is expanding at a much faster rate than was formerly anticipated (Makrilakis & Katsilambros, 2003). Previously, T2DM was considered as a disease of ageing and the elderly but now this perception has turned out to be a complete

misconception and individuals with type 2 diabetes mellitus in developing nations, including Pakistan are presented at a younger age (Shera, Jawad, & Maqsood, 2007). Acceleration in rates of T2DM in Pakistan is posing threats to the economy and quality of life of individuals due to poor glycemic control and very high rates of complications (Basit, Hydrie, Hakeem, Ahmedani, & Masood, 2004; Khoharo & Qureshi, 2008; Moin, Gondal, & Bano, 2008).

1.6 Diabetes care in Pakistan

There is no cure for T2DM, but the condition is controllable with a combination of medical care, patient education and self-management (American Diabetes Association, 2009). Diabetes complications present a considerable burden of morbidity and mortality, with the danger of both macrovascular and microvascular complications (UK Prospective Diabetes Study Group, 1998).

Multiple diabetes complications in Pakistani patients with T2DM have been reported in literature. A study highlighted that 21% of individuals with T2DM suffer from macrovascular complications which include angina pectoris, myocardial infarction and stroke (17%, 5% and 2.6%, respectively) and microvascular complications, including 43% retinopathy, 39.6% neuropathy, 20.2% nephropathy and 4% foot ulcers (Shera et al., 2004). Previous studies on T2DM in Pakistan reported that a large proportion of patients with T2DM had poor or suboptimal glycemic control and the mean glycated hemoglobin (HbA1c) was higher than the prescribed level as per international guidelines (Badruddin, Basit, Hydrie, & Hakeem, 2002; Khattab, Khader, Al-Khawaldeh, & Ajlouni, 2010; Mahmood & Aamir, 2005; Zuberi, Syed, & Bhatti, 2011). Additionally, the medical care cost is projected to be very high

(Khowaja et al., 2007). Resource imperatives society, lack of medical repayment and inadequate allocation of health care budget are barriers to quality medical care whereby the vast majority of the patients are unable to bear the high cost of treatment (Govender, Ghaffar, & Nishtar, 2007; Khuwaja, Khowaja, & Cosgrove, 2010). Institutions specializing in diabetes care are limited in number and are concentrated in the big cities. There is no personnel support and very few specialized dieticians and pharmacists are available for the patients (Jawad, 2003). Family physicians have little time (the average time spent with a person with diabetes was 8.5 minutes) for counselling that makes issues more complicated for the patients (Shera, Jawad, & Basit, 2002).

1.7 T2DM-related knowledge and Diabetes Self-management Education

A low level of T2DM-related awareness within the population and a low priority to initiate an appropriate preventive and curative plan have been recognized as major issues in the management of T2DM (Ooyub, Ismail, & Daud, 2004). Poor T2DM-related knowledge and management skills among patients is frequently reported in literature (Al Shafaee et al., 2008; Angeles-Llerenas, Carbajal-Sánchez, Allen, Zamora-Muñoz, & Lazcano-Ponce, 2005; Bell, Passaro, Lengerich, & Norman, 1997; Bruce, Davis, Cull, & Davis, 2003; Çaliskan, Ozdemir, Ocaktan, & Idil, 2006; Gunay et al., 2006; Habib & Aslam, 2003; Kamel, Badawy, El Zeiny, & Merdan, 1999; McClean, McElnay, & Andrews, 2001; Murata et al., 2003; Murugesan, Snehalatha, Shobhana, Roglic, & Ramachandran, 2007; Speight & Bradley, 2001; West & Goldberg, 2002). Additionally, another key element of effective disease management for T2DM is the support of patients' self-management capacity building. In order to achieve optimal health, T2DM patients are usually advised strict, rigorous and

permanent lifestyle changes that include dietary interventions, physical activity, strict adherence to medication regimes, good metabolic control and regular medical examinations of eyes, foot and kidney (Khan et al., 2012). However, if patients do not adhere to these guidelines, their diabetes is more likely to be poorly controlled with an increased risk of developing further health problems. Therefore, adherence is a key factor associated with the effectiveness of all pharmacological therapies and foremost the most important factor for medications prescribed for chronic conditions like T2DM (Osterberg & Blaschke, 2005). Consequently, among different strategies for diabetes control, improving adherence plays a key role in optimizing metabolic control (Albano, Crozet, & d'Ivernois, 2008; Lindenmeyer et al., 2006).

Furthermore, to overcome the poor acquaintance towards T2DM, Diabetes Self-management Education (DSME) is considered an integral part of care for individuals who want to achieve successful outcomes (Haas et al., 2013). T2DM needs lifetime care and management; however, 50–80% of patients with T2DM do not posses enough skills and knowledge for self-care of the disease (Clement, 1995). A study reported that the 62.6% of the diabetic population of Pakistan had a poor level of awareness regarding T2DM and its management (Mahmood et al., 2011). Monitoring of metabolic markers, i.e. blood pressure, body weight, lipid profile, blood glucose and HbA1c are is essential in clinical management as hypertension, obesity, and dyslipidemia are well-known risk factors of atherosclerosis and are frequently reported among diabetic patients (Tripathi & Srivastava, 2006). Previous studies have shown that DSME programs improve homeostasis of metabolism and healthy lifestyles prevent the development of atherosclerosis in patients with T2DM (Kim et al., 2006; Mulnier et al., 2013). Therefore, diabetes education is considered to be an

essential element in reaching a good glycemic control (Berger & Mühlhauser, 1999). However, in real practice, modest improvements in glycemic control have been found after the educational intervention focused on diabetes patients (Farsaei, Sabzghabaee, Zargarzadeh, & Amini, 2010; Koev, Tankova, & Kozlovski, 2003; Wens et al., 2008). Centrally focused interventions without the inputs of pharmacists or nurses, patients' non-involvement, poorly structured programs and non-need assessments are among the few reasons of the failure of T2DM-related interventions (Jimmy & Jose, 2011). Therefore, it is now established that a well-structured health education program with the involvement all healthcare professionals and a prior need assessment is necessary for the improvement of diabetes-related outcomes in term of glycemic control and other metabolic complications (Pal, Pal, Barua, & Ghosh, 2010).

1.8 Rationale of the study

T2DM management is a lifelong process that requires efforts from diabetic healthcare providers and patients. However, T2DM Individuals themselves are a key factor in the successful management of the disease and prevention of serious complications (Haas et al., 2013). Diabetes self-care requires patients to adapt dietary and lifestyle modifications, regular blood glucose monitoring and appropriate medication intake with the help of healthcare providers for maintaining a higher level of self-confidence leading to successful behavioural change (Funnell & Anderson, 2004; UK Prospective Diabetes Study Group, 1998). In developing countries like Pakistan, the emergence of this pandemic at an early age is attributable to rapid cultural changes and a high degree of urbanization leading people to adopt unhealthy lifestyles and decreased physical activity. The obesity along with a sedentary lifestyle and increase in caloric intake played a major role in the recent explosion of this chronic illness (Iqbal, 2007).

Non adherence to the prescribed treatment regimen is common in patients with diabetes ranging from 23-77%, making optimal glycemic control difficult to achieve (Riaz, Basit, Fawwad, Ahmedani, & Rizvi, 2014).

Therefore, it is important to explore the patients' perception about T2DM, its management and interaction between patients and healthcare providers. It is also essential to understand the contribution of general T2DM diabetes knowledge among patients and their adherence to medication in order to promote better self-care for T2DM. Within this context, it is recommended that T2DM-related education should be promoted through a pharmacist led medication therapy management (MTM) program (Johannigman et al., 2010; S. L. Pinto, Bechtol, & Partha, 2012). A unique attribute of MTM program is the engagement of the pharmacist in a wider set of activities other than simply counselling about the disease and medications.

1.9 Significance of the study

The incidence and prevalence of T2DM continues to grow worldwide and requires continuous medical care and patient self-management education to prevent acute complications and to reduce the risk of long-term complications (American Diabetes Association, 2009). The importance of glycemic control in reducing future complications in T2DM is highly related to medication adherence and T2DM-related knowledge (Browne, Avery, Turner, Kerr, & Cavan, 2000; Okuno et al., 1999). Therefore, the assessment of the patient's disease-related knowledge and medication adherence is important for better therapeutic outcomes (Rothman et al., 2003).

This study, therefore, will attempt to explore the association between patients' diabetes-related knowledge, medication adherence, glycemic control and its effect on

Health Related Quality of Life (HRQoL). Based on the results, a pharmacist-led MTM program will be offered to T2DM patients attending public health facilities in Sargodha city, Pakistan. It is hoped that the MTM will optimize therapeutic outcomes by reducing drug associated adverse events, improved medication adherence and increased patients' understanding of their diseases and prescribed drugs. In this study, healthcare professionals and policy makers will have a clear picture of T2DM-related problems and will help in planning and developing didactic programs for patients in the near future.

1.10 Study objectives

The primary objective of this study is to evaluate the effectiveness of a pharmacist-led MTM program to control and minimize T2DM-related complications by improving diabetes-related knowledge, medication adherence, glycemic control and HRQoL. In addition, the secondary objectives of this study are as under:

1. To assess diabetes-related knowledge, HRQoL, medication adherence and glycemic control among T2DM patients attending a public healthcare institute in Sargodha, Pakistan.

2. To assess the relationship between diabetes-related knowledge, medication adherence, HRQoL and HbA1c.

3. To implement a pharmacist-led MTM program focusing to improve diabetes-related knowledge, medication adherence, glycemic control and HRQoL among the study population.

4. A post- evaluation to assess the effectiveness of the pharmacist-led MTM program.

1.11 Thesis overview

In this thesis, chapter 2 reviews the literature related to the study with the definition of key terms and provides a conceptual framework for the study. A brief discussion of the importance of diabetes related knowledge, medication adherence, glycemic control and HRQoL is also presented. The literature review finishes with conclusion stating that a pharmacist-led intervention through MTM has the potential to improve medication adherence in diabetes and to reduce levels of HbA1c and other biochemical parameters. A thorough review of literature relevant to the study, concentrating on patient education, medication adherence, glycemic control and HRQoL among T2DM patients forms the bulk of this chapter.

Chapter 3 starts with a systematic discussion of the methodology used for conducting the study. The tools used for data collection, randomization of patients, and implementation of intervention through the MTM program is thoroughly discussed.

Chapter 4 demonstrates the assessment of diabetes-related knowledge, medication adherence, glycemic control and HRQoL among T2DM patients. The detailed methodology, findings and conclusions of the assessment of patient knowledge about diabetes, medication adherence, glycemic control and HRQoL is described.

Chapter 5 illustrates the pre- and post- interventional assessment of diabetes related knowledge, medication adherence, glycemic control and HRQoL and the impact of the intervention is evaluated.

Chapter 6 includes the conclusions of the thesis and along with a set of recommendations for further research work.

CHAPTER 2

PHARMACISTS' INTERVENTIONS TO IMPROVE CONTROL AND MANAGEMENT IN TYPE 2 DIABETES MELLITUS: LITERATURE REVIEW

2.1 Introduction

T2DM is a metabolic disorder characterized by chronic hyperglycemia, polyuria, polydypsia, polyphagia, emaciation, and weakness due to disturbances in carbohydrate, fat, and protein metabolism, which are associated with an absolute or relative deficiency in insulin secretion and/or insulin action (Balkau & Eschwege, 2003; Deb & Dutta, 2006; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997; Kumar. P, 2002; Lindberg G, Lindblad U, & Melander A, 2004).

Diabetes is the most well-known endocrinal disorder, and as of the year 2010, it was evaluated that more than 200 million individuals worldwide had T2DM with 300 million subsequently to have the diabetes by 2025 (Amos, McCarty, & Zimmet, 1997; King, Aubert, & Herman, 1998; Zimmet, 2000). Diabetes may be categorized into several types, but the two major types are type 1 and type two (Zimmet, Cowie, Ekoe, & Shaw, 2004). Table 1 contrasts the features of type 1 and type 2 DM (H., 2010).

Table 2.1: Contrasting Features of Type 1 and Type 2 Diabetes Mellitus (Tripathi, 2006)

Features	Type 1	Type 2
Frequency [a]	10-20%	80-90%
Age of onset	Early below 35 years	Late after 40 years
Type of onset	Abrupt and severe	Gradual and insidious
Weight	Normal	Obese or non-obese
*HLA (human leukocyte antigen)	Linked to ^DR3, HLA DR4,HLA DQ	No HLA association
Family history	< 20%	About60%
Genetic locus	Unknown	Chromosomes 6
Diabetes in identical twins	50% concordance	80% concordance
Pathogenesis	Autoimmune destruction of β cells	Insulin resistance impaired insulin secretion
Islets of cell antibodies	Yes	No
Blood insulin level	Decreased insulin	Normal or increased insulin
Islet-cell changes	Insulin cell depletion	No insulitis, later fibrosis
Amyloidosis	Infrequent	Common in chronic cases
Clinical management	Insulin, diet	Diet, exercise, oral drugs, insulin
Acute complications	Ketoacidosis	Hyperosmolar coma

HLA: Human Leukocyte Antigen
^HLA-DR3: Human Leukocyte Antigen - antigen D Related,
^HLA-DR4: Human Leukocyte Antigen - antigen D Related
^HLA-DQ: is a cell surface receptor protein found on antigen presenting cells
[a]Proportion of sample from the population

2.2 Type 1 Diabetes

β-Cell destruction happens in pancreatic islets. Most of the cases include autoimmune antibodies that destroy β-cells and that are detectable in the blood, but some cases are idiopathic. In all type 1 diabetes cases, levels of circulating insulin are low or very low, and patients are more susceptible to ketosis. This type is less common and has a low degree of genetic predisposition.

2.3 Type 2 Diabetes

Either a β-cell mass does not exist or a moderate reduction has occurred. The insulin in circulation is low or normal, but can be high. No anti-β-cell antibodies are demonstrable, and the DM has a high rate of late onset in patients' lives. More than 90% of cases of diabetes are type 2 DM (KD, 2007).

2.4 Pharmacist' intervention in diabetes management

To reap the benefits of advanced medical treatments, more efficient and effective interventions are required to help individuals in following medical regimens (Haynes, McDonald, Garg, & Montague, 2002). Recently, interest has been increasing in extending the role of the pharmacist in public health, beyond the traditional product orientated functions of dispensing and distributing medication (O'Loughlin, Masson, Déry, & Fagnan, 1999). The pharmacy profession is increasingly being recognized as having a strategic position in health promotion, due to their in-depth knowledge of the rational use of medicines (Olsson, Tuyet, Nguyen, & Lundborg, 2002). The role of the pharmacist as part of a multidisciplinary approach cannot be overemphasized. Pharmacists are now a critical part of health care teams, and they are taking more

responsibility for clinical outcomes of drug therapy (Narhi, Airaksinen, Tanskanen, & Erlund, 2000).

A number of limitations exist in the potential role of pharmacists, such as their lack of prescribing power and a shortage in some countries of suitably qualified pharmacists with clinical experience. These issues may be further compounded by economic constraints, particularly in developing countries. Adherence to therapy is also a vital component of any medication regimen, and pharmacists are ideally positioned at the interface between the patient and his or her medicine to influence medication adherence in a positive manner (Bogden, Abbott, Williamson, Onopa, & Koontz, 1998).

The World Health Organization expressed, "*pharmacists have a critical role to play, which is considerably more than selling medicines*" hence addressing the problem of low adherence to long-term therapy for chronic conditions (World Health Organization). The organization summarized its view, indicating that the pharmacist's role fits the 7-star concept, in which the pharmacist is described as a caregiver, communicator, decision-maker, teacher, lifelong learner, leader, and manager and, thus, is perfectly positioned to carry out effective interventions. These roles enable him/her to carry out interventions successfully, improving the effectiveness of drug therapy, reducing costs, preventing undesirable side effects, and improving clinical outcomes for patients (Dorevitch & Perl, 1996). Increasingly, it is being accepted that pharmacists are well equipped and well trained to provide interventions for chronic conditions. Intervention programs involving the community pharmacist are one of the few techniques that have proven successful, generating benefits that are 10 times greater than the costs (I Côté, Moisan, Chabot, & Grégoire, 2005). All of the roles that

a pharmacist can play as part of a multidisciplinary team depend on the pharmacist being suitably qualified in a number of competencies, which may not always be the case, especially in developing countries. Evidence has shown that pharmacist involvement in managing therapeutic regimens through a medication therapy management (MTM) program for populations of patients with complex chronic diseases such as diabetes, hypertension, (Cranor, Bunting, & Christensen, 2003) heart failure, (M. D. Murray, Ritchey, Wu, & Tu, 2009; M. D. Murray et al., 2007) and hypercholesterolemia (Bunting & Cranor, 2006) results in better clinical outcomes.

MTM is a pharmacist led professional service aimed at reducing drug associated adverse events, improving patient medication adherence, and increasing patient understanding of their diseases and prescribed drugs. MTM "is a distinct service or group of services that optimizes therapeutic outcomes for individual patients" (American Pharmacists Association National Association of Chain Drug Stores Foundation, 2008).

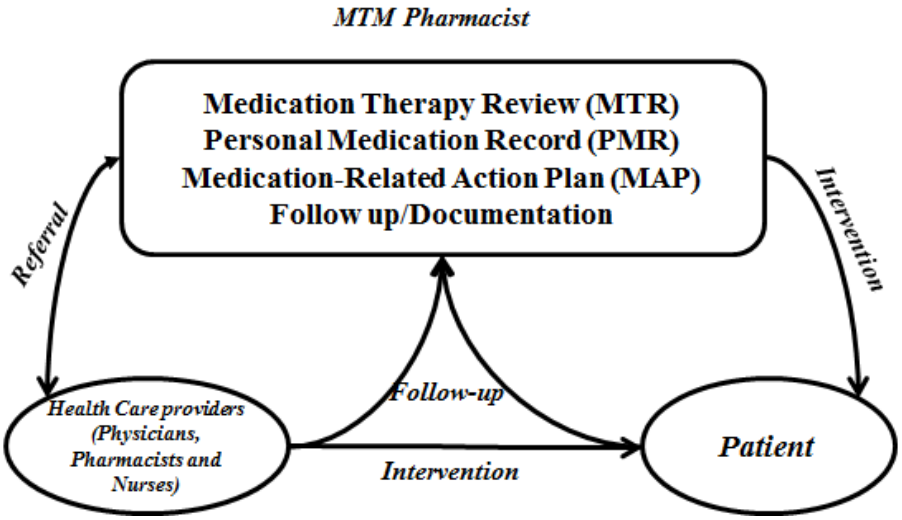

Figure 2.1: Outlines of the core elements of MTM services and how MTM integrates with other health care providers and the final recipient of the care process—the patient (Hussein & Brown, 2012).

Therefore, the current review examines the contributions of pharmacists to the improvement of the long-term prognoses of patients with DM by improving its control and management. It is the authors' hypothesis that pharmacists can play a major role in reducing HbA1c and improving both glycemic control and HRQoL.

The search terms were diabetes mellitus and pharmacist intervention. All available years in each database were searched. The studies included in this review were identified through a search of Cochrane Library Databases, Medline, EMBASE, PsychINFO, ERIC, Dissertation, and PubMed. Only papers that were published in English and that used human participants were considered. An initial search, using the above terms in searches of abstracts, identified 35 published articles. Full texts of all articles were obtained and independently read in full by the authors to identify those papers suitable for inclusion in this review. Studies that took place in the community, outpatient, primary care, and hospital (secondary care) settings were all included. Randomized controlled trials and retrospective cohort reviews were included. Using a

Microsoft Excel spreadsheet, data were extracted from the chosen studies. No blinding regarding a journal or author was done. Data were extracted for authors, year of publication, randomization quality criteria, patient details, intervention details, endpoint and outcome measures, baseline and post intervention results, and main findings. To assess the methodological quality of the described studies, we noted how the randomization and allocation concealment were conducted.

2.5 Interventional effects on HbA1c, lipids, and the cardiovascular System

Diabetic patients with concomitant dyslipidemia are often soft targets for cardiovascular disease and deaths. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular morbidity and mortality. HbA1c is routinely used as a marker to indicate long-term glycemic control. The American Diabetes Association estimated the risk of diabetes related mortality increased 25% for each 1% increase in HbA1c. A strong correlation has been shown between lipid profile and coronary artery disease. One study lasting 12 months with 228 diabetic patients at 7 independent pharmacies in Lucas County, Ohio, was conducted to evaluate the management of medication therapy. In the study, their pharmacists counselled patients at 6-month intervals regarding their diets and lifestyle modifications, including smoking cessation and adherence to exercise plans. The measured outcomes included HbA1c and systolic blood pressure (SBP). Because of the interventions, means (±SD) HbA1c values reduced from 7.08 ± 1.54% to 6.89 ± 1.30% at 12 months. Patients with an HbA1c level more than 7% at baseline averaged a decrease of 0.5% at 6 months and 0.75% at 12 months and SBP became normal. Caffeine, liquor consumption, and smoking decreased and physical activity increased (S. L. Pinto, Bechtol, & Partha, 2011).

A 6-month randomized controlled trial was conducted at the endocrine clinic at Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Malaysia. Type 2 diabetes mellitus patients ($n = 73$) attending an endocrine clinic at Universiti Kebangsaan Malaysia Medical Centre (UKMMC) were randomized to either control ($n = 36$) or intervention group ($n = 37$) after the screening. Patients in the intervention group received an intervention from a pharmacist during the enrollment, after three and six months of the enrollment. Outcome measures such as HbA1c, BMI, lipid profile, Morisky scores and quality of life (QoL) scores were assessed at the enrollment and after 6 months of the study in both groups. Patients in the control group did not undergo intervention or educational module other than the standard care at UKMMC. The HbA1c values reduced significantly from 9.66% to 8.47% ($P = 0.001$) in the intervention group. However, no significant changes were noted in the control group (9.64–9.26%, $P = 0.14$). BMI values showed significant reduction in the intervention group (29.34–28.92 kg/m^2; $P = 0.03$) and lipid profiles were unchanged in both groups. Morisky adherence scores significantly increased from 5.83 to 6.77 ($P = 0.02$) in the intervention group; however, no significant change was observed in the control group (5.95–5.98, $P = 0.85$). HRQoL profiles produced mixed results (Butt, Ali, Bakry, & Mustafa, 2015).

A 6-month randomized, controlled, parallel-group trial with 135 diabetic patients was conducted in Belgium to assess the effectiveness of community pharmacist interventions in diabetic care. Patients at 66 community pharmacies were randomly assigned to receive a pharmacist's care. The interventions mainly focused on correct use of medication, medication adherence, healthy lifestyle promotion, and changes in pharmacotherapy (i.e., type and/or dose of hypoglycemic agents). The results showed

a significant reduction (1.05%) in HbA1c in those patients whose pharmacotherapy plans were changed by a pharmacist's intervention (Mehuys et al., 2011).

To evaluate the effectiveness of a diabetes-care management program, 179,249 patients at Kaiser Permanente Northern California with diabetes were enrolled in another study. In the 32-week study, patients were divided into 2 groups, one of which was monitored after 12 and 24 weeks under a managed care program, whereas the other group acted as controls. Pre- and post-program, HbA1c levels, lipid profiles, and SBPs were compared between groups. It was found that a statistically significant decrease in levels of HbA1c and low density lipoprotein cholesterol (LDL) occurred in patients who participated in the managed care program (Schmittdiel, Uratsu, Fireman, & Selby, 2009).

To evaluate the effects of medication management in patients having diabetes and hypertension, a randomized control trial of 36 weeks, with 52 patients from Tulsa, Oklahoma assessed the interventions of community pharmacists in patients' therapies. The intervention group participants received MTM services for hypertension and diabetes management on a monthly basis. The mean intervention group SBP decreased 17.32 mm Hg, whereas the mean control group SBP level increased 2.73 mm Hg ($p = 0.003$). The percentage of patients at goal BP increased from 16.0% to 48.0% in the intervention group and decreased from 20.0% to 6.67% in the control group. Intervention group participants were 12.92 times more likely than control group participants to achieve goal BP ($p = 0.021$). Although the mean adherence rate in the intervention group increased 7.0%, while remaining fairly constant in the control group (-0.7%), this group difference was not statistically significant (Planas, Crosby, Mitchell, & Farmer, 2009).

A 53-week study was conducted with 43 patients at Penang Hospital in Malaysia to evaluate a Diabetes Medication Therapy Adherence Clinic (DMTAC) managed by pharmacists. Patients having HbA1c of more than 8% were included in the study. The patient's demographics, medication regimens, and adherence to therapy were evaluated, and the pharmacists' 6-week interventions were reviewed. HbA1c, fasting blood glucose (FBG), LDL, triglycerides (TG), and high-density lipoprotein (HDL) cholesterol was evaluated. A mean reduction in HbA1c of 1.73% ($p < 0.001$), mean reduction in FBG, and a mean reduction in LDL cholesterol of 0.38 mmol/L ($p = 0.007$) was achieved. The difference in TG and HDL cholesterol were not significant. Patient adherence to medication regimens improved significantly with an increase in the mean MMMAS score from 7.00 to 10.84 ($p < 0.001$) after completion of the DMTAC program (Phei Ching & Kelvin, 2010).

In a study intended to evaluate the clinical pharmacist's role in a multidisciplinary health care team, which included physicians, clinical pharmacists, registered nurses, and a registered dietician, diabetic patients in multispecialty ambulatory care medical group in suburban Chicago were seen by clinical pharmacists for interventions; education, initiation, or adjustment of pharmacotherapy plans; and ordering of pertinent laboratory tests. A substantial drop in HbA1c levels occurred, which exhibited that the involvement of a pharmacist in a health care professional team could improve patient results (Brooks, Rihani, & Derus, 2007).

To assess clinical outcomes for patients with DM who received medication management every 2 to 6 weeks as determined by the severity of their illness or level of educational need from a pharmacist. Once the initial goals were met, a patient would be asked to return in 3 to 6 months for a follow-up appointment. A 1.5-year

study was conducted in collaboration with private physicians. Patients who were older than 18 years of age and who had type 1 or type 2 DM were included in this study. HbA1c, body weight, and BP were observed at 3 intervals. A significant reduction in HbA1c was found, but no changes in BP or reductions in weight were observed (Nkansah, Brewer, Connors, & Shermock, 2008).

Recently, a 53-week study was conducted in Massachusetts to evaluate the outcomes of implementation of a pharmacist-supervised at the Veterans Affairs diabetic clinic. A total of 160 T2DM patients who were taking either an oral hypoglycemic medication or insulin, were included in the study. The patients met with pharmacist after 12 weeks for review of clinical outcomes. A mean reduction of more than 1% (9.12% ± 1.41% to 7.94% ± 1.18%) in the HbA1c value was observed. Further HbA1c improvements were documented in patients followed for 6 months after clinical enrollment. This study revealed that a pharmacist's intervention can have a positive impact on patients' therapy outcomes (Collier & Baker, 2014).

To measure the effects of a pharmacist-run medication management program on medication adherence, glycemic control, and total health care expenditures, Scott & White Health Plan (SWHP) claims data were evaluated. High-risk patients (n = 46) having HbA1c greater than 7.5% and spending more than $600 for their medications were included in this study. A control group was also identified. The study was conducted for 1 year. Patients in the intervention group showed greater improvement (9.5% to 8.2%) in HbA1c values than controls, who moved from a baseline of 9.5% to 8.7% at the end of the study. The total monthly health care costs were increased in both groups, but the increase was lower in the intervention group. Patients in the