A Systematic Review of Factors Influencing Medication Adherence in Type 2 Diabetes Mellitus Patients

Major (Dr) Saifulsyahira Jaaman*, Rosliza Abdul Manaf** & Muhammad Hanafiah Jun**

*Health Services Division of Malaysian Armed Forces, Jalan Yap Kwang Seng, Kuala Lumpur, Malaysia

ABSTRACT

INTRODUCTION Medication adherence is an important factor in controlling Type 2 Diabetes Mellitus (T2DM). There is a lack of consensus on which factors influencing medication adherence and which technique was widely used in assessing medication adherence.

METHODS A rigorous systematic search conducted to identify robustly implicated factors, found that all were observational studies that studied factors influencing medication adherence. The search was narrowed to 16 observational studies (total N= 6419) relating to medication adherence and T2DM, medication adherence assessments and medication adherence rate. Five domain of factors influencing medication adherence were identified. These were patient-related factors, socio-economic factors, condition-related factors, health-system/health-care related factors and therapy-related factors. The assessment used for medication adherence were all indirect methods, either pill count, dosage method or questionnaire.

RESULTS Good medication adherence rate ranged from 35.4% to 83.3%.

CONCLUSION This review showed that poor medication adherence was likely associated with young age, low income, poor diabetic knowledge, multiple anti-diabetic treatments used, health service dissatisfaction and poor glycemic control. It also revealed that the older the patient the better adherence to medication, and also good glycemic control.

KEYWORDS Medication Adherence, Type 2 Diabetes Mellitus, Factors Influencing, Medication Adherence Rate, Medication Adherence Assessment

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a growing problem worldwide with a worldwide prevalence of 9.8% and 9.2% in adult men and women, respectively ^{1,2}. Its prevalence and incidence are growing in both Western countries and the Asia Pacific region ²⁻⁴. Poor glycemic control was associated with increased incidence of stroke, all-cause mortality and cardiovascular deaths ². The World Health Organization (WHO) estimated a rise in the number of diabetic population from 170 million in 2000 to 366 million in 2030 ⁵.

Alongside this increased prevalence comes an increased burden of disease from complications, which are potentially preventable ⁶. The importance of patient education and promoting self-care has long been recognized as a key component in chronic disease management and improving patient outcomes ². One component of self-care is adherence to often complicated medication regimes. Good adherence is associated with reduced risk of diabetes complications, reduced mortality and reduced economic burden. However, a substantial proportion of people with T2DM does not take medication as prescribed, with only 67–85% of oral medication doses taken and approximately 60% of insulin doses ⁷.

A wide range of terms has been used to describe patient use (or non-use) of prescribed medications including adherence, compliance, concordance and persistence. Two distinct patterns of medication use are described by these terms; missed medication doses (generally described by the terms adherence, compliance and concordance) and duration of use before termination (persistence). The term concordance is preferred by some to emphasize the joint agreement by the prescribing physician and the patient to use the prescribed medication in a certain way 8. 'Adherence' is the term recommended for use by WHO. The WHO defines adherence to long-term therapy as the extent to which a persons' behaviour taking medication, following a diet, and/or executing lifestyle changes corresponds with agreed recommendations from a health-care provider 19,22,30,31. The terms 'adherence' and 'compliance' are often used interchangeably 9.

WHO has identified five dimensions associated with medication adherence which are patient-related factors i.e age, gender, smoking habit, impulsivity and ethnic minority groups; socio-economic factors i.e socioeconomic status, financial resources, medication costs, education level, family support, condition-related factors i.e depression or other chronic diseases, duration of diabetes, diabetes complications; health system / health-care related i.e healthcare center / clinic, distance to nearest pharmacy, lower continuity of care and therapy-related factors i.e concurrent medication use, adverse effects, previous experience with medication 1.2,9,19,21-29,31-33.

Adherence to anti-diabetic treatment is one of the major factors of handling diabetic management. This is where a T2DM patient can achieve their HbA1c target and also to avoid diabetic complication. Medication adherence is the extent to which patients take medications as prescribed by their healthcare providers and as agreed upon in the treatment plan ^{9,19,22,30,31}.

^{**}Department of Community Health, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor, Malaysia.

Medication adherence is essential to optimize patient outcomes in nearly any disease. Non-adherence to medications is associated with worsening of disease, increased mortality, and greater health care costs. Direct and indirect methods are available to assess medication adherence. Direct methods include observing patients taking medications and measuring drug or metabolite concentrations in the blood or urine. Indirect methods include asking patients, patient diaries, refill rates, pill counting, monitoring for clinical response, electronic monitoring devices, and patient scales or surveys 1,10,19.

Medication adherence rates to drug regimens in patients with T2DM are relatively low and vary widely among populations with adherence rates between 36% to 94% ¹¹. Epidemiological studies have found many factors associated with medication adherence ⁹⁻¹¹. Reviews report that adherence has been associated with patient factors, social and medical support, and medication related aspects ¹⁴. Patient factors are for example the patient's age (older patients being more adherent), economic status (patients with a higher economic status being more adherent) and health beliefs (patients with beliefs about medicines as something harmful were less adherent) ^{11,14,18}.

Social and medical support include among others family help and the patient-healthcare provider relationship, and patients with more support were more adherent. Medication related factors take into account the attitude towards medicines, the complexity of the medication regimen and the experience of side effects 10-12. A positive attitude towards medicines, a less complex medication regimen and less experience of side effects were related to higher adherence rates 7. Studies found that health beliefs, quality of the doctor/patient relationship, the course of diabetes and quality of information influenced medication adherence. Examples of these findings are that health beliefs could lead to reduced adherence due to lack of understanding of diabetes and its treatment. Within the doctor/ patient relationship patients perceived the doctor blaming the patient for negative health outcomes, and physicians not understanding the patient's difficulties as obstacles to medication adherence. With respect to information, lack of knowledge and conflicting information about the treatment could influence medication adherence negatively 7,8,10. In view of the limited information surrounding the issue of adherence, this systematic review aims to find out the factors associated with medication adherence whether good or poor.

METHOD

A systematic review of articles was based on a search of electronic databases and of bibliographies of studies and previous reviews. A broad search of databases was conducted initially using generic terms to identify the relevant search terms During the development of the search strategy, consideration was given to the diverse terminology used and the spelling of keywords as this would influence the identification of relevant studies. A combination of keywords including "factors influencing" and "diabetes mellitus", "diabetes type 2", "medication adherence", "medication compliant", "anti-diabetic treatment", "non-insulin dependent diabetes mellitus treatment", "patient compliance", "adherence to anti-diabetic treatment", "self-care", "self-management" were used. In order to ensure complete coverage of the literature, the search strategies were developed to be sensitive (broad) rather than specific. The databases searched included were Medline, CINAHL and PubMed from 2005 until 2016. The PRISMA flow diagram for the search strategy is summarized in the figure below.

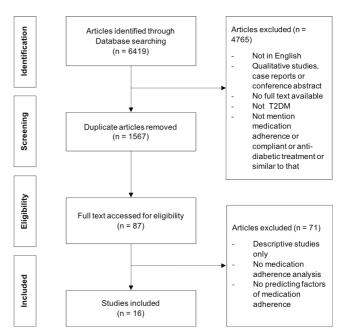


Figure 1. Flowchart of The Systematic Review Process

RESULT

Study Selection

Sixteen studies were included in this systematic review; Figure 1 describes the study selection process. Four thousand eight hundred and fifty-two articles were identified after duplicates were removed, of which 4765 articles were excluded based on titles and abstracts for not meeting selection criteria. A further 71 articles were excluded after assessing full-text versions for eligibility, leading to a final sample of 16 articles. Inclusion criteria for this review are as follows; all articles in English and has full-text access, participants must diagnose T2DM, accessing medication adherence factors on diabetic treatment and finally analyzing associated factors with medication adherence and also predictors.

Study Characteristics

All studies have good medication adherence proportion between 39%-83.3% with varieties of measurement used for medication adherence. All sixteen studies used indirect method as medication adherence measurement with Morisky Medication Adherence Scale (MMAS) (6 studies), self-reporting questionnaire (5 studies), medication possession ratio (MPR) (2 studies), medication compliant questionnaire (1 study), continuous multiple interval measure of gaps in therapy method (CMG) (1 study) and dosage count in 3 month (1 study). There were two studies who were using two measurements in their studies simultaneously ^{20,32}. The majority of the study design was cross-sectional studies (12 studies). Only four cohort studies were analyzed in this review. Only three studies were from Malaysia populations 19, 30, 31, others were scattered all over the world. Individual study result is shown in Table 1.

Based on the WHO dimension of factors associated with medication adherence in diabetic patients we segregate the studies according to factors discussed, namely; patient related, socio-economic, condition-related, health system or health-care related and therapy-related factors.

Patient-Related Factors

Out of sixteen studies, ten studies have patient-related factors associated with medication adherence 19,21-23,25,27,28,31-33. Younger age is one of the major factor contributing to poor medication adherence 19,28,31,32. One study observed older age group (> 60 years) old was the predictor of poor medication adherence 23. These differences could due to culture and socio-demographic status of the study being held. There was also a study that observed older age group was the compliance factor 21. Other factors such as concern on drug adverse 27, belief on medication are harmful 27, non-European 28, no knowledge of complication 23 and patients' negative belief regarding diabetes and sugar control ²⁵ were the contributing factors. In other side patients' who have knowledge about diabetes 33 and patients' who live in rural area 21 have good medication adherence.

Socio-economic Factors

Out of sixteen studies, six studies have socioeconomic factors associated with medication adherence ^{19,21,27,28,29,31}. Patients who have poor economic status or have financial difficulties were poor medication adherence ^{28,29} but one study reported that patients' who high income was poor medication adherence ¹⁹. One study reported that patients who have low socio-economic status have good medication compliance ²¹. These differences could due to the different geographical area and gross domestic product (GDP) per capita of different countries. In terms of knowledge, there were studies reported low knowledge score as the contributing factors of poor medication adherence ^{27,31}.

There is also a study showing that professional profession was the factor of poor medication adherence in T2DM ²⁸. Another important factor of poor medication adherence in T2DM is the lack of family support ²⁸.

Condition Related Factors

There were eight studies which reported condition-related factors with medication adherence ^{19,20,22,23,26,27,28,31}. Patients who have a long duration of T2DM, mostly more than five years were prone to have poor medication adherence ^{20,23} but a study from Africa showed patients who have a duration of T2DM more than three years have good medication adherence ²². Patients who chronic condition or associated with comorbidity also have poor medication adherence ^{27,31}. Patients' who have a complication due to T2DM reported having poor medication adherence ²⁸. Depression or patients who have distress symptoms also associated with poor medication adherence ^{19,26}.

Health System / Health-care Related Factors

There were only five studies have health system / health-care related factors with medication adherence ^{1,21,22,28,29}. In terms of health services, a study reported poor medication adherence due to service dissatisfaction29, difficulties to take medication (pharmacy far from home) ²⁸ and patients were follow-ups by specialist ²⁸. Availability of anti-diabetic drug at a pharmacy and first treatment received were oral anti-diabetic (OAD) were reported to be factors contributed to good medication adherence ^{21,22}. Patients' health-care related factors such poor acceptability of medical condition, a decision on medication solely made by patients, need for information on treatment, reporting no confidence and need for medical support became the factors of poor medication adherence ²⁸. Regular exercise was factor contributed to good medication adherence ¹.

Therapy-Related Factors

Ten studies were reported to have therapy-related factors associated with medication adherence 1,20,21,23,24,27,28,29,30,32. Four studies out of ten, reported that poor glycemic control (HbA1c > 6.5%) or increasing trend in HbA1c associated with poor medication adherence 20,30,32,28. Good medication adherence was reported when patients have low HbA1c1. The consequence of T2DM such as high systolic blood pressure (SBP) and high cholesterol was associated with poor medication adherence 20. Increase in a number of anti-diabetic medication, medication dose increase and poly-pharmacy associated with poor medication adhrence ^{23,24,27,30}. Surprisingly a study showed good medication adherence when patients received more than five anti-diabetic drugs 21. Patients who went for traditional treatment also showed poor medication adherence to anti-diabetic drugs 29.

Risk of Bias within Studies

All studies have their own sample selection processes. Five studies didn't have contained detailed and comprehensive explanations of their subject eligibility criteria ^{21,26,28,30,33}. All studies have their interpretation of medication adherence except four studies that used WHO definition of medication adherence ^{19,22,30,31}. The reliability and validity of a number of measurements could not be established in nearly half of the studies ^{20,22,23,24,26,28,32,33}. Reporting of statistical methods used was detailed in all studies. Seven studies provided sufficient descriptions of study limitations as well as the source and role of potential funding ^{1,23,24,25,27,28,31}.

DISCUSSION

Following a systemic review with detailed inclusion and exclusion criteria, this review aimed at providing an updated summary of currently identified factors influencing medication adherence in T2DM patients.

Synthesis of the Results

Variation of adherence rates generally corresponded to the definition of medication adherence itself, a study categorized adherence as good, medium and poor adherence28, another study categorized as high, medium and low adherence29 and the majority have only two categories which were good and poor ^{21,22,23,26,27,31} or high and low ^{1,19,25,30,32} or adhere and non-adhere ^{20,24,33}. These made the medication adherence rate wide between 12% (low medication adherence) to 83.3% (high medication adherence). Other factors also contributed to the variation of the adherence rate such as patient-related factors, socio-economic factors, condition-related factors, health system / health-care related factors and therapy-related factors.

Synthesis of Patient-Related Factors

Patient-related factors were quite dominant factors contributing to poor medication adherence with young age was the major factor ^{19,28,31,32}. Younger generation sometimes was hardly serious on their disease progression and in one of the studies stated younger patients lead to busy lifestyle ^{31,32}. Different situation to another study where older age group (>60 years old) was the factor poor adherence. This was due to older patients tend to forget easily (forgetfulness) ²³. It stated that when the patients become older their medication adherence becomes better due to disease awareness and afraid they will have diabetes complication ^{21,23,28,31}. Other factors such as negative belief on harmful medication or regarding sugar control were due to inadequate knowledge on diabetes control and diet ^{23,33,37}.

Synthesis of Socio-economic Factors

One of the factors of poor medication adherence was

poor economic status or financial difficulties ^{28,29}. This was due to socio-economic of the country population country was poor ²⁹ and because of the higher cost of diabetic treatment and in-availability of social insurance to the ethnic minority ²⁸. Different finding in another study where high-income patients have poor medication adherence. This was due to these patients have more resourceful in health-seeking endeavors ¹⁹. Poor family and social support were one of the contributing factors of poor medication adherence. This can lead to diabetes complication due to the disease progress and poor glycemic control ²⁸. It made the patient less confident on self-managing diabetes treatment and has poor knowledge on diabetes ^{27,31}.

Synthesis of Condition Related Factors

Patients who were diagnosed T2DM more than five years were prone to poor medication adherence. This was because when the disease progress, patients start to get complications in systemic function such as eye complication (blurring of vision) or periphery nerve function. The health-care practitioner prone to add medication doses or to add some more anti-diabetic drugs that lead to poor medication adherence 20,23,27,31. There was a conflicting study showed that longer the duration of diabetes the more adherence to anti-diabetic treatment. The author stated this was maybe due to information bias due to self-report questionnaire 22. But in daily life in Uganda, from the health-care observations, patients who have a longer duration of diabetes have a good relationship with their health-care provider and have a better understanding of anti-diabetic regimen 22. Depression also stated to be an associated factor of poor adherence. This is because the longer the disease progress the more complications will occur if the patients have poor insight regarding diabetes. Complications and multiple chronic diseases made patients hopeless and become depress 19,26.

Synthesis of Health System / Health-care Related Factors

Unsatisfactory health-care service such as the long waiting time at the pharmacy and unavailability of medication in pharmacy can lead to poor medication adherence. The long distance between home and pharmacy also lead to poor adherence 28.29. Surprisingly patients who were follow-up by specialist also have poor medication adherence. This could due to poly-pharmacy that a specialist always prescribes to diabetic patients or prescribing medication in the specialist category that was not familiar to patients 28. Patients' health-care related factors such poor acceptability of medical condition, the decision on medication solely made by patients, need for information on treatment, reporting no confidence and need for medical support became the factors of poor medication adherence 28. This due to sometimes patients didn't accept the reality of current conditions such as having kidney complications or need to start on insulin due to complication. This made the patients need more information on disease progress and anti-diabetic treatment.

Lack of diabetic self-management and self-efficacy lead to poor diabetic control and medication adherence. Regular exercise was the factor contributed to good medication adherence ¹. Patients who exercise regularly always have positive behaviour towards their disease. They think positively on anti-diabetic treatment ¹.

Synthesis of Therapy-Related Factors

Poor glycemic control was the major factor in poor medication adherence. This was because of a patient who has poor control also has poor compliance with anti-diabetic treatment and diet. This lead to progress of the disease ^{20,28,30,32}. Almost all patients who have poor glycemic control also have high cholesterol and high SBP. This lead to physician decision to start on poly-pharmacy and combination therapy. The increase in a number of medication, increase in dose and multiple modes of medication lead to poor medication adherence 23,24,27,30. Patients' felt the burden and difficult to digest the information they got from their health-care provider. When this happens they tend to choose traditional healer or treatment which are simpler and no medication adverse effect 29. The majority of under developed countries patients choose traditional treatment as their first choice of treatment 22,29. Contradicting study at Canada showed their diabetic patients are willing to accept poly-therapy or need to take more than five anti-diabetic treatment. This is because they have easy access to a drug plan whether public or private. In this study also patients who live in rural regions were more likely to persist and comply with their anti-diabetic treatment compare with those living in urban setting 21.

CONCLUSION

There is five main domain of factors influencing medication adherence which are patient-related factors, socio-economic factors, condition-related factors, health system / health-care related factors and therapy-related factors. Each domain has its own factors and predictors of medication adherence. Poor medication adherence was likely associated with young age, low income, poor diabetic knowledge, multiple anti-diabetic treatments used, health service dissatisfaction and poor glycemic control. The older the patient the better adherence to medication and also has good glycemic control.

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Correspondence: Major (Dr) Saifulsyahira Jaaman, Health Services Division of Malaysian Armed Forces, Jalan Yap Kwang Seng, Kuala Lumpur, Malaysia. Telephone: +60192287779. e-mail: shirajeri@gmail.com