



## MEDICATION ADHERENCE IN TYPE 2 DIABETES MELLITUS AND FACTORS INFLUENCING ITS NON-ADHERENCE: A NARRATIVE REVIEW

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### ABSTRACT

**Objective:** To evaluate the medication adherence in Type 2 Diabetes Mellitus and factors influencing its non-adherence. **Background:** Patient adherence to prescribed therapies in type 2 diabetes mellitus (T2DM) is an area of enormous importance because of the strong correlations between adherence, patient outcomes, and treatment costs. In T2DM, non-adherence to regimens may compromise glycemic control, which can, in turn increase morbidity and mortality rates. **Method:** A literature search was performed to identify studies reporting adherence to anti-diabetic medications and highlighting the factors affecting its non-adherence. The search was limited to RCTs written in English with a freely available abstract. **Data sources:** PubMed (2013-2018). **Review methods:** Studies which are not reporting adherence to medications or highlighting factors associated with its non-adherence in T2DM, and those with gestational diabetes and type I diabetes were excluded. Eligible reports are discussed narratively. **Results:** Low adherent patients constituted majority of the study population in all the included studies. The major determinants of non adherence were found to be age, duration of therapy, educational status, cost of medications, knowledge and complexity of medication regimen. **Conclusion:** Medication adherence is influenced by multifactorial issues and they have a detrimental impact on the quality of life of patients. We recommend that adoption of certain interventions like improving interactions with patients, reducing the complexity of medication regimen, educational initiatives, reminder systems and reduced costs may result in the desired patient outcome which is euglycemia.

**Key Words:-** Type 2 Diabetes Mellitus; Medication Adherence; Factors; Medication Non- Adherence.

#### Access this article online

Home page:

<http://ijptjournal.com/>

DOI:

<http://dx.doi.org/10.21276/ijpt.2018.9.4.3>

Quick Response code



Received:25.08.18

Revised:12.09.18

Accepted:15.09.18

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### INTRODUCTION

Diabetes Mellitus refers to a group of common metabolic disorders that shares the phenotype of hyperglycemia. The prevalence of diabetes mellitus is growing rapidly worldwide and is reaching epidemic proportions. It is a chronic disease, which, due to its high and constantly increasing prevalence, its lifelong presence as well as its concomitant complications and disabilities, remains as a major medical problem. It puts a heavy burden on the individual affected, their families and society as a whole, not only financially, but also in psychological and social terms. Diabetes mellitus is one of the most common chronic diseases across the world and the number of diabetic patients is on rise (Definition, Diagnosis and Classification of Diabetes Mellitus, 2017)

The prevalence of type 2 diabetes is at epidemic proportions worldwide, and the incidence and prevalence of T2DM continue to increase. This is of critical concern because T2DM represents the largest budget item in many health care systems, primarily due to the high rates of morbidity and mortality associated with the disease. Even worse, it has been well documented that this cost burden has been inexorably growing worldwide (Global Status Report on Non-Communicable Diseases, 2017).

The CODE-2 (Cost of Diabetes in Europe-type 2) showed that the total cost of treating more than 10 million patients with type 2 diabetes in countries studied was approximately 29 billion US Dollars, which represents an average of 5% of the total health care expenditure in each country. Furthermore, that cost increases 2 to 3.5 fold once patients develop preventable micro-vascular and macro-vascular complications (Benedetti M, 2017). Hospitalization costs, which include the treatment of long-term complications such as heart disease, account for 30-65% of the overall costs of the disease, the largest proportion of costs. Clearly, if health systems could be more effective in promoting adherence to self-management of diabetes, the human, social and economic benefits would be substantial (World Health Organization, 2016).

A key contributor to the remarkably high rates of morbidity and mortality is chronic poor metabolic control, especially poor glycemic control. Although a wide array of options are now available for treating T2DM, including several new pharmacological classes of drugs that are included in the current American Diabetes Association/European Association for the Study of Diabetes (ADA/EASD) and American Association of Clinical Endocrinologists (AACE) recommendations, ~50% of patients with T2DM fail to achieve adequate glycemic control (glycated hemoglobin [HbA1c] <7%). Using data from the National Health and Nutrition Examination Survey, targets for glycemic control (HbA1c) were achieved by only 55.5% of participants during 2016–2017. A number of factors contribute to poor glycemic control, including lack of integrated care in many health care systems, clinical inertia among health care providers, and poor patient adherence to self-care recommendations. Among them, it is evident that poor medication adherence looms large (Polonsky WH and Henry RR, 2016).

Medication adherence in T2DM remains poor despite the availability of many new classes of medications and increased efforts toward patient education and targeted interventions that address adherence. New non-pharmacologic and pharmacologic approaches are needed that will have a clinically significant and sustained long-term impact on adherence. Innovative strategies for addressing treatment burden as well as patients' problematic beliefs about their medications are needed. Toward this end, novel drugs or

delivery systems that remove the need for daily, weekly, or even monthly dosing should be available in the near future, offering the potential for greatly increased adherence accompanied by markedly improved glycemic control, reduced complications of diabetes, and lower health care costs and resource use.

Patient adherence to prescribed therapies in type 2 diabetes is an area of enormous importance because of the strong correlations between adherence, patient outcomes, and treatment costs. Since diabetes is a chronic condition, long term adherence to therapy is necessary. Improvements in adherence would improve glycemic control, that would help reduce morbidity and mortality related to uncontrolled T2DM. A recent report by WHO stated that, because the magnitude of non-adherence and the scope of its sequelae are so alarming, more health benefits worldwide would result from improving adherence to existing treatments than by developing new medical treatments (Majed HT *et al.*, 2014).

There is a continuing need to routinely assess the like reasons for non-adherence among patients with diabetes in clinical practice. Determining the significance of non-adherence and identification of factors leading to non-adherence to a prescribed treatment through a continued research can assist in planning interventions to overcome barriers. Hence this study will be carried out to give information on patient non-adherence and related factors, give information based on the respondent's response on different aspects of disease and design an interventional method that can solve problems associated with non adherence in diabetic patients.

## METHOD

A literature search using PubMed was performed. Keywords used in database searches were "type 2 diabetes mellitus", "medication adherence", "medication non-adherence" and "factors". Consideration of type 1 diabetes and gestational diabetes were beyond the scope of our search and review, and so the search terms excluded these conditions. Searches were limited to articles in the English language, published between 2013-2018. The findings from the search are presented as a narrative review.

## SEARCH OUTCOME

Using the above search methodology, 191 references were retrieved. These were screened to exclude studies not reporting medication adherence in type 2 diabetes mellitus and factors influencing its non-adherence ( $n=170$ ).

## DATA ABSTRACTION AND SYNTHESIS

The 21 studies meeting the selection criteria were evaluated and discussed in light of the authors' knowledge of the topic and clinical experience.

## RESULTS AND DISCUSSION

### Characteristics of studies identified by literature search

Of 191 search results, 21 studies were identified as relevant, reporting medication adherence in type 2 diabetes mellitus and factors influencing its non-adherence. Characteristics of the 21 reviewed studies are summarized in Table 1.

### Medication Adherence Measurement

There are several methods for measuring adherence each having its own advantages and disadvantages. This includes many direct and indirect methods. Considering the articles used in our review, all of them are based on questionnaires which is an indirect method

### Factors influencing Non-Adherence

#### Age

Mixed conclusions were obtained regarding the effect of age on adherence. In most of the studies improved adherence was in the old age group. Vijayakarhikeyan *et al.* (Vijayakarhikeyan M *et al.*, 2017) found that adherence was higher in the age group of >60 years. Conversely the study conducted by Shaimol *et al.* (Shaimol T *et al.*, 2014) and Shuvankar *et al.* (Mukherjee S *et al.*, 2013) showed that high adherence was seen in young age groups.

#### Gender

All the studies showed that there was no significant relation between gender and medication adherence.

#### Duration of therapy

Most of the studies showed that patients who were new to therapy or those with a short duration of therapy had a lower adherence. Elhami E *et al.* found that only 7.69% adherence was seen in patients new to anti-diabetic therapy (Elhami E *et al.*, 2016). But the study by Shrestha JS *et al.* emphasized that association between duration and adherence was insignificant (Shrestha JS *et al.*, 2017).

#### Educational status

A comparison of educational status and medication adherence was seen in some of the studies and all of them concluded that those with a poor educational background showed lesser adherence. A study conducted by Manobharathi M *et al.* found that illiteracy was seen in 43.8% of the non complaint patients (Manobharathi M *et al.*, 2014). Alternatively in a study of Vijayakarhikeyan *et al.* illiteracy was the least reason (16.8%) for non adherence (Vijayakarhikeyan M *et al.*, 2017)

### Co-morbidities

Various co morbidities was seen in most of the patients in all the studies with the most common being hypertension followed by heart and renal diseases. They were found to have a significant co relation with medication adherence. Hana T *et al.* deduced that patients with associated co-morbidities had triple the risk of being non adherent to the therapy and hypertension increased the risk of non-adherence by 90% (Majed HT *et al.*, 2014)

### Cost, Frequencies, Polypharmacy and Forgetfulness

Cost is one of the common factors for non adherence seen in most of the studies. As per the study of Sontakke S *et al.* for 65% of the patients high cost of medicines was the major reason for non-adherence (Sontakke S *et al.*, 2015). Also a study conducted by Awodele O *et al.* in Nigeria showed that the free health scheme for elderly which avail them free drugs helped in enhancing the overall adherence of the elderly population (Awodele O and Jemeela AO, 2015).

Polypharmacy and frequent dosing stand as a hindrance for adherence in many of the patients. Taruna *et al.* in their study stated that frequent dosing and multiple drugs attributed to forgetfulness in various age groups and more than half of them desired a reduction in the number and frequency of medications. Complimenting their study, the study of Mukherjee S *et al.* deduced forgetfulness (44.7%) as the major reason for non-adherence (Mukherjee S *et al.*, 2013). Conversely, a study done by Shrestha *et al.* cited there was no significant co-relation between number of medications and adherence (Shrestha JS *et al.*, 2017).

### Knowledge

Knowledge was seen as a key factor in measuring adherence and many studies used separate questionnaires to assess the knowledge in study population. According to the study by Awodele O 14.5% of study population had no idea about the disease (Awodele O and Jemeela AO, 2011). Similarly, Khotkar *et al.* and Sharma T *et al.* found that about 50% of the patients were unaware about the consequences of missing the drugs or doses (Khotkar K *et al.*, 2017; Sharma T *et al.*, 2014).

### Other factors

Many other factors were also seen co relating to non adherence. Belief of the patients is one such factor. A study conducted by Khotkar *et al.* cited some of patients stopped taking medicines on their own as they believed that their diabetes was under control (Khotkar K *et al.*, 2017). A study by Praveen Kumar *et al.* deduced side effects as a major reason for non adherence and it resulted in self decision and omission of drugs (Praveen KG, 2013). Another one by Arulmozhi S *et al.* showed

that patients with poor family support showed 60.8% non adherence and in the multivariate analysis of their study

only family support had significant influence on adherence (Arulmozhi S and Mahalakshmy S, 2014).

**Table 1. Characteristics of the included studies**

SL. No	Reference	Study type	No. Of patients	Methods used in assessing adherence
1	Smitha S <i>et al.</i> , 2015	Prospective Cross Sectional Study	150	MMAS, KAP
2	Manobharathi M <i>et al.</i> , 2017	Descriptive Cross Sectional Study	108	MMAS
3	Susheela RS <i>et al.</i> , 2016	Prospective Cross Sectional Observational Study	300	MMAS, KAP
4	Awodele A <i>et al.</i> , 2015	Both descriptive and prospective Study	100	KAP, MMAS
5	Mukherjee S <i>et al.</i> , 2013	Cross Sectional Study	470	Pre-designed, pre-tested structured questionnaire
6	Uma VS <i>et al.</i> , 2013	Community based Cross Sectional Study	346	MMAS-8
7	Shrestha JS <i>et al.</i> , 2017	Prospective Observational Study	120	Semi-structured Questionnaires
8	Hana TA <i>et al.</i> , 2014	Cross Sectional Case Control Study	693	Specially Designed Questionnaire
9	Elena LB <i>et al.</i> , 2017	Observational Cross-Sectional Study	963	Electronic Self-Administered Questionnaire and TSQM(5- Point Likert Scale)
10	Lotta W <i>et al.</i> , 2014	Cross Sectional Multicentered Study	430	Self- report adherence and barriers questionnaire (5- Point Likert Scale & 8- Point Likert Scale), Treatment Satisfaction Questionnaire for Medication
11	Arjun KA <i>et al.</i> , 2018	Cross Sectional Observational Study	100	KAP, MMAS
12	Praveen KG, 2013	Prospective Observational Study	154	MMAS
13	Taruna S <i>et al.</i> , 2014	Cross Sectional Research Study	600	MMAS
14	Khotkar K <i>et al.</i> , 2017	Cross Sectional Observational Study	100	MMAS
15	Perwitasari DA and Urbayatun S. 2016	Prospective Cross Sectional Study	65	BMQ Diabetes Quality of Life Clinical Trial Questionnaire
16	Baishnab S <i>et al.</i> , 2015	Prospective Observational Study	151	MMAS
17	Vijayakarhikeyan M <i>et al.</i> , 2017	Community Based Descriptive Cross Sectional Study	360	MMAS
18	Shaimol T <i>et al.</i> , 2014	Prospective Cross Sectional study	141	MMAS
19	Arulmozhi S, Mahalakshmy T	Descriptive Cross	150	Pre-designed, pre-tested

	<i>et al.</i> , 2014	Sectional Study		structured questionnaire MMAS (5- Point Likert Scale)
20	Abebe SM <i>et al.</i> , 2014	Cross Sectional Study with internal comparison	391	MMAS
21	Kassahun A <i>et al.</i> , 2014	Descriptive Cross Sectional Study	285	MMAS

## CONCLUSION

Hippocrates exhortation to the physician to “not only be prepared to do what is right himself, but also to make the patient cooperate has consistently failed for more than 2000 years. Low adherent patients constituted the majority of the study population in all our included studies. Therapeutic non-compliance results in treatment failure and makes diabetes a serious problem to both individuals and health care professionals. We concluded that the major reasons for non-adherence were age, duration of therapy, educational status, cost of medications, knowledge and complexity of medication regimen. Innovative methods are required to assist

patients with lower adherence. Health professionals can play major role in improving adherence by increasing the interaction with patients followed by adopting some measures like reducing the complexity of medication regimen, educational initiatives, reminder systems and reduced costs.

## ACKNOWLEDGEMENT

Nil

## CONFLICT OF INTEREST

No interest

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**Cite this article:**

Sriram Shanmugam, Merlin Mathews, Nimitha Treesa Baby, Praveen Raj, Reema Annie Ninan. Medication Adherence in Type 2 Diabetes Mellitus and Factors Influencing Its Non-Adherence: A Narrative Review. *International Journal of Pharmacy & Therapeutics*, 9(4), 2018,119-124. DOI: <http://dx.doi.org/10.21276/ijpt.2018.9.4.3>



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