CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187

Available online at: http://www.iajps.com *Review Article*

ADHERENCE TO ANTI-DIABETIC MEDICATIONS AMONG SAUDI DIABETIC PATIENTS - A SYSTEMATIC REVIEW

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Article Received: October 2022 **Accepted:** October 2022 **Published: October** 2022

Abstract:

Background: *A significant public health issue and a significant risk factor for the emergence of diabetes complications is poor and insufficient glycemic control among type 2 diabetes patients. Social scientists and medical professionals are both concerned about the rising prevalence of non-adherence to medical treatment. As a result, a sizable portion of patients do not benefit sufficiently from medical care, which leads to subpar health outcomes, a decreased quality of life, and higher healthcare costs.*

Objectives: *This study aims to assess the extent of anti-diabetic drug adherence and determine factors associated with non-adherence among patients with type 2 diabetes mellitus in Saudi Arabia.*

Methods: *For article selection, the PubMed database was used. All relevant articles relevant with our topic and other articles were used in our review. Other articles that were not related to this field were excluded. The data was extracted in a specific format that was reviewed by the group members.*

Conclusion: *The study included 13 studies in different region in Saudi Arabia. Moderated level of adherence was noted generally in Saudi Arabia. The highest levels of adherence was reported in Tabuk. Young age and polypharmacy were significantly correlated with adherence. Despite the availability of numerous new medication classes, increased patient education efforts, and targeted interventions that address adherence, medication adherence in T2D remains low.*

Keywords: diabetes, adherence, compliance, barriers, Saudi Arabia, T2DM, T1DM

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Please cite this article in Bandar Abdullah Alagl et al, ***Adherence To Anti-Diabetic Medications Among Saudi Diabetic Patients - A Systematic Review****., Indo Am. J. P. Sci, 2022; 09(10).*

INTRODUCTION:

The most prevalent endocrine condition in the world is diabetes mellitus, which is a serious major health issue. As of right now, 285 million people were impacted, and by 2030, that number is expected to rise to 438 million [1].

T2DM is thought to affect roughly 23% of people in Saudi Arabia, with pre-diabetes affecting an additional 25.5% of people who are 30 years of age or older. T2DM is anticipated to double in prevalence in Saudi Arabia by 2035 and account for an estimated 7.5 million cases [2, 3].

Although several drugs have been demonstrated to lower blood sugar (glycemia), modern management has been unable to achieve and maintain the best glycemic control for diabetic patients. Uncontrolled T2DM is known to cause adverse health outcomes like blindness, kidney failure, lower limb amputation, and other issues, all of which have been shown to have a negative impact on patients' quality of life [4, 5].

The degree to which a person is following a doctor's orders and taking their medication on time is known as medication adherence or compliance. Patients with chronic illnesses frequently struggle to follow the recommended treatments, and as a result, they do not always benefit fully from the drug therapy they are prescribed [3, 6].

A healthy lifestyle, a dietary approach, and medication are all part of managing type 2 diabetes. The core of diabetes holistic care is following the management plan. Inadequate care can lead to complications related to the disease, a rise in the need for medical services, a decline in life quality, and an increase in the cost of medical care [6, 7].

A major global health concern is patients' non-adherence to therapeutic plans. The failure to take medications as directed by a doctor has repeatedly been linked to poor glycemic control and microvascular complications like neuropathy, nephropathy, and retinopathy with detrimental effects on the patients and the community at large [8].

Financial difficulties, forgetfulness, youth, level of education, pre-existing diabetes complications, and difficulties taking the medications alone are some of the factors that have been linked to non-adherence to anti-diabetic medication. Poor drug access, high drug costs, unequal distribution of health providers between urban and rural areas, and cultural barriers all make it difficult for people in developing nations to take care of themselves [5. 9].

One of the most important factors in achieving good health outcomes in T2DM is patient adherence to the prescribed treatment plan. Drug therapy has been shown to have advantages in terms of better glycemic control and a subsequent decrease in morbidity and microvascular, macrovascular, and other complications. Adherence to oral antidiabetic drugs (OADs) is linked to improved glycemic control, a lower risk of complications from diabetes, and a lower financial burden [10].

Study Objective:

This study aims to assess the extent of anti-diabetic drug adherence and determine factors associated with non-adherence among patients with type 2 diabetes mellitus in Saudi Arabia.

METHODS:

Study design

In order to define a coherent empirical research agenda that builds on prior knowledge, a systematic review of the current evidence on awareness of anti-diabetic drug adherence in Saudi Arabia is regarded as a reliable method of identifying and synthesising the peer-reviewed articles for evidence in this area. Only qualitative evidence was used in this review to support an interpretation. Additionally, a synthesis of qualitative data aims to produce conclusions that are meaningful, pertinent, and appropriate for individuals, to guide future research, and ultimately to improve Saudi Arabia's practises for anti-diabetic drug adherence. The review will combine, integrate, and interpret the data from the included papers using qualitative synthesis techniques, whenever possible.

The review aims to move beyond the aggregation of available data to provide further interpretive insights into awareness of anti-diabetic drug adherence in Saudi Arabia and define where future research can add to what is known.

Study eligibility criteria

Peer-reviewed qualitative studies were included in the review. Mixed-methods studies' qualitative data was screened for inclusion and added if the qualitative component is relevant. All peer-reviewed articles that discuss anti-diabetic drug adherence from the viewpoint of the general public, healthcare professionals, and the healthcare delivery system and are published in English was included.

The studies had to have been published between January 2012 and August 2022 in order to be considered for the review, ensuring the work's

currency and enabling the identification of emerging issues from a variety of perspectives.

Study Inclusion and Exclusion criteria

The project's relevance, the articles' English-language quality, and their geographic limitation to Saudi Arabia all were taken into account when choosing which ones to use. All other articles, repeated studies, reviews of studies, and articles that did not have one of these topics as their primary end were disregarded. Studies not available in English, conference abstracts, books, grey literature, and editorial comments all were disregarded by the reviewers. Studies that only present qualitative data won't be considered.

Search strategy

A systematic search strategy was developed using a combination of Medical Subject Headings (MeSH) and controlled vocabulary to identify peer-reviewed articles on anti-diabetic drug adherence in Saudi Arabia. The PubMed/MEDLINE database was chosen for data collection.

Selection of study

The selection procedures and outcomes were presented in accordance with the ENTREQ guidelines for reporting qualitative systematic reviews. To help with duplication removal, all retrieved studies first imported into the Endnote library. The two reviewers shared the Endnote library after the duplicates have been eliminated in order to independently screen the articles by title and abstract while being guided by the eligibility requirements. The studies that the two reviewers would have selected was reviewed in full. Any disagreements between the two reviewers were resolved by a third reviewer. Each eligible study had its entire text reviewed independently by the two reviewers. When there are disagreements between the two reviewers, the third reviewer was consulted to discuss the differences in order to reach a consensus. Finally, the full texts of all relevant studies found to meet the inclusion criteria was retained for the final framework synthesis.

Data extraction

Two reviewers independently extracted data from eligible studies onto a customised data extraction form, filling it with variables related to the study population and the relevant phenomena. The third review author double-checked and confirm the extracted articles. Name of the first author, publication year, data collection period, and geographical location are just a few of the study characteristics that was extracted. Then, specific study information such as the study's design, population, sample size, sampling techniques, and data collection methods was recorded.

Data synthesis and analysis

No software was utilized to analyze the data. The reviewers sorted the data by theme and present the themes in the form of an analysis table (chart). The columns and rows of the table reflect the studies, and related themes and enable us to compare findings of the studies across different themes and subthemes.
The reviewers used charts to define the identified concepts and map the range and nature of the phenomena. Our review explored associations between the themes to help clarify the findings.

RESULTS:

Figure 1 shows the selection and identification of studies. The search of the mentioned databases returned a total of 314 studies that were included for title screening. 213 of them were included for abstract screening, which lead to the exclusion of 67 articles. The remaining 146 publications full-texts were reviewed. The full-text revision led to the exclusion of 133 studies due to difference in study objectives, and 13 were enrolled for final data extraction **(Table 1).**

According to table (1), the study included 13 studies in different region in Saudi Arabia (4 in Riyadh region, 2 in Khobar City, 1 in Bisha governorate, 1 in Tabuk, 1 in Najran, 1 in Qassim, 1 in Al Hasa, and 1 in Jeddah).

Highest adherence rates were reported in Tabuk region in a rate of (76.44%) [16] followed by Jeddah as 74.9% of participants reported subpar levels of adherence followed by Riyadh (69%) [17]. Khobar city showed adherence rated of 33- 35.8% [11, 12]. Central region reported adherence in 48.6% [15]. Lowest adherence rates were reported in a study in different regions of the kingdom as 54.8% had a low adherence level, 10.7% had a high level, and 34.5% had a medium level [14].

The use of alternatives, lack of time, polypharmacy, a strained relationship with the doctor, cultural beliefs, self-adjusting doses, exposure of side effects, ineffective medications, refusal of insulin, numerous doctor visits, an uncontrolled diet, and forgetfulness were the main noted barriers to adherence [19].
Younger age, employment, the lack of a reminder, and non-commitment to appointments are all predictors of subpar adherence [23].

The included studies had different study designs.

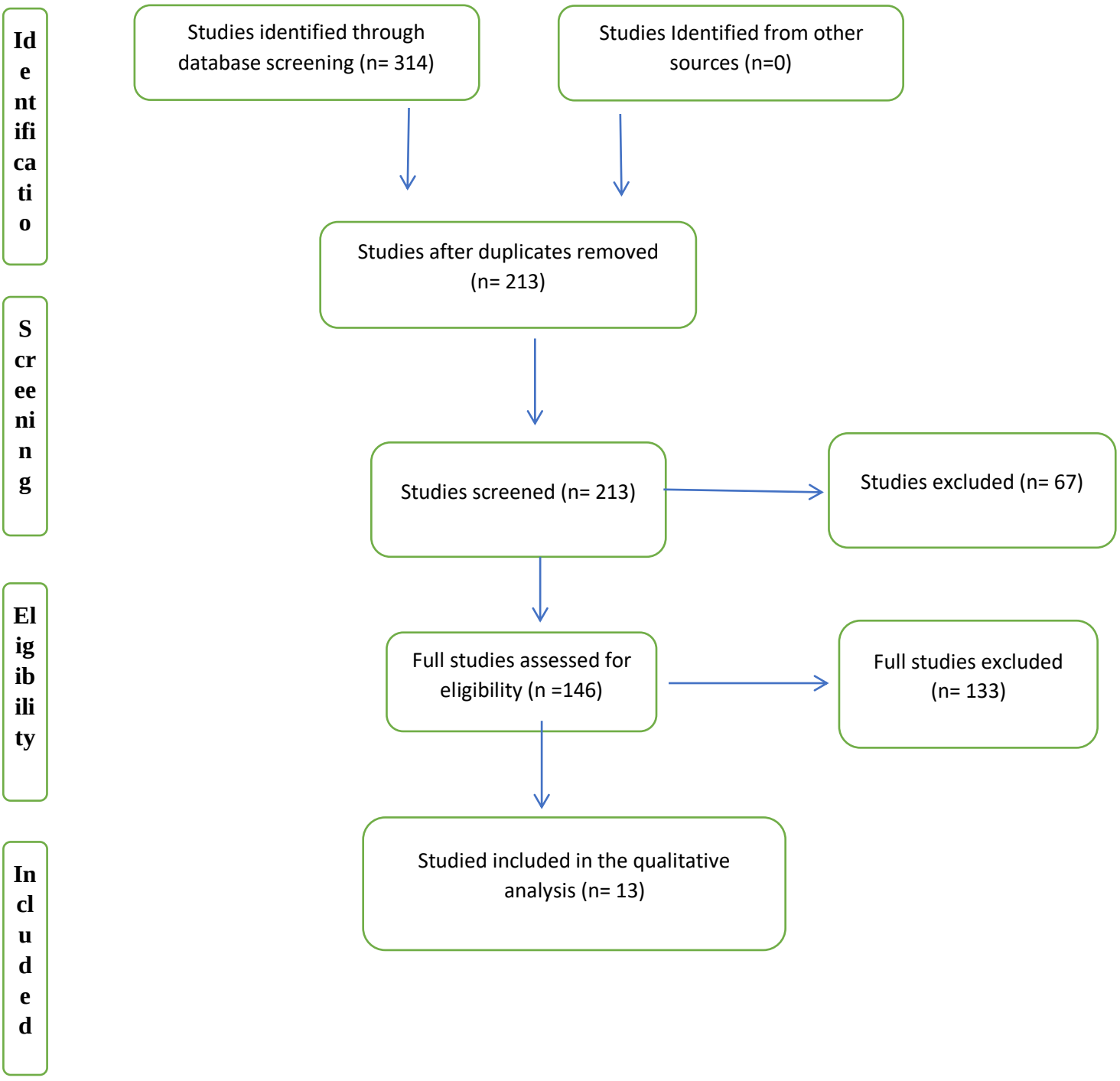

Table 1: Author, country, year of publication, methodology and outcome:

Author, Publishing Year	Study region	Methodology	Outcome
AlQarni, Khaled et al. (2019) [11].	Khobar City	Type 2 DM out-patients were the subject of a quantitative cross-sectional study. The General Medication Adherence Scale (GMAS) was used in the study to track medication adherence in this population.	(35.8%) had a high level of medication adherence. The relationship between the HbA1c level and the adherence score was weak but negatively correlated. In this population, education did not influence adherence.
AlShayban, Dhfer Mahdi et al. (2020) [12]	Khobar City	Patients with type 2 diabetes who visited three neighbourhood pharmacies in Khobar, Saudi Arabia, were the subjects of a three-month cross-sectional study. The Michigan Diabetes Knowledge Test and the General Medication Adherence Scale, both available in Arabic, were used to measure the patients' knowledge of their diseases and their adherence to their prescribed treatments.	8.1% was the mean HbA1c value. Half of patients (50.9%) had disease knowledge between 51% and 75%, and a third of patients (33%) had high adherence. It was found that there is a significantly weak-to-moderately positive correlation between medication adherence and disease awareness.
Alqarni, Abdullah M et al. (2018) [13]	Bisha governorate	375 type 1 and type 2 Saudi diabetic patients who were PHCC patients under the Bisha governorate's Health Affairs were the sample for a cross-sectional study. The four-item Morisky Green Levine Medication Adherence Scale was used to measure adherence to diabetes medication (MGLS). Every participant filled out a self-report questionnaire with sociodemographic and clinical information.	Patients had moderate adherence (42.9%) and low adherence (21.4%), respectively. Occupational status, current medication use, glycated haemoglobin (A1c), and the number of related comorbidities were all factors associated with the level of adherence in univariate analysis. A1c 7 and the absence of comorbid conditions variables persisted as significantly correlated with adherence in multivariable analyses.
Ahmed, Nahid Osman et al. (2017) [14]		a web-based descriptive cross-sectional study. Adherence was evaluated using the eight-item Morisky medication adherence scale.	54.8% had a low adherence level, 10.7% had a high level, and 34.5% had a medium level. Age and adherence score had a positive and significant correlation. The level of adherence and gender were found to have an identically strong correlation. However, neither the number of hypoglycemic medications used nor the duration of the diabetes disease were significantly correlated with adherence.
Balkhi, Bander et al. (2019) [15]	central region	In a sizable tertiary hospital in Saudi Arabia's central province, a cross-sectional retrospective study was conducted. 5457 patients who are at least 18 years old and have been diagnosed with T2DM. As a proximate indicator of OAD adherence, the modified medication possession ratio (mMPR) was calculated. Multinomial logistic regression models were used to evaluate the factors related to OAD non-adherence and medication oversupply. The secondary objectives measured the relationship between glycemic control and OAD adherence.	Glycated haemoglobin was 8.2±1.67 on average. 48.6% of the participants in the study had good medication adherence, and 8.6% had a medication oversupply. When compared to men, women with T2DM had a higher likelihood of having poor adherence in the multivariate analysis. Additionally, patients with hyperpolypharmacy, comorbid osteoarthritis, and non-Saudi patients had a higher likelihood of experiencing medication oversupply.
Prabahar, Kousalya et al. (2021) [16]	Tabuk	In Tabuk, Saudi Arabia, a tertiary care hospital undertook a cross-sectional study. To learn more about participants' adherence to their medication, participants were chosen and interviewed. The degree of adherence	Nearly one-quarter of patients were nonadherent to their medications, and participants adhered to their medications in a rate of (76.44%). There were no statistically significant differences in the medication

		among study participants was assessed using a medication adherence rating scale questionnaire.	adherence of male and female patients. Side effects and forgetfulness, respectively, were the main intentional and unintentional causes of nonadherence.
Alyami, Mohsen et al. (2019) [17]	Najran	An outpatient diabetes clinic provided 115 adults with T2D as a convenience sample. The administration of validated self-reported measures of medication adherence, illness perceptions, medical beliefs, and God locus of control for health was done. The most recent HbA1c values for patients were taken from medical records.	More than 69% of patients reported having trouble staying on top of their medication. Adherence was connected to every domain of illness perception, belief in medicine, and locus of control of health by God. Age, perceptions of the consequences of the illness, illness identity, and illness coherence all independently predicted adherence. Two thirds of patients (67%) had suboptimal HbA1c, and higher HbA1c was linked to perceptions of a cyclical timeline and less effective insulin.
Alsayed, Khalid A, and Medhat Khalifa Ghoraba. (2019) [18]	Riyadh	Patients in the diabetic care section of the Security Forces Hospital in Riyadh, Saudi Arabia, were given a pre-validated questionnaire with 18 questions.	With basal bolus insulin therapy, adherence rates were 61.9%. With 31.62% and 31.58%, respectively, there is little difference between the adherence levels of male and female respondents. The highest levels of adherence (65.75%) were seen in the younger age groups (14-29). Patient literacy levels as well as location are positively correlated with adherence.
Alodhaib, Ghaida et al. (2021) [19]	Qassim	face-to-face interviews using a qualitative method were conducted with adult Saudi patients who had diabetes mellitus and uncontrolled (fasting blood glucose >7.2 mmol/L or glycosylated haemoglobin >7%). Each interview was audio recorded before being thematically analysed. For 68 patients, interviews were conducted.	The use of alternatives, lack of time, polypharmacy, a strained relationship with the doctor, cultural beliefs, self-adjusting doses, exposure of side effects, ineffective medications, refusal of insulin, numerous doctor visits, an uncontrolled diet, and forgetfulness were the main obstacles noted.
Al Harbi, Turki J et al. (2015) [20]	Riyadh	450 adults with type 2 diabetes participated in a one-year historical prospective study between October 2010 and September 2011 at a Saudi Arabian primary care facility. The 2010 ADA standards of diabetic care processes and targets were used in the study.	Medication compliance varied from 82.2% for antiplatelets to 92.4% for dyslipidemia. 24.2% of the patients met the required HbA1c level of 7% for the outcomes. Only 7.2% of patients had LDL levels that were within target range, controlled blood pressure, and glycemic control. During follow-up, a rising trend of patients achieving glycemic control (7%) was observed.
Alhabib, Mohammed Y et al. (2022) [21]	Riyadh	a cross-sectional study focused on elderly patients receiving outpatient care for chronic illnesses. The General Medication Adherence Scale (GMAS), a validated instrument scale, was used to collect data from participants via telephone interviews. Its goal is to measure key determinants impacting adherence, including patient behaviour, cost, comorbidity, and pill burden.	The Mean overall score for GMAS was 29.9±3.1 out of 33. (64.9%) of the patients had a high level of medication adherence. The patients had a high adherence on the domain of patient behavior related non-adherence (PBNA) (13.5±1.9) out of 15, a high adherence on the domain of additional disease and pill burden (ADPB) (11.2±1.4) out of 12, and good to high adherence on the cost-related non-adherence (CRNA) (5.25±1.1) out of 6.
Khan, Ataur R et al. (2012) [22]	Al Hasa	A cross-sectional survey was carried out in the Al Hasa area. 535 diabetic patients were chosen through random sampling from three centres for chronic diseases located	Overall, 67.9% of participants had therapeutic non-compliance. Male non-compliance was greater than female non-compliance (69.34% vs. 65.45%). Urban participants had a non-

		throughout Al Hasa. By using interviewing questionnaires and file records, the data were gathered. Any patient with a Hb1AC of more than 7% at the time of the interview who had been prescribed the best course of treatment and received appropriate advice on diet and exercise for their diabetes but did not follow the medical advice was regarded as non-compliant.	compliance rate that was significantly higher than rural participants' (71.04 vs. 60.15%). The following factors were found to be significantly linked to non-compliance by bi-variate analysis: female gender, low educational attainment (illiteracy), urban population, irregular follow-up, non-adherence to prescription medication, non-adherence to exercise programme, insulin, and insulin when combined with oral metformin.
Khayyat, Yara A Jr et al. (2022) [23]	Jeddah	Using an electronic, self-created, validated questionnaire, 383 patients with type 2 diabetes mellitus were interviewed for an analytical, cross-sectional study. Through stratified random sampling, patients were selected from all Ministry of Health facilities located throughout Jeddah.	74.9% of the participants reported subpar levels of adherence. Younger age, employment, the lack of a reminder, and non-commitment to appointments are all predictors of subpar adherence.

DISCUSSION:

Chronic disease treatment depends on patient adherence to medication, and non-adherence among elderly patients is a problem for healthcare professionals. According to prior research, assessing adherence and patient compliance is challenging and frequently patient-dependent [4].

Adherence to the entire prescribed regimen is necessary for the drugs and lifestyle changes to be effective in controlling type 2 diabetes and related conditions. According to data from the World Health Organization (WHO), the average rate of long-term therapy compliance for chronic illnesses in developed nations is only about 50% [24].

According to a hospital-based study conducted in the United Arab Emirates, 84% of people adhere to their anti-diabetic medication regimens [25], whereas similar studies conducted in Ethiopia and Uganda found 85.1 and 83.3%, respectively [26, 27]. In contrast, research from Switzerland and Botswana revealed lower prevalence rates of 40 and 52%, respectively [28, 29]

Large claim databases have been used in studies to identify key demographic factors that are linked to poor medication adherence in T2D, including younger age, lower education, and lower income. However, it may be more important to pinpoint those critical factors that may be modifiable. Six major factors are identified by the data that are currently available: perceived treatment efficacy, hypoglycemia, treatment convenience and cost, medication beliefs, and physician trust. It should be noted that the existing literature has described a number of additional factors (eg, depression, forgetfulness, and limited diabetes knowledge) [30].

If a patient can comprehend how their treatment plan is positively and relatively immediately affecting their outcome, their adherence to treatment is more likely to improve [31]. According to a systematic review of numerous chronic diseases, medication compliance is correlated with perceived need, and patients are more likely to be compliant the more strongly they believe the prescribed medication is actually necessary [32]. According to another study, patients with T2D believed that medication would result in undesirable side effects in 32.8% of cases and that weight gain might result in 13.9% of cases, which may have contributed to decreased adherence [33]. In one study of individuals with type 1 and type 2 diabetes, non-adherence to insulin was attributed to a variety of factors, including adverse reactions at the injection site, fear of hypoglycemia, time commitment, disruption of physical activity, and a lack of instructions [34]. Medication administration was found to be a significant barrier to adherence in a qualitative meta-synthesis of the various perspectives of medication non-adherence among patients and healthcare professionals [35].

T2D treatment is a lifelong process, and the complexity of the various therapies frequently rises over time. A systematic review of 51 studies on the relationship between medication adherence and dosing frequency in chronic diseases, such as diabetes, found that medication adherence decreased with increasing daily frequency of medication:

compared to once-daily dosing, the differences for twice-daily, three times daily, and four times daily dosing were, respectively, -6.7%, -13.5%, and -19.2% [36]. The increasing complexity of treatment has a clear impact on treatment compliance. Treatment for diabetes and its complications may involve multiple tablets with daily dosing. The frequency of dosing was found to be inversely related to medication adherence in a systematic review of 76 studies. Adherence was significantly higher for once-daily dosing (79%) than for three times-daily dosing (65%) (p 008), for once-daily dosing than for four-daily dosing (51%; p 0.001), and for twice-daily dosing (69%) than for four-daily dosing (p 0.001) [37].

According to research by Hauber et al, increased cardiovascular risk and weight gain in T2D patients as a result of treatment were linked to a higher likelihood of non-adherence [38]. In 430 T2D patients receiving metformin and a sulfonylurea, Walz et al. [39] discovered that 34% of patients showed signs of hypoglycemia, and 19% had moderate or severe hypoglycemia. Despite the lower HbA1c levels, this was linked to poor treatment adherence and lower treatment satisfaction. Low adherence to treatment was linked to hypoglycemic events in a database study involving 212,061 T2D patients. Sulfonylureas, other OHAs (such as meglitinide and -glucosidase inhibitors), and insulin were all linked to a higher risk of hypoglycemia. Low risk of hypoglycemia was associated with thiazolidinediones, metformin, and dipeptidyl peptidase-4 (DPP-4) [40]. Longer medication persistence, according to a retrospective observational study, was linked to better glycemic control; however, the associations varied significantly between drug classes, with only metformin, sulfonylureas, and sodium-glucose co-transporter-2 (SGLT-2) inhibitors having >50% persistence at 2 years. 38 The drug with the longest median persistence, excluding SGLT-2 inhibitors, was metformin. For SGLT-2 inhibitors, there was only a brief follow-up period available, but they showed promise for good persistence [41].

The importance of patient education in highlighting the necessity of medication adherence as well as the directions and timing for taking medications on regular days, during the month of Ramadan, and while travelling. The doctors should also clear up any misunderstandings that patients have about the complications and side effects of the medications. In addition to teaching patients how to adjust their insulin doses or use their mobile devices to do so, they should also encourage and inform those who refuse to take insulin about its advantages. Re-education and illustrated pictures were two instructional strategies used in an Iranian randomized controlled trial study to increase diabetic patients' knowledge of diabetes [42].

CONCLUSION:

The study included 13 studies in different territories in Saudi Arabia. Moderated level of adherence was noted generally in Saudi Arabia. The highest levels of adherence was reported in Tabuk. Young age and polypharmacy were significantly correlated with adherence.

Despite the availability of numerous new medication classes, increased patient education efforts, and targeted interventions that address adherence, medication adherence in T2D remains low. New nonpharmacologic and pharmaceutical strategies are required to improve adherence in a clinically significant and long-lasting manner. Innovative approaches are required to address the burden of treatment as well as patients' unhelpful drug-related beliefs.

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