Assessing the Influential Factors Associated with Medication Non-adherence and Self-care Practices Among Type 2 Diabetes Mellitus Patients in Tripoli, Libya

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Abstract: Influential factors causing poor adherence to antidiabetic medications and self-care practices among type 2 diabetes mellitus (T2DM) patients have not been reported before in Libya. To assess such factors that contribute to non-adherence, a single health facility, cross-sectional descriptive study was carried out on T2DM patients attending the NCDE in Tripoli/ Libya; using a pre-tested questionnaire. Crude odds ratios in the binary logistic regression were used to describe the associations between medication adherence and various independent factors using SPSS version 26. Adjusted odds ratios with their corresponding 95% confidence intervals were further generated in the multivariable analysis, to determine variables which were independently associated with medication adherence and were considered significant at a p-value of <0.05. Of the 380 study participants, only 225(67.1%) were adherent. 159(41.8%) were non-adherence to physician recommendations and were careless when taking their medication, 200(52.6%) found difficulty maintaining recommended dietary restrictions, 211(55.5%) and 97(25.5%) didn't adhere to regular exercise or blood glucose monitoring; respectively. Factors significant association with non-adherence were; medication being taken; especially patients who were prescribed OHA and insulin ([AOR] [95% CI] = 0.214[0.073-0.632]), being careless and not taking prescribed medication as recommended ([AOR] [95% CI] = 2.880 [1.387- 5.983]), forgetfulness ([AOR] [95% CI] =0.199 [0.070- 0.570], stop taking prescribed antidiabetic medication when feeling well ([AOR] [95% CI] = 0.153[0.058- 0.402], medications side effects ([AOR] [95% CI]=0.382 [0.181- 0.809] and unawareness of the consequences of not adhering to medication as recommended and the consequences skipping doses ([AOR] [95% CI] = 0.146 [0.037- 0.581]). Adherence to recommended medication and self-care practices in Libya is unsatisfactory. Diabetes education, awareness programs, and regular monitoring of T2DM individuals' medication adherence and self-care practices are vitally required.

1. Introduction

Diabetes mellitus (DM) is a serious global issue and a public health care concern rapidly expanding worldwide (1). It has the highest psychological and behavioural demands of all chronic illnesses (2). There is no indication that the prevalence of DM will reverse as it continues to rise globally (3). DM prevalence in the Middle East and North Africa (MENA) area; which Libya is part of, had the highest regional prevalence rate of 12.2% and 16.2% in 2019 and 2021; respectively (4,5). During 1990 and 2019, the region witnessed an increase in the average mortality rate of 0.2% (24.8 to 25.2) (6). Most mortalities (24.5%) from diabetes in working-age

adults occur in the MENA Region. The MENA area will have 136 million diabetics by 2045 and an estimated growth of 86 %, which is the second-highest rate in the world (5). Although it has been estimated that the prevalence of DM in Libya might reach 14.1%, the exact prevalence is unclear (7). According to survey findings by Beshyah, the incidence of non-communicable illnesses like DM is frighteningly high (16.4%) (8). By 2045, DM cases will reach 762.500 in Libya, up from 442.500 in 2017, in which adults had a diabetes prevalence of 11.2% (9).

Although adherence to medication therapy is a well-known issue in clinical practice, medication adherence of DM patients reportedly varies, and non-adherence is a significant obstacle in providing diabetic care and treatment delivery (10). Over $100 billion is estimated to be spent yearly on managing the consequences of inadequate medication adherence (11). Patients who do not adhere to their drug therapy might do so on purpose or accidentally (i.e., intentional or unintentional non-adherence) (12). However, a medicine should be taken as directed to attain its intended effectiveness (13).

Poor medication adherence is a significant contributor to uncontrolled hyperglycaemia (14). Acute and chronic DM complications can result from inadequate and poorly controlled hyperglycaemia. Several of these complications are permanent and can cause impairment and failure to many body organs, particularly the nerves, eyes, and kidneys, if they are not managed (15). Chronic diabetes complications are the main reason for the high hospitalization rate of DM patients in Libya, despite the fact that effective treatments and medications that lower glycaemia levels are available nationwide (16).

Studies have investigated and identified possible influential factors and reasons for non-adherence to medication across a broad spectrum of illnesses, including DM. Numerous types of research have revealed inadequate and poor levels of DM patients' adherence to medication (17,18) and self-care practice (19,20). Due to differences in study size and methods, the association of different factors to adherence is conflicting.

For T2DM patients to adhere to therapy better, they must have good knowledge and a better understanding of the disease since having enough knowledge about DM promotes excellent self-care practices, the knowledge of T2DM patients and their awareness of the disease is directly influenced by their social and demographic characteristics (21). These characteristics are important determinants and influential factors that can impact how successfully a patient comprehends and adheres to their medication and self-care practice (22). Age (23-27), gender (28,29), education (27,29,30), and occupation (25,28) are some of the commonly cited social-demographic factors. The WHO has identified four additional factors and social-demographic variables that are likely to contribute to non-adherence. These include; patient-related, condition-related, therapy-related, and healthcare /system-related factors (31). Patient-related factors frequently cited include forgetting to take medication/s (26,28,32-35), stopping taking medication/s either when feeling well (36) or felling worse (23), and lack of finance (33,35,37-40). Condition-related factors have also been reported as the duration of having the disease (24,30), associated comorbidities (41,42), and taking other medications (25). Therapy-related factors such as side effects (26,36,37,40,41,43) and medication cost (24,36,44) were commonly associated with non-adherence.

Given the absence of research that identifies influential factors that may explain non-adherence behaviour among T2DM patients in Libya, there is a need to determine the adherence status of T2DM patients to both antidiabetic medication and self-care practices, as well as the possible factors that can contribute to non-adherence of these patients to these two facets of therapy in the country. This study performs a much-needed service by filling in that knowledge gap. The finding of this study will be beneficial for Libya's healthcare system and will make an essential contribution to non-adherence knowledge in Africa.

2.   Material and Methods

2.1   Ethics Approval and Consent to Participate

Ethical approval was obtained from the ethical committee at the Biotechnology Research Centre and given a reference number of BEC-BTRC 33-2020. All participant patients received voluntary informed consent and were assured that their information was kept confidential since their names were not requested. The participants were also informed that their participation was strictly voluntary and that they were free to refuse to participate in the study at any time without any consequences.

2.2   Study Setting and Study Participants

A descriptive cross-sectional study in a single health facility using a pre-tested questionnaire was carried out on T2DM who sought care at the National Centre for Diabetes and Endocrinology (NCDE) in Tripoli/ Libya. The NCDE provides outpatients with diabetes follow-up, medications, and laboratory testing despite operating as a referral clinic. The study was conducted for eight months (Starting June 2019) to investigate the reasons and factors influencing the non-adherence behaviour of these patients to their diabetic treatment. The study included patients of both genders attending the NCDE who are diagnosed with T2DM, aged ≥25 years old, with a fasting blood glucose level > 126 mg/dl and are being treated for at least six months with oral anti-hyperglycaemic (OAH) medication with/or without insulin. All these patients agreed to participate of their free will. A nurse participated in looking over the patient file to make sure that the type 1 diabetes was excluded from the study. The study also excluded patients who were recently diagnosed with diabetes (≤ 6 months). Being newly diagnosed can be confusing and overwhelming, and because patients may have trouble adjusting to life with DM, they were excluded. Patients who could not speak either Arabic or English were ruled out. The study also excluded patients who were very sick, unable, and unwilling to participate in the survey.

2.3   Sample Size Determination

The sample size for this study was calculated using the formula mentioned in Naing et al. review (45):

$$n = \frac{Z^2 P(1-P)}{d^2} \qquad \text{Eq. 1}$$

N = the estimated sample size of patients, Z = confidence level of which 95% is conventional, Z = 1.96, and P = the expected prevalence and the population assumed to be non-adherent to diabetic treatment. According to Mesquida et al., 50-60% of diabetic patients show poor medication adherence (46). The mean of this percentage will be the target population, i.e., P = 0.55, 1-P is the probability of diabetic adherent patients (1-P = 45%), and d is the precision and accepted margin of error (5%, d = 0.05).

The outcome of the sample size formula is the required sample group for this study (i.e., 380 patients).

2.4   Data Collection and Sampling Technique

A self-report, pre-tested questionnaire was used to collected the data. It consisted mainly of closed-ended questions with few open-ended questions. These questions were collected from previous and similar literature (41,47,48). The questionnaire contained four main sections. The first section had six questions regarding the socio-demographic characteristics of the participants, such as; age, gender, marital status, education level, employment, and family income. The second section contained six questions regarding participants' medical conditions; duration of having diabetes, medications prescribed, duration of taking diabetes medication/s, frequency of drug intake, dosage regimen, and what associated chronic disease/s they have besides T2DM. Since no golden standard is available for medication adherence assessment (49),

adherence to diabetic medication was determined by asking patients to recall if they missed any doses of medication as least once in the past seven days (50). Using a dichotomous response scale (i.e., yes/no), the third section contained four adherence indicators that were used to evaluate medication adherence and diabetic self-care practices of the patients. They include taking prescribed medication as recommended, maintaining and not having difficulty following recommended dietary restrictions, performing exercise regularly and monitoring blood glucose levels regularly. Since outdoor exercise is uncommon for Libyan women, regular exercise was defined as doing all the household routines by oneself as cooking, cleaning, and washing. The last section was also a dichotomous scale (i.e., yes/no), which contained twelve reasons and influential factors causing non-adherence to medication, taking other medications, having associated chronic disease, forgetting to take prescribed antidiabetic medication, being aware of the consequences of skipping doses and not adhering to medication as recommended, stop taking prescribed antidiabetic medication without physician recommendation, stop taking it when feeling well and symptoms under control, stop taking it when not feeling well and symptoms not under control, taking alternative treatment instead of medication, medication price, monitoring blood glucose level is cumbersome, sleep disturbance because of frequent urination, and experiencing side effects from antidiabetic medicines. Three final year B. Pharm. students from the Faculty of the Pharmacy / University of Tripoli helped to distribute and collect the questionnaires from the patients at the NCDE. Using a convenient sampling method, a nurse working at the clinic was asked to help select patients who were willing to participate and met the study's inclusion criteria. Patients who only met the requirements were given the questionnaire. The study's objective was clarified to the selected patient on the explanatory letter attached to the questionnaire. The nurse was asked to fill out the questionnaire for illiterate patients, and the rest of the participants completed the questionnaire themselves. The students went through all sections to ensure no missing data in the collected questionnaires. Data's completeness was checked regularly until the required sample size was ordered.

2.5 Operational Definition of Adherence to Antidiabetic Medication

This study's operational definition of adherence was 100 % adherence to the recommended medical prescription. Missing a single dose out of more than one prescribed dose was considered non-adherent. Patients who did not miss a dose in the previous seven days were considered adherent. These patients were given a score of "1".

2.6 Data Management and Quality Assurance

Before distributing the questionnaire, it was first prepared in English. It was then translated into the local Arabic language by the principal investigator, using iterative translation to enhance the quality of the translation (51). Five T2DM patients at the NCDE were asked if the questions were clear, simple to understand, and not ambiguous. All five patients confirmed that the questions' meanings were interpreted the same as intended (52). These patients were not included in the study. The internal consistency of the questionnaire was pilot-tested on 30 patients. A default sample size of 30 participants is advised in pre-tests of questionnaires (53). Because the questions are a dichotomous response scale (yes/no), Kuder–Richardson 20 test (KR-20) was used to assess the reliability using Microsoft Excel 2016. The KR-20 obtained (0.806) was above the accepted limit of 0.70, which indicates reliability (54). To manage the data obtained and ensure its quality, the principal investigator monitored the data collection process throughout the study.

2.7 Data Analysis

Data collected in this study were coded, entered using double data entry to ensure completeness and was analyzed using Statistical Packages for Social Sciences (SPSS) version 26 (SPSS Inc., Chicago, IL, USA).

Categorical and numerical variables were tabulated and expressed as frequencies and percentages. Binary logistic regression was used to assess the association between medication adherence and each independent explanatory variable as socio-demographic parameters, duration of diabetes, diabetic treatment, comorbid conditions, other medications taken with diabetic treatment, and the different factors influencing non-adherence (i.e., between dependent and independent variables). Furthermore, multivariate logistic regression was performed to further analyze all independent variables with a *p*-value of less than 0.25 at a 95% confidence interval (CI) in the binary logistic regression analysis. Using the model of the Hosmer–Lemeshow goodness of fit test in multivariable logistic regression, the adjusted odds ratios (AORs) at 95% CI were estimated to identify non-adherence associated factors, and the association was considered statistically significant when the *p*-value is equal to 0.05 or less.

3. Result

3.1 Participants Socio-demographic Characteristics

The socio-demographic parameters of the 380 participants are shown in Table 1. Out of the total participants, more than a quarter of the patients, 105 (27.6%), aged between 51- 60 years, more than half 227 (59.7%), were males, and the majority, 322 (84.7%), were married. Regarding education status, 216 (56.8%) of the participants have an education degree, either university or another degree, and 54(14.2 %) of the subjects had no formal education. Regarding occupation, 228(60 %) of the patients were employed, and 136(35.8%) had per capita monthly income of less than 500 L.D.

Table 1. Socio-demographic characteristics and adherence association of the participants.

Variable	Category	Total Frequency (%) (n=380)	Non-adherent (n=125)(%)	Adherent (n=255)(%)	COR [95% CI]	*p-value*
Age (years)	25-30	17(4.5)	3(2.4)	14(5.5)	1.00	
	31-40	52(13.7)	12(9.6)	40(15.7)	0.714 [0.175-2.908]	0.639
	41-50	92(24.2)	23(18.4)	69(27.1)	0.643[0.169-2.439]	0.516
	51-60	105(27.6)	36(28.8)	69(27.1)	0.411 [0.111-1.523]	0.183
	61-70	84(22.1)	37(29.6)	47(18.4)	0.272 [0.073-1.018]	0.053
	71-80	27(7.1)	13(10.4)	14(5.5)	0.231 [0.054-0.991]	0.049*
	81-90	3(0.8)	1(0.8)	2(0.8)	0.429 [0.029-6.409]	0.539
Gender	Male	227(59.7)	77(61.6)	150(58.8)	1.00	
	Female	153(40.3)	48(38.4)	105(41.2)	1.123[0.724-1.741]	0.604
Marital status	Single	35(9.2)	8(6.4)	27(10.6)	1.00	
	Married	322(84.7)	108(86.4)	214(83.9)	0.587[0.258-1.336]	0.204
	Divorce/widow	23(6.1)	9(7.2)	14(5.5)	0.461[0.146-1.456]	0.187
Educational level	Not educated	54(14.2)	24(19.2)	30(11.8)	1.00	
	Primary school	26(6.8)	6(4.8)	20(7.8)	2.667[0.925-7.685]	0.069
	Secondary school	84(22.1)	34(27.2)	50(19.6)	1.176[0.589-2.349]	0.645
	University	136(35.8)	33(26.4)	103(40.4)	2.497[1.285-4.854]	0.007*
	Other education	80(21.1)	28(22.4)	52(20.4)	1.486[0.733-3.011]	0.272
Employment	Not employed	152(40.0)	57(45.6)	95(37.3)	1.00	
	Employed	228(60.0)	68(54.4)	160(62.7)	1.412[0.915-2.179]	0.119
Family monthly income (L.D)	< 500	136(35.8)	50(40)	86(33.7)	1.00	
	500 -1000	98(25.8)	27(21.6)	71(27.8)	1.529[0.870-2.687]	0.14
	> 1000	109(28.7)	38(30.4)	71(27.8)	1.086[0.642-1.838]	0.758
	No answer	37(9.7)	10(8)	27(10.6)	1.570[0.702-3.511]	0.272

Note: L.D=Libyan dinar; COR=Crude odd ratio; CI=Confidence interval; ***** Indicates statistical significance (*P*<0.05).

3.2   Participants' Medication Adherence Status

The adherence to diabetic medication among the study participants was 67.1 %. These patients did not miss a single dose of medication in the past seven days. Whereas; 125 (32.9%) of the participants were non-adherent and did miss to take the prescribed medication at least once.

3.3   Adherence Indicators to Diabetic Self-care Practices

The T2DM participant patients were assessed for their diabetic self-care practices. 221 (58.2%) of the patients were not careless and took their prescribed medication as recommended by their physician, 180(47.4%) maintained and did not find difficulty in following recommended dietary restrictions, 169(44.5%) performed exercise regularly, and 283(74.5%) monitoring their blood glucose level regularly (See Table 2).

Table 2. Adherence indicators and diabetic self-care practices of the participants.

Adherent Indicators		Frequency (%) (n=380)	Non-adherent (n=125)(%)	Adherent (n=255)(%)	COR [95% CI]	*p-value*
Taking prescribed medication as recommended and not being careless	No	159(41.8%)	87(69.6)	72(28.2)	1.00	
	Yes	221(58.2%)	38(30.4)	183(71.8)	5.819[3.642-9.298]	0.000*
Maintaining and not finding difficulty in following recommended dietary restrictions.	No	200(52.6%)	79(63.2)	121(47.5)	1.00	
	Yes	180(47.4%)	46(36.8)	134(52.5)	1.902 [1.226-2.95]	0.004*
Performing exercise regularly	No	211(55.5%)	90(72)	121(47.5)	1.00	
	Yes	169(44.5%)	35(28)	134(52.2)	2.848[1.795-4.517]	0.000*
Monitoring blood glucose levels regularly	No	97(25.5%)	43(34.4)	54(21.2)	1.00	
	Yes	283(74.5%)	82(65.6)	201(78.8)	1.952[1.213-3.141]	0.006*

Note: COR=Crude odd ratio; CI=Confidence interval; * Indicates statistical significance ($P<0.05$).

3.4   Participants' Clinical and Medication Characteristics

The clinical and medication-related characteristics of the participants are shown in Table 3. One-third of the participants, 132(34.7%), have had diabetes for more than ten years, 129(33.9%) have been taking diabetic medication for less than 5 years, 153(40.3%) were taking OHA with insulin, 168(44.2%) were taking two dose unit per day, and 227(59.7%) of the patients were taking their medication twice a day. Of the patients taking OHA, 59(15.5%) were on monotherapy, while 131(34.5%) were on combination therapy. Metformin alone was taken by 53 (13.9%) of the patients. The most frequently prescribed combination therapy was a dual OHA containing metformin and glimepiride 57 (15%), followed by metformin and glibenclamide 26 (6.8 %). Triple OHA was also prescribed, in which 13 (3.4%) of the patient were taking a combination therapy of metformin, sitagliptin, and glimepiride. More than a third of the patients, 153(40.3%), took OHA with insulin. Metformin was the most typical combined OAH medication with insulin 138 (36.3%). 145(38.2%) of the patients have associated comorbidities. Hypertension 67(17.6%) was the most frequent among the participants, followed by heart disease 22(5.8%). Whereas; 21(5.5%) of the patients had hypertension and heart disease.

3.5   Binary Logistic Regression Association to Adherence

In the crude binary logistic analysis, patients aged between 71-80 years were 77% less to adhere to the prescribed anti-diabetic medications than those aged 25 -30 years (Crude OR [COR] [95% CI] =0.231 [0.054-

0.991]). Participants who had a university education were 2.49 times more adhered to medication than those who were illiterate ([COR] [95% CI] =02.497[1.285-4.854]). See Table 1.

As seen in Table 2, patients who maintain and follow recommended dietary restriction ([COR] [95% CI] =1.902 [1.226-2.950]) and regularly monitor their glucose level ([COR] [95% CI] =1.952[1.213-3.141]) are two times more likely to be adherent to their antidiabetic medication. Whereas; those who perform regular exercise ([COR] [95% CI] =2.848[1.795-4.517]) are three times more likely to be adherent.

Table 3. Adherence association of the participant's clinical and medication-related characteristics.

Variable	Category	Total Frequency (%) (n=380)	Non-adherent (n=125)(%)	Adherent (n=255)(%)	COR [95% CI]	p-value
Duration of DM (years)	< 5	123(32.4)	26(20.8)	97(38)	1.00	
	05-10	125(32.9)	48(38.4)	77(30.2)	0.430[0.245-0.755]	0.003*
	> 10	132(34.7)	51(40.8)	81(31.8)	0.426[0.244-0.743]	0.003*
Taking medication for (years)	< 5	129(33.9)	29(23.2)	100(39.2)	1.00	
	05-10	125(32.9)	47(37.6)	78(30.6)	0.481[0.278-0.834]	0.009*
	> 10	126(33.2)	49(39.2)	77(30.2)	0.456[0.264-0.787]	0.005*
Type of medication	Single OHA	59(15.5)	15(12)	44(17.3)	1.00	
	Multi- OHA	131(34.5)	31(24.8)	100(39.2)	1.100[0.540-2.239]	0.793
	OHA +Insulin	153(40.3)	75(60)	78(30.6)	0.355[0.182-0.690]	0.002*
	Insulin only	37(9.7)	4(3.2)	33(12.9)	2.812[0.854-9.261]	0.089
No. of dose unit	Insulin only	37(9.7)	4(3.2)	33(12.9)	1.00	
	1	103(27.1)	42(33.6)	61(23.9)	0.176[0.058-0.534]	0.002*
	2	168(44.2)	58(46.4)	110(43.1)	0.230[0.078-0.681]	0.008*
	3	72(18.9)	21(16.8)	51(20)	0.294[0.093-0.935]	0.038*
No. of doses	Once daily	101(26.6)	42(33.6)	59(23.1)	1.00	
	Twice daily	227(59.7)	67(53.6)	160(62.7)	1.700[1.044-2.769]	0.033*
	Three times daily	52(13.7)	16(12.8)	36(14.1)	1.602[0.788-3.256]	0.193
Associated comorbidities	Absent	235(61.8)	57(45.6)	178(69.8)	1.00	
	Hypertension	67(17.6)	33(26.4)	34(13.3)	0.330[0.188-0.580]	0.000*
	Heart disease	22(5.8)	12(9.6)	10(3.9)	0.267[0.110-0.650]	0.004*
	Both	21(5.5)	10(8)	11(4.3)	0.352[0.142-0.872]	0.024*
	Asthma	15(3.9)	9(7.2)	6(2.4)	0.213[0.073-0.626]	0.005*
	Hyperlipidemia	7(1.8)	2(1.6)	5(2)	0.801[0.151-4.239]	0.794
	Others	13(3.4)	2(1.6)	11(4.3)	1.761 [0.379-8.182]	0.47

Note: OAH=oral anti-hyperglycaemic; COR=Crude odd ratio; CI=Confidence interval; * Indicates statistical significance (*P*<0.05).

Patients having DM for five years or more were 57% less likely to adhere to medication than patients who have had diabetes for less than five years ([COR] [95% CI] =0.430[0.245-0.755] and 0.426[0.244-0.743] respectively). Participants who are taking OHA with Insulin are 65% less adherent to their medications than patients who are on single OHA ([COR] [95% CI] =0.355[0.182-0.690]). T2DM patients who have comorbidities such as hypertension, heart disease, or both and asthma are 67%, 73%, 65%, and 79% less likely to adhere to medication than respondents who have no associated comorbidities ([COR] [95% CI] = 0.330[0.188-0.580], 0.267[0.110-0.650], 0.352[0.142-0.872] and 0.213[0.073-0.626]); respectively. Details are in Table 3.

3.6 Reasons for Medication Non-adherence

Details of the factors contributing to non-adherence that were assessed in this study are presented in Table 4. More than a third of the participants, 145(38.2%), have associated chronic disease, 154(40.5) are taking other medications besides their diabetic medicine, and 273(71.8%) respond that they forget to take prescribed antidiabetic drugs. Nearly a quarter of the participants, 77 (20.3%), stopped taking their prescribed

anti-diabetic medication without physician recommendation, 60 (15.8%) stopped taking it when they were feeling well, and 66 (17.4 %) stopped taking their medication when not feeling well and symptoms not under control. 50 (13.2%) of the participants admitted taking alternative treatment instead of the prescribed anti-diabetic medication, and 359 (94.5%) said they would take medication more regularly if it were provided for free or affordable. Monitoring blood glucose levels is cumbersome for 153 (40.3%) participants, and 177 (46.6%) are disturbed at night during sleep because of frequent urination. Side effects from the anti-diabetic medication were experienced by 104 (27.4%) of the patients, and 29 (7.6%) were unaware of the consequences of not adhering to medication as recommended and the consequences of skipping doses. All of these factors in the binary logistic analysis were associated with medication non-adherence except stopping prescribed antidiabetic medication when not feeling well, taking medication more regularly if provided at an accessible or affordable price, and monitoring glucose level is cumbersome. Participants who answered yes to the influential factors are (50.9%-87.6%) less likely to adhere to medication than participants who answered 'no'.

Table 4. Factors and reasons contributing to non-adherence behaviour among T2DM participants.

Factors / reasons influencing non-adherence		Total Frequency (%) (n=380)	Non-adherent (n=125)(%)	Adherent (n=255)(%)	COR [95% CI]	*p-value*
Associated chronic disease	No	235(61.8)	57(45.6)	178(69.8)	1.00	
	Yes	145(38.2)	68(54.4)	77(30.2)	0.363 [0.233-0.564]	<0.001
Taking other medications	No	226(59.5)	51(40.8)	175(68.6)	1.00	
	Yes	154(40.5)	74(59.2)	80(31.4)	0.315 [0.202-0.491]	< 0.001
Forget to take prescribed antidiabetic medication.	No	107(28.2%)	9(7.2)	98(38.4)	1.00	
	Yes	273(71.8%)	116(92.8)	157(61.6)	0.124 [0.060- 0.256]	< 0.001
Stop taking prescribed medication without a physician's recommendation.	No	303 (79.7%)	84(67.2)	219(85.9)	1.00	
	Yes	77 (20.3%)	41(32.8)	36(14.1)	0.337[0.202-0.563]	< 0.001
Feeling well and symptoms under control.	No	320(84.2%)	85(68)	235(92.2)	1.00	
	Yes	60 (15.8%)	40(32)	20(7.8)	0.181 [0.100- 0.327]	< 0.001
Not feeling well and symptoms not under control.	No	314(82.6%)	99(79.2)	215(84.3)	1.00	
	Yes	66 (17.4 %)	26(20.8)	40(15.7)	0.708 [0.409-1.226]	0.218
Taking alternative treatment instead of prescribed medication.	No	330(86.8%)	100(80)	230(90.2)	1.00	
	Yes	50 (13.2%)	25(20)	25(9.8)	0.435 [0.238-0.794]	0.007
Take medication more regularly if it is provided for a free or affordable price.	No	21 (5.5%)	7(5.6)	14(5.5)	1.00	
	Yes	359 (94.5)	118(94.4)	241(94.5)	1.021 [0.401- 2.598]	0.965
Monitoring blood glucose levels is cumbersome.	No	227 (59.7%)	66(52.8)	161(63.1)	1.00	
	Yes	153 (40.3%)	59(47.2)	94(36.9)	0.653 [0.423- 1.008]	0.054
Disturbed at night during sleep because of frequent urination.	No	203 (53.4%)	52(41.6)	151(59.2)	1.00	
	Yes	177 (46.6%)	73(58.4)	104(40.8)	0.491 [0.318- 0.758]	0.001
Experience side effects from antidiabetic medication	No	276 (72.6%)	72(57.6)	204(80)	1.00	
	Yes	104 (27.4%)	53(42.4)	51(20)	0.340 [0.212- 0.543]	< 0.001
Not aware of the consequences of medication non-adherence and the consequences of skipping doses.	No	351 (92.4%)	105(84)	246(96.5)	1.00	
	Yes	29 (7.6%)	57(45.6)	178(69.8)	0.192 [0.085- 0.436]	< 0.001

Note: COR=Crude odd ratio; CI=Confidence interval; * Indicates statistical significance (*P*<0.05).

3.7 Factors Associated with Medication Non-adherence

Factors that were found to have a statistically significant association with non-adherence in the multivariable logistic regression analysis, as illustrated in Table 5, are; the type of medications being prescribed ([AOR] [95% CI] = 0.214[0.073-0.632]), carelessness ([AOR] [95% CI] = 2.880 [1.387- 5.983]), forgetfulness ([AOR] [95% CI] =0.199 [0.070- 0.570], feeling well ([AOR] [95% CI] = 0.153[0.058- 0.402]),

medications side effects ([AOR] [95% CI]=0.382 [0.181- 0.809]) and unawareness ([AOR] [95% CI] = 0.146 [0.037- 0.581]).

Table 5. Influential factors associated with non-adherence in T2DM patients.

Possible factors causing non-adherence	B	S.E.	Wald	AOR [95% CI]	P value
Taking OHA and Insulin	-1.539	0.551	7.797	0.214 [0.073-0.632]	0.005
Being careless and not taking prescribed medication as recommended	1.058	0.373	8.044	2.880 [1.387- 5.983]	0.005
Forget to take prescribed antidiabetic medication.	-1.613	0.536	9.065	0.199 [0.070- 0.570]	0.003
Stop taking prescribed antidiabetic medication when feeling well and symptoms under control.	-1.879	0.493	14.497	0.153[0.058- 0.402]	< 0.001
Experience side effects from the antidiabetic medication?	-0.962	0.383	6.319	0.382 [0.181- 0.809]	0.012
Not aware of the consequences of not adhering to medication as recommended and the consequences of skipping doses.	-1.921	0.703	7.467	0.146 [0.037- 0.581]	0.006

Note: B=Unstandardized beta; S.E=Standard error; AOR=Adjusted odd ratio; CI=Confidence interval; * Indicates statistical significance ($P<0.05$).

T2DM patients who were prescribed OHA and insulin, forget to take prescribed antidiabetic medication, stop taking prescribed anti-diabetic medication when feeling well and symptoms under control, who experience side effects from antidiabetic medicines, and those who are not aware of the consequences of not adhering to medication as recommended and the consequences skipping doses are 79 %, 80%, 84%, 62% and 85% less likely to be adherent to their diabetic treatment; respectively. Being careless and not taking prescribed medication as recommended is 2.8 times non-adherent to therapy.

4.   Discussion

To the author's knowledge, the influential factors causing poor adherence to diabetic medication and self-care practices among T2DM patients have not been reported before in Libya. For this reason, T2DM patients attending the NCDE in Tripoli, Libya, were assessed in this study for their medication adherence, self-care activities, and the influential factors associated with the non-adherence of these patients to these two facets of therapy in the country. Few studies on adherence to anti-diabetic medication among T2DM patients in Libya were identified (55-57). Two of these studies took place in Benghazi Diabetes Centre and targeted both T1 and 2 DM patients at different periods. The first aimed to assess patients' practices and knowledge (55). The other study also assessed patients' ability in addition to factors that improve adherence to the condition's treatment and management (56). A most recent study, which took place in Tripoli at the NCDE, assessed the influence of illness perceptions on medication adherence among T2DM patients (57). Each of these research utilized a different adherence measure. Still, none of these studies have focused on the influential factors causing poor adherence to diabetic medication and self-care practices in the country.

The status of adherence to anti-diabetic medication reported by this study was unsatisfactory 67.1% but reasonable when compared to other developing African countries such as Egypt (38.9%) (58), Sudan (45%) (59), Ethiopia (95.7%) (47) and Nigeria (86.8%) (60). Patients may also have difficulty remembering their medication-taking regimens. This was minimized by asking the participants to recall events over a short period which was from the preceding week. Similar findings of adherence level were reported in the previously mentioned Libyan studies. The prevalence of low medication adherence which was measured using the eight-item Morisky medication adherence scale, was 36.1% according to Ashus et al., (57). Whereas; 27.1% of diabetics reported by Roaeid et al. not take their medications regularly (55). A much higher percentage of low

adherence levels was reported by Elkharam et al., which assessed adherence using HbA1c and showed that 63.2% of diabetic patients had poor glycaemic control (56). All these findings highlighted the low adherence levels among the diabetic Libyan population.

According to this study, males were found to have a higher prevalence of T2DM than females in the Libyan population. This outcome was consistent with earlier studies conducted in other nations, where T2DM prevalence was lower in females than males (61). The distribution of body fat varies by gender. Females tend to have more subcutaneous and peripheral fat, which increases their insulin sensitivity and helps protect them from T2DM. In contrast, males are linked to insulin resistance because they have a more significant proportion of visceral and hepatic fat. Laziness in the lifestyle of the male gender is another contributing factor to developing T2DM (61).

Treatment protocols for T2DM patients include pharmacological and non-pharmacological measures (27). These patients rely on insulin and OAH that should be taken on schedule in addition to a healthy diet, frequent blood sugar testing, and regular exercise to achieve satisfactory control of blood glucose levels (62). Medication adherence and self-care practices are the most crucial aspects of diabetes control (63). Because patients alone are responsible for 98% of the self-care activities, adherence to these two facets of therapy is difficult, demanding, and challenging (64). Adherence to anti-hyperglycaemic medication, diet, and exercise is, therefore, essential and must be maintained to sustain blood glucose levels and minimize complications over the long term (65). When comparing patients who don't follow these non-pharmacological routines in the binary logistic analysis, self-care adherent practices are up to three times more medication adherence. It is a matter of need for cognitive training programs and behavioural therapy on lifestyle modifications, dietary restrictions, physical work out, diabetic foot care, and regular ophthalmology examinations. All these therapy measures have shown to enhance patients' life expectancy and quality (48).

This study revealed that non-adherence was a statistically significant association with patients who were prescribed OHA and insulin. Such patients are 79 % less likely to be adherent to their medication ([AOR] [95% CI] = 0.214[0.073-0.632]). More than a third of the participants, 153(40.3%), were using combination therapy. This may be due to the Libyan market's high cost of insulin injections. Contrary to this study's finding, glibenclamide monotherapy was administered to 74.3% of the patients (40). Combination therapy is aligned with the indicated strict management of blood glucose levels, and such patients may have felt better and stopped taking medication accordingly. This may explain why 60 (15.8%) stop taking their prescribed antidiabetic medication when feeling well, and their symptoms are under control and are less likely to be adherent. A tailored treatment strategy and individualized blood glucose target for each patient may be essential. It is of equal importance and necessary to develop approaches to educating patients about their medication regimens. This will assist in reducing the already enormous disease burden associated with non-adherence and diabetic complications.

In coincide with similar studies (21,26,28,32-35); that indicated that forgetfulness and being unaware of the consequences of not adhering to medication as recommended and the consequences of skipping doses were significantly associated with medication non-adherence, this current study revealed that almost three-quarters of the patients 273(71.8%) forget to take their prescribed antidiabetic medication and 159(41.8%) were being careless and not taking prescribed medication as recommended. Since 228(60%) of the patients are employed, and the majority are of working age, they may become distracted at work and forget to take their prescriptions. Furthermore, one-third of the research population comprises patients aged 60 and

beyond, which may account for forgetfulness. As people age, their cognitive ability drops. This pertains to individuals aging with multi-comorbidities and taking multi-medications. Measures must be developed to lessen forgetfulness and unawareness. These factors may result from the patient not receiving the ongoing assistance they require after the prescribed medication. Patients unaware of their disease must have regular meetings with diabetes educators to raise their awareness, and of equal importance is to keep the period between consultations with health professionals as minimal as possible.

T2DM patients who experience side effects from anti-diabetic medication were found in this current study to be 62% less likely to be adherent to their medication and showed a statistically significant association. In the same way, Manobharathi et al. and several other studies have stated that side effects of drugs as one of the critical associated factors for non-adherence (26,36,37,40,41,43). Anti-diabetic medications may not have been the only cause of the side effects seen during treatment. Since more than a third of the study population have comorbidities, medications such as antibiotics, antihypertensive, angiotensin receptor blockers, β -blockers, calcium channel blockers, and vitamins may have contributed. These adverse effects may be mistakenly thought to result from anti-diabetic medications (61).

Associated comorbidities were found to be insignificantly associated with medication adherence in this study. This finding differs from a Saudi Arabia study which revealed that patients with no comorbid disorders had a significant association with good adherence (66). Patients with chronic illnesses, in general, and DM in particular, may struggle to adhere to the prescribed therapy due to cumbersome and inconvenient dosing regimens caused by multi-medication and the concern of consuming too many medicines. Due to the multi-medications administered to T2DM patients with associated comorbidities, poor adherence appears to hinder achieving a satisfactory clinical outcome in such patients substantially. The associated comorbidities of these patients will determine how many medications they will take and are dependent mainly on their disease severity. Such patients are, therefore, challenging and present a problem to healthcare practitioners since they may have difficulty adhering to all prescribed medications belonging to numerous different pharmacological classes. In this study, Hypertension 67(17.6%) and heart disease 22(5.8%) were the most associated comorbidities among the patients studied.

The cost of medications, low monthly income, and unemployment are deterrent factors affecting patients' medication adherence. Although these economic factors were found to be insignificant similar to research from South India finding (67), medication non-adherence is potential because these patients may be unable to purchase most of their medications, resulting in missed doses. However, this can cause sub-optimal drug levels if the medications are not taken regularly and timely. Only 21 (5.5%) of respondents answered no when asked if they would take their prescription more frequently if it were free or inexpensive, which may account for the lack of a significant association. This may be since after and during the covid-19 break out. The Libyan healthcare system had suffered a clear scarcity of medications and pharmaceutical products previously offered to the general population free of charge in all public healthcare systems. Therefore, chronic disease medications should be available at medical facilities so that patients who cannot afford them can easily obtain them.

In further assessing the factors that affect medication adherence, it was found that some diabetic patients, 50 (13%), shifted to alternative treatment, cupping (bloodletting), and herbal medication instead of their antidiabetic medications. The Libyan nation commonly uses alternative therapies, especially herbal medicine, in their culture. Libya has a rich source of medical plants (68). A study by Ashur et al. showed that seventy-seven different traditional medicine products were utilized by 28.9% of diabetes patients, with herbs

being the most frequently used (69). Another study by Gupta et al. revealed that numerous herbs could cause drug-herbal interaction when taken with anti-diabetic medication. Such interaction could alert the pharmacokinetic and pharmacodynamics features of such medications and also can have both risks and benefits to diabetic patients (70).

The utilization of a self-report questionnaire has limitations as an estimate of patients medication adherence levels. Although a cost-effective, reliable, and a method that helps health care providers to identify patients who are more likely to have poor adherence; it's not the real medication-taking behaviour. Self-reports might be subjective and may overestimate patient's adherence status when compared to other methods. Social desirability is another disadvantage of self-reporting questionnaires. The possibility of meaning loss during translation cannot be neglected. Another methodological limitation of the study is convenience sampling, which has the potential to produce samples that are either under or over-represented in the research population. The obtained results do not represent medication adherence of diabetic patients in the entire city or country because it was a cross-sectional survey conducted in a single diabetes centre. The findings' generalizability may have been improved with a multicentre investigation. Selection bias is another study limitation because, typically, patients who visit NCDE are often more concerned about their health and were the selected participants. Because the study assessed adherence by just using a questionnaire and did not consider the consequence of non-adherence, future researchers need to narrow these gaps by using different analysis methods. For example, analysis of patient's medication record, pill counts, and medication use control in addition to using a questionnaire. These methods would greatly improve the value of clinical analysis and allow further evaluation of the impact of non-adherence to anti-diabetic medication.

5. Conclusion

Non-adherence to recommended medication and self-care practices exists among T2DM patients in Libya and is unsatisfactory but reasonable compared to other developing countries. Influential factors contributing to non-adherence behaviour are the type of prescribed medications, carelessness, unawareness, forgetfulness, stopping taking prescribed antidiabetic medication when feeling well and symptoms under control, and medication side effects. Monitoring T2DM individuals' medication adherence levels and self-care practices through regular follow-up and providing these patients with the necessary education is vital. This will make it easier for medical practitioners to recognize patients who don't take their medications as prescribed, aid in creating effective programs, and facilitate the establishment of successful measures to encourage medication adherence and self-care practices and eventually prevent diabetic complications. If the patient does not follow the specified treatment plan, all attempts, time, and funds spent on diagnosing, prescribing, and educating them on their condition will be squandered.

Data Availability

The data supporting this study's findings are available from the corresponding author upon reasonable request.

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