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Medication adherence and associated costs among patients with type 2 diabetes accessing care at a tertiary health care facility in Nigeria: a cross-sectional study

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Abstract

Background: Diabetes mellitus (DM) affects a significant proportion of the Nigerian population with substantial health and economic burden. Adherence to medication is critical to achieving effective control of diabetes, as poor adherence causes suboptimal glycemic control and diabetic complications, increasing the disease health and economic burden. The study aimed to assess the current state of adherence to anti-diabetic medication and associated costs among a population of patients with T2DM attending medical outpatient's clinic in a tertiary healthcare facility, south-east, Nigeria.

Method: A cross-sectional study was carried out using a structured questionnaire incorporating the 8-item Morisky medication adherence questions, to determine adherence and associated factors of non-adherence to anti-diabetic medications among a population of outpatients at the Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi. Demographic characteristics, clinical and medication adherence information were collected from participants. Patients' records were reviewed to abstract information on drug use pattern and associated costs of medication. Data was analyzed with SPSS version 16 and GraphPad Prism version 5.03 software, summarized using descriptive statistics and multiple regression analysis.

Findings: A total of 208 patients diagnosed with T2DM were interviewed using questionnaires while 300 prescriptions of anti-diabetic medications were analyzed. Mean age of patients was 53.5 (±0.5) years. Approximately 53% of participants were adherent while up to 47.1% were non-adherent to anti-diabetic medications. Socio-demographic, clinical and medication characteristics of participants showed no association with medication adherence. Multiple medications and associated costs were the most common factors associated with non-adherence. Mean cost of prescription amounted to $13.30 per patient, at $0.53 per patient per day. Metformin was the most prescribed anti-diabetic medication, constituting up to 16% of the total cost of medication

Conclusion: There was a significant sub-optimal adherence to anti-diabetic medication among the diabetes patients. Multiple medication and associated costs contributed most to non-adherence suggesting scope for improved rational use of medicines to enhance patient's adherence and improved outcome.

Keywords: Medication Adherence, Anti-diabetics, Type-2 Diabetes, Medical Outpatients, Treatment Cost, Rational Drug Use

Background

Diabetes mellitus (DM) is a chronic disease of public health importance affecting a significant proportion of the global population. It is the leading cause of disability and death [1]. The prevalence of diabetes mellitus is growing rapidly worldwide and is reaching epidemic proportions. Epidemiological data indicate that all nations, rich and poor, suffer the impact of diabetes epidemic [2], but low- and middle-income countries (LMICs) appear to currently face the greatest challenge of the disease, particularly sub-Sahara Africa (SSA) already burdened by communicable and non-communicable diseases [3-5].

In Nigeria, between 1% and 10% of the population is said to be affected by diabetes mellitus, in particular type 2 (T2DM), constituting a major public health concern, with substantial economic burden [6 – 9]. The disease affects all segments of the Nigerian population as one of the leading causes of premature death and disability. As a chronic life-long disease, DM imposes significant health and economic burden on households and society, through healthcare utilization and loss of productivity.

Management of diabetes mellitus takes both pharmacological and non-pharmacological approaches. Non-pharmacological approach includes lifestyle, dietary modifications and physical exercise. Pharmacotherapy for type 2 diabetes mellitus has changed dramatically in the last few years with the addition of several new drug classes and recommendations to achieve more stringent glycemic control. Sufficient glycemic control is achieved through a combined approach using diet control, physical exercise and medication. This effectively prevents both short- andlong-term related complications [10, 11]. Inclusion of statins and good control of blood pressure further helps to reduce cardio-vascular events and deaths.[12]

Effective control of diabetes relies heavily on the patient's ability to pursue self-care, through lifestyle modifications such as dietary controls and regular exercises, as well as regular self-monitoring of blood glucose and medication adherence. Adherence to medication in the management and control of T2DM is critical to achieving the goals of pharmacotherapy, effectively maintaining glycemic control. However, several studies on medication adherence have reported low adherence patterns [13 -15]. Poor adherence to medication is a major impediment to effective management, leading to complications and increasing disease burdens [16]. Drop in medication adherence has been noted to be most dramatic after the first six months of therapy among patients with chronic conditions such as T2DM [17]. The WHO had estimated that only about half of patients with chronic diseases adhere to medication [16]. A systemic review of medication adherence among T2DM patients showed average adherence to range between 36% and 93%, while adherence to other treatment recommendations especially dietary recommendations remains poor [18]. In Nigeria, related adherence studies have reported non-adherence to range between 25 and 50% among the patients [19-22].

Many factors have been identified to contribute to non-adherence to anti-diabetic medication, such as cost of medication, poor knowledge of anti-diabetic medications, poor access to health care facilities, side effects of anti-diabetic medications, complexity of medication (number, doses per day etc) [23, 24]. Medication may contribute to non-

adherence due to side effects and cost, while poor patient-health care provider relationships may also be a major determinant of non-adherence [2]. These constitute significant burden to the health care system and the society as a whole, impacting greatly on the Nigerian economy and leading to a series of diabetic complications and increased disease burden. Cost of medication remains a major factor affecting adherence [5, 25] especially among the low-income population, who cannot afford high costs of medication, leading to non-adherence. Hence, quality of anti-diabetic medication prescribed to patients is critical to enhanced adherence and successful control of DM. Prescriptions of inappropriate and/or high-cost medications will always lead to poor adherence. Acquisition cost of medication becomes important consideration in disease management especially in low-income countries such as Nigeria where out-of-pocket (OOP) expenditure remains the main source of health care finance [26].

Currently, there is insufficient information on medication adherence among patients with T2DM in Nigeria, particularly south eastern part where incidence of diabetes is significant. Regular adherence studies remain useful to generate evidence to inform improved diabetic control. This study aimed to assess the extent of adherence to anti-diabetic medications among a cohort of patients attending diabetic outpatient clinic in a tertiary healthcare in Nigeria. The study further aimed to identify both patient and non-patient related factors of adherence or non-adherence to anti-diabetic medications. Pattern of drugs prescription and associated costs of medication were analyzed as part of non-patient/health system related factors of non-adherence.

Methods

Study setting

The study was conducted at the Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, south-east Nigeria. It is a tertiary healthcare facility providing specialized clinical and teaching services to a surrounding population of over 300,000 inhabitants. The facility has a bed space for 500 inpatients. It is a major referral health center in Anambra state, owned by the federal government. A work force of over 2400 staff is spread across various clinical and non-clinical departments. Over 21,000 patients are treated annually at the outpatient's unit of the hospital. Diabetes Mellitus (both Types 1 & 2) is one of the major conditions treated in the medical outpatient's unit (MOP), offering diabetic services to an estimated 2000 patients per annum. Diabetic cases are treated every Monday of the week at the clinic located in the endocrinology department. Patients pay for their drugs at the hospital pharmacy while out-of-stock medicines are purchased from community pharmacies outside the hospital. Hence, with OOP payments, cost of drugs may constitute a major issue affecting medication adherence among the patients.

Study design

A cross-sectional study design was used to evaluate patients' adherence to anti-diabetic medication in the facility. The 8-item Morisky Medication Adherence Questionnaire [27] was used to determine the patients' self-reported adherence to anti-diabetic medication [13, 19]. A structured questionnaire was used to collect socio-demographic information and factors of adherence from patients treated for T2DM, to determine factors of adherence/non-adherence to medication. Patients' records were systematically reviewed to obtain data to analyze the

pattern of drug prescription and use. The study was conducted over a three-month period, between July and September 2017.

Study population and sampling

The study population consists of previously diagnosed patients with T2DM receiving anti-diabetic medication during the study period at the medical out-patients (MOP) unit of the hospital. Patients were included if they were previously diagnosed with T2DM, above 18years of age, on anti-diabetic medication for greater than six months, and signed consent form. They were excluded if they have type 1 or gestational diabetes, very ill patients or non-Nigerian citizen.

The study adopted the sample size formula for estimating a minimum sample size for a descriptive prevalence study as described previously [28]. It has a standard score of 95% confidence level and margin of error 5%. The minimum population size of diabetic patients from the MOP was estimated to be about 400, seen between July and September 2017 and thus used in calculating the sample size based on the formula thus;

$n = N / (1+N(e)^2)$ [28]

where: n=sample size

N=population size = 400

e=margin of error

=0.05 based on research condition

This resulted to a minimum sample size of 200 patients. However, the sample size was increased by 10% to 220, to accommodate for dropouts or withdrawals.

Data collection

Baseline data and prescription information were collected from patients' hospital records. Up to 300 prescription data was extracted to assess the pattern and associated costs of prescription. Semi-structured questionnaires were administered on the subjects to obtain demographic information such as age, sex, duration of T2DM, level of adherence of patients on anti-diabetic medication, causes of non-adherence, and more. The interviews took place on Mondays, the diabetic clinic days at the MOP unit. Only patients who signed the informed consent form participated in the study. Patient records were reviewed to obtain information on drug use pattern and associated costs of prescribed medications. Other information from the records included clinical characteristics, past medical history and reported diabetic complications.

The study used a structured questionnaire divided into sections A and B to obtain demographic and medication adherence information respectively. Section A consisted of demographic data of the patients such as age, sex, educational level, marital status and clinical and medical characteristics of the patients, such as type of diabetes, duration of diabetes, treatment modality, number of oral hypoglycemic agents (OHA) in use, and diabetic complications. Section B comprised self-reported 8-item Morisky type questions on medication adherence, as was used in previous studies [13, 29]. Of the eight questions, seven were answered with a yes/no response, which corresponded to 1 and 0 values [13]. To measure adherence to medication, the responses were categorized using the following scores: 0 corresponds to high adherence; 1 or 2 = medium adherence while greater than 2 = low adherence [13, 28, 29]

Data analysis

Data were recorded in a predesigned excel work sheet and analyzed using SPSS version 16 and GraphPad Prism 5.03 software, to determine non-adherence to prescribed regimen, patient and non-patient

related factors associated with non-adherence, demographic related factors, drug use pattern, average cost of prescription, the most prescribed anti-diabetic medication. In line with previous studies, medication adherence was categorized as either adherent or non-adherent based on the Morisky response score of between 0 and 2, where 0 represent adherence, 1 = medium adherence and 2 low/non-adherence. Descriptive statistics including frequency, percentage, mean and standard deviation were used to summarize the data. Association between variables (relationship between adherence/non-adherence and participants' characteristics) was assessed using both univariate and multivariate logistic regression and chi square statistics. Findings were significant at the level p≤0.05

Ethical consideration

The study sought and received ethical approval from the NAUTH Ethical Review Committee with the number, NAUTH/CS/66/VOL10/124/2017/048. All participants signed the informed consent form before interview, with their right of refusal or withdrawal assured.

Results

Socio-demographic characteristics

A total of 208 patients with T2DM were included in the study and interviewed. There were more females (57.7%) than males, (42.3%). The mean age of study participants was 59.8(±18.5) years, with majority falling between 51-65 years. Most of the participants had formal education while 81.7% was currently married. Table 1 summarizes the socio-demographic data of the respondents.

The summary of clinical and medication characteristics of study participants is presented in Table 2 which shows that all the patients interviewed were of T2DM. As regards the duration of diagnosed diabetes, nearly half of the patients (44.9%) had been diagnosed between 5-10years. Over 90% were either on oral hypoglycemic agents (OHA) or a combination of OHA and insulin. Majority (67.3%) of the patients had diabetic complications with eye complications (55.8%) as the most reported case. Nearly two thirds (58.7%) were HIV negative while for 40.4%, the HIV-status was unknown.

Adherence to anti-diabetic medications

The prevalence of high adherence to anti-diabetic medication according to the Morisky scale was 52.9%. Medium and low adherences were 19.2% and 27.9% respectively, accounting for 47.1% of non-adherent group Figure 1.

Factors of adherence to anti-diabetic medications

Association between socio-demographic, clinical and medication characteristics of study participants and medication adherence are presented in Table 3. Overall, the analysis of correlation of medication adherence to age, sex, marital status, duration of diabetes, educational level, modality of treatment, HIV-status revealed no statistical association as p>0.05.

Figure 2 shows greatest adherence was achieved among patients greater than 65 years, where non-adherence was similarly the lowest (π^2 =13.18; p<0.05). Consequently, ratio of adherence to non-adherence within this age group was the highest. Conversely, greatest non-adherence was observed between the ages 51 – 65 years.

Table 1: Socio-demographic characteristics of study participants (N= 208)

Variable	Characteristics	n(%)
Sex	Female	120 (57.7)
	Male	88 (42.3)
Age	18 – 36	26 (12.5)
	37 – 50	54(25.9)
	51 – 65	74 (35.6)
	>66	54(26.0)
Age	Mean (Standard Deviation)	59.8(±18.5)
Education	No formal education	30 (14.4)
	Less than primary school	18 (8.7)
	Primary school completed	44 (21.2)
	Secondary school completed	48 (23.1)
	College/University completed	52 (25)
	Post-graduate education	16 (7.7)
Marital status	Never married	8 (3.9)
	Currently married	170 (81.7)
	Divorced	4 (1.9)
	Widowed	26 (12.5)

Factors of non-adherence

The distribution of factors influencing patients' non-adherence to anti-diabetic medication among the participants are presented in Table 4. Findings show that multiple medication (28%), forgetfulness and cost of medication (24%) as the three most influencing factors of non-adherence.

Prescription pattern of anti-diabetes medication

The study analyzed 300 prescriptions with a total of 2807 drugs. Of these, anti-diabetic drugs alone accounted for 964 (34.3%). Drugs for cardiovascular diseases (CVD) were the most co-prescribed/non-anti-diabetic medications, with a total of 733(26.1%) drugs.

Biguanides (Metformin) was the most prescribed anti-diabetic drug class either alone 356 (36.9%) or in combination with other agents, followed by sulfonylurea (glibenclamide) at (25.8%). Metformin-glibenclamide was the most prescribed combination (Table 5). In general, up to 39% of the drugs were prescribed using generic names while the rest 61% were prescribed non-generics. However, for anti-diabetics alone, only 38% were prescribed as generics while majority (62%) were non-generics (Table 6). Each prescription had an average of 5.02(±1.09) drugs. The drug use indicators that summarize the prescription data are presented in Table 7.

Table 2: Clinical and medication characteristics of study participants (N= 208)

Variable	Clinical/Medication Characteristics	n(%)
Diabetes type	Type 1	0 (0)
	Type 2	208 (100)
Duration of diabetes	<5	48 (22)
	5 -10	96 (45)
	>10	64 (30)
Treatment modality	Oral hypoglycemic agents (OHA)	142 (68)
	Insulin	8 (4)
	Both OHA and insulin	58 (28)
	Diet Only	0 (0)
Number of OHA currently in use	1-3	138 (66)
	4-6	60 (29)
	6-10	8 (4)
	Missing	2 (1)
Presence of Diabetic complications	Yes	140 (67)
	No	68 (33)
Type of Diabetic complications		
	Eye complications	116 (55.8)
	Skin complications with or without itching	32 (15.4)
	Postural hypotension	16 (7.7)
	Palpitations	40 (19.2)
	Gastro-paresis	14 (6.3)
	Erectile dysfunction	4 (1.2)
	Neuropathy	14(6.3)
	Heart failure	60 (28.4)
	Diabetic foot/hand with or without ulcer	68 (32.6)
	Kidney complications(nephropathy)	0(0)
	Stroke	10(4.8)
HIV Status		
	Positive	2(0.9)
	Negative	122(58.7)
	Unknown	84(40.4)

HIV = Human Immunodeficiency Virus

Cost of medication

Analysis of prescription costs shows that the mean cost of medication was N4,654.58 ±2,195 ($13.30) per patient, including co-medication. This translated to a mean daily cost of N186.18 ($0.53) per patient per day, ranging from N44.8 ($0.13) to N634.04 ($1.81) per patient per day. A patient spends a monthly average cost of N5,213.04 ($14.89) to treat diabetes including at least one co-morbidity.

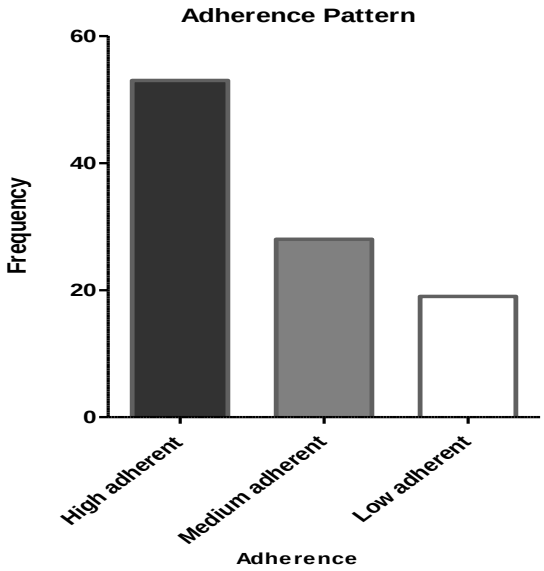

Figure 1: Prevalence of adherence to anti-diabetic medication using the Morisky scale

Table 3: The relationship between socio-demographic, clinical and other characteristics on adherence to anti-diabetic medication

Variable	Characteristics	Adherent (n)	Non-adherent (n)	p-value
Age group	18 – 36	12	14	
	37 – 50	24	30	0.32
	51 – 65	34	40	
	>66	40	14	
Sex	Female	64	56	0.53
	Male	46	42	
Education	No/Primary	62	34	0.20
	Secondary & Higher	48	64	
Marital status	Not married	2	6	
	Married	92	78	
	Divorced	0	4	0.81
	Widowed	16	10	
HIV Status	Negative	60	60	
	Positive	0	4	0.417
	Unknown	50	36	
Duration of Diabetes	<5	38	18	
	5 -10	40	52	0.125
	>10	32	28	
Modality of treatment	OHA	40	62	
	Insulin	0	6	0.149
	Insulin +OHA	15	30	
	Diet only	0	0	

OHA = Oral hypoglycemic agent

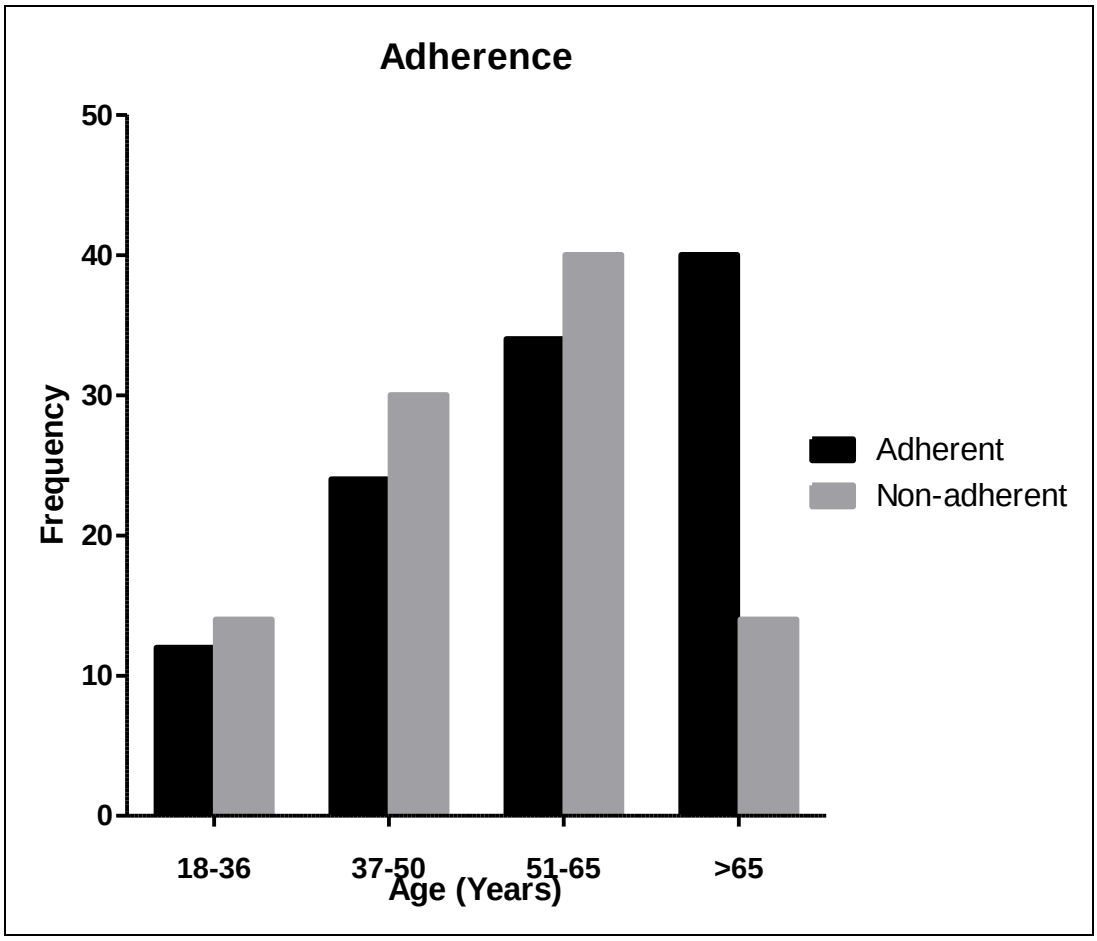

Figure 2: Pattern of adherence vs. non-adherence across age categories (π^2 =13.18; p<0.05)

The highest cost was spent by a diabetic patient placed on combined anti-diabetic medication (4 combinations) with cardiovascular co-morbidity and also treated for hyperlipidemia, while the lowest expenditure was made by a patient placed on metformin mono-therapy treated for malaria co-morbidity.

For anti-diabetic medications alone, the biguanides (Metformin) as monotherapy, which was the most prescribed anti-diabetics, accounted for a total cost of N178,048 ($508.71) representing the third highest proportion (16%) of the total cost of the medication. The 4-combination therapy of Thiazolidinediones + sulphonylureas + biguanides + dipeptidyl peptidase-4-inhibitors accounted for the highest proportion of the total cost at 35.7% as the most expensive prescription even though it was the least prescribed. It was followed the biguanides + sulphonylureas combination which accounted for 18.9% of the total cost. (Table 8). ($USD1 = N350.00)

Discussion

This study assessed the adherence to anti-diabetes treatment among patients attending outpatient clinics in tertiary healthcare facility in Nigeria. It shows that 53% of the patients reported good adherence which occurred mostly among older patients. Medium and low adherence to anti-diabetic medication were 19% and 28% respectively accounting for 47.1% of the non-adherent group.

Table 4: Factors affecting adherence to anti-diabetic medications

Factors	n(%)
Forgetfulness	54(24.0)
Cost of medication	50(24.0)
Side effect of the drug	24(11.5)
Lack of trust in the efficacy of the drug	18(8.7)
Multiple medication	58(28.0)
Complexity of drug regimen	22(10.6)
Interference with meal plan	36(17.3)
Poor family support	10(4.8)
Presumed intake of high dose	14(6.7)
Long duration of drug intake	48(23.1)

Table 5: Classes of prescribe anti-diabetics

Classes of Anti-Diabetics	n(%)
Biguanides (Metformin) only	356(36.9)
Sulphonylureas only	249(25.8)
Insulin only	41(4.3)
Insulin + Metformin	11(1.1)
Insulin + Sulphonylureas	4(0.4)
Biguanides+Sulphonylureas	164(17.0)
Biguanides+ Thiazolidinediones	44(4.6)
Sulphonylureas+Thiazolidinediones	15(1.6)
Insulin+Sulphonylureas+Biguanides	5(0.5)
Thiazolidinediones+Sulphonylureas+Biguanides	2(0.2)
Thiazolidinediones+Sulphonylureas+Biguanides+Dipeptidyl Peptidase-4-Inhibitors	73(7.6)
Total	**964(100)**

Overall, adherence to anti-diabetic medication was found to be suboptimal with only 53% of the patients demonstrating good adherence. This finding is however higher than that of a study conducted in a tertiary health care facility in Ogbomosho city, south west Nigeria, which reported only 40.6% of high medication adherence among the patients [19].

Table 6: Generic vs non-generic prescribing

Class of drug	Generic n(%)	Non-generic n(%)	Total
Anti-Diabetics	365(38)	599(62)	964
Drugs For CVD	418(57)	315(43)	733
Anti-malaria	10(25.91)	29(74.09)	39
Drugs For Ulcer	69(39)	109(60.9)	178
Anti-Neuropathy	39(77)	12(23)	51
Antibiotics	81(74.8)	28(25.2)	109
Vitamins/Haematinics	90(80.6)	22(19.4)	112
Low Dose ASA	25(11.0)	198(89)	223
Others	103(26.1)	295(74.1)	398
Total	**918(39.2)**	**1209(60.9)**	**2807**

Table 7: Drug use indicators for T2DM (n=964)

Indicator Variable	No (frequency)	Percentage (%)
Average number of drugs per prescription (std. dev) (n=2806)	5.02 (±1.09)	-
Average cost per prescription (std. dev) (including co-medication, n=2806)	N4,654.58 ± 2,195.42 ($13.34)	-
Monotherapy anti-diabetics (n=964	646	67.0
Combination therapy (n=964)	318	33
Fixed dose combination anti-diabetics (n=964)	27	2.8
Generic anti-diabetic prescription (n=964)	365	37.9
Oral administration (n=964)	923	95.8
Parenteral/Subcutaneous route (n=964)	41	4.3

However, the adherence rate in this study is low compared to some previous studies carried out in Nigeria [21] which reported adherence rate of 72.5%, as well as in Uganda [30] with 71% adherence. Similarly, a study in Tanzania by Rwegerera *et. al* (2017) reported an adherence rate of 72%. These differences may be partly explained by the differences in the methods used to estimate adherence. While this study used the widely acclaimed and validated Morisky scale for estimating adherence as applied in many studies [13, 19, 31], these other studies used the patients' recall on adherence or pill counts to assess the level of adherence [13]. Consequently, findings of this study were

more consistent with those of similar studies that applied the Morisky scale.

Table 8: Cost distribution of anti-diabetic medications

Classes of Anti-Diabetics	Cost (Naira)	Cost (%)
Biguanides only	178,048	16.4
Sulphonylureas only	115,470	10.6
Thiazolidinediones only	45,600	4.2
Insulin Only	68,890	6.3
Insulin + Metformin	23,508	2.2
Insulin + Sulphonylureas	10,121	0.9
Biguanides+Sulphonylureas	206,127	18.9
Sulphonylureas+Thiazolidinediones	31,996	2.9
Insulin+Sulphonylureas+Biguanides	2,068	0.2
Thiazolidinediones+Sulphonylureas+Biguanides	5,115	0.5
Thiazolidinediones+Sulphonylureas+Biguanides+Dipeptidyl Peptidase-4-Inhibitors	388,529	35.7
Total	**1,088,318**	**100**

The findings on demographic characteristics of the study population such as age, gender, were similar with related diabetic studies in Nigeria and other settings [19, 21, 32, 33], reflecting the general trends among diabetic patients. The findings suggest that T2DM appear to be more prevalent among women than men, with mean age hovering around 60 years of age.

This study indicates that the highest adherence occurred among older adults, which is consistent with findings of previous studies that reported similar findings [23, 34]. The study in Tanzania by Rwegerera 2014, reported more adherences among patients older than 61 years, suggesting that older adult diabetics are more likely to adhere to medications compared to younger categories[35]. This has been partly explained by the presence of more co-morbid conditions among the older adults, which makes them obtain more information on the benefits of adherence and the subsequent need to comply. Hence, co-morbidity among diabetes has been reported to be significantly associated with good adherence to anti-diabetic medications [23]. Similar to other previous studies in Tanzania and the United Kingdom [23, 36], this study found no association between gender and medication adherence among the participants.

The study identified multiple medication, forgetfulness and cost of medication as the three most common causes of non-adherence among the patients. This is not surprising given that as a chronic disease

requiring lifetime management, taking many drugs at the same time will likely lead to forgetfulness. Similarly, the use of many drugs will certainly lead to increased cost of medication, becoming unaffordable to many patients. Previous studies have documented similar findings in Nigeria and other settings [21, 23, 30, 33]. The administration of multiple tablets in T2DM management is necessitated by progressive failure of beta cells in type 2 diabetes, requiring the successive addition of different medications to achieve optimum glycemic control [37-39]. In addition, majority patients with DM are further subjected to co-morbidities which require medication, consequently increasing the pill burden. The resulting multiple medications becomes a burden to the patient identified to be one of the factors responsible for poor adherence to oral anti-diabetic medication. The use of fixed drug combinations (FDC) can be a useful means of addressing this concern to improve adherence. Study has reported successful application of the FDC method in patients treated for HIV/AIDS, tuberculosis, hypertension resulting in about 26% reduction in the risk of non-compliance compared with individual drug component regimen [40]. In this study, FDC accounted for only 2.8% of the anti-diabetic medications.

The adherence to anti-diabetic medication showed no association with socio-demographic and clinical characteristics as the different p-values are not statistically significant. Similarly, the study conducted in Botswana did not show any association between adherence and socio-demographic and clinical characteristics of the patients [13]. However, some previous studies showed contrasting results on the association of adherence with some socio-demographics and clinical characteristics of the patients such as age, gender and education[30, 41]. The study conducted in a referral hospital, Ethiopia showed a significant association between social-demographic characteristics such as age and marital status with medication adherence [2]. The reason for this variation again reflects the differences in methodological approaches and settings of the research, as well as the variation in factors affecting adherence, indicating the need for further investigation.

This study also analyzed prescription pattern among T2DM patients, to partly explore the possible influence on medication adherence or non-adherence. Analysis of prescription records of the patients shows an average number of 5 drugs per prescription, higher than the WHO standard recommendation of 2-3 drugs for developing countries. Even though higher number of drugs may be justified among diabetes due to co-morbidity, increase in number of prescribed medications has been known to lower medication adherence [19, 42]. Hence, the poly-pharmacy in this study could partly explain the non-adherence among the patients especially in younger adults with little or no co-morbidity. High number of drugs increases medication complexity in terms of dosing and frequencies, risks of side effects, increasing costs and burden of medication, all contributing to poor compliance to medication. Consequently, multiple medications and forgetfulness were the leading causes of non-adherence reported by the participants in this study.

The multiple medication should further explain the high average cost of drugs per prescription in this study which came to N4,564.58 (US $13.34) per patient, for a low-income population that pay OOP, lacking in financial risk protection. Patients paid up to

N634 ($1.81) per day for medication alone, as the highest medication cost. This expectedly becomes unaffordable and catastrophic for patients living below the poverty line of $1 per day. For such people with co-morbidity and multiple medications (taking up to nine drugs) it was not surprising that affordability was a major issue and hence non-adherent for a significant number of the study participants. Further to high cost of medication is the high rate of non-generic prescription where less than 50% of prescribed medication was generic, contrary to the policy that makes generic prescription standard practice for public healthcare facilities. This underscores the need to enforce generic prescription to reduce the cost of medication thereby improving medication adherence. While it is understood that newer anti-diabetics do not presently have generic alternatives, the most commonly prescribed OHA (metformin and glibenclamide) have many low costs generic alternatives which should lower the daily cost of medication for the patients. The importance of generic medication in reducing costs of care and improving health outcome cannot be overemphasized. The use of generics and enhanced lifestyle modification become very essential in reducing the cost of care for the diabetes patients. In this study generic metformin was the cheapest medication alternative for diabetes management at a cost of N44.80 ($0.13) per patient per day.

Study limitations

The study reports some limitations that will require caution in the use of the findings.

First, the low sample size and single center study may affect the generalizability of the findings to the general population. Larger sample size may have been more appropriate to produce a better association between medication adherence and other variables, especially in those areas that had no significant association. However, the tertiary institution attends to a wide variety of the population as a leading healthcare facility in the region, hence the similarity of the findings with previous studies in Nigeria. Secondly, the study did not determine association between the medication adherence and glycemic control as was the case in some previous studies. This was due to some logistic issues and lack of finances in measuring glycosylated heamoglobin (HbA1c) which is not a routine in most hospitals. Thirdly, the study included only pharmacotherapy aspects and did not address physical exercise, dietary modification and self-monitoring of blood glucose as other key components of diabetes care that affect glycemic control for improved patient's outcome. Finally, the study further recognizes the non-inclusion of psychosocial factors as was done in some previous studies, given the contribution of such factors as language, education, social support etc. to poor adherence [13]. We only focused on the medication adherence and not on these other factors.

Conclusion

The study indicates significant non-adherence to anti-diabetic medication among the study participants, a major concern on effective control of diabetes in the country. Key determinants of non-adherence include modifiable factors which are both patient and non-patient related. While prescription practices suggest substantial compliance to treatment guidelines in diabetes management, there is scope for enhanced rational drug use, especially in non-patient related factors such as medication complexity and costs, to improve adherence and patients' outcomes.

Policy interventions such as patient education and enhanced access to affordable medicines are necessary to increase medication adherence so that patients can realize the full benefits of prescribed medications. Policy on the use of generic medication especially in public health institutions needs to be enforced and encouraged to reduce the cost of medication for improved adherence.

Abbreviations

CVDs: Cardiovascular diseases
DM: Diabetes Mellitus
HIV: Human Immunodeficiency Virus
LMICS: Low- and Middle-Income Countries
MOP: Medical Outpatient
NAUTH: Nnamdi Azikiwe University Nnewi
OHA: Oral hypoglycemic agent
OOP: Out-of-pocket
T2DM: Type 2 Diabetes Mellitus
WHO:World Health Organization

Declarations

Consent for publication

Participants were informed that information may be published but confidentiality will be maintained.

Availability of data and material

Generated dataset for the study is available on reasonable request from the corresponding author

Competing interests

Authors declare no competing interests

Funding

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Authors' contribution

CCE: Participated in the study design, data collection and analysis and drafted the manuscript.

ICO: Participated in drafting the study, data collection and analysis.

CCN: Participated in drafting, data collection and analysis.

All authors read and approved final manuscript

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