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Pattern of drug utilization, medication adherence, and treatment satisfaction among diabetic patients in a secondary hospital in southern Nigeria

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ABSTRACT

Background: Drug use evaluations provide insights into the efficiency of drug use and may promote rational use of drugs, medication adherence and patient satisfaction with treatment.
This study seeks to determine the current pattern of utilization of antidiabetic drugs, patient's adherence, and satisfaction with treatment among diabetic patients in a secondary hospital in southern Nigeria.
Methods: A cross sectional prospective antidiabetic drug utilization study was conducted among patients with diabetes mellitus receiving care at General Hospital, Ikot Ekpene between November 2019 and February 2020. Data on antidiabetic drug use pattern was obtained via an assessment of patients' prescriptions. Patients' medication adherence and satisfaction with treatment offered was assessed using the 4-Item Morisky Medication-Taking Adherence Scale and the Treatment Satisfaction Questionnaire for Medication (Version 1.4). Descriptive statistics was used to summarize data, inferential statistics was used where applicable with statistical significance set at $p<0.05$.
Results: The Sulphonylureas were the most frequently prescribed class of antidiabetic drugs (69.2%). A combination of antidiabetic agents was prescribed in 80.8% of the patients. Clinically significant and potentially dangerous drug-drug interactions was identified in 91.7% of the prescriptions. The mean global satisfaction with treatment scores of the patients was 61.4(±8.3). The mean medication adherence scores of the patients was 2.1(±1.2). There was a statistically significant relationship between patients' global satisfaction with treatment score and the medication adherence score ($r = 0.350$; $p = 0.0001$).
Conclusion: Sulphonylureas were the most frequently used class of antidiabetic agents in this population. Patients were generally satisfied the treatment offered. However, the level of adherence to prescribed antidiabetic drugs was poor. There is a compelling need for greater involvement of pharmacists in the provision of clinical services for patients with diabetes mellitus.

1. Introduction

Diabetes mellitus is a multifactorial, complex, genetically derived endocrine disorder. It is a syndrome of impaired carbohydrates, fats and protein metabolism caused either by lack of insulin secretion or decreased sensitivity of tissues to insulin [1]. It is considered a major health problem in Nigeria and globally [1]. It is a major risk factor for macrovascular and microvascular complications such as retinopathy, nephropathy, neuropathy, atherosclerosis, ischemic heart disease, stroke, and peripheral vascular diseases. The condition affects quality of life of patients as well as their life expectancy [2]. Diabetes-related complications and disease progression can be prevented by early detection of the disease, lifestyle modification, and optimal glycemic control using suitable therapeutic regimens [2].

Drug use evaluation (DUE) helps the healthcare system to understand, interpret and improve the prescribing, administration and use of medication [3]. Such studies provide insights into the efficiency of drug use. It promotes the rational use of drugs in populations. Rational use of drugs among patients involves the prescription of a well-documented drug in an optimal dose on the right indication, with the correct information and at an affordable price [3]. Without knowledge on how drugs are being used, it is difficult to initiate a discussion on rational drug use and to suggest measures to improve prescribing habits for the

better [3, 4]. DUE is a method of obtaining information to identify problems of drug use [4]. If properly developed, it would provide a means of identifying drug use problems and also provide a means to correct the problem and thus contributes to rational drug therapy [4]. Assessing medication adherence is of immense importance to both researchers and clinicians. A wrong estimation of medication adherence can result in several problems affecting patients and the healthcare system. This is because poor adherence can cause an effective intervention to be seen as being ineffective, leading to the ordering of expensive diagnostic procedures, and an unnecessary intensification of therapy [5]. Poor adherence to prescribed medication is reported to be a serious challenge affecting the successful management of type 2 diabetes. It often results in uncontrolled diabetes, serious complications, and wastage of health care resources [6.7]. A study by Abebaw *et al.* reported about 85.1% adherence among patients with type II diabetes in Ethiopia [8]. Earlier studies in New York, Malaysia, Iran, Uganda, and Nigeria reported 72%, 66%, 74.8%, 71%, and 72.5 % adherence respectively [9-13].

Patients' satisfaction with treatment is often believed to be a determinant of medication adherence. In a bid to promote patient-focused outcome measurements, the United States food and drug administration (FDA) had highlighted the importance of undertaking assessments of clinical outcomes in patients receiving therapeutic interventions. The treatment satisfaction questionnaire for medication (TSQM) was designed as a general measure of treatment satisfaction with medication [14].

Reports suggests a variability in diabetes treatment satisfaction, medication adherence, and glycemic control from in different parts of the world [15]. In Nigeria, satisfaction to treatment among diabetes patients is a significant challenge and may affect medication adherence and eventually blood glucose control [15]. This study was aimed at determining the current pattern of utilization of antidiabetic drugs, patient's adherence and satisfaction with the antidiabetic treatment offered in a secondary hospital in southern Nigeria. The study also sought to determine the relationship between patient satisfaction with treatment and adherence to drug therapy.

2. Methods

2.1 Study Setting and design

This study was carried out at General Hospital Ikot Ekpene (GH-IK) in Akawa Ibom state, Southern Nigeria. GH-IK is a major secondary healthcare facility in Akwa Ibom state, southern Nigeria. The facility provides health care to the people of Ikot Ekpene local government area and its environs. The mission of the hospital is to ensure the provision of safe, quality, affordable, adequate, equitable and accessible health services to all. This cross sectional prospective study was conducted among 120 patients with diabetes mellitus receiving treatment at GH-IK.

Patients attending clinic appointments at the medical outpatient clinic of GH-IK as well as those admitted into the medical wards of the hospital were recruited into the study. All patients with diabetes mellitus who met the following eligibility criteria were recruited into the study.The eligibility criteria for recruitment into the study were patients diagnosed with diabetes mellitus and receiving treatment at the hospital within the period of the study; patients who provided a written informed consent to participate in the study. Sample size was determined by using the formula described by Yamane $\{n = N/1+N(e^2)\}$ [16]. Where n = calculated sample size; N = Population of HIV/AIDS patients that attended clinic within the period of the study; e = level of precision ($\pm$ 5%).

A total of who 120 patients who fulfilled the eligibility criteria participated in the study. The study protocol was approved by the Health Research Ethics Committee of the Akwa Ibom State Ministry of Health (MH/PRS/99/VOL.V/713). Furthermore, institutional approval was obtained from the Management of General Hospital Ikot Ekpene. A written informed consent was also obtained from the participants and strict confidentiality was ensured during the data collection and handling.

2.2 Data Collection Instruments

Data on the demographic and clinical characteristics of the patients was obtained using a suitably designed, pre-piloted data collection instrument. The first draft of the instrument was pre-tested with the case notes of ten patients at the study site to assess completeness and relevance of data capture. The final draft of the instrument was modified based on the results of pre-testing, but the data collected during pre-testing was not included in the final result. The data collected from patients' case notes included: patient's gender, patient's age, educational level, duration of illness, presence of co-morbidity, type of co-morbidity (if present), prescribed antidiabetic agent(s) and prescribed non-antidiabetic agent(s).

Data was obtained via patient interview and from their case notes using the pre-piloted clinical data collection instrument. Secondary data extracted from the patients' case notes were clinically significant/potentially dangerous drug-drug interactions, and contraindications to antidiabetic drugs administered. Furthermore, data on the extent of patients' satisfaction with the treatment offered, as well as medication adherence was obtained using the

Treatment Satisfaction Questionnaire for Medication (Version 1.4) [14], and the 4-Item Morisky Medication Taking Adherence Scale (MMAS-4) [17] respectively.

2.2.1 The Treatment Satisfaction Questionnaire for Medication

The Treatment Satisfaction Questionnaire for Medication (TSQM) version 1.4 comprises 14 questions covering 4 domains for treatment satisfaction: TSQM effectiveness (questions 1-3), side effects (questions 4-8), convenience (questions 9-11), and global satisfaction (questions 12-14). Each score on each domain ranges from 0 (extremely dissatisfied) to 100 (extremely satisfied) [6].

2.2.2 The 4-Item Morisky Medication-Taking Adherence Scale (MMAS)

The Morisky medication adherence scale is a validated assessment tool used to measure non-adherence in a variety of patient population. The tool uses a number of brief behavioral questions targeted at avoiding "yes-response" bias often noted with chronic care patients. The questions were presented in a manner that prevents answers that tend to follow certain behavioral patterns, thus allowing the patients to respond to questions regarding medication non-adherence in a spirit of full disclosure for the clinician. The MMAS has been found to be a useful resource to address the challenges of medication adherence, including patients forgetting to take their medications or discontinuing medications without proper clinical guidance. Patients scoring higher on the scale, are considered to be more adherent while those with lower scores on the scale are presumed to be struggling with non-adherence [17].

In addition to the scoring template of the 4-Item MMAS, a medication adherence level was deduced, where adherence scores of < 3 was considered a low level of adherence; and adherence scores of 3 and 4 were considered medium and high medication adherence levels respectively.

2.3 Data Analysis

The appropriateness of the antidiabetic drug doses, dosing and clinically significant drug interactions, and contraindications were assessed using the Medscape App V 6.5.1 [18].

Quantitative data was analyzed using Statistical Program and Service Solutions (SPSS) version 25.0 computer package. Descriptive statistics was used to summarize data, inferential statistics was used where applicable with statistical significance set at $p<0.05$.

3.0 Results

3.1 Sociodemographic and Clinical Characteristics of the patients.

The demographic and clinical characteristics of the patients is presented in Table 1. Almost half of the study participants (48.33%) were aged 60 years and above. About 65% of the patients were also being managed for conditions other than diabetes mellitus with hypertension being the most frequently observed co-morbidity.

Table 1: Demographic/Clinical Characteristics of the Patients

Characteristics	Frequency	Percent (%)
Gender		
Male	62	51.7
Female	58	48.3
Age (years)		
15 – 30	3	2.5
31 – 50	16	13.3
51 – 60	43	35.8
>60	58	48.3
Educational Level		
Primary	9	7.5
Secondary	68	56.7
Tertiary	43	35.8
Duration of Illness		
1month – 5years	75	62.5
6 – 10years	33	27.5
11 – 15years	9	7.5
= 16years	3	2.5
Presence of Co-morbidity		
None	42	35.0
Yes	78	65.0
Type of Co-morbidity		
Hypertension (HTN)	56	71.8
HTN & BPH	4	5.1
HTN & CKD	4	5.1
Asthma	4	5.1
HTN & Asthma	2	2.6
HIV	2	2.6
Arthritis	2	2.56
PUD	2	2.56
HTN & HIV	1	1.28
HTN & Arthritis	1	1.28

*BPH = Benign Prostatic Hyperplasia; HTN = Hyperetension; PUD = Peptic Ulcer Disease; CKD = Chronic Kidney Dsease; HIV = Human Immuno Deficiency Virus

Pattern of Utilization of Antidiabetic Medication

The sulphonyl ureas , Glibenclamide were the most frequently prescribed antidiabetic medicines. Monotherapy was prescribed in only about 19% of the patients. The antidiabetic drug doses and dosing interval, as documented were adequate with no contraindications in all the cases studied. The pattern of utilization of antidiabetic drugs in the study site is as presented Table 2

Table 2: Pattern of Utilization of Antidiabetic Drugs

Antidiabetic Drugs/Combinations	Frequency	Proportion	
Biguanides (*n=63*)			**52.5**
Metformin	63	100	52.5
Thiazolidinedione (*n=40*)			**33.3**
Pioglitazone	40	100	33.3
Sulphonyl Ureas (*n=83*)			**69.2**
Glibenclamide	81	97.6	67.5
Glimepiride	2	2.4	1.7
Insulins (*n=72*)			**60.0**
Monotherapy (*n=23*)			**19.17**
Polytherapy (*n=97*)			**80.83**
Metformin/Insulin	7	7.22	5.83
Metformin/Pioglitazone	2	2.06	1.67
Metformin/Glibenclamide	13	13.4	10.83
Insulin/Glibenclamide	22	22.68	18.33
Pioglitazone/Glimepiride	1	1.03	0.83
Metformin/Pioglitazone/Insulin	3	3.09	2.5
Metformin/Glibenclamide/Pioglitazone	16	16.49	13.33
Insulin/Pioglitazone/Glibenclamide	9	9.28	7.5
Metformin/Glibenclamide/Insulin	18	18.56	15
Metformin/Glimepiride/Pioglitazone	1	1.03	0.83
Metformin/Glibenclamide/Pioglitazone/Insulin	1	1.03	0.83
Clinically Significant Drug-Drug Interactions			
Present (*n=110*)			91.7
Absent (*n=10*)			8.33

*Monotherapy = Patients placed on a single antidiabetic drug; Polytherapy = Patients placed on a combination of two or more antidiabetic drugs

Clinically Significant and Potentially Dangerous Drug-Drug Interactions

One hundred and twenty-seven clinically significant, potentially dangerous drug-drug interactions were identified. Table 3 and Appendix I respectively shows the frequency of occurrence of each identified drug-drug interaction and the details of the frequently encountered drug interaction including the therapeutic recommendations.

Table 3: Frequency of Clinically Significant/Potentially Dangerous Drug-Drug Interactions

Drug interaction	Frequency	Proportion (n =127)
Lisinopril + metformin	20	15.8
Amlodipine + metformin	19	15.0
ACT + pioglitazone	11	8.7
Metronidazole + pioglitazone	8	6.3
Ciprofloxacin + metformin	8	6.3
Aspirin + insulin	7	5.5
Hydrochlorothiazide + metformin	5	3.9
Levofloxacin + metformin	5	3.9
Levofloxacin + pioglitazone	4	3.2
Lisinopril + insulin	4	3.2
Levofloxacin + insulin	3	2.4
Ciprofloxacin + pioglitazone	3	2.4
Prednisolone + pioglitazone	3	2.4
Metformin + cyanocobalamin	3	2.4
Frusemide + metformin	3	2.4
Hydrocortisone + pioglitazone	2	1.6
Hydrochlorothiazide + pioglitazone	2	1.6
Hydrochlorothiazide + insulin	2	1.6
Prednisolone + metformin	2	1.6
Ciprofloxacin + insulin	2	1.6
Ciprofloxacin + glimepiride	2	1.6
Aspirin + glimepiride	2	1.6
Digoxin + metformin	1	0.8
Lisinopril + glimepiride	1	0.8
Nifedipine + metformin	1	0.8
Losartan + insulin	1	0.8
Hydrocortisone + metformin	1	0.8
Cotrimoxazole + metformin	1	0.8
Dexamethasone + metformin	1	0.8

*(ACT = Artemether/Lumefantrine combination)

3.4 Patients' Satisfaction with Treatment

The mean scores of patient satisfaction with medication (using the treatment satisfaction questionnaire for medication), based on 4 domains namely; Medication effectiveness, Side effects, Convenience, and Global satisfaction, is as presented in **Table 4**.

Table 4: Mean Scores of Patient Satisfaction with Treatment

Domains	Mean Scores	Standard Deviation
Medication Effectiveness	69.85	12.53
Medication Side Effects	91.53	21.36
Convenience	62.48	7.94
Global Satisfaction	61.36	8.32

3.5 Patients' Adherence to Antidiabetic Medications

The medication adherence scores of the patients based on the 4-Item Morisky medication-taking adherence scale is as presented in Figure1. The mean medication adherence scores of the patients was 2.12 (±1.22).

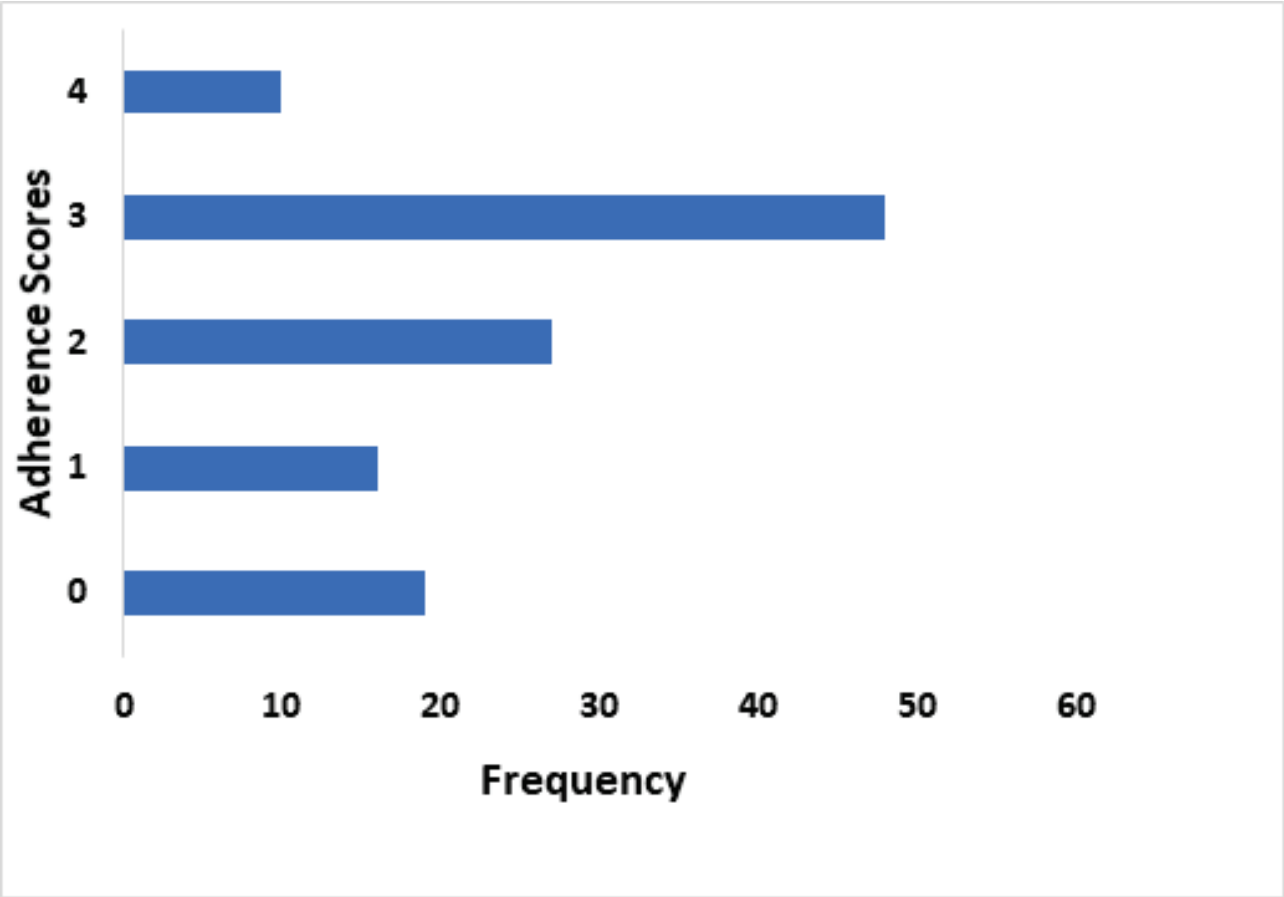

Figure 1: Chart of Patients' Medication Adherence Scores

Based on the deduced medication adherence level, where medication adherence scores of < 3 was considered a low level of adherence, adherence scores of 3 and 4 were considered medium and high levels of medication adherence respectively, we found that 51.7% (62) of the patients had a low level of medication adherence, 40% (48) of the patients had a medium level of medication adherence, while only 8.3% (10) of the patients had a high level of adherence to prescribed antidiabetic medicines.

3.6 Relationship between Patients' Satisfaction with Drug Therapy and Medication Adherence

There were statistically significant positive relationships between the following;

i. Patients' satisfaction with the medication's effectiveness score and the medication adherence scores ($r = 0.345$; $p = 0.0001$),
ii. Patients' satisfaction with the ease of taking the medicine score and the medication adherence score ($r = 0.217$; $p = 0.018$), and
iii. Patients' global satisfaction with treatment score and the medication adherence score ($r = 0.350$; $p = 0.0001$).

This suggests that the higher the patients' satisfaction with the medication effectiveness, the ease of taking the medicine, and the overall satisfaction with treatment given, the higher their adherence to the prescribed drugs.

4.0 Discussion

Drug utilization research is an important aspect of pharmaco-epidemiology. It describes the extent, nature, and determinant of drug exposure. It provides insight into the extent, profile and trends of drug use. It can contribute to the promotion of rational evidence-based drug therapy that can in turn help to improve patient care and treatment [19].

In our study, we found that the sulphonylureas were the most frequently prescribed antidiabetic drugs in the population studied. Among the sulphonylureas, glibenclamide was the most frequently prescribed sulphonylureas, accounting for about 98% of the sulphonylureas used in the population. This is in consonance with previous reports from other study populations [20-24]. We also observed that majority, over 80%, of the antidiabetic drugs were prescribed as combination therapy, and a metformin-based combination therapy was the most frequently used antidiabetic drug combination in this population. Similar studies have identified metformin as being frequently used either in monotherapy or polytherapy [2,25-27]. Satpathy *et al.* in their study reported that metformin monotherapy and combination therapy was used in 66.8% of the population studied and was also the single most frequently prescribed anti-diabetic drug [2]. Upadhyay *et al*. reported that biguanides accounted for 51.2% of the total antidiabetic medications in the study population [25]. In Canada, Johnson *et al*. reported that 65% of the patients received metformin, alone or in combination [27]. The high utilization of metformin may be due to its endorsement as the preferred antidiabetic agent by clinical guidelines [28]. Metformin has been recommended as the first-choice oral medication for patients with diabetes mellitus. It has a better safety profile, greater general tolerability and relatively lower cost when compared with other antidiabetic medications. Generally speaking, combination therapy has significant advantages over monotherapy. Clinical studies have shown that the combination of sulphonylureas and metformin can achieve optimal glycemic control even in advance type-2 diabetes mellitus [29]. Antidiabetics with different mechanism of action demonstrate greater synergy.

Insulin was used in 60% of the cases studied. In a similar study by Satpathy *et al* in a tertiary care hospital in north east India, insulin was used in only 23% of the population [2]. Insulin is indicated when there is poor glucose control with optimal doses of oral hypoglycemic agents and deterioration of the condition with substantial weight loss. The high utilization of insulin therapy in the study population may be suggestive of the extent of disease progression in the patients studied.

The doses and dosing interval of the antidiabetic drugs used in the population were appropriate. Furthermore, there was no contraindication to the use of any of the antidiabetic drugs in the cases studied. This is highly commendable and may be an indication of the quality of clinicians in the study site. However, we found clinically significant drug-drug interactions in about 92% of the cases studied. The most frequently encountered clinically significant and potentially dangerous drug-drug interactions identified in this study was a co-administration of lisinopril and metformin, followed by the co-administration of amlodipine with metformin. Lisinopril is reported to increase the toxicity of metformin by an unspecified interaction mechanism. It increases the risk of hypoglycemia associated with metformin. The clinicians are advised to monitor blood level closely. On the other hand, amlodipine decreases the effect of metformin by pharmacodynamic antagonism. Clinicians are also advised to monitor the patient closely for loss of blood glucose control. In spite of these recommendations, we did not find any evidence of close monitoring of blood glucose levels in patients who were co-administered metformin with lisinopril as well as those who were co-administered metformin with amlodipine. This is worrisome and calls for suitable pharmaceutical care interventions by pharmacists.

In this study, the treatment satisfaction questionnaire for medication was used in assessing patient satisfaction with treatment. Our analysis revealed that the general satisfaction with treatment in the population studied was high. Our analysis of the individual components of the TSQM revealed that the patients' satisfaction with the side-effects profile of their medicines had the highest score. Adverse effects of drugs are a major cause of treatment dissatisfaction that may affect adherence resulting in therapeutic failure. Fernandes *et al.* evaluated treatment satisfaction with injectable disease modifying therapies in patients with relapsing-remitting multiple-sclerosis [30]. They found that the patients were reasonably satisfied with their treatment. Their results suggested that the main source of patient dissatisfaction with treatment is the inconvenience of administration regimen. They also reported that patients who discontinue their treatment within the first 6 months were more likely to be unsatisfied with their treatment.

In our study, most of the patients expressed confidence in the effectiveness of the prescribed drugs in treating their condition. Perceptions of efficacy are believed to be an important factor in boosting patient satisfaction with treatment [31].

We found that over 50% of the patients had low adherence to prescribed antidiabetic drug therapy. Medication adherence is an important part of patient care and is indispensable in the attainment of clinical goals. Medication non-adherence results in poor clinical outcomes, increase in morbidity and mortality, as well as increase in healthcare expenditure. Research reports indicate that about 50-60% of patients are non-adherent to the medicines prescribed by their physician, particularly, those with chronic illness [5]. Medication non-adherence has

been associated with increased rates of relapse and greater health resource utilization [32]. The poor medication adherence by majority of the cohort studied may be an indication of a poor involvement of pharmacists in the provision of care to the diabetic patients in the study site. Health education has been shown to improve the adherence of patients to their medication [33]. It has been observed that patients' knowledge and understanding of their condition has a significant role to play in providing good quality outcomes for the patients. Randomized controlled studies have demonstrated the efficacy of a comprehensive pharmacy care program to improve medication adherence among patients with chronic disease conditions [34, 35]. Pharmacists can contribute to positive therapeutic outcomes by educating patients to empower them to follow their pharmacotherapeutic regimens. The Pharmacist has the responsibility of providing patient education and counselling in the context of pharmaceutical care. Pharmacists should encourage patients to seek education and should eliminate barriers to providing it [36,37].

One factor that may affect adherence to pharmacotherapy is treatment satisfaction [30]. We found that patient satisfaction with medication effectiveness, ease of taking medicine and overall satisfaction with the treatment was positively correlated with their medication adherence. Our findings show that patients who were more satisfied with the treatment were more likely to be adherent to their antidiabetic medications. Across many clinical settings, patient satisfaction with medication, resulting from factors such as the effectiveness, convenience (e.g., route of administration, dosing frequency), or side effects of the medication, has been associated with better adherence to, and persistence with, treatment [6, 38, 39]. Many studies on chronic disease conditions have demonstrated an association between treatment satisfaction and adherence to medication [40, 41]. An association between treatment satisfaction and health related quality of life has also been reported. These reports suggest that improved treatment satisfaction results in better medication adherence and a corresponding improvement in the health-related quality of life of patients with chronic disease conditions. Treatment satisfaction has been identified as the major factor affecting medication adherence. Factors affecting the acceptance of treatment will in turn affect adherence to therapy [42, 43]. An understanding of the factors that affect patients' treatment satisfaction could enhance medication adherence and result in a better therapeutic outcome.

5. Conclusion

Glibenclamides was the most frequently used antidiabetic agent in this population and most of the antidiabetic agents were used in combination (polytherapy). The incidence of clinically significant, potentially dangerous drug-drug interaction was high. Most of the patients were satisfied with the treatment offered. However, most of the patients had low adherence to the prescribed antidiabetic drugs. There is a statistically significant positive relationship between patient satisfaction with treatment and medication adherence. There is a compelling need for greater involvement of pharmacists in the provision of clinical services for patients with diabetes mellitus.

Conflict of interest

The authors hereby declare that there is no conflict of interest.

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