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ANTIDIABETIC DRUGS UTILIZATION PATTERNS IN A NIGERIAN TERTIARY HEALTHCARE FACILITY

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ABSTRACT

Worldwide, diabetes mellitus (DM) is considered a public health care problem. Studies have shown that DM is on an alarming rise in Nigeria, and antidiabetic medications are the mainstay for its management. Rational use of antidiabetics is important in achieving desired therapeutic outcomes. Therefore, this study aimed at assessing antidiabetic drug utilization patterns at the Medical Out-Patients Department (MOPD) of Ahmadu Bello University Teaching Hospital (ABUTH). A prospective, cross-sectional study design was used for data collection on a sample of 603 patients who attended the facility between 8th June and 28th September 2015. Data were collected according to the World Health Organization (WHO) method for drug utilization studies. The results showed that an average of 1.8 antidiabetics was observed per prescription. Oral antidiabetic drugs (OADs) (with 6.045 Defined Daily Dose, DDD/1000 patients/day) were 49.55 times more utilized than insulin (with 0.122 DDD/1000 patients/day). Metformin, with 4.358 DDD/1000 patients/day was the most utilized OAD. The cost/DDD within the DU90% segment was NGN 1,786.46 (US$8.97). In conclusion, metformin was the most utilized antidiabetic and the costs of antidiabetics were high in the facility. It is therefore recommended that interventions to curtail the cost of drugs in the facility should be adopted.

Keywords: Antidiabetic Drugs; Defined Daily Dose; Diabetes Mellitus; Drug Utilization; Metformin

INTRODUCTION

Worldwide, diabetes has emerged as one of the most significant public health challenges (Desai *et al*., 2012). In Nigeria, reports have shown that there is an increased prevalence and burden of type 2 diabetes mellitus, DM., (Adisa *et al*., 2009; Chinenye & Ogbera, 2013). DM accounted for 15% of all medical admissions and 22% of all medical deaths in the country (Adibe *et al*., 2009). Diabetes mellitus, as a chronic illness, requires continuing medical care and patient self-management education and support to prevent acute complications and to reduce the risk of long-term complications (American Diabetes Association, 2018). The ultimate goal of diabetes therapy is to prevent micro and macro-vascular complications to improve life expectancy and quality of life (Benhalima & Mathieu, 2009). Besides, adequate glycaemic control is required for the improvement of diabetes clinical, economic, and humanistic outcomes (Adisa *et al*., 2011). This is mostly achieved through the use of insulin and oral hypoglycaemic agents (Egde *et al*., 2012).

World Health Organization (WHO) defined drug utilization as the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences (WHO, 2003). Drug utilization is an invaluable tool used to assess the rational use of medicine in a facility (Akhtar *et al*., 2012). Appropriate drug utilization has a huge contribution to the global reduction in morbidity and mortality of a disease with consequent medical, social, and economic benefits (Tamuno and Fadare, 2012). Rational prescribing ensures that patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period, and at the lowest cost to them and their community (Hardon *et al*., 2004; WHO, 2003). In contrast, irrational use of drugs has been recognized as a global problem. It includes inappropriate and unnecessary use of drugs, polypharmacy, inappropriate dosage, underdosing, and use of parenteral drugs despite the availability of oral drugs, misuse, and overuse of antibiotics (Gangopadhyay *et al*., 2016). This study aimed to assess the antidiabetics utilization pattern at a Nigerian tertiary healthcare facility. Noteworthy, stated that without the knowledge of how drugs are being prescribed and used, it is difficult to initiate a discussion on rational drug use or to suggest measures to improve prescribing habits (WHO, 2003).

MATERIALS AND METHODS

Ethical approval

The study was approved by the Health Research Ethics Committee of Ahmadu Bello University Teaching Hospital Zaria, Nigeria. Both written and verbal consent of patients were sought prior to data collection.

Study design

A prospective, cross-sectional study was conducted on a sample of 603 patients attending the diabetic clinic at the MOPD, ABUTH-Zaria. The World Health Organization has recommended using at least 600 encounters or prescriptions for drug utilization studies (World Health Organization, 1993).

Eligibility criteria

Prescriptions of consenting patients with an established diagnosis of type 2 diabetes mellitus who came to the hospital pharmacy to fill their prescriptions were included in this study. However, prescriptions from inpatients, critically ill patients, prescriptions containing supplements, and patients who declined to participate in the study were excluded.

Data collection

Pertinent data were collected using forms adopted from the WHO method on how to investigate drug use in health facilities. The data were collected over a period of 16 weeks between 8th June and 28th September 2015 from the prescriptions of patients attending the MOPD of Ahmadu Bello University Teaching Hospital. The following data were collected as stated in the WHO document.

1. Prescribing indicators: Average number of drugs per encounter, percentage of drugs prescribed by generic name, percentage of encounters with an antibiotic prescribed, percentage of encounters with an injection prescribed and percentage of drugs prescribed from national essential drug list.
2. Patient Care Indicators: Average consultation time, average dispensing time, percentage of drugs actually dispensed and patients' knowledge of correct dosage by asking a question.

3. Facility indicators: Availability of a copy of Essential Drug List (EDL) of the hospital, availability of key drugs.
4. Complementary indicators: Percentage of patients treated without drugs, average drug cost per encounter, percentage of drug costs spent on injection.

Data analysis

Data were analysed using Microsoft Excel 2013 and presented as descriptive statistics. The drugs were sorted and coded according to the Anatomical Therapeutic Chemical (ATC)/defined daily dose (DDD) classification system (World Health Organization, 2013). All calculations were done according to WHO methods of drug utilization World Health Organization, (1993) as stated below:

1. Prescribing indicators

i. Average number of drugs per encounter was calculated by dividing the total number of different drug products prescribed by the number of encounters surveyed.
ii. Percentage of drugs prescribed by generic name was determined by dividing the number of drugs prescribed by generic name by the total number of drugs prescribed, multiplied by 100.
iii. Percentage of encounters with antibiotics/injection was determined by dividing the number of encounters with antibiotics/injection by the total number of drugs prescribed, multiplied by 100.
iv. Percentage of drugs prescribed from the essential drug list was determined by dividing the number of products prescribed from the essential drug list of the hospital by the total number of drugs prescribed, multiplied by 100.

2. Patient care indicators

i. Average consultation time was determined by dividing the total time for a series of consultations, by the actual number of consultations.
ii. Average dispensing time was calculated by dividing the total time for dispensing drugs to a series of patients, by the number of encounters.
iii. Percentage of drugs actually dispensed was worked out by dividing the number of drugs actually dispensed at the health facility by the total number of drugs prescribed, multiplied by 100.
iv. Patients' knowledge of correct dosage was found by dividing the number of patients who can adequately report the dosage schedule for all drugs, by the total number of patients interviewed, multiplied by 100.

3. Facility indicators

i. Availability of copy of EDL: By stating yes (or) no.
ii. Availability of key drugs was calculated by dividing the number of specified products actually in stock by the total number of drugs on the checklist of essential drugs multiplied by 100.

4. Complementary indicators

i. Average drug cost per encounter was determined by dividing the total cost of all drugs prescribed by the number of encounters surveyed.
ii. Percentage of drug costs spent on injection was determined by dividing the cost of injections prescribed by the total drug cost.

The formulas for other parameters are shown below:

$$DDD/1000\ diabetic\ patients/day = \frac{Total\ amount\ of\ drugs\ used\ during\ study\ period(mg, units) \times 1000}{DDD\ (mg, units)\ \times Duration\ of\ study \times total\ sample\ size}$$

$$cost/DDD = \frac{Cost\ of\ one\ tablet\ or\ vial\ of\ insulin\ (₦) \times DDD(mg, units)}{Strenght\ of\ one\ tablet\ or\ vial\ of\ insulin(mg, unit)}$$

The drug utilization 90% (DU90%) segment was computed as described by WHO collaborating centre for drug statistics methodology (Blix, 2016; World Health Organization, 2013). The drugs were ranked by volume of their DDDs and the cumulative values corresponded to within and beyond DU90% were obtained. The costs of the drugs were obtained from the hospital pharmacy price list.

RESULTS

A total of 603 prescriptions were collected during the study period which contained a total of 1,085 drugs with an average of 1.8 drugs per prescription. The majority of the patients, 57% were female. Most of the prescriptions (99%) had the names of the patients written on them while 98% had the names of the prescribers. Only 91.5% of the prescriptions were dated. The age of the patients and signatures of the prescribers accounted for 32% and 99.7% respectively. Drug use indicators were presented in tables 1 and 2. Antidiabetics' utilization within DU90% and total DU90% were 6.115 and 6.167 DDDs/1000 patients/day respectively.

Table 1: Drug use indicators data in Ahmadu Bello University Teaching Hospital during the period under review

Core indicator	Facility value	WHO recommended values
Prescribing indicators		
Average number of drugs prescribed (n)	1.8	1.6-1.8
Percentage of drugs prescribed by generics name	57.9	100
Percentage of encounters with antibiotics	5.8	≤30
Percentage of encounters with injections	43.4	13.4-24.1
Percentage of drugs prescribed from EDL	82.9	100
Patient care indicators		
Average consulting time (minute)	8	>10
Average dispensing time (minute)	3	>5
Percentage of drugs actually dispensed	83.6	100
Adequate knowledge of correct dosage (%)	90.3	100
Facility indicators		
Availability of EDL	Yes	Yes
Percentage of key drugs available	100	100
Complementary indicators		
Average drugs cost per prescription (₦)	1,462	-
Percentage of drugs cost spent on injection	96.8	-

EDL means Essential Drug List

Table 2: Utilization of antidiabetics (A10) in this facility expressed as a percentage, number of DDD/1000 patients/day, and Cost/DDD in Naira observed during the study period.

ATC code	Drug prescribed	Percentage	DDD/1000 patients/day	Cost/DDD (N)
A10BA02	Metformin	46.80	4.368	49.46
A10BB12	Glimepiride	16.07	1.500	51.00
A10BB01	Glibenclamide	8.90	0.166	22.00
A10AB05	Insulin aspart	8.88	0.041	832.00
A10AC04	Insulin lispro	8.56	0.040	832.00
Within DU90% segment		**89.21**	**6.115**	**1,786.46**
A10AE04	Insulin glargine	5.20	0.024	844.00
A10AB01	Soluble insulin	3.45	0.016	1,311.00
A10BG03	Pioglitazone	1.78	0.011	79.00
A10AC01	Insulintard	0.36	0.0005	1,240.00
Beyond DU90% segment		**10.53**	**0.052**	**2,234.00**
Total = within DU90% + beyond DU90%		100.00	6.167	4,020.46

ATC = Anatomical and Therapeutic Classification, DDD = Defined Daily Dose and DU90% = 90% of Drug Utilized

DISCUSSION

Drug utilization studies provide useful insights into current prescribing practices and also identify irrational prescribing. The consequences of irrational prescribing include non-adherence to medications, which can result in complications due to uncontrolled blood glucose levels and also escalate the costs of drugs and health care (Soumya *et al*., 2015).

The higher number of females observed in this study could be due to the high prevalence of diabetes among females as observed in a study by Hilawe and coworkers (2013). In urban areas, the incidence of diabetes is slightly higher among females due to the simple reason that men are involved in strenuous physical activities that tend to burn off most of the excess carbohydrates and fats which could lead to obesity and insulin resistance (Udonwa & Okoi, 2013). Furthermore, it has been known that females are more willing to seek medical advice (Fitzgerald *et al*., 1995) and comply with treatment (Babwah *et al*., 2006).

The average number of drugs per prescription observed in this study agreed with the WHO recommended value. An average number of drugs per prescription is used to assess for the presence of polypharmacy. Eze and Odunayo (2010) have shown that polypharmacy is common among diabetic patients in Nigeria (Eze & Odunayo, 2010). This may results in an increased risk of irrational drug use often due to the need for additional drugs to treat comorbidities (Patel *et al*., 2013). Furthermore, polypharmacy is associated with an increase in drug interactions, adverse drug reactions, nonadherence, and financial burden to the patients (Abidi *et al*., 2016; Parveen *et al*., 2016; World Health Organization, 1985).

The prescription trend in the facility showed that generic drug prescription was suboptimal with 82.9 % of drugs prescribed from the National Essential Drug List. This implies that the prescribers deviated from the standard norm by prescribing proprietary or branded drug products (Eze & Odunayo, 2010). However, uncontrolled advertisements of drugs to doctors by pharmaceutical sales representatives and stock out of drugs in hospital pharmacies are known to promote brand-name prescriptions (Ashar *et al*., 2016) which are very common

in our hospitals. WHO has promoted generic drug prescription which has an advantage for cost containment of drugs (Babalola *et al*., 2011). This facilitates better communication among healthcare providers (Mudenda *et al*., 2016). According to Patel *et al*., (2013), generic prescribing allows flexibility of stocking and dispensing various brands of a particular drug that are cheaper and as effective as proprietary brands. Generic drug prescriptions are known to differ widely in Nigeria. However, the value observed in this study was in agreement with the reported values of 55-61 % in most facilities (Chedi *et al*., 2015).

The percentage of prescriptions with antibiotics was within the WHO cut-off values of less than 30 %. The findings from this study were in agreement with others by Adibe *et al*., (2009), and Ogbonna and Ezenduka, (2014) in their studies in south-eastern Nigeria. Also, Eze and Odunayo, (2010) reported a value of 9.4 % in south-western Nigeria. Appropriate use of antibiotics is required to prevent the emergence of drug-resistant bacteria. According to figures gathered by surveys presented to WHO, in 2000, about 60% of antibiotics in Nigeria were prescribed unnecessarily (Akande & Ologe, 2007).

The high use of injectable in this study could be due to the frequent use of insulin injection in patients who do not tolerate or respond properly to the oral agents, or in conditions where there are contraindications to the use of oral agents (American Diabetes Association, 2013b, 2013a; WHO and IDF, 2004). Furthermore, it has been cited by Hardon *et al*., (2004) that health workers and patients in many countries believe that injections are more effective than tablets. As a consequence, the preference for injection has led to the high cost of prescription as manifested by the finding of this study. This was because injections contributed the highest share of the average cost (96.8 %) of a prescription in this facility. The use of injections is always expensive compared to other dosage forms and it requires trained personnel for its administration. Unhygienic use of injections can increase the risk of transmission of blood-borne diseases such as HIV (Angamo *et al*., 2011; Ashar *et al*., 2016; Hardon *et al*., 2004). In contrast, patients with T2DM who do not achieve optimal glycaemic control with oral antidiabetics alone may require insulin therapy and studies by the National Institute for Health and Care Excellence (NICE) guidelines suggest that combination therapy with insulin and metformin, or insulin and a sulfonylurea, show significantly lower glycated haemoglobin levels compared to insulin monotherapy (Hasan *et al*., 2015). In practice, insulin is used in the management of T2DM due to lack of patient compliance, clinical inertia, insulin resistance, lack of optimum exercise and dietary control that may lead to unsatisfactory control of hyperglycaemia (Agarwal *et al*., 2014). In addition, the use of injections in this facility has significantly contributed high cost (96.8 % of the total cost of drugs) of prescription in this facility.

The average consultation and dispensing times were below the WHO standard. Due to this many patients were left without vital knowledge about their disease and medications. Many studies in Nigeria reported short consultations and dispensing times (Adibe *et al*., 2009; Chedi, *et al*., 2010; Chedi *et al*., 2015). This could be attributed to a lack of adequate manpower to cater to a large number of patients, inadequate motivation, and monitoring of healthcare personnel. Adequate knowledge of the correct dosage of drugs by the patients was also below the WHO standard. This could be due attributed to the short consultation and dispensing times. Longer

dispensing times allow pharmacists to offer adequate drug information to patients about the correct dosage, side effects they may experience, and counselling which in turn enhances compliance to treatment and better treatment outcomes (Mudenda *et al*., 2016).

Metformin was the most utilized antidiabetic agent in the facility as indicated by the highest as indicated by DDD/1000 patients/day of 4.368. The high use of metformin in the facility is not surprising since it is considered as the first-line agent for type 2 diabetes in most treatment guidelines. This agreed with the reports of studies from Nigeria and other countries as reported by Acharya *et al*., (2016); Adibe *et al*., (2009); Agarwal *et al*., (2014); Alam *et al*., (2014); Ogbonna and Ezenduka, (2014); Patel *et al*., (2013). This implies that there is adherence to the prescribing guidelines for diabetes in the facility. However, metformin and glimepiride combination was the most used combination therapy. This is perhaps because glimepiride and glipizide have a lower tendency to cause hypoglycaemia when compared with other sulfonylureas (Abidi *et al*., 2016). This may explain their high usage in the facility.

The drug utilization 90% (DU90%) segment has been described as an inexpensive, flexible, and simple method of assessing the quality of drug prescribing in routine healthcare (Bergman *et al*., 1998; Igboeli *et al*., 2010). The present study revealed that only metformin, glimepiride glibenclamide, insulin aspart and insulin lispro fall within the DU90% which conformed to the drug of the first choice for the treatment of diabetes according to the national and international treatment guidelines. This is an indication of rational utilization of antidiabetic drugs in this facility as the fewer the number of drugs and adherence to standard treatment guidelines are suggestive of rational and quality use of medicines in a facility (Bergman *et al*., 1998; Kulkarni *et al*, 2016; Vlahovic-Palcevski *et al*, 2002). In comparison, a study in the south-eastern part of the country reported metformin, glibenclamide, chlorpropamide, and fast-acting insulin within the DU90% segment (Adibe *et al*., 2009). In contrast to the within DU90% segment, beyond DU90% (DU10%) segment account for drugs that are not being used in large volume and are not priority to be procured except on an emergency (Prihayati, 2019). Further to this, management guidelines for diabetes have shown that drugs that fall beyond DU90% are often used in combination with either insulin or metformin for effective therapy. Similarly, the cost/DDD within the DU90% segment for this study was found to be lower than the cost beyond the DU90% segment as expected. Cost/DDD is used as a measure of cost-effectiveness of a treatment (Blix, 2016) and it is expected that high-volume medications are known to be available at a cheaper price (Bergman *et al*., 1998).

CONCLUSION

The findings of this study demonstrated that metformin was the most commonly prescribed oral antidiabetic in the facility. Generic drug prescription was remarkably lower, consultation and dispensing times were also lower than the recommended standards. While the cost of drugs was high, which can be reduced by adherence to generic drug prescribing. In addition, a shifting trend towards the use of insulin for the management of type 2 diabetes was observed. It is recommended that strategies to reduce the cost and irrational use of antidiabetics in the facility should be adopted.

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