Official Publication of the Faculty of Basic Medical Sciences University of Ibadan, Nigeria

Arch. Bas. App. Med. 5 (2017) 11 – 16
www.archivesbamui.com

ARCHIVES OF BASIC & APPLIED MEDICINE

Research Article

Anti-Diabetic Drug Utilization and Assessment of Glycemic Control Using Glycated Hemoglobin in Patients with Diabetes Mellitus Attending a Tertiary Hospital in South-West Nigeria

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Received: January, 2017; Accepted in final form: February 2017

Abstract

Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. This study focuses on antidiabetic drug utilization and assessment of glycemic control using glycated hemoglobin in patients with diabetes. This was a prospective cross-sectional study carried out from August to November 2015 in the University College Hospital, Ibadan. Data were collected from patients' case notes for drug utilization study and an assessment of glycemic level using glycated hemoglobin (HbA1c) was executed, patients were interviewed for socio-demographic data and adherence. Data were analyzed and interpreted using SPSS 13 version. A total of 201 case notes were reviewed. Female patients made 67.16% and male 32.84%. Average age range was 60 – 69 years. Average number of drugs per encounter was 2.7 and 87.3% of the drugs were prescribed by their generic names. Percentage encounter containing antibiotics and injections were 3.7% and 13.4% respectively, 92.5% of drugs prescribed were from the essential drug list, others include: antidiabetics 175 (32.6%), Antihypertensive 175 (32.7%), non-steroidal anti-inflammatory drugs 45 (8.4%), statins 40 (7.5%), vitamins 13 (2.4%), antibiotics 20 (3.7%), central nervous system drugs 9 (1.7%), others 59 (11.0%). The most prescribed antidiabetic drug was the biguanides (B) occurring in 23.38%. B plus sulfonylureas (SU) were the most prescribed combinations occurring in 30.35% of prescription. SU showed most effective glycemic control of 60% compared to B, 53.3% or its combination, not statistically significant (P>0.05). This reveals a rational drug use pattern and good compliance to drug therapy.

Keywords: Drug utilization, Diabetes mellitus, glycated hemoglobin, glycemic control, South-west Nigeria

INTRODUCTION

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels (ADA, 2012). Type 2 diabetes mellitus is the most common form of diabetes comprising of 90% to 95% of all diabetes cases with the rest accounting for type 1 diabetes and other forms of diabetes like gestational diabetes (Qaseem, 2012). An estimated 346 million people worldwide live with diabetes, resulting in 3.4 million deaths in 2004, with more than 80% of these deaths occurring in low- and middle income countries (WHO, 2011).

In Africa, the estimated prevalence of diabetes is 1% in rural areas, up to 7% in urban sub-Sahara Africa, and between 8-13% in more developed areas such as South Africa and in population of Indian origin (Motala, 2002). The prevalence in Nigeria varies from 0.65% in rural Mangu (North) to 11% in urban Lagos (South) (Akinkingbe, 1997), and data from the World Health Organization (WHO) suggests that Nigeria has the greatest number of people living with diabetes in Africa (Wild *et al.*, 2004)

The most widely used clinical test in diabetes is the measurement of blood glycated hemoglobin (also called $HbA1_C$) (Krishmnamurti and Steffes, 2001) which is a form of hemoglobin used primarily to identify the average, plasma glucose concentration over prolonged periods of time. It is formed in a non-enzymatic pathway by hemoglobin's normal exposure to high plasma levels of glucose. Glycation of hemoglobin has been associated with cardiovascular disease, nephropathy and retinopathy in diabetes mellitus. It gives an assessment of long term glycemic control. In general, the reference range (that found in healthy persons), is about 4.0%-5.9% (Larsen *et al.*, 1990).

Drug utilization (DU) has been defined as the marketing, distribution, prescription, and use of drugs in a society, with emphasis on the resulting medical and social consequences (WHO, 1997). The principal aim of drug utilization studies (DUS) is to facilitate the rational use of drugs in population. DUS is an essential part of pharmacoepidemiology as it describes the extent, nature and determinants of drug exposure and it is used to identify treatment adherence problems (Sincree *et al.*, 2006).

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The goal of treatment of DM is to control blood glucose and ultimately prevent long-term complications, as shown by the United Kingdom Prospective Diabetes Study group and Diabetes Control and Complications Trial (BMARPSGB, 2003).

MATERIALS AND METHODS

Study design: The aim of this study is to assess the most effective antidiabetic drug in the treatment of diabetes mellitus and the drug utilization pattern of antidiabetic drugs. This study was a prospective cross-sectional study carried out for four months from August 2015 to November 2015 on antidiabetic DU and glycemic control using $HBA1_C$ among patients with DM attending the General Outpatient (GOP) department clinic and the endocrinology clinic of the medical Outpatient (MOP) department of the University College Hospital (UCH), Ibadan, Oyo State, south-west, Nigeria. The UCH is an 850 bedded Hospital, and a major referral center within the south-western region of Nigeria. Ibadan is the largest indigenous town in Africa, south of the Sahara and it is located in south-western Nigeria, 125 kilometers from Lagos. It has a calculated population of 3,800,000, while the Yoruba comprise its principal inhabitants (Enwere *et al.*, 2006)

Ethical approval: Ethical approval for this study was issued by the University of Ibadan (UI)/UCH ethical review committee with an IRB Research approval number of UI/EC/15/0091.

Study population and selection: A total of 306 patients were screened, out of which 201 met the inclusion criteria which includes: all consenting diabetic patients, patients with diabetes and other co-morbid condition like hypertension, stroke, tuberculosis and arthritis, and prescriptions of patients who are diagnosed with diabetes both males and females were included for the study, 186 were interviewed for adherence to therapy.

Data collection: Structured questionnaires were administered and explained to the patient in a language they could understand. Patients case notes were reviewed and demographic data, detailed medical history, medications for DM, concomitant medications for co morbid diseases, questions regarding lifestyle, dietary pattern, and exercise program with laboratory investigations were recorded in the study proforma. Compliance, adverse effects and change in drug therapy were noted during the subsequent visits done at monthly intervals (Sivasankari *et al.*, 2013).

Blood collection and analysis: Blood samples were collected from patients for $HbA1_C$ test using the CLOVER® $A1_C$ analyzer machine and results obtained were properly recorded. The HbA1c target for patients with diabetes according to the American Diabetes Association below 7%, patients with HbA1c value of 7% and above were considered to have poor glycemic control.

Statistical analysis: Descriptive statistics was used for data presentation, Chi-square statistics was used to determine the effect of anti-diabetic drug classes on glycemic control using the glycated hemoglobin values. Correlation and multiple regressions were carried out to examine the relationship between glycemic control and predictive variables (age, sex). Data analysis was performed using SPSS version 13 and Microsoft excel version 2007.

RESULTS

Of the 201 patients who met the inclusion criteria and consented, 66(32.8%) were males and 135 (67.2%) were females. Patients with type 2 diabetes were most prevalent within the age range of 60-69 years followed by 50-59 years. The socio demographic characteristics of the participants are presented in (Table 1). Most of the patients fell within the age range of 60 – 69 years (Table 1); fewer patients were less than 40 years.

Table I:
Sociodemographic characteristics of study participants (N=201)

Parameters	Values
Sex	
Male	66 (32.8%)
Female	135 (67.2%)
Marital Status	
Single	2 (1%)
Married	193 (96%)
Divorced	6 (3%)
Educational Level	
Illiterate	32 (15.9%)
Below Secondary school	78 (38.8%)
Secondary school and above	91 (45.3%)
Occupation	
White collar	25 (12.4%)
Self employed	19 (9.5%)
Blue collar	94 (46.8%)
Unemployed/Retired	63 (31.3%)
Age Range	
Below 40	9 (4.5%)
40-49	21 (10.4%)
50-59	58 (28.9%)
60-69	74 (36.8%)
70 and above	39 (19.4%)

Table 2:
Percentages and frequencies of drugs prescribed in both clinics

Drugs Prescribed	Frequency	Percentage
Antidiabetics	175	32.6%
Calcium channel blockers	70	13.1%
ACE inhibitors	75	14.0%
NSAIDS	45	8.4%
Antidyslipidemia drugs	40	7.5%
Beta blockers	9	1.7%
Angiotensin II receptor blockers	21	3.9%
CNS drugs	9	1.7%
Vitamins	13	2.4%
Antibiotics	20	3.7%
Others	59	11.0%
Total	536	100.0%

Out of all the medications prescribed in both clinics, 32.6% were antidiabetics, other co-medication prescribed include; Calcium channel blockers (CCB – 13.1%), Angiotensin

converting enzyme inhibitors (ACEI – 14.0%), Non-steroidal anti-inflamatory drugs, (NSAIDs – 8.4%), antihyperlipidemias (statins – 7.5%), Beta blockers (BB – 1.7%), Angiotensin II receptor blockers (ARB – 3.9%), Vitamins (2.4%), Antibiotics (3.7%), Central nervous system drugs (CNS drugs – 1.7%), others (11.0%) as shown in Table 2.

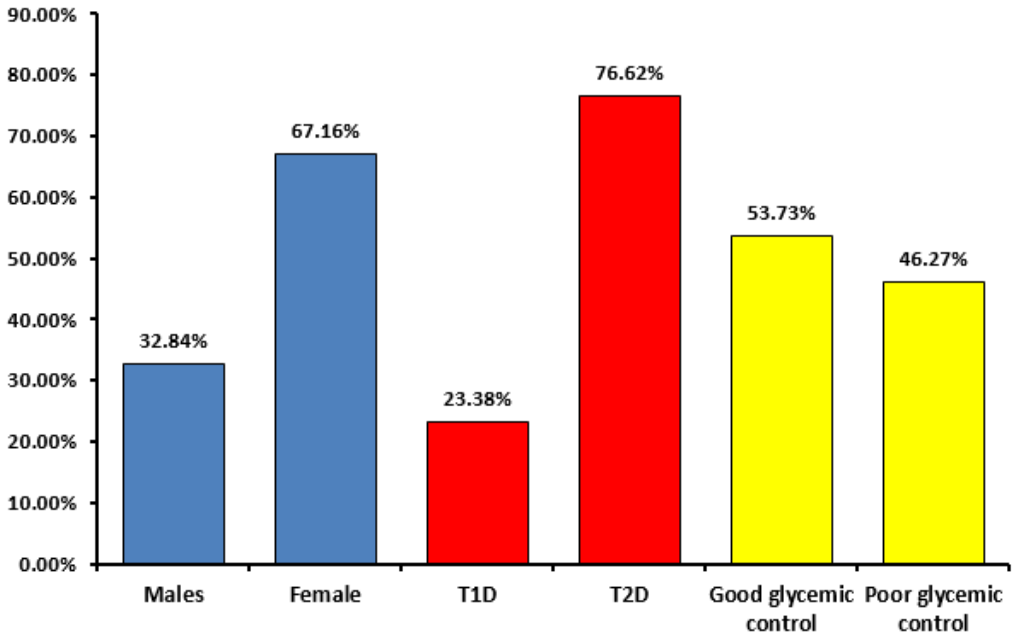

Figure 1:
Patients socio-demographic parameters in both clinics (T1D = Type 1 diabetes; T2D = Type 2 diabetes)
There was higher number of females (67.16%) in this study as compared to males (37.84%) in both clinics as shown in Figure I

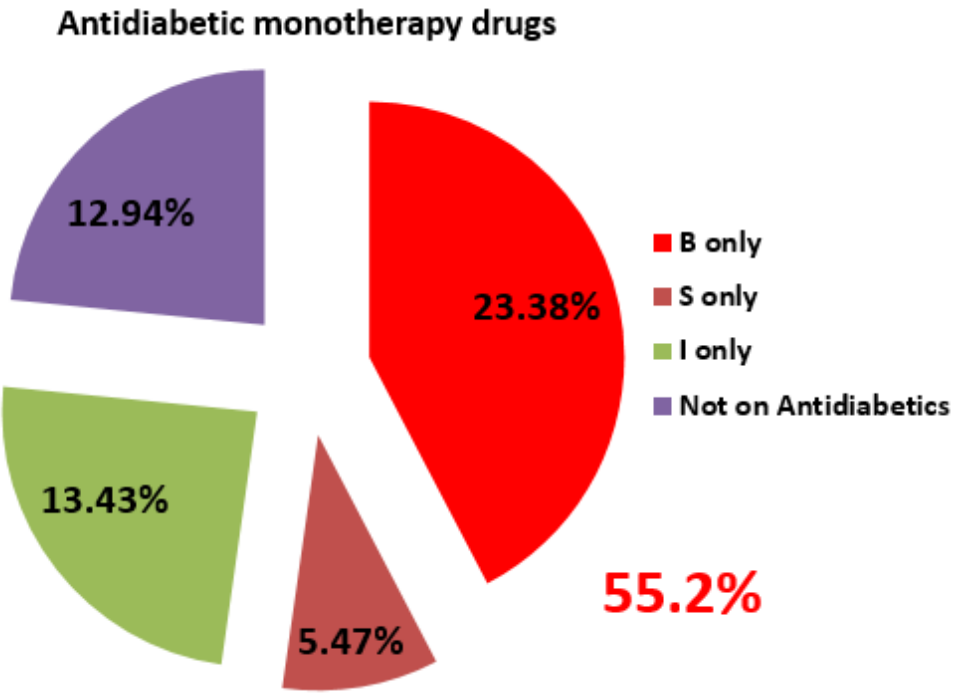

Figure 2:
Percentages of antidiabetic monotherapy drugs prescribed in both clinics [B = Biguanides (23.38%); S =Sulfonylureas (5.47%); I = Insulin (13.43%); Not on Antidiabetics, dietary control (12.94%)]

The percentage of patients on antidiabetic monotherapy was 42.28%, metformin alone (23.38%) was the most prescribed antidiabetic followed by insulin (13.43%) and then Sulfonylureas (5.47%). Patients not on any of the antidiabetics

made up 12.94%. Biguanide plus sulfonylurea (30.35%) was the most prescribed combination therapy followed by Insulin plus Biguanide (9.95%) and others (4.5%).

Patients showing good adherence to therapy showed a better glycemic control (55.3%) compared to those with poor adherence (44.7%).

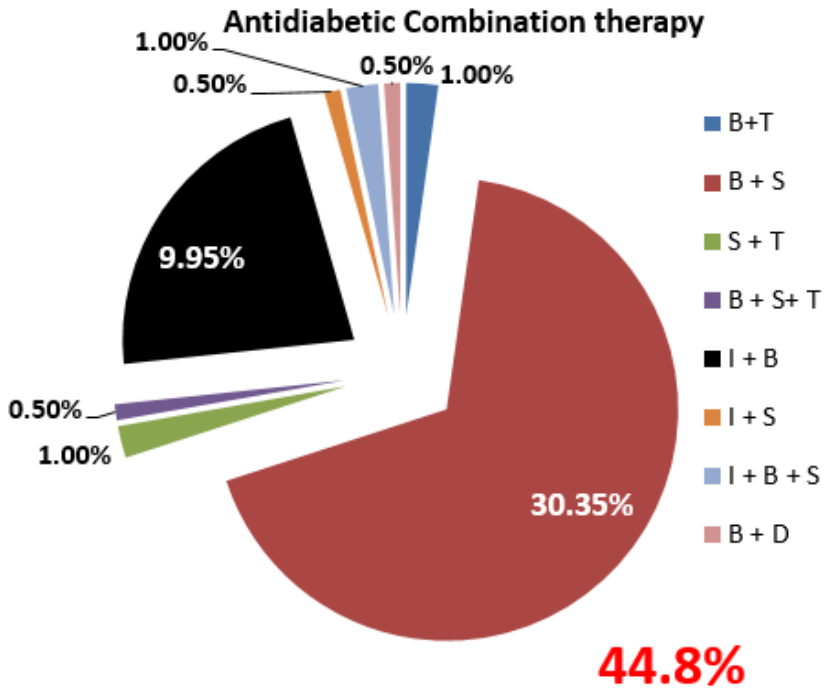

Figure 3:
Percentages of antidiabetic combination therapy prescribed in both clinics. B+T = Biguanides + Thiazolidinediones (1.00%); B+S = Biguanides + Sulfonylureas (30.35%); S+T = Sulfonylureas + Thiazolidinediones (1.00%); B+S+T = Biguanides+Sulfonylureas+Thiazolidinediones (0.50%); I+B = Insulin + Biguanide (9.95%); I+S = Insulin + Sulfonylureas (0.50%); I+B+S = Insulin + Biguanide +Sulfonylureas (1.00%); B+D = Biguanide + Dipeptidylpeptidase (0.50%). The combination therapy of Biguanides and Sulfonylureas was discovered to be the most prescribed especially in patients with type 2 diabetes mellitus.

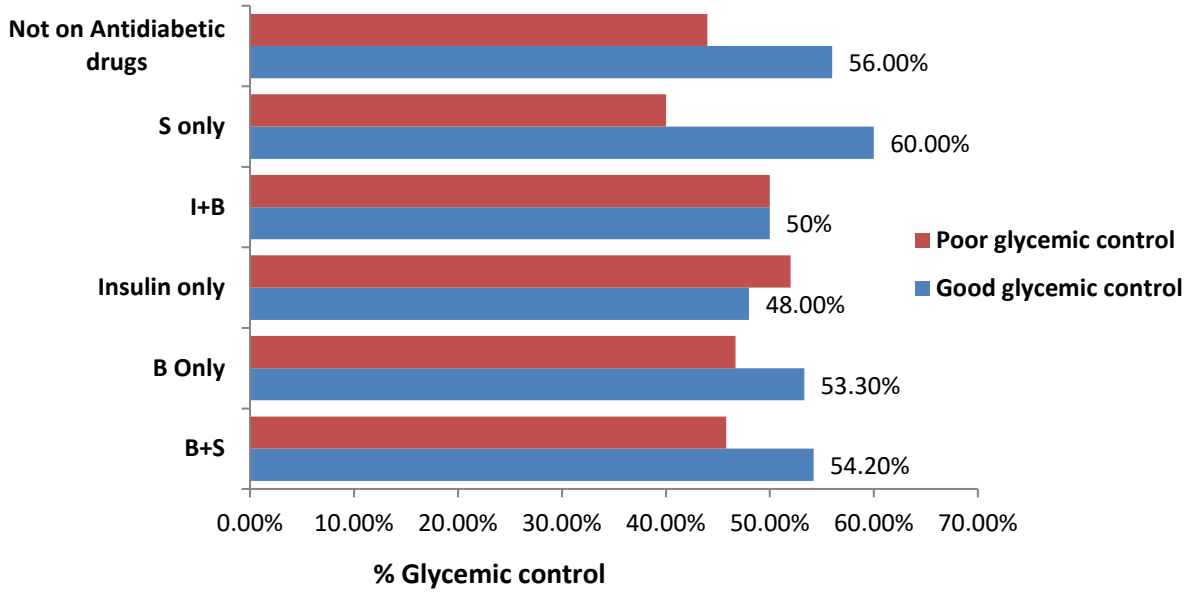

Figure 4:
Percentages of glycemic control of various antidiabetic drugs utilized by patients in both clinics [S = Sulfonylureas (60.0% GGC; 40.00% PGC); I+B = Insulin + Biguanide (50.0% GCC; 50.00% PGC); B =Biguanide (53.30% GGC; 46.70% PGC); B+S = Biguanide + Sulfonylureas (54.20% GCC; 45.80% PGC); Insulin (48.0% GCC; 52.00% PGC); Not on Antidiabetic drugs (56.0% GGC; 44.00% PGC); GCC = Good glycemic control; PGC = Poor glycemic control.]. The sulfonylurea class of drug showed a better glycemic control compared to the other classes of antidiabetics and their combinations.

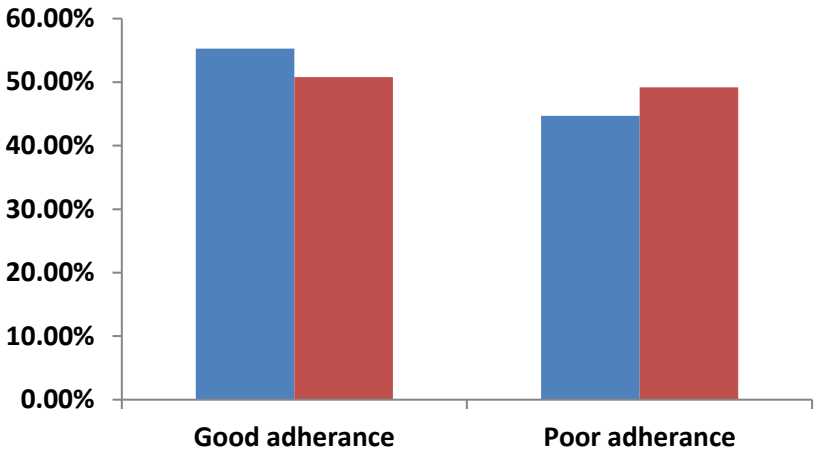

Figure 5:
Percentages of glycemic control in relation to patient's adherence.

DISCUSSION

A prescription is an order that is written by the physician or a medical signature by a physician to tell the pharmacist what medication he/she wants for his/her patients at a particular time in the management of such patients' disorder. A prescription is expected to reflect some elemental components as the name, phone number and signature of prescriber, and the name and age of patient (Practitioner's manual, 2006). In this study, metformin and its combination was found to be mostly prescribed compared to any other antidiabetic drug combination which agrees with other reports from Nigeria (Adibe *et al.,* 2009; Upadhyay *et al.,* 2007) and also in line with the findings of Johnson *et al.,* 2001; Yurgin *et al.,* 2007; Sultana *et al.,* 2010 but in contrast with the findings of Cantrill, 1999; who reported that glibenclamide (SU) is the drug of choice in the monotherapy of moderate hyperglycemia in non-obese Type II diabetes mellitus. The high prescription pattern of metformin in this zone is most likely due to the perceived fact that metformin is seen as a more preferable and safe antidiabetic drug with low hypoglycemic side effect, however, this finding is in contrast to the reports of some studies done in Hong Kong (Lau *et al.,* 1996) which reported that Glibenclamide (SU) was the most commonly prescribed anti-diabetic drug.

Despite the high prescription pattern of metformin, results from our study shows that the sulfonylureas class of drugs had a better glycemic control of 60% compared to other antidiabetic drug therapies. The reason why patients might have shown such a good glycemic control with the use of sulfonylureas might be associated with cost and the mechanism of action of sulfonylureas which act by inhibiting the efflux of potassium ion (K^+) (K^+ channel blockers) from pancreatic ß-cells via a sulfonylurea receptor which may be closely linked to an ATP-sensitive K^+-channel. The inhibition of efflux of K^+ leads to depolarization of the ß-cell membrane and, as a consequence, voltage-dependent calcium ion (Ca^{++}) channels on the ß-cell membrane then open to permit entry of Ca^{++}. The resultant increased binding of Ca^{++} to calmodulin results in activation of kinases associated with endocrine secretory granules thereby promoting the exocytosis of insulin-containing secretory granules, it also reduces serum glucagon levels possibly contributing to its hypoglycemic effects. The precise mechanism by which this occurs remains unclear but may result from indirect (secondary) inhibition due to enhanced release of both somatostatin and insulin. Sulfonylureas may also potentiate insulin action at target tissues (drug-dependent characteristic) (Gribble and Reiman, 2003).

Clinical distribution from our study showed that most patients were from the endocrinology clinic medical outpatient department (91.54%) as compared to the general outpatient department (8.46%); this is expected as diabetes is directly related to the endocrine system. Diabetes is known to be accompanied by some complications as a result of its co-morbid nature. The associated co morbid conditions seen with diabetes mellitus are hypertension, dyslipidaemia, neuropathy, nephropathy and retinopathy. In this study, 81.50% of the patients had hypertensive heart disease and were prescribed antihypertensives drugs alongside their antidiabetic medication while 13.10% of the drugs prescribed were angiotensin converting enzyme inhibitors (ACEI). The high antihypertensive prescriptions reflect the high rate of co-morbidity of hypertension and diabetes and the high rate of prescription of ACEI observed in the study is consistent with its documented benefit in preventing nephropathy (Ontarget investigators *et al.*, 2008).

Patients with glycated hemoglobin level less than 7% were said to have good glycemic control while those with values of 7% and above were said to have bad glycemic control. 53.73% of the patients in both clinics showed a good glycemic control which is an evidence of good adherence or compliance to drug therapy compared to 46.27% of the patients who showed poor glycemic control. Patients with good adherence showed better glycemic control compared to patients with poor adherence and a total of 53.73% of the patients in both clinics showed a good glycemic. This study also reveals a rational drug utilization pattern and good compliance to therapy by patients attending the MOP and GOP of the University College Hospital, Ibadan. Results from this research will help Clinicians in better prescription of antidiabetic drugs and in drug utilization patterns; it will also help the Government make good policies in regards to antidiabetic drug utilization. A good relationship should be encouraged between the endocrinology clinic and the cardiology clinic considering the fact that hypertension is one of the most common co morbid diseases frequently observed in patients with diabetes and also, more sensitization should be encouraged on patient's lifestyle and compliance to drug therapy.

In conclusion, this study reveals that the SUs showed a good glycemic control which compared to the most prescribed biguanide (metformin) and its combination B+SU in patients with diabetes in both clinics, therefore, it is advisable that the prescription of sulfonylureas should be encouraged by clinicians where necessary as they are inexpensive, more affordable and accessible to the patients as well as having a better glycemic control compared to other more costly antidiabetic drugs in the market. This will further enhance good adherence to medication.

Competing interest: There was no competing interest between authors in the course of carrying out this research

Authors Contribution

Jerry V. Amwe was involved with design of the research, carried out the research and also drafted the manuscript; Aduragbenro D.A. Adedapo conceived the idea, was involved with the design and supervised the research work. She also contributed to the manuscript for publication; Jokotade Adeleye consultant in charge of endocrinology was involved with the design, monitoring of collection of data and interviewing of patients in the clinic, and approved of the manuscript.

Acknowledgements: *Dr. Adigun of General Outpatient Department, UCH for assistance with patients enrolment and Dr. Tunde Adedokun of the Department of Epidemiology and Medical Statistics, University of Ibadan for assistance with statistical analysis.*

Funding/Financial Disclosure: *The research was self-funded with no external funding or grant*

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