

## Pharmacoepidemiological Survey on the Use of Anti-Diabetic Agents in a Teaching Hospital in South Eastern Nigeria

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### Abstract

**Background:** Periodic evaluation of Information on diabetes mellitus in every country is required for effective monitoring and follow up and treatment approach.

**Objectives:** This study evaluated drug utilization pattern in diabetic patients with reference to a tertiary hospital in South-Eastern Nigeria.

**Methods:** Four hundred folders of diabetic patients who attended the University of Nigeria Teaching Hospital (UNTH) diabetic specialist clinic over five (5) years, from 2013 - 2018 were selected for the study using a proforma. Data analysis was carried out using statistical package for social sciences (SPSS) software.

**Results:** The study shows that 62.3% of the patients were females, while 37.8% were males. Prevalent symptoms reported among diabetic patients include polyuria (38%), polydipsia (27%), polyphagia (14.0%), and weight loss (13.6%). Hypertension (90.5%) was the major risk factor among others reported. Prevalence of diabetes was associated with age, as patients above 60 years of age formed a greater proportion of the respondents. Also, 50% of patients showed a positive family history of diabetes in relation to their parents, while 32.69% and 17.31% of the patients' family history were related to their siblings and other relation respectively. Higher proportion of patients (75.5%) was diagnosed of diabetes in less than five years. The most prescribed drug was Metformin (51%) followed by insulin (39.9%).

**Conclusion:** The study revealed that Metformin is the most utilized anti-diabetic drug among the elderly (especially women), who were most vulnerable to diabetes in South-Eastern Nigeria.

**Keywords:** Drug Utilization; Metformin; Anti-Diabetic Agents; Nigeria; South East

### Introduction

Diabetes mellitus (DM) is an endocrine-metabolic disease characterized by chronic hyperglycemia giving rise to the risk of micro vascular and macro vascular damage, with associated reduced life expectancy and weakened quality of life [1].

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It is an enormous healthcare and socio-economic burden which affects any person irrespective of age, race, sex, and economic status [2,3]. About 6 percent of the world population is affected by DM [4], and by the year 2030, diabetes cases are expected to reach 366 million [5], while by 2025, the total expenditure globally will be between 213 -396 billion dollars [6].

According to the World Health Organization (WHO), Nigeria, with the highest population of about 200 million in Africa also has the highest number of diabetes cases with a prevalence of 0.65% in rural areas and 11% in urban areas [3].

A recent study revealed that about 5.8% (approximately 6 million) of adult Nigerians are suffering from DM, even though two-thirds of diabetes cases have not been diagnosed [7,8].

Rigorous efforts through proper diagnosis, risk factor identification, lifestyle modification and the use of anti-diabetic drugs have been made to curb the rising cases of DM.

Utilization of oral hypoglycaemic agents as single or combination therapies remains a preferential approach against the huge epidemic of DM [9].

Prescription and utilization pattern is required for rational use of drugs in a given population. They are resources to studying pharmacovigilance, pharmacoepidemiology, pharmacogenetics and pharmacoeconomics concept in such population [4].

The world health organization (WHO) defines drug utilization as the marketing, distribution, prescription and use of drugs in a society [10]. Contemporary measures in the management of DM encompasses prevention, screening of high risk individuals and serious intervention via the pharmacotherapy approach using insulin and oral hypoglycaemic agents [10].

Thus, inappropriate prescription could eventually diminish the effectiveness of drug therapy, producing non-adherence, escalation of the incidence of adverse drug reaction (ADR) and amplification of the cost of medical care [5].

In the Eastern part of Nigeria, there is currently no updated data on diabetes prevalence, diagnosis and intervention, considering the population scope. In this study, we estimated the incidence of diabetes from 2013-2018 using a Tertiary Teaching Hospital in South Eastern Nigeria. Age bracket, type of diabetes, age of onset, risk factors, complications as well as drug utilization pattern in the management of diabetes were targeted variables.

The study will serve as a guide for hospitals to plan intervention programmes and also to ensure improved quality of life among diabetics.

## Materials and Methods

### Study design

The study is a cross sectional, retrospective survey of clinical records of DM patients who received treatment from 2013 to 2018 (5 years period) at the University of Nigeria Teaching Hospital (UNTH), Enugu State in South Eastern Nigeria.

### Study setting

The study was carried out in the records department at UNTH, ItukuOzalla, Enugu State. UNTH is situated 21 kilometers from Enugu city along Enugu- Port-Harcourt express way. The hospital is one of the international standard teaching hospitals in Nigeria. As at the time of the study, there were 41 departments in the hospital, one of which is the diabetic unit, mapped out for this study. The sample size includes the first four hundred (400) folders of diabetic patients enrolled between 2013 and 2018.

**Sampling**

The hospital record of the patients was secured with the help of medical personnel in charge of medical record unit. Sampling was done randomly and each folder was picked after every other folder starting from 2013 and ending in 2018. Confidentiality of the patients’ data was maintained throughout the study by use of numbers for identification, their names were not taken. The participants whose folders were used were the ones that met the inclusion criteria for the study.

**Study instrument and data collection**

Data from the medical record of qualified participants was extracted by using a proforma. Content and facial validity of the proforma was carried out by team of medical record experts working in the hospital. Relevant data extracted include socio-demographic data, symptoms, presence of complications, and drug regimen.

**Inclusion criteria**

Only medical folders of patients with established diabetes or impaired glucose tolerance within 2013 - 2018 were used for the study.

**Exclusion criteria**

Pregnant women were excluded from the study to avoid possible impact of pregnancy on anthropometrics and laboratory parameters.

**Ethical consideration**

Ethical permission for research investigation was given for this research to be conducted by the health research and ethics committee of UNTH, Enugu State with approval number, NHREC/05/01/2008B-FWA00002458-1RB00002323 on 30<sup>th</sup> September, 2019.

**Data analysis**

The data obtained with the proforma was coded into the microsoft excel spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS/IBM, version 20). Descriptive statistics such as frequency and percentage distribution were used to summarize the data. Analyzed outcomes include drug utilization pattern, percentage of complications and socio demographics of patients.

**Results**

**Socio-demographics**

From table 1, 43.8% of the patients were above 60 years, 26.8% were between 51 - 60 years, 10% were of the range 41 - 50 years, 7.8% were between 31 - 40 years, while 7.3% and 4.5% account for 21 - 30 years and below 20 years respectively. Majority of patient (62.3%) were females while minorities (37.8%) were males. While 86.3% of the patients were married, only 10.5% of them were not married, and very few fraction, 1% and 2.3% were separated/divorced or widowed respectively. In terms of employment status, majorities (69.3%) were self-employed (Table 1).

*Table 1: Demographic data of patients.*

	Category	Frequency	Percentage (%)
Age	Less than 20	18	4.5
	21 - 30	29	7.3
	31 - 40	31	7.8
	41 - 50	40	10.0
	51 - 60	107	26.8
	Above 60	175	43.8
	Total	400	100.0

Gender	Male	151	37.8
	Female	249	62.3
	Total	400	100.0
Marital status	Single	42	10.5
	Married	345	86.3
	Separated\Divorced	4	1.0
	Widowed	9	2.3
	Total	400	100.0
Employment	Student/Unemployed	38	9.5
	Self Employed	277	69.3
	Civil Servant	72	18.0
	Retired	13	3.3
	Total	400	100.0

**Family history and risk factors**

A total of 50% of the total patient showed a positive family history of diabetes in relation to the parents, while 32.69% and 17.31% of the patient were of the view of diabetes being among their siblings and other relation respectively. Under risk factors, 90.5% was hypertensive, while very few proportion, 6.9% and 2.6% had obesity and overweight respectively (Table 2).

**Table 2:** Family history and risk factors of DM.

	Category	Frequency	Percentage (%)
Family history	Parents	26	50.00
	Siblings	17	32.69
	Other Relation	9	17.31
	Total	52	100
Risk Factors	Hypertension	313	90.5
	Obesity	24	6.9
	Overweight	9	2.6
	Total	346	100.0

**Chief complaint amongst patient and duration since diagnosis and complications of DM**

From table 3, majority, 38%, of the patients complained of polyuria, 27% polydipsia, 14.0% polyphagia, 13.6% weight loss, and 6.5% and 1% nocturia and shock respectively.

Majority of the patients amounting to 75.5% were diagnosed less than five years, 17.3% were diagnosed 5 - 10 years ago, 3.3%, 2.3% and 1.8% were diagnosed 11 - 15, 16 - 20 and above 20 years respectively.

Among complications, diabetic foot ulcer accounted for 34.60%, nephropathy accounted for 30.11%, retinopathy accounted for 24.54% while septicemia and heart failure account for 6.32% and 4.50% respectively (Table 3).

**Table 3:** Chief complaint amongst patients, duration since diagnosis and complications of DM.

	Category	Frequency	Percentage
Chief complaint	Polyuria	193	38.0
	Polydipsia	137	27.0
	Polyphagia	71	14.0
	Nocturia	5	1.0
	Shock	33	6.5
	Weight Loss	69	13.6
	Total	508	100.0
Duration since diagnosis (years)	< 5	302	75.5
	5 - 10	69	17.3
	11 - 15	13	3.3
	16 - 20	9	2.3
	> 20	7	1.8
	Total	400	100.0
Complications of DM	Nephropathy	81	30.11
	Retinopathy	66	24.54
	Septicemia	17	6.32
	Diabetic Foot Ulcer	93	34.60
	Heart Failure	12	4.50
	Total	269	100.0

**Complications of DM in relation to different age groups**

Patients above 60 years of age had more diabetes complications (nephropathy, 53.1%, retinopathy, 37.3%, diabetic foot ulcer, 55.9%, heart failure, 58.3%) than other lower age categories. Septicemia was absent among patients above 60 years (Table 4).

Patients between 51 - 60 years had lower complications than patients above 60 years, while patients between 41 - 50 years had less complication than patients between 51 - 60 years. Similar, trend was observed among patients in lower age categories. Interestingly, patients below 20 years had no complication except 2 (3.0%) cases of retinopathy (Table 4).

**Table 4:** Complications of DM in relation to different age groups.

Age	Complication						Total
	Nephropathy	Retinopathy	Septicemia	Diabetic foot ulcer	Heart failure	Nil	
< 20	0(0)	2 (3.0)	0 (0)	0 (0)	0 (0)	16 (11.7)	18 (4.5)
21 - 30	0 (0)	4 (6.0)	1 (10.0)	0 (0)	0 (0)	24 (17.5)	29 (7.3)
31 - 40	5 (6.2)	8 (11.9)	1(10.0)	3 (3.2)	0 (0)	14 (10.2)	31 (7.8)
41 - 50	7 (8.6)	9 (13.4)	3 (30.0)	5 (5.4)	1 (8.3)	15 (10.9)	40 (10.0)
51 - 60	26 (32.1)	19 (28.4)	5 (50.0)	33 (35.5)	4 (33.3)	20 (14.6)	107 (26.8)
Above 60	43 (53.1)	25 (37.3)	0 (0)	52 (55.9)	7 (58.3)	48 (35.0)	175 (43.8)
Total	81	67	10	93	12	137	400

Numbers in parenthesis indicate responses expressed in percentage.

**Drugs prescribed by physician in the management of DM**

From the prescription pattern, majority of patients (353, 51.0%) used metformin in DM management, followed by insulin (276, 39.9%), glimepiride (39, 5.6%), glibenclamide (12, 1.7%), vildagliptin (4, 0.6%), rosiglitazone (5, 0.7%) and saxagliptin (3, 0.4%) (Table 5).

**Table 5:** Drugs prescribed by physician in the management of DM.

Drugs	Frequency	Percent
Metformin	353	51.0
Insulin	276	39.9
Glimepiride	39	5.6
Glibenclamide	12	1.7
Vildagliptin	4	.6
Saxagliptin	3	.4
Rosiglitazone	5	.7
Total	692	100.0

**Drug employed in the management of DM in relation to different age groups**

From the table 6 below, the relationship between age and level of utilization of various drugs in diabetes management is very clear. Metformin (11, 1.7%) was mostly prescribed and utilized.

**Table 6:** Drug employed in the management of DM in relation to different age groups.

Drugs	Age category						Total
	< 20	21 - 30	31 - 40	41 - 50	51 - 60	> 60	
Metformin	11 (1.7)	25 (3.6)	27 (3.9)	35 (5.1)	102 (14.7)	152 (22.0)	353 (51.0)
Insulin	0 (0)	12 (1.7)	18 (2.6)	27 (3.9)	91 (13.2)	128 (18.5)	276 (39.9)
Glimepiride	0 (0)	0 (0)	3 (0.4)	15 (2.2)	12 (1.7)	9(1.3)	39 (5.6)
Glibenclamide	0 (0)	0 (0)	1 (0.1)	1 (0.1)	4(0.6)	6(0.9)	12 (1.7)
Vildagliptin	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.4)	1 (0.1)	4 (0.6)
Saxagliptin	0 (0)	0 (0)	0 (0)	0 (0)	2 (0.3)	1 (0.1)	3 (0.4)
Rosiglitazone	0(0)	0 (0)	0 (0)	0 (0)	2 (0.3)	3 (0.4)	5 (0.7)
Total	12 (1.7)	37 (5.3)	49 (7.1)	78 (11.3)	216 (31.2)	300 (43.4)	692 (100.0)

*Numbers in parenthesis indicate responses expressed in percentage.*

In relation to age group, majority of patients above 60 years (152, 22.0%) used metformin most, followed by those between 51 - 60 years (102, 14.7%). The trend reduces as the age range reduces. Vildagliptin, Saxagliptin and Rosiglitazone were never prescribed or used by diabetic patients in < 20, 21 - 30, 31 - 40 and 41 - 50 years, but only very few proportion of patients between 51 - 60 and above 60 years utilized them.

Use of glibenclamide and glimepiride were not reported for patients below 20 years and those between 21-30 years, but their utilization increase with age. Similar trend was observed with insulin, where 12 (1.7%), 18 (2.6%), 27 (3.9%), 91 (13.2%), 128 (18.5%), and 276 (39.9%) patients in 21 - 30, 31 - 40, 41 - 50, 51 - 60 and above 60 years age category respectively used it.

## Discussion

The research was done with 400 patients folders selected randomly from the medical records of diabetic specialist clinic over the five (5) year period, from 2013 - 2018.

Out of these, 151 (37.8%) patients were males and 249 (62.3%) were females. These figures are consistent with previous study conducted in Ibadan, South-Western Nigeria where women were found to have higher risks of DM than men [11]. This could be attributed to the proposition of Muhammad., *et al.* [3] that most females engage in sedentary lifestyle such as home keeping which makes them to be physically less active compared to males who engage more on active works such as office activities, businesses and farming. Also, elevated body fat, weight and stress can increase their DM risks [12,13]. This is contrary to a study carried out in Saudi Arabia where more males had diabetes than females [5].

The incidence of diabetes in patients increases with increasing age. This observation has been reported in Sudan [14] and other parts of Nigeria [3]. DM was mostly seen among patients greater than 60 years of age, conforming to the fact that the prevalence of DM increases with age as reported by Jian., *et al.* [10]. This is substantiated by studies in Nigeria and other Africa countries where ages 55 and 64 years were most susceptible to diabetes [3,15].

Also, 50% of the patients showed a positive family history of diabetes in relation to the parents, while 32.69% and 17.31% of the patient were of the view of diabetes being among their siblings and other relation respectively. Higher prevalence of diabetes among parents could be attributed to age, which is associated with incidence of diabetes. Similar trend was observed in study of Oyenusi., *et al.* [16] in Nigeria.

Subsequently, majority of the patients amounting to 75.5% were diagnosed in less than five years, 17.3% were diagnosed 5 - 10 years, 3.3%, 2.3% and 1.8% were diagnosed 11 - 15, 16 - 20 and above 20 years respectively before this study. It is important to note that higher positive diagnosed cases of diabetes were reported in recent years compared to the past years in this study, which corroborate the rising cases of DM among the populace. Interestingly, a systematic review conducted by Uloko., *et al.* [7] revealed increase in the incidence of DM in Nigeria, affecting all regions of the country, where South-South geopolitical zone recorded the highest prevalence.

Metformin, a biguanide was the most recommended anti-diabetic drug with 51% of the total prescription, while insulin (39.9%) was the next commonly prescribed agent. Preponderance of metformin as an anti-diabetic drug has also been reported in other studies [10]. Also, studies have recommended metformin as a therapy of choice for overweight and obese patients with type 2 DM [6,17] due to its advantages such as its ability to acts as a peripheral enhancer of insulin, reduction of cardiovascular mortality rates compared to sulfonylurea, absence of severe hypoglycemia [10]. A related study by Adibe., *et al.* [18] in South-Eastern Nigeria revealed Metformin as the most utilized anti-diabetic drug.

The chief complaints among the patient were majorly polyuria which accounted for 38%, polydipsia accounted for 27%, polyphagia 14.0%, weight loss complaints was at 13.6% while nocturnal and shock formed the less complaints at 6.5% and 1% respectively.

Diabetic foot ulcer, a known complication of diabetes was the most common with frequency of 34.60% amongst all other complications that were reported by these patients which is at variance with other studies carried out in Nigeria [19].

Hypertension is a risk factor of DM, with 40 - 50% of diabetic patient having hypertension than non-diabetic population [20]. This is substantiated by our study where majority (90.5%) of patients were hypertensive.

In the same vein, patients below 20 years form the minority with only 3%, suffering from retinopathy.

### Conclusion

From the assessment, prevalence of DM increases with age. It was also found to be more prevalent in women than in men. Metformin has the highest prescription rate among other anti-diabetic drug. Further studies relating to patients compliance to treatment, cost considerations, prescription trend of combination therapy should be investigated.

### Limitations of the Study

The drawback of the study include the restriction of data collection from medic which is a little fraction of the diabetes related admissions in the hospital, as well as the use of a single health facility.

### Statement of Ethics

Research was done following the guidelines for human studies and conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Ethical permission for research investigation was given for this research to be conducted by the health research and ethics committee of UNTH, Enugu State, with approval number, NHREC/05/01/2008B-FWA00002458-1RB00002323 30<sup>th</sup> September, 2019. Thereafter, consent was given to access patients folder starting from 2013 and ending in 2018.

### Disclosure Statement

Authors declare that no conflict of interest exist among them and other bodies with respect to this work.

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### Author Contribution

M.O.A. and C.I.O designed the work. E.O.E. and T.C.A. wrote the manuscript draft. C.I.O. collected data. A.I.O. and C.I. did statistical analyses and also reviewed the manuscript. All authors approved the final version of the manuscript before the submission.

### Data Availability Statement

Data are not available publicly due to privacy and confidentiality. Such data will be made available upon request from the correspondence author with proper explanation.

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