Retrospective Study of the Prescription Pattern of Antidiabetic Drugs and Their Outcome in a Tertiary Hospital in Southeast Nigeria

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Abstract

Background: Diabetes mellitus is a condition characterized by hyperglycemia resulting from either insulin insufficiency or from receptor resistance to insulin, and is accompanied with vascular complications in the long run. It is managed with insulin and oral antidiabetics. We identified the prescribing pattern of antidiabetics and the outcome in a tertiary hospital in a tertiary hospital in Nigeria.

Methods: The study was a retrospective survey of prescription data. Relevant information for the study was obtained from study population of 402 diabetic patients. We collected data from prescriptions and folders of adult patients 18 years and above with diabetes who had been diagnosed for atleast 12 months and have been on anti diabetes medications.

Results: The average patients' age was 56.93 years with more females than males. Insulin accounts for only 10.5% of all the antidiabetics prescribed while oral antidiabetics accounted for 89.5% of the antidiabetics prescribed. Meglitinide was the least prescribed class of oral antidiabetics (0.2%) while biguanide was the most prescribed (37.9%). Ditherapy had a frequency of 172 prescriptions while quintetherapy had frequency of 14 prescriptions.

Conclusion: The presence of biguanide in triple therapy, sulphonylureas and meglitinides in quadriple reduced the glycemic level significantly.

Abbreviations

USD- United States Dollar, IDF- International Diabetes Federation, MOPD- Medical Out Patient Department, ESUTH- Enugu State University Teaching Hospital, ESUT- Enugu State University of Science and Technology, DM- Diabetes mellitus, T2DM- type 2 diabetes mellitus

Introduction

Diabetes mellitus, a disease characterized by persistent hyperglycemia continues to increase the cost of healthcare provision worldwide. This disease has proven to be a pandemic and has been on the increase since history can remember, with data collected worldwide, showing that over 151 million cases were reported in the year 2000, approximately 194 million cases in 2003, 246 million in 2006, 285 million in 2010, and 415 million cases in 2015. The Diabetes Atlas Ninth 2019 edition of the International Diabetes Federation gave the following statistics: that approximately 463 million adults were presently living with diabetes mellitus, and by 2045 the number will increase to 700 million diabetic patients; of whom 79% of adults living in low and middle-income countries with 1 in 2 (a total of 232 million) people with diabetes mellitus shall remain undiagnosed. Diabetes mellitus caused 4.2 million deaths and at least USD 760 billion dollars in health expenditure in just the 2019 calendar year alone being 10 percent of total spending on adults [1].

Diabetes mellitus can thus be said to be worldwide problem since even the World Health Organization predicts a 50% increase in the deaths associated with diabetes mellitus over the next ten years with already having 1.5 million direct diabetic deaths and an additional 2.2 million deaths resulting from complications in the year 2012, and that by 2030 diabetes mellitus would be seventh leading cause of death worldwide [2]. As of 1992, the Nigerian National Non-Communicable Disease Monitoring Survey estimated a prevalence of 2.2% DM patients in Nigeria [3], however in 2017 the disease prevalence had increased to 2.4 [4]. All these extrapolations are worrisome and underscore thus the need for this study to review the prescription pattern of antidiabetic agents, insulin and the oral hypoglycemic agents inclusive, of their outcomes to determine the most appropriate strategies in the effective management of diabetes mellitus.

Prescription or Medical Prescription often abbreviated Rx or Px is a health care program or order written by a physician or any other qualified medical practitioner to the pharmacist to compound and/or dispense specific medication(s) for the patient. Prescription Pattern explains the extent and profile of drug use, trends, quality of drug guidelines, usage of drugs from essential medicine list and use of generic drug and compliance with regional, state, or national guidelines [5]. It can further be said that prescription pattern monitoring, is a study tool for assessing the prescribing, dispensing and distribution of medicines. The main aim for this practice is to facilitate rational use of medicines. Rational Drug Use ensures that a patient receives the medication appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time and at the lowest cost available to them and their community [6]. Antidiabetic Agents these are drugs used in the treatment/management of diabetes mellitus by altering the glucose level in the blood via different mechanisms of actions. Examples of such drugs include insulin, biguanides, sulfonylurea, meglitinides, thiazolidinedione, dipeptidyl peptidase IV inhibitors and alpha glycosidase inhibitors. Outcome simply means the result and for this research outcome entails the efficacy of the prescription given to the antidiabetic patients. We analyzed the prescription pattern of antidiabetics, both insulin and oral hypoglycemics, treatment and its combination therapy in patients with diabetes mellitus with or without co-morbidities that visited the medical outpatient department of a Nigerian tertiary hospital.

Methods

Material

The medical chart used for the study contained the following information: serial numbers of the patient, the fasting blood glucose reading of the patient the first and the last day the patient visited the hospital within the data collection period and the drugs prescribed that were relevant to the study.

Study Design

This is a retrospective study carried out by collecting the relevant information from the case note of the diabetic patients in Medical Out Patient Department (MOPD) of the ESUT Teaching Hospital, Enugu.

Study Population

Overall, 402 diabetic patients that visited the medical outpatient department of ESUT Teaching Hospital within the study duration were recruited into study as shown in Table 1.

Ethical Consideration

Ethical approval was obtained from the research and ethics committee of ESUTH with the registeration number: ESUTHP/C-MAC/RA1034/VOL. 1/258

Study Duration

The research was carried out using the case notes of the diabetic patients who visited the Medical Outpatient Department of ESUT Teaching Hospital from 2017-2020

Study Setting

The research was carried out in the Medical Outpatient Department of Enugu State University of Science and Technology Teaching Hospital. ESUTTH metamorphosed from the then Nursing Home established in 1903 for the colonial masters to a first-class hospital for government officials and elites in the society in 1952. During the Nigerian civil war of 1967-1970, it was converted to a general hospital and used extensively to treat the wounded. Gradual and progressive expansion led to establishment of Surgical, Maternity, Theatre and Pediatric facilities in 1985. It was then approved for the training of house officers, became a specialist hospital in November 2005 and then progressed to a teaching hospital in May 2006. Qualified employees were thereafter recruited and specialized working in the aforementioned departments to carry daily care of pateints' care including complex procedures such as cholecystectomy, ovariectomy, skin grafting, dialysis, cystolithotomy, myomectomy, vaginal hysterectomy and mastectomy [7].

Source of Data

All relevant and necessary information for the research was collected from the patients' case notes and prescriptions.

Inclusion Criteria

We collected data from prescriptions and folders of adult patients 18 years and above with diabetes who had been diagnosed for atleast 12 months and have been on anti diabetes medications.

Exclusion Criteria

We excluded prescriptions and folders with incomplete information or data and those with gestational diabetes.

Data Collection

This study was carried out by meticulously going through the case notes of 402 diabetic pateints that visited the medical outpatient department. Using their case notes, information such as patient age, patient gender, patient fasting blood glucose, and all the antidiabetic drugs prescribed to the patients. $P < 0.05$ was considered as statistically significant. All the data collected was analyzed using statistical package for social science version 20.0 for calculations. The analysis carried out on the data included;

1. Categorization of the patients based on the therapy administered

2. Determination of the frequencies of the different classes of antidiabetics therapeutic regimens

3. Determination of the different combinations obtained in the study

4. Determination of the different age groups and their frequencies in the different therapeutic regimens present in the study.

5. Frequency of gender in the different therapies.

6. Frequency and percentage of the final fasting blood glucose of the patients.

7. Use of the Pearson Chi-square association analysis to determine if the different therapies statistically had any control on the glycemic level of the patients

Results

Table 1: The distribution of study subjects by age group

Variables	n	%
Males	149	37.1
Females	253	62.9
Total	402	100
Patients' Age Group (years)	n	%
<19	1	0.2
20-29	0	0
30-39	24	6.0
40-49	64	15.9
50-59	124	31.0
60-69	142	35.2
70-79	43	10.7
80-89	4	1.0
Total	402	100.0

Table 2: Frequency of drugs prescribed for the different classes of antidiabetics

Class of antidiabetic prescribed	Frequency of drugs in each Class of antidiabetics (n=1017)	Proportion expressed as (%)
Insulin	107	10.5
Biguanide	385	37.9
Sulphonylurea	325	32.0

Dipeptidyl peptidase Inhibitor	67	6.6
Thiazolidinedione	116	11.4
Meglitinide	2	0.2
Alpha glycosidase Inhibitor	15	1.5

Table 3: Prescription frequency of the different classes of antidiabetics

Class of antidiabetic	Monotherapy	Di-therapy	Tri-therapy	Quadruple-therapy	Quinte-therapy
Insulin	4	14	44	33	14
Biguanide	36	171	118	53	14
Sulphonylurea	1	158	107	51	14
Dipeptidyl peptidase Inhibitor	1	0	18	32	14
Thiazolidinedione	1	3	66	36	14
Meglitinide	0	0	0	2	0
Inhibitor	0	0	7	5	0
Total	43	346	360	212	70
Proportion (%)	4.2	33.6	34.9	20.6	6.8

Table 4: The different combination therapies

Ditherapy		Tri-therapy		Quadruple-therapy		Quinte-therapy	
I + B	13	I + B + S	29	I + B + S + D	11	I + B + S + D + T	14
I + S	1	I + B + D	5	I + B + S + T	12	-	
B + S	158	I + B + T	8	I + B + S + A	4	-	
B + T	4	B + S + D	12	I + B + T + M	2	-	
-	-	B + S + T	59	B + S + D + T	20	-	
-	-	B + S + A	7	-	-	-	
Total	176		120		49	14	

Where
I = Insulin
B = Biguanide
S = Sulphonylurea
D = Dipeptidyl peptidase Inhibitor
T = Thiazolidine
M = Meglitinide
A = Alpha glycosidase Inhibitor

Table 5: Frequency of age groups in the different therapeutic combinations

Age Groups (years)	Monotherapy	Ditherapy	Triple Therapy	Quadruple-Therapy	Quinte-Therapy
<19 Years	-	-	1	1	-
20-29	-	-	-	-	-
30-39	2	4	10	3	2
40-49	7	31	15	8	2
50-59	16	53	38	19	2
60-69	10	59	47	18	6
70-79	8	24	8	4	-
80-89	-	1	1	-	2
Total	**43**	**172**	**120**	**53**	**14**

Table 6: Frequency and percentage of the final fasting blood glucose of the patients

FBG (mg/dl)	Frequency	Percentage (%)
≤66	2	0.7
67-76	5	1.2
77-86	9	2.2
87-96	31	7.7
97-106	92	22.8
107-116	84	20.8
117-126	93	23.1
127-136	23	5.7
137-146	15	3.7
≥147	48	11.9
Total	402	100.0

Table 7: Result for the chi square association analyses on the effect of antidiabetics combinations

Variable	Monotherapy p-value	Di Therapy p-value	Tri-Therapy p-value	Quadruple-Therapy p-value	Quinte-Therapy p-value
Insulin	0.122	0.977	0.595	0.358	ND
Biguanide	0.468	0.850	0.000	-	ND
Sulphonylurea	0.869	0.946	0.448	0.001	ND

Dipeptidyl peptidase Inhibitor	0.955	-	0.144	0.276	ND
Thiazolidinedione	0.908	0.953	0.106	0.101	ND
Meglitinide	-	-	-	0.001	ND
Alphaglycosidase Inhibitor	-	-	0.883	0.854	ND

ND=Not done

Discussion

This study made an attempt to study and describe the prescription pattern of antidiabetics along with its outcome in the management of glycemic level of the blood in diabetic patients who visited the medical outpatient department of Enugu State University of Science and Technology Teaching Hospital in Enugu State, South Eastern part of the Nigeria The case notes of 402 patients were used for this study, 149 were males while 253 were females this could be because men especially those in the middle class visited the hospital only at extreme ill conditions. This could also be because women often had to cope with both their own healthcare and that of their families, [8] thus they always have the need to visit the hospital. Also, the fact that women when pregnant had to go to the hospital for antenatal visits, in so doing might find out about their diabetic health condition and thus commence treatment. The number of antidiabetics drugs per prescription was 1-5. Other studies previously carried out in hospital settings reported 2-5 antidiabetic drugs per prescription [9-12]. The average number of antidiabetics per prescription in this study is 1.6 which is like 1.4 reported by another study [13]. Though it is lower than 3.3 reported by Adibe [14] thus prescription of antidiabetics in ESUT-TH is preceding away from polypharmacy.

Biguanides (385 of 1017 prescriptions or 37.9%) was the most prescribed class of antidiabetics, which was not in tandem with other studies that had been previously carried out which suggested that sulfonylurea is the most prescribed class of antidiabetics [15-18]. The reason for my result could be because biguanide was used mostly in monotherapy which was like several other studied [14,19]. Biguanide was followed by sulphonylureas (325 of 1017 prescriptions or 32.0%), showing that biguanides and sulphonylureas were the drugs of choice for the physicians at ESUT-TH and it was also in alignment with every other study carried out on the prescription pattern of antidiabetics. This study shows that there was low frequency for the prescription of newer antidiabetic drug classes which was similar to the study by Ameya et al. [16]. The least prescribed class from the study was meglitinide followed by alpha glycosidase inhibitor and then dipeptidyl peptidase inhibitor.

Insulin accounted for 10.5% (107 of 1017 prescriptions) of the total antidiabetics prescribed, thus from the study it was the fourth most prescribed class of antidiabetics. This percentage is not in tandem with previous studies which suggested higher percentage of insulin prescription [18,20]. This shows that prescribing was pulling away from insulin preparation in ESUT-TH and this could be because the physicians were avoiding the incidence of hypoglycemia which was the frequent adverse effect of insulin administration. Thus, this study strongly suggests that oral hypoglycemic agents are preferred over parenteral, insulin, and was in

tandem with the work by Ashkay [15]. However, there was need for constant monitoring of the blood glucose level so that the therapy could be intensified by the addition of other antidiabetics or increment in the dose in order to obtain optimal glycemic control.

In this study, almost all the drugs were prescribed by brand name suggesting the popularity of brands amongst the physicians and the influence of pharmaceutical companies on the physicians' decision or perhaps the physicians were looking out for economic outcome. The therapies differed in the order of diatherapy > tritherapy > quadripletherapy > monotherapy> quintetherapy. Monotherapy was the second to least used combination, this could be because the physicians were not willing to take chances with their patients thus preferred the use of combination therapy unlike the study carried out by Willey et al (2022) who documented a good glycemic control on monotherapy.

Majority of the patients on the antidiabetics had controlled glycemic levels, which fell within the range of various other studies which had documented 50%-86% glycemic control. These variations in glycemic control in the different studies could be due to differences in race, differences in the study population, method for the measurement of blood glucose levels, methods of data collection and the cut-off point for adequate glycemic control. The presence of certain drugs in the therapies yielded statistically significant result ($P < 0.05$) such as biguanide in tritherapy gave an association of glycemic control, <0.001, also the presence of sulphonylureas and meglitinides in quadruple therapy both gave the same association of glycemic control, 0.001. [20-22]. Thus, glycemic level was adequately controlled in the presence of biguanide in a tritherapy and either sulphonyl urea or meglitinide in quadruple therapy. The research did not consider the role of exercise and dietary measures. This could be due to poor documentation of the patients' case note or probably because the patients did not visit the dietician as they ought to have done.

Limitation of the Study

The blood glucose level was measured using the fasting blood glucose instead of using the HbA1c measurement which was considered the gold standard and gave better judgement of 3 months glycemic control. The Accu-Chek Active glucometer was used for this purpose, obviously due to its ease of use. The information used for this study was obtained from the patients folders, thus the privilege of interacting with the patients was ruled out. Due to the economic condition in Nigeria, most patients did not show up for their checkup, and often showed up only when their condition may have worsened, thus the fluctuations and unexpected results in most of the final glucose readings. The study did not take into account adequate separation of the different types of diabetes mellitus. The research also had uncontrolled confounding variables such as exercise and dietary measures (lifestyle modifications).

Conclusion

Oral hypoglycemic agents were the dominants in the prescribing pattern of antidiabetics. Biguanides were the most frequently prescribed while meglitinides were the least prescribed class of antidiabetics. The age bracket of 60-69 has the highest occurrence of type 2 diabetes mellitus. Ditherapy was the most used combination while quintetherapy was used the least. The use of biguanide in tritherapy, meglitinide and sulphonyl urea in quadruple proved effective in reduction of blood glucose level.

Conflict of Interest: The authors have no conflict of interest to declare

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