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IDENTIFICATION OF DRUG THERAPY PROBLEMS IN PATIENTS WITH DIABETES TREATED IN A SECONDARY CARE FACILITY IN BENIN CITY

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ABSTRACT
This study aims to identify the types and frequency of drug therapy problems (DTPs) as well as the treatment pattern of patients with diabetes admitted to the medical wards of the Central hospital Benin City. A prospective descriptive survey of 40 patients was undertaken during a 3 month period in the male and female medical wards of Central Hospital Benin City. Patient specific subjective and objective data were collected through interview, and review of medical records and prescriptions using pharmaceutical care forms. Data collection began on admission and ended on discharge in respect of each patient. The data were evaluated and identified. The number of male **patients 27(67.5%) was twice that of the female. There were varying diagnosis and several co-morbidities and/or complications. The most commonly used oral antidiabetic was metformin (57.5%) followed by glibenclamide (45%). Soluble insulin was the most prescribed of the insulin preparations occurring in 23 (57.5%) patients. Of the patients with diabetes who had hypertension, 15 (37.5%) were on lisinopril while 5 (12.5%) were on amlodipine and nifedipine respectively. There was a statistically significant difference in the FBS, Systolic BP and Diastolic BP on admission and discharge, P < 0.01. All the diabetic patients experienced DTPs (potential or actual) which could have been easily identified by a clinically trained pharmacist. The mean rate of DTP was 4.05 ± 1.96. The most frequently encountered DTP was wrong drug 23.9% followed by adverse drug reaction 16.4%, needs additional drug therapy 14.5% and dosage too high 14.47%. Others include inappropriate compliance 13.8%, dosage too low 11.3% and unnecessary drug therapy 5.6%. The findings of this study suggest a high incidence of drug therapy problems in the health facility and this makes a case for the presence of a pharmacist who is trained in the pharmaceutical care of diabetes in our health care system to help identify, prevent and resolve DTPs.**

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease with a high prevalence worldwide. In Nigeria the number of persons with DM was 1.7 million in 2000 and it is estimated that in 2030 will rise to 4.8 million (Wild *et al* 2004.) Diabetes has reached epidemic proportions in many developing and newly industrialised nations and because of the high rate of morbidity and mortality as well as high cost of managing the disease a multidisciplinary approach has been recommended for its management (ADA 2000.) Pharmaceutical care is a patient oriented care whereby the pharmacist takes responsibility for drug therapy problems. Here the pharmacist's duty is to identify, prevent and resolve drug therapy problems. A drug therapy problem is

any undesirable event experienced by the patient that involves or is suspected to involve drug therapy and that actually or potentially interferes with a desired patient outcome (Cipolle *et al* 2004) The occurrence of drug related problems, can be significantly reduced and the desired outcomes of pharmacotherapy achieved if the principles of pharmaceutical care are applied (Hepler *et al* 1990., Mc Donough *et al* 2003., Strand *et al* 2004., Rao *et al* 2007., Pereira de Lyra *et al* 2008).

Cipolle *et al* 1998 identified eight categories of drug therapy problems and they include [1] Unnecessary drug therapy; [2] Wrong drug; [3] Dosage too low; [4] Dosage too high; [5] Adverse drug reaction; [6] Drug interaction; [7] Inappropriate adherence; [8] Additional drug therapy.

Diabetes has high hospital admissions from acute complications such as hypoglycaemia, Diabetic Ketoacidosis (DKA), Hyper osmolar non ketotic state (HONK), lactic acidosis and readmissions from uncontrolled DM others are chronic complications/co-morbidities of the disease and drug therapy. When patients receive medications, the medications are expected to improve the quality of life of the patient and achieve definite outcomes. Increasingly, however, patients are not only being managed for their diseases but also problems arising from the use of medications (Passarelli *et al.,* 2005., Johnson *et al* 1997., Olivier *et al.,* 2009.) thus creating a health care need. This need however, is often not met and traditional efforts geared towards addressing it are often fragmented. Diabetes Mellitus as a disease is usually associated with complications and comorbidities that require use of complex pharmacotherapeutic regimens in the course of its management.

This study aims to identify the types and frequency of drug therapy problems as well as the treatment pattern of patients with diabetes admitted to the medical words of the Central hospital Benin City.

METHODS

SETTING

This study was a prospective descriptive survey conducted at the male and female medical wards of Central Hospital Benin City, Nigeria. The hospital is a 450 bed secondary health care institution founded in 1904, offering clinical, surgical and public health services to people of Edo South senatorial district. The hospital serves as one of the referral centres to many clinics and hospitals in these areas as well as a teaching hospital for Igbinedion University medical students and Pharmacy students from the University of Benin. It is approved for specialist training by the West Africa College of Medicine in 2 areas: Obstetrics and Gynaecology and family medicine.

POPULATION/SAMPLE

The study sample was drawn from all consenting patients with diabetes admitted into the male and female medical wards during a period of three months. The inclusion criteria were: Adult patients with diagnosed diabetes mellitus admitted to the male or female wards during the study period. Patients who did not give their consent and all other medical patients were excluded from the study.

DATA COLLECTION

Two methods were employed in collecting patient's specific data. First was the review of patients' case notes and then a patient interview conducted using a pharmaceutical care data collection form The demographics of

the patients were noted and the prescriber's assessment of the patient's condition was recorded as the indication for drug therapy. Drug therapy problems were classified according to categories established by Hepler and Strand (Hepler *et al* 1990*).*

USE OF PHARMACEUTICAL CARE FORMS

A pharmaceutical care data collection form was used to collect needed information from the patient. These procedures yielded subjective and objective data that included: Patient demographics e.g. name, age, gender and so on. Others include diagnosis, present and past medical history, including herbal medication, allergies and intolerances, Smoking, caffeine, alcohol and drug use history and compliance history.

DATA ANALYSIS

Raw data were entered into Microsoft Excel Software, checked for accuracy and then analysed using the Statistical Package for Social Science SPSS Version (11.0) for descriptive statistical analysis and Graphpad Instat (Version 3) for inferential analysis. Mean scores with standard deviations and percentage frequencies were determined. Inferential statistics were calculated with the aid of Graphpad Instat, which reports the unpaired t-test and P–values; P-value of less than 0.05 was interpreted as significant.

RESULTS

A total of 40 patients who met the inclusion criteria were included in the study 27 (67.5%) were males and 13(32.5%) females. The mean age of the patients was 58.38 years, with a range of 16 to 99 years, and they were admitted for a mean duration of 8.27 days ± 6.98 (range 1 – 30 days).

Only 7(17.5%) claimed they had a known family history of DM. 37 (92.5%) of the patients were resident in Benin City. There were varying diagnoses for the patients and they are as shown in Table 2. Multiple co-morbidities and/or complications were encountered. All but two 2 (5%) of the patients had more than one co-morbidity and/or complications. Hypertension (HTN) was the most frequently occurring 14 (35%) followed by hyper osmolar non ketotic state (HONKS) 5 (12.5%), Diabetes keto acidosis (DKA) 5 (12.5%), CVD 5 (12.5%), others include Diabetic foot ulcer (DFU) 3 (7.5%), Chronic renal failure (CRF) 3 (7.5%), Chronic cardiac failure (CCF) 2 (5%) etc. (Table 2).

Lisinopril, amlodipine and nifedipine were the most commonly prescribed antihypertensive drugs for the patients who had co-existing hypertension occurring at a proportion of 45.1%, 16.1% and 16.1% respectively of all anti hypertensive medications prescribed (Table 3)

Metformin and Glibenclamide were the most frequently encountered oral hypoglycaemic agents (OHA) occurring at a proportion of 57.5% and 45% respectively of the patients' OHA prescription. Different types of insulin preparations were also prescribed, 16 (40%) of the patients were on insulin preparations alone while 13(32.5%) of them were on a combination of insulin and an OHA. The remaining 11(27.5%) were prescribed only OHAs. Overall of the 29 patients prescribed insulin either singly or in combination with other agents, soluble insulin was the most frequently prescribed occurring in 23(79.3%) of the cases (Table 4).

The Fasting blood sugar and/or Random blood sugar and systolic and diastolic blood pressure levels of the patients at the time of admission and on discharge were recorded and compared. Results showed a statistically significant decrease i.e.

Table 1: Demographics

VARIABLE	FREQUENCY	PERCENTAGE (%)
Sex		
Female	13	32.5
Male	27	67.5
Family History of DM		
No	33	82.5
Yes	7	17.5
Ethnic group		
Bini	24	60.0
Esan	8	20.0
Etsako	1	2.5
Ibo	1	2.5
Igbanke	2	5.0
Itsekiri	1	2.5
Urhobo	2	5.0
Yoruba	1	2.5
Residence		
Benin City	37	92.5
Lagos	3	7.5
Smoking History		
No	33	82.5
Yes	7	17.5
Alcohol History		
No	21	52.5
Yes	19	47.5

positive clinical change in these parameters on discharge $P < 0.01$. Patients BMI values could not be reported because they were not recorded. Similarly, serum lipids were ordered for only 3 patients and these were within normal limits.

All the types of DTPs were observed in the study and all the patients had at least one DTP giving a 100% DTP encounter. The mean rate of DTP was 4.05 ± 1.961. The most frequently occurring DTP was wrong drug followed by adverse drug reaction, needs additional drug and dosage too high. These occurred in the following proportions: 23.9%, 16.4%, 14.5% and 14.5% respectively. Others are as shown in Table 5. The mortality outcome for the patients was high, 12(30%) of the patients died due to complications of renal failure and hypoglycaemia.

The study identified drug therapy problems and determined their frequencies and distributions. There were varying diagnoses for the patients. This could be as a result of the fact that diabetes is not a single disease but a syndrome or a cluster of disorders usually encompassing obesity, hypertension, dyslipidemia, atherosclerotic heart disease. The name syndrome X, or insulin resistance syndrome has been used to identify this pathological entity (Bhattacharyya *et al* 2001., and Wikipedia 2009). The most frequently prescribed antihypertensive agent in this study

Table 2: Patients diagnosis

	FREQUENCY	**PERCENT**
AUGB, DM, CRF	1	2.5
CCF, S. HTN, RVD, T.M, DM	1	2.5
CRF, DFU UDM	1	2.5
CRF, HTN, UDM	1	2.5
CRF, UDM, PTB	1	2.5
CVD, DKA, S. HTN	1	2.5
CVD, UDM, S. HTN	1	2.5
D. NEPH., CCF, S. HTN	1	2.5
D. NEPH., S. HTN, DM	1	2.5
DFU, HTN, DM	1	2.5
DFU, MF, DKA	1	2.5
DFU, UDM	1	2.5
DKA	5	12.5
DKA COMA	1	2.5
DKA, DFU	1	2.5
DM	1	2.5
DM, CVD, SD	1	2.5
GASTRO, S. ANAEMIA, DM	1	2.5
GASTRO, UDM	1	2.5
HONK S. DFU	1	2.5
SEPT. M. HTN	1	2.5
HONK STATE	1	2.5
HONK STATE, HTN	1	2.5
HONK, VULVOVAG	1	2.5
HONK, S. HTN	1	2.5
HTN, CVA, UDM	1	2.5
HTNS WE ENCEPH, UDM	1	2.5
HYPOGLY. COMA, CVD	1	2.5
LF, UDM, CA.H. OF PANC	1	2.5
MF, CCF, L.L. PNEUM, DM	1	2.5
MF, DM	2	5.0
RL PNEUM. UDM	1	2.5
MF, UDM	1	2.5
UDM, SHTN, MF	1	2.5
UDM, SHTN	1	2.5
UDM, MF	1	2.5
Total	**40**	**100.0**

AUGB= Acute upper gastrointestinal bleeding, CCF= Congestive Cardiac Failure, CRF=Chronic Renal Failure, CVA=Cerebrovascular Accident, CVD=Cerebrovascular Disease, DFU=Diabetic Foot Ulcer, DKA=Diabetic, Ketoacidosis,DM=Diabeticmellitus,D.NEPH=DiabeticNephropathy, ENCEPH=Encephalopathy,GASTRO=Gastroenteritis, HTN=Hypertension, L.L.PNEUM=Left Lobar Pneumonia, M.F=Malaria fever, M HTN=Moderate Hypertension, PTB=Pulmonary Tuberculosis, R.L. PNEUM=Right lobar pneumonia,S.D.=Seizure Disorder, SEPT=Septicaemia, SHTN =Severe Hypertension, T.M.=Thyroid mass, UDM=Uncontrolled Diabetes Mellitus, Vulvovag=Vulvovaginitis, S. Anaemia=severe Anaemia, CA.H. OF PANC=Cancer of head of Pancreas, S.D=Seizure Disorder,

TABLE 3: Pattern of prescription of antihypertensive medication

Antihypertensive	Monotherapy	Combination	N(%)
ACEI			
Lisinopril	8	6	14(45.1)
CCB			
Nifedipine	1	4	5(16.1)
Amlodipine	1	4	5(16.1)
BB			
Atenolol		1	1((3.2)
DIURETICS			
Hydrochlorothiazide(HCTZ)		1	1((3.2)
HCTZ + Amiloride	1	3	4(12.9)
OTHERS			
Aldomet		1	1(3.2)
Total	11	20	31(99.8)

was lisinopril followed by amlodipine and nifedipine. Sandeep and Rodney 2008. In their study on treatment of hypertension in type 2 diabetes mellitus noted that thiazide diuretics, angiotensin Ⅱ receptor blockers, and perhaps angiotensin – converting enzyme (ACE) inhibitors may be the preferred first – line agents for treatment of hypertension in diabetes (ACEI or ARB can reduce progression of micro – macrovascular complications). Evidence for the choice of ACE inhibitors as first – line agent is also supported by the HOPE study which shows a HTN – independent benefit on mortality (HOPE Study, 2000*)*. However, these benefits were not apparent in ALLHAT study (ALLHAT study 2002). There is evidence that ACE inhibitors may be superior to calcium channel blockers, thus calcium channel blockers are probably best used as second or third line treatment for HTN in diabetes. (Estacio *et al.,* 1998., Agardh *et al.,* 1996)

The most frequently prescribed oral hypoglycaemic agent was metformin followed by glibenclamide. This is consistent with the United Kingdom Prospective Diabetes Study (UKPDS) where metformin was recommended as the preferred oral agent and when contraindicated, sulphonylureas (glibenclamide) and glitazones are acceptable secondary choices. (UKPDS 1998) Metformin is associated with weight loss or weight maintenance, tolerable and low cost.

Sulphonylurea is relatively inexpensive. Soluble insulin was the most frequently prescribed of the insulin preparations. Short acting insulin is used in stress situations such as infections, myocardial infarction, coma, DKA, HONK, diabetes and dehydration. This finding of soluble insulin as the most frequently prescribed insulin preparation is consistent with the Diabetes Control and Complication Trial (DCCT) finding. (DCCT 1993) Regular insulin has a plasma half life of 5 – 6 hours

Table 4: Type and frequency of antidiabetic medications used

	Frequency	**Percent**
AMARYL, MET	2	5.0
GLIB	1	2.5
GLIB., MET	8	20.0
GLIB., MET, HUM $^{70}/_{30}$	1	2.5
GLIB, MET, MIXTARD	2	5.0
GLIB, MET, SOL	2	5.0
GLIB, MET, SOL HUM $^{70}/_{30}$	4	10.0
HUM $^{70}/_{30}$	1	2.5
MET, HUM $^{70}/_{30}$	1	2.5
MET, SOL	1	2.5
MET, SOL, HUM	2	5.0
MIXTARD	1	2.5
SOL	9	22.5
SOL, HUM $^{70}/_{30}$	2	5.0
SOL, MIXTARD	3	7.5
Total	**40**	**100.0**

MET=Metformin, GLIB= Glibenclamide, SOL=Soluble insulin, HUM=Humulin,

Table 5: Types, Distribution and Frequency of DTPS

Type of DTPs	Frequency				Total No of Occurrence N	%	Total No of Patients N	%
	One	Two	Three	Four				
Wrong drug	18	5	2	1	38	(23.90)	26	(65)
Adverse drug reaction	10	3	3	1	26	(16.35)	17	(42.5)
Dosage too high	9	7			23	(14.47)	16	(40)
Needs additional drug therapy	13	3		1	23	(14.47)	17	(42.5)
Inappropriate Compliance	18	2			22	(13.84)	20	(50)
Dosage too low	12	3			18	(11.32)	15	(37.5)
Unnecessary drug therapy	5	2			9	(5.66)	7	(17.5)
Total					159	(100.0)		

Table 6: Comparison of FBS, RBS Systolic and Diastolic BP of Patients at Time of Admission and Discharge

	N	Mean	SD	P
FBS on admission	15	256.16	119.4	0.01
FBS on discharge	15	153.5	102.0	
RBS on admission	24	340.8	143.3	0.06
RBS on discharge	9	233.4	134.9	
Systolic BP on admission	40	142.5	36.6	0.01
Systolic BP on discharge	34	124.7	26.1	
Diastolic BP on admission	40	88.25	22.2	0.01
Diastolic BP on discharge	34	80.0	16.3	

and needs to be given 4 times daily. The DCCT used regular insulin 3 or 4 times daily for the intensive insulin therapy group and the conventional group received one or two insulin injections per day (intermediate or long acting insulin i.e. NPH or glargine). The result showed that the intensive group had better outcome.

A noticeable omission in the drug therapy of the patients was the absence of cholesterol lowering drugs, not a single one was prescribed, and this is a significant flaw in the drug management of these patients. The reason for this is traceable to the fact that routine laboratory investigation for these patients was not readily done.

The frequency of DTP in this study is alarmingly high. 100% of the patients had at least 1 or more DTP, this rate of DTP is similar to that of a UK study which reported a frequency of 97% (Joel *et al* 2006) but higher than the frequencies reported by an Indian (Smith *et al* 1996) and Canadian (Kassam *et al* 2007) study which reported a DTP frequency of 78% and 75.5% respectively. The mean DTP per patient was 4.05 ± 1.96, this is much higher than that found in a similar study (Kassam *et al* 2007*)* with 2.5 ± 1.35 DTP per patient. In this study all the classes of DTPs were encountered, however, the most frequently occurring was wrong drug followed by adverse drug reactions. The least occurring was unnecessary drug therapy. This finding differs from the Canadian study (Kassam *et al* 2007*)* in terms of the ranking of DTPs, where needs additional therapy was the most frequent DTP followed by adverse drug reaction. The least was dosage too high.

Comparing the patients' FBS and BP levels on admission and discharge, there was an appreciable decrease in these parameters. This shows that despite the high rate DTPs the pharmacological management of the patients while on admission yielded positive intermediate outcomes with regard to the afore mentioned parameters i.e. FBS and BP.

CONCLUSION

There is a very high occurrence of DTPs among the DM patients treated in the surveyed facility. This study indicates the need for a multidisciplinary management approach which includes a pharmacist whose role will be to identify, prevent and resolve DTP

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