

DRUG UTILISATION AND GLYCAEMIC CONTROL IN DIABETIC-HYPERTENSIVE PATIENTS ATTENDING CLINIC AT STATE SPECIALIST HOSPITAL GOMBE, NORTH EAST NIGERIA

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Abstract

Background: The coexistence of hypertension and diabetes in individuals often necessitate the prescription of multiple medications. Some antihypertensive medications are known to potentially worsen hyperglycaemia, though this occurrence is not extensively documented.

Objectives: This study describes drug utilisation in the treatment of diabetic-hypertensive patients at State Specialist Hospital, Gombe, and compares glucose control in those using glucose-friendly versus non-glucose-friendly antihypertensive medications.

Method: In a cross-sectional study with 223 diabetic-hypertensive patients on oral anti-diabetic and antihypertensive medications for ≥ 6 months, folders were selected using a simple random sampling technique. A researcher-developed data collection form was used to capture patients' socio-demographic and clinical details. Statistical Product and Services Solution version 23.0 was employed for analyses, presenting continuous variables as mean (\pm standard deviation) while categorical data was expressed as frequencies and percentages. The glycaemic control of patients receiving glucose-friendly was compared with that of non-glucose-friendly antihypertensive users using the student t-test. Variables with $p < 0.05$ at a 95% confidence interval were deemed significant.

Results: Of the 223 diabetic-hypertensive patients, the majority were female (69.5%), ≤ 50 years old (60.5%), married (96.4%), and lacked formal education (66.8%). Metformin and angiotensin-converting enzyme inhibitors were the primary anti-diabetic (98.7%) and antihypertensive (82.0%) medications used in the study setting. There was no significant difference between glycaemic control of patients using glucose-friendly and non-glucose-friendly antihypertensive medications (8.49 mmol/L vs. 8.75 mmol/L; $p = 0.639$).

Conclusion: Majority of the patients used metformin and lisinopril. No significant difference was observed between the glycaemia of patients receiving glucose-friendly and non-friendly antihypertensive medication.

Keywords: Glycaemic Control; Diabetic-Antihypertensive Patients; Gombe State, Nigeria

Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterised by high blood sugar levels over a prolonged period^[1]. Hypertension, also known as high blood pressure (HBP) is a leading predictor of complications in diabetic patients^[2]. Hypertension is defined as a long-term medical condition in which the blood pressure in the arteries is persistently elevated between 130-140 mmHg systolic and 80-90 mmHg diastolic^[2]. Theories on antihypertensive-induced glycaemic defects are multifaceted. While some theories have been substantiated, others remain contradictory. These theories broadly fall into four categories: effects on peripheral blood flow, insulin receptors, liver function, and insulin release. Medications like alpha-blockers and ACEIs or ARBs, which enhance peripheral blood flow, may improve insulin sensitivity and glucose uptake. In contrast, drugs that diminish blood flow, such as nonselective beta-blockers, potentially reduce glucose disposal. This is also evidenced by the observation that lower capillary density in skeletal muscles increases susceptibility to the glycaemic effects of beta-blockers^[3]. Furthermore, various antihypertensive agents could alter glucose transport

proteins (GLUT 1 and GLUT 4), tyrosine kinase activity, or insulin receptor binding affinity, however, more information is needed to evaluate these effects [4]. Two other potential sources of altered glucose control include hepatic insulin resistance and impaired insulin release. Inhibition of insulin release can lead to hyperglycaemia, and beta-blockers have long been considered to inhibit insulin release through pancreatic beta-receptor blockade. Similarly, diuretic therapy has also been associated with impaired insulin release through the depletion of serum potassium [3]. However, because insulin levels are higher than normal in most patients with diabetes, this mechanism is unlikely to be of major importance. Hypertension in diabetic individuals markedly increases the risk and accelerates the course of complications [5]. Hypertension and diabetes mellitus (DM) represent two of the major risk factors for cardiovascular disease (CVD) [6]. In many individuals, hypertension and T2DM accompany other CVD risk factors such as visceral adiposity and dyslipidaemia, in the so-called Metabolic or Insulin Resistance Syndrome. This combination appears to accelerate the development of atherosclerosis, adding substantial cardiovascular risk beyond that of the individual risk factors [7]. Treatment of CVD risk factors such as hypertension aims primarily to reduce cardiovascular morbidity and mortality [8]. Some blood pressure-lowering drugs are known to have hyperglycaemic side effects, which may complicate or even counter the beneficial effects of antidiabetic medications. There is no doubt that β -blockers and diuretics have adverse metabolic effects. The European Society of Hypertension (ESH) guidelines therefore argue against the inclusion of diuretics and β -blockers in the medication for known diabetic hypertensive patients. The benefit of tight blood pressure and glucose control in diabetes has been extensively reported in previous publications [5]. However, these therapeutic goals are not easily or frequently reached in patients with diabetes. Furthermore, no conclusive evidence exists on whether treatment strategies that combine multiple antihypertensive agents and glucose control further reduce or increase the marked increase in macrovascular and microvascular complications typical of diabetic hypertensive patients [5]. This study aimed to describe the pattern of medications used in the management of diabetic-hypertensive patients and compare the glucose control between patients taking glucose-friendly and non-glucose-friendly blood pressure lowering drugs among patients attending clinic at the Gombe State Specialist Hospital, Gombe (GSSH).

Methods

Study Location

The survey was conducted at the State Specialist Hospital domiciled within Gombe Metropolis in North-east Nigeria. The metropolis lies between latitude 110 81 N and 110 241 N, longitude 110 021 E and 110 181 E. The temperature averages 30°C with an annual rainfall of 52 cm. The hospital is the largest state government-owned secondary health facility that is meant to cater for referral cases from other secondary (general hospitals) and primary health facilities scattered across the 11 local governments of the state. Hence the hospital patient demographics may be largely a fair reflection of the entire state. Based on the Nigerian National Population Commission Census 2006 figures projected for 2014, Gombe State has an estimated total population of about 3 million (3,028,459) at an annual growth rate of 3.2%. The metropolis has a projected population of 344, 804 inhabitants.

Study Design

A retrospective study design was employed for data collection from patients' case folders that met the inclusion criteria. Case folders of patients who attended the diabetes clinic between January 2018 to October 2019 were retrieved and reviewed.

Sampling technique

Unique identity numbers were assigned to folders of patients with diabetes and hypertension. Simple random technique was adopted and folders of patients that meet the inclusion criteria were selected for the study until the sample size was obtained.

Inclusion Criteria

Folders of adult diabetic-hypertensive patients aged ≥ 18 years, receiving oral anti-diabetic and anti-hypertensive therapy and attending clinic for not less than six months.

Exclusion Criteria

Folders were excluded from the study if the patient was pregnant, had type 1 diabetes or incomplete data.

Sample Size determination

This formula, $N = Z^2Pq/d^2$ was used to determine the sample size [9].

Where, n= Minimum sample size, Z= Standard deviation (1.96), P= Prevalence of DM in Nigeria 10.89 % [10], d= precision set at 5%, $q=1-P$ (1-0.5) = 0.5

Therefore:

$$\begin{aligned} n &= [1.96/0.05]^2 \times 0.1089 \times (1-0.1089) \\ &= 39.22 \times 0.1089 \times 0.8911 \\ &= 149.12 \end{aligned}$$

An attrition rate of 50% was considered, resulting in a minimum required sample size of 223 participants.

Data Collection Method

The data was collected from the patients' case folders using a predesigned data collection form. A total of 223 patients' folders were sampled and screened. The demographic and clinical characteristics, prescribed medications, blood pressure and fasting plasma glucose were recorded on the predesigned data collection form and analysed.

Ethical consideration

Ethical approval was obtained from the Research and Ethics Department of the Gombe State Ministry of Health according to the Declaration of Helsinki and Good Clinical Practice guidelines (ICH GCP) Ref No. MOH/ADM/621/VOL.I/124, dated 26 June 2019 and, all patient information extracted was handled confidentially.

Data Management

The data obtained was imputed into Statistical Product and Services Solution (SPSS) version 23.0 and analysed using descriptive statistics and Chi-square. Continuous variables were expressed as Mean/SD and categorical variables were expressed as frequencies/percentages in tables, while the two groups of blood pressure-lowering agents were compared using student t-test analysis.

Results

Of the 223 case folders of diabetic hypertensive patients retrieved and reviewed, 155 (69.5 %) were females. More than half (60.5 %) were aged 50 years and above, 215 (96.4 %) were married and two-thirds (66.8 %) had no formal education. Business entrepreneurs, civil servants, students, and farmers were 63.2 %, 19.3 %, 1.8 % and 15.7 % respectively.

Table 1: Socio-Demographic Characteristics of Patients (n = 223)

Variable	Frequency (n)	Percent (%)
Gender		
Male	68	30.5
Female	155	69.5
Age (years)		
18-28	1	0.4
29-39	21	9.4
40-50	66	29.6
Above 50	135	60.5

Marital Status		
Single	8	3.6
Married	215	96.4
Level of Education		
No formal education	149	66.8
Primary School	33	14.8
Secondary School	34	15.2
Tertiary Education	7	3.1
Occupation		
Civil Servants	43	19.3
Farmers	35	15.7
Businessmen	141	63.2
Student	4	1.8

More than half (59.2 %) of the patients in this study had normal Body Mass Index, 85 (38.1 %) were obese and 6 (2.7 %) underweight. Two-thirds were moderately active (68.2 %), nearly all (96.0 %) had a family history of diabetes, 91.9 % denied the use of alcohol and 99.6 % did not smoke. The duration of T2DM was between 2 and 6 years for over half (61.4 %) of the patients, all the patients (100.0 %) had Hypertension (100.0 %), dyslipidaemia (8.5 %) and others had Obesity (38.1 %).

Table 2: Clinical and Behavioural Characteristics of Patients (n=223)

Variable	Frequency (n)	Percent (%)
BMI Status (kg/m²)		
Less than 18.5	6	2.7
18.5 – 24.9	132	59.2
25 – 29.9	84	37.7
Above 30	1	0.4
Physical Activity		
Low	55	24.7
Moderate	152	68.2
High	16	7.2
Family History of DM		
Yes	5	2.2
No	214	96.0
Alcohol Consumption		
Yes	18	8.1
No	205	91.9
Smoking		
Yes	1	0.4
No	222	99.6
Duration of DM (Years)		
6mths – 1	39	17.5
2 – 6	137	61.4
7 – 12	34	15.2
13 and above	13	5.8
Comorbidities		
Hypertension	223	100
Dyslipidaemia	19	8.5
Obesity	85	38.1

The medications prescribed are presented in Table 3. The majority (98.7 %) of the patients received biguanides for the treatment of DM, followed by Sulphonylureas (67.3 %) and thiazolidinediones (21.1 %). The most prescribed antihypertensive in the study setting was Angiotensin-converting enzyme inhibitors (82%), followed by calcium channel blockers (39.5%), thiazide diuretics (23.3%), beta-blockers (13.9%), angiotensin receptor blockers (2.7%), centrally acting agents (0.9%), while 8.5 % used HMG-CoA Reductase Inhibitors for lipid treatment.

Table 3: Medication Prescribed for patients (n = 223)

Name of Drugs	Frequency (n)	Percent (%)
Antidiabetics		
Biguanides (BIG)	217	98.7
Sulphonylureas (SU)	150	67.3
Thiazolidinediones (TZD)	47	21.1
Antihypertensives		
<i>A. Glucose-non-friendly</i>		
Thiazide Diuretics (TD)	52	23.3
Beta-blockers (BBs)	31	13.9
<i>B. Glucose-friendly</i>		
Calcium Channel Blockers (CCBs)	88	39.5
Angiotensin Converting Enzyme Inhibitors (ACEIs)	182	82.0
Angiotensin Receptor Blockers (ARBs)	6	2.7
Centrally Acting (CA)	2	0.9
Antilipidemics		
HMG-CoA Reductase Inhibitors	19	8.5

An equal proportion of patients demonstrated hyperglycaemia and controlled glycaemic status (49.8 % vs. 49.8 %), while 0.4 % had hypoglycaemia.

Table 4: Patients' Distribution Based on Fasting Plasma Glucose (n=223)

FPG (mmol/L)	Frequency (n)	Percent (%)
Less than 3.9	1	0.4
3.9-7.2	111	49.8
Above 7.2	111	49.8

The test for comparison of glycaemic control between patients receiving glucose-friendly antihypertensive and non-glucose-friendly antihypertensive agents showed that there is no statistically significant difference between the groups (mean glucose 8.49 mmol/L vs. 8.75 mmol/L; $p = 0.639$).

Table 5: Comparison of Glycaemic Control of Patients on Glucose-Friendly and Non- Glucose-Friendly Antihypertensive Agents (n=223)

Anti-hypertensive Agents	N	Mean	SD	T-Test	Df	P
Glucose-friendly antihypertensive	153	8.49	3.79	-0.47	221	0.639
Non-glucose-friendly antihypertensive	70	8.75	4.25			

Dependent Variable: FPG- Fasting Blood Glucose, $p < 0.05$, SD-Standard deviation, n-frequency, Df-Degree of freedom

Discussion

This study sought to provide baseline data on drug utilisation and glycaemic control of diabetic-hypertensive patients receiving care at the SSHG between January 2018 and October 2019. Notably, the management of hypertension in diabetic patients remains a pivotal concern^[11], as underscored by current International Society of Hypertension (ISH) guidelines^[12]. These guidelines recommend the use of angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCBs) to achieve targeted blood pressure control ($< 140/90$ mmHg). This practice was reflected in the prescription patterns observed in this study with the majority of patients using ACEIs and CCBs (Table 3). Available epidemiological data recommends the use of ACEIs because of their reno-protective properties through lowering of proteinuria, tolerability and affordability^[13], while CCBs provide additional benefits to diabetic patients by slowing down the advancement of atherosclerosis, addressing intracellular calcium abnormalities that could be involved in the development of diabetic cardiomyopathy, and safeguarding against the escalation of chronic renal disease and cardiovascular events^[14,15].

The effective management of individuals with diabetes and hypertension necessitates the use of multiple medications. The careful selection of a treatment plan with favourable tolerability and simplified dosing is essential for optimising positive outcomes in this high-risk population. These findings align with existing literature, underscoring that the classes of antihypertensive agents have diverse effects on glucose tolerance, consistent with earlier research^[11,13]. The results also suggest that ACEIs and CCBs may be more favourable regarding glucose metabolism than thiazide diuretics and beta-blockers.

Table 4 showed that nearly 50 % of patients receiving diabetes care at SSHG had hyperglycaemia while a few demonstrated hypoglycaemia.

Similarly, poor glycaemic control has been reported among diabetic patients by various studies conducted in different parts of Nigeria, ranging between 34% and 74%^[16,17,18,19]. Poor glycaemic control increases the risk of developing diabetes complications which are the leading cause of blindness, chronic kidney disease, lower limb amputation, sudden cardiac death, and cerebrovascular disease among patients with DM^[20,21,22,23]. The inability to achieve target therapeutic goals may be due to various factors, including lack of diabetes awareness, weak health promotion activities and absence of medication therapy counselling services, especially in most resource-limited settings (RLS) like Nigeria^[24,25,26,27,28,29].

Comparing glycaemic control between patients who received glucose-friendly and non-glucose-friendly antihypertensive medications (Table 5) revealed that the mean glycaemic control for both groups was poor (8.49 mmol/L vs. 8.75 mmol/L). Various categories of antihypertensive drugs have demonstrated specific impacts on blood glucose metabolism. Specifically, certain agents such as β -blockers and thiazide diuretics have been associated with negative effects on blood glucose, in contrast to other classes such as ACEIs, angiotensin receptor blockers (ARBs), and CCBs^[30]. While this study did not reveal a statistically significant difference between the groups ($p < 0.639$), a systematic review of randomised controlled trials aimed at quantifying the impact of non-glucose-friendly antihypertensive agents on glycaemic control in adults diagnosed with diabetes clinically indicated a moderate increase in diabetic patients who received beta blockers and thiazide diuretics.^[31] The lack of a substantial distinction in glucose control among patients in the two groups could be attributed to factors such as study design, sample size, study duration, study population characteristics, and adherence to prescribed medication.

Conclusion

This study found that nearly half of the patients were unable to achieve satisfactory glycaemic control. Notably, there was no significant distinction between the glycaemic status of patients receiving antihypertensive agents deemed friendly to glucose and those of non-glucose-friendly counterparts. Nevertheless, it's worth mentioning that the utilisation of ACEIs and CCBs in this study aligns with international best practices and recommendations.

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Author Statement

Conflict of interest statement

The authors declared no conflict of interest.

Author contributions

Concept – P.P., E.A.D.

Design – P.P., E.A.D.

Supervision – E.A.D.

Resources – P.P., E.A.D.

Materials – P.P., E.A.D.

Data Collection and/or Processing – P.P., E.A.D.

Analysis and/or Interpretation – P.P., E.A.D.

Literature Search – P.P., E.A.D.

Writing – P.P.

Critical Reviews – P.P., E.A.D.

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