



CARDIOVASCULAR RISK FACTORS AND PRESCRIPTION PATTERN AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS IN NORTH-EAST NIGERIA

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ABSTRACT

Cardiovascular diseases are the leading cause of morbidity and mortality among diabetic patients. This study was a 12-months retrospective cross sectional audit of case folders of adult (>18 years) type 2 diabetic patients, who attended clinic at two (2) referral hospitals in North-East Nigeria, between June 2017 and May 2018. Patients' data including socio-demographic characteristics, cardiovascular risk factors, medication history and clinical characteristics were retrieved. The data were presented as proportions and percentages in tables and pie chart formats. The analysis was done using statistical package for social sciences (SPSS) version 21.0. Of the 807 case folders that were reviewed, 64.5% were female patients, with majority (61.3%) below 50 years of age and 90.2% were married. Over 50% had secondary/primary education and most (57.9%) were unskilled labourers. About one-third (34.6%) were engaged in moderate to regular physical activities. The prevalence of hypertension, dyslipidaemia and obesity was 84.8%, 5.1% and 47.1% respectively. More than three quarters of the patients (87%) were on multiple oral antidiabetic agents and metformin was the most prescribed medication (93.8%). The antihypertensive agents with the highest prescription rate was lisinopril (57.9%), while 50.9%, 6.5%, and 2.7% received low dose acetylsalicylic acid, lipid lowering agents and pregabalin respectively. Hypertension was the most prevalent cardiovascular risk factor in the study population, followed by overweight/obesity. The prescription rate of metformin and Lisinopril is commendable, but there is need to increase the use of statins and pregabalin in the study settings.

Keywords: Type 2 Diabetes Mellitus; Cardiovascular Risk Factors; Prescription Pattern; Nigeria

INTRODUCTION

Diabetes mellitus (DM) is defined as a chronic degenerative disease, which affect carbohydrate, protein and fat metabolism (ADA, 2009; WHO, 2021). It is characterized by persistent hyperglycaemia, resulting from insufficient insulin secretion or sensitivity or both (ADA, 2009; WHO, 2021). The prevalence of DM has risen to an epidemic status in recent times, with type 2 diabetes

mellitus (T2DM) accounting for approximately 95% of DM population worldwide (Chilton *et al.*, 2011; Saeedi, *et al.*, 2019; IDF, 2021). Sub-Sahara Africa (SSA) and other low- and middle-income countries (LMICs) bear the greatest burden of diabetes globally (IDF, 2017). The comorbid occurrence of hypertension, overweight/obesity and dyslipidaemia in persons with T2DM has been implicated in

the increasing incidence and prevalence of cardiovascular disease and mortality (Colosia *et al.*, 2013; Zazuli *et al.*, 2017).

In a systemic review of observational studies of 30 European and 26 Asian published research articles, Colosia and colleagues reported hypertension rates of greater than 70% in Asia and above 80% in Europe, while there were lower, but not less than 30% rates in North and South America (Colosia *et al.*, 2013). A case-controlled study in Lebanon reported 78.3% hypertension rates and 65.8% dyslipidaemia in patients with T2DM (Diab *et al.*, 2019), while in another study involving 2,784 T2DM patients from three Sub-Sahara African (SSA) countries, 71% of the participants had hypertension, 34% had hyperlipidaemia and 27% had obesity (Ekoru *et al.*, 2019).

Furthermore, literature search revealed that the prevalence of hypertension among patients with T2DM in Nigeria is between 31.9% and 85.5%, obesity occurs in 32.8% to 60%, while up to 39.6% have dyslipidaemia (Awosan *et al.*, 2013; Kayode *et al.*, 2015; Chen *et al.*, 2016; Abdulghani *et al.*, 2018; Mata-Cases *et al.*, 2019, David *et al.*, 2019). Most Nigerian studies are single facility-based research, with less than 500 participants, and without extensive study on the prevalence of cardiovascular risk factors among diabetic patients. Evidence has shown that the risk of long-term vascular complications such as peripheral arterial disease, coronary artery disease and stroke is exacerbated in the presence of hypertension, obesity and dyslipidaemia, leading to increased need for multiple medication use in patients with T2DM (Colosia *et al.*, 2013; Zazuli *et al.*, 2017; Govender *et al.*, 2019; Fuchs & Whelton, 2020). This study was aimed to estimate the prevalence of cardiovascular risk factors associated with T2DM and describe medication prescription pattern among T2DM

patients attending diabetic clinic at two health institutions in North-East Nigeria.

MATERIALS AND METHODS

Study Design and Setting

This study was a retrospective cross sectional audit of 807 randomly selected case folders of ambulatory patients with T2DM, attending clinics at Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH), Bauchi State and State Specialist Hospital Gombe (SSHG), between June 2017 and May 2018. Abubakar Tafawa Balewa Teaching Hospital is a tertiary hospital while SSHG is a secondary health facility located in the North-East region of Nigeria. Both institutions are situated within the state capitals of Bauchi and Gombe respective and serve as referral hospitals to other health centres within and outside the states.

Sample Size Determination

The following formula (Daniel, 1999; Pourhoseingholi *et al.*, 2013) was used to estimate the required sample size for individual study site:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where 'n' is the sample size, 'Z' is the statistic corresponding to level of confidence, 'P' is expected prevalence (that can be obtained from similar studies or a pilot study conducted by the researchers) and 'd' is precision (corresponding to effect size) at 95% confidence interval (CI). A total of 845 folders (768 + 10% attrition) were estimated for the two hospitals and 807 case folders of patients with T2DM were randomly selected, representing 95.5% of the required sample size.

Data Collection

A predesigned proforma for data collection was used to retrieve patients' socio-

demographic characteristics (age, gender, height, weight, educational status and occupational status), cardiovascular risk factors and prescribed medications, while patients with incomplete data were invited and their height (m²) and weight (kg) were measured using a stadiometre. The Body mass index (BMI) for each patient was computed in kilogram per metre squared (kg/m²) and categorized as underweight (< 18.5kg/m²), normal weight (18.5kg/m² – 24.9kg/m²) or overweight/obese (≥ 25.0kg/m²) (WHO, 2021).

Ethical Consideration

The study received ethical approval from the research and ethics committee (REC) of Abubakar Tafawa Balewa University Teaching Hospital, Bauchi State and Gombe State Ministry of Health, Gombe.

Data Analysis

The data obtained was entered into an excel spreadsheet on Microsoft office package and exported to Statistical Package for Social Sciences (SPSS) Version 20.0 (IBM Corp, Armonk, New York, USA). Data was analysed and presented as frequencies and proportions.

RESULTS

Socio-demographic Characteristics

A total of 807 case folders of patients with T2DM were assessed for the presence of cardiovascular risk factors. There were more female patients in the study (64.5%), with majority (61.3%) below 50 years of age and 90.2% were married. Over 50% had secondary/primary education and 57.9% were engaged in unskilled labours. Approximately one-third (34.6%) practiced moderate to regular physical activity (Table 1).

Table 1: Socio-demographic Characteristics of patients (n = 807)

Characteristics	Frequency (n)	Percentage (%)
Gender		
Male	286	35.5
Female	521	64.5
Age		
< 50	495	61.3
>50	312	38.7
Marital status		
Single	79	9.8
Married	728	90.2
Education		
No formal education	233	28.9
Primary/secondary	437	54.1
Tertiary	137	17
Occupation		
Unskilled worker	468	57.9
Skilled worker	182	22.6
Students	23	2.9
No paid worker	134	16.6
Physical Activity Status		
Low	528	65.4
Moderate	182	22.5
Regular	98	12.1

Cardiovascular Risk Factors

More than three-quarters (84.8%) of the population had hypertension, followed by 47.1% who were either overweight or obese, while few (5.1%) had dyslipidaemia (Table 2).

Table 2: Prevalence of Cardiovascular Risk Factors (n = 807)

Characteristics	Frequency (n)	Percentage (%)
Hypertension		
Present	684	84.8
Absent	123	15.2
Dyslipidaemia		
Present	41	5.1
Absent	766	94.9
Body Mass Index (kg/m²)		
< 18.5	76	9.4
18.5 -24.9	351	43.5
≥ 25.0	380	47.1

Medication Prescription

The review of 807 case folders revealed that 87% of patients received multiple medications, while 13% were on monotherapy (figure 1). Table 3 showed that the most prescribed antidiabetes agent was metformin (93.8%), followed by sulfonylureas {glibenclamide (44%), glimepiride (16%) and gliclazide (0.1%)}. Pioglitazone, a thiazolidinedione was prescribed in 10.2% of the population and 0.1% patient received sitagliptin (DPP-4 Inhibitor). The most prescribed antihypertensive agent were lisinopril (59.7%), belonging to the angiotensin converting enzyme inhibitors (ACEIs) and amlodipine (48.1%), a calcium channel blocker (CCBs), while bisoprolol and carvedilol which belong to beta/alpha-beta receptor blockers were the least prescribed (0.4%). The statins (atorvastatin and simvastatin) were prescribed in 5.5% patients for the management of lipids, while a fibrate (fenofibrate) was used in 0.1% patient. Approximately half (50.9%) and slightly more than one-quarter (26.7%) of

patients received acetyl salicylic acid and clopidogrel respectively to provide antiplatelet or antithrombotic activity, while pregabalin (2.7%), carbamazepine (3.0%) and diclofenac (1.0%) were prescribed to ameliorate neuropathic pains (Table 3)

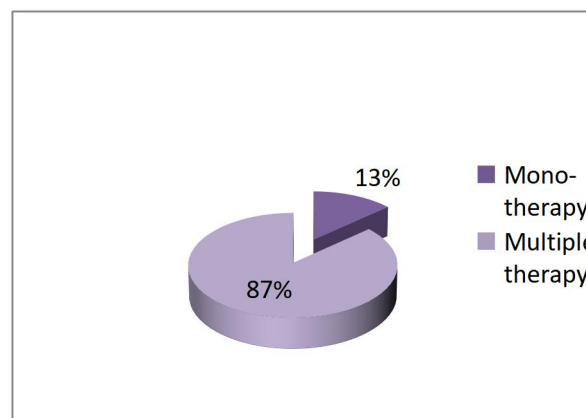


Figure 1: Proportion of Antidiabetes Agent Prescribed as Mono or Multiple Therapy

DISCUSSION

Socio-demographic Characteristics

The International Diabetes Federation (IDF) estimated that cardiovascular disease accounts for up to 80% deaths among people with DM and it is often associated with the comorbid occurrence of hypertension, obesity, dyslipidaemia in patients with T2DM (IDF, 2013). This study found that most of the patients were married female, below the age of 50 years and engaged in low to moderate levels of physical activity. Similar socio-demographic characteristics was observed in previous studies conducted in Nigeria (Enwere *et al.*, 2006; Adibe *et al.*, 2009; Jimoh *et al.*, 2011; Eze *et al.*, 2011; Dada *et al.*, 2021). This may be related to the fact that the health seeking behaviour of most urban dwellers in the country is relatively comparable and more female visit the public hospital compared to the male counterparts (Adams & Carter, 2011). But another study conducted in Saudi Arabia reported more

male (76.2%) visiting the clinic than female (23.8%) (Misbahuddin *et al.*, 2018).

Table 3: Prescribed Medication (n = 807)

Description	Medication	Frequency (n)	Percentage (%)
Antidiabetes Agents			
	Metformin	757	93.8
	Glibenclamide	355	44.0
	Gliclazide	1	0.1
	Glimepiride	129	16.0
	Pioglitazone	82	10.2
	Sitagliptin	1	0.1
	Insulin	8	1.0
Antihypertensive Agents			
	Nifedipine	23	2.9
	Amlodipine	337	41.8
	Lisinopril	482	59.7
	Losartan	38	4.71
	Telmisartan	6	0.7
	Bendrofluazide	84	10.4
	Amiloride Hydrochlorothiazide	9	1.1
	Spironolactone	11	1.4
	Atenolol	69	8.6
	Bisoprolol	3	0.4
	Carvedilol	3	0.4
Antilipidaemic Agents			
	Simvastatin	20	2.5
	Atorvastatin	24	3.0
	Fenofibrate	1	0.1
Others			
	Clopidogrel	215	26.7
	Acetyl salicylic Acid 75mg	411	50.9
	Pregabalin	22	2.7
	Carbamazepine	24	3.0
	Diclofenac	8	1.0

Cardiovascular Risk Factors

Evidence has shown that there is a strong correlation between DM and cardiovascular death, ranging from 1-3 in males and 2-5 in

females compared to non-diabetic individuals (Colosia *et al.*, 2013; Zazuli *et al.*, 2017; Sharma *et al.*, 2020). The prevalence of hypertension observed in this study was as high as 84.8%, while almost half of the patients were overweight or obese and only few (5.1%) had



dyslipidemia (Table 2). In a cross-sectional descriptive epidemiological study by Akin and Boluk, the prevalence of hypertension in 1024 Turkish type 2 diabetic patients was consistent with our result (84.8% vs 84.9%), while the prevalence of obesity in their population was slightly higher than the rate reported in this study (54.4% vs 47.1%) (Akin and Boluk, 2020). Similarly, studies conducted in Spain and Lebanon also demonstrated high prevalence of hypertension (72% and 78.3%) and approximately the same proportion of obesity (45% vs 47.1%) as observed in our study (Mata-Cases *et al.*, 2019; Diab *et al.*, 2019). A multi-centered study conducted in three SSA countries reported lower proportion of obesity (27%; 95% CI 25-29) in contrast to this study, while the same population demonstrated high prevalence of hypertension (71%; 95% CI 89-73) and moderate proportion of hyperlipidaemic cases (34%; 95% CI 32-36) (Ekoru *et al.*, 2019). Contrary to the low prevalence of dyslipidaemia observed in this study, some researchers reported prevalence rates of between 60% and 65.8% (Mata-Cases *et al.*, 2019; Diab *et al.*, 2019; Akin and Boluk, 2020). The differences may be due to the variations in cultural and feeding habits among different study populations. In addition, paucity of data with regards to lipid disorders in our study settings and other geographical differences between Africa, Europe and Asia could explain the observed differences.

Furthermore, it was also noted that some older studies conducted in Nigeria reported lower prevalence of hypertension (25% to 54.2%) (Osuntokun *et al.*, 1972; Okesina *et al.*, 1995; Chuhwak *et al.*, 2002; Unadike *et al.*, 2011; Odeyinka and Ajayi, 2017), but not less than 30% occurrence of dyslipidaemia and obesity (Awosan *et al.*, 2013). But in agreement with our findings, more recent studies in the country have shown higher proportions of hypertension (74% and 85.5%) and obesity (60% and 51.2%) in patients with T2DM (Onyenekwe *et al.*, 2019;

David *et al.*, 2019). This steady increase in cardiovascular risk factors among diabetic population in Nigeria from 25% in 1972 (Osuntokun *et al.*, 1972) to 85.5% in 2019 (David *et al.*, 2019) may be related to westernised lifestyle, nutrition transition, rapid urbanization, increased sedentary lifestyle, physical inactivity, ageing population and poor glycaemic control (Hu *et al.*, 2011; ADA, 2022).

Medication Therapy Prescription Pattern

Medication therapy, lifestyle intervention and routine blood glucose monitoring are collectively regarded as indispensable and complimentary cornerstone strategies in the management of DM. These strategies promote good glycaemic control and minimize the risk of developing complications (Chaudhury *et al.*, 2017). Of the 807 patients' case folders that were reviewed, 87% were on multiple medications, with 99.4% patients receiving oral antidiabetic medications and 0.6% on insulin therapy. Metformin was the most prescribed anti-diabetes agents (93.8%), while sitagliptin was the least preferred (0.1%). The finding in this study was similar to results of other studies conducted in Nigeria and India (Jimoh *et al.*, 2011; Ashutosh *et al.*, 2017; Pushpa *et al.*, 2020; Das *et al.*, 2021; Dada *et al.*, 2021), where between 67.1% and 97.4% patients received combination of oral anti diabetic medications. In a private medical facility based in South-West Nigeria, Amao and colleagues reported a total of 100% patients who received prescription containing metformin, while the least prescribed oral antidiabetic agents were vildagliptin and saxagliptin (Amao *et al.*, 2018). The use of metformin as a drug of first choice either alone or in combination with other antidiabetic agents in the management of T2DM is supported by international guidelines, especially because of its weight loss advantage, tolerability, little or no hypoglycaemic effect and affordability (ADA, 2019).



Sulfonylureas (SUs) were the second most preferred oral antidiabetic agents in the study settings, either as single agents or in combination with metformin. This finding is corroborated by other studies where 20% to 45% of study participants received SUs as monotherapy or in combination with metformin (Ashutosh *et al.*, 2017; Misbahuddin *et al.*, 2018; Das *et al.*, 2021). But our finding was not consistent with some studies where SUs were preferred as first-line medication (Yusuff *et al.*, 2008; Hasamnis & Patil, 2008; Agarwal *et al.*, 2014). The preference for metformin as drug of first choice in this study, followed by SUs is supported by the result of a recent survey among 103 prescribers in Saudi Arabia (Allyhiani *et al.*, 2022). Majority (95%) subscribed to the use of metformin as first-line medication and agreed that SUs could be added for improved beneficial effect or in cases where metformin is contraindicated. The prescribers preferred the combination of DPP4- inhibitor plus metformin only in patients with established cardiovascular disease as recommended by the guidelines (Allyhiani *et al.*, 2022; ADA, 2022). Evidence has shown that the DPP-4 inhibitors have commendable adverse-effect profile, with low risk of hypoglycaemic event, no effect on weight and very effective in patients who are close to their target glycated haemoglobin concentration, but often experience elevated post prandial hyperglycaemia (Rolee & Bridgeman, 2010; Ashutosh *et al.*, 2017).

In line with recommendations and international best practice (ADA, 2022), the most preferred antihypertensive agents in this study were ACEIs (Lisinopril: 59.7%) and CCBs (Amlodipine: 41.8%). Similar result was reported by Jimoh *et al.* 2011, where 38.2% out of 206 diabetic-hypertensive patients received ACEIs or angiotensin receptor blockers (ARBs). But our study reported a minimal use of Losartan (4.71%), an ARB. The use of ACEIs or ARBs is encouraged because of their renoprotective property, cost effectiveness and

tolerability (ADA, 2019). Furthermore, it was observed that the use of lipid lowering drugs was scanty (5.6%) in this study. This is a variation from the ADA guidelines, which recommends the prescription of statins and other lipid lowering medications for overweight/obese patients with T2DM who are ≥ 40 years, to minimize the risk of developing cardiovascular complications (ADA, 2019). Other drugs that were prescribed in the study population include low dose acetylsalicylic acid (ASA 75mg) (50.9%), clopidogrel (26.7%), carbamazepine (3%) and pregabalin (2.7%). This practice is consistent with guidelines and was done to treat and/or prevent atherothrombotic events and diabetic peripheral neuropathy (DPN), which are commonly associated with cardiovascular morbidity and mortality in patients with T2DM (Fedele *et al.*, 1997; Frampton & Scott, 2004; Patel *et al.*, 2014; Salam *et al.*, 2019; Liang *et al.*, 2020). These events occur through a complex mechanism involving platelets, calcium, hyperglycaemia and insulin resistance, coupled with the short platelets lifespan caused by the presence of DM. The end result is increased platelet aggregation and adhesion, which culminates in cardiovascular complications such as stroke (also known as cerebrovascular accident), coronary artery disease or peripheral arterial disease (Kario *et al.*, 1995; Keating *et al.*, 2003; Ferreira *et al.*, 2004; Salam *et al.*, 2019).

CONCLUSION

This study found that most diabetic patients in the two study settings had hypertension and about half were either overweight or obese. The use of metformin as drug of first choice, lisinopril and antiplatelet agents is supported by international guidelines and quite commendation. However, there is need to improve on the prescription of DPP-4 Inhibitors, statins and anti-neuropatic agents. We recommend a prospective and intervention study to address diabetes comorbidity, complications and



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improve the standard of care in ATBUTH, Bauchi and SSHG.

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