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Prescription Pattern and Glycaemic Control Using Glycated Haemoglobin in Type 2 Diabetic Patients: A Cross-Sectional Survey

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Abstract:-

➢ ***Background:-***

Irrational medication prescribing and paucity of glycated hemoglobin testing in resource-limited settings leads to poor health outcomes in patients with type 2 diabetes mellitus

➢ ***Objectives:***

This study aims to describe prescription pattern and assess glycaemic control using Glycated hemoglobin among type 2 diabetic patients attending clinic at Abubakar Tafawa Balewa University Teaching Hospital. Bauchi, Nigeria.

➢ ***Methods:***

A 6 months prospective, cross sectional, observational survey, conducted in 200 patients with uncontrolled type 2 diabetes mellitus (≥ 7mmol/L fasting blood glucose). Prescribed medications and socio-demographic characteristics were obtained through face-to-face interview, body mass index was computed using weight and height measurements and 4µl sample of capillary blood obtained from finger prick of individual subject was used for Glycated haemoglobin test. Data was analysed using SPSS version 20.0 and results were expressed in descriptive and inferential statistics.

➢ ***Results:***

A total of 200 type 2 diabetic patients, with uncontrolled glycaemia participated in the study. Majority were ≥ 40 years (82.5%), female (67.5%), married (86.5%) and engaged in low level of physical activity (81%). About half had no formal education (47%) and 51.5% had family history of diabetes. (Metformin was the most commonly prescribed antidiabetes agents (91.5%), while only 5.5% of the study population received antilipidaemic medication. Furthermore, chi square analysis showed that no factor was associated with uncontrolled glycaemia using Glycated haemoglobin test ($P > 0.05$).

➢ ***Conclusion:***

Insufficient prescribing of antilipidaemic agents was observed and about half (46%) of the participants had controlled glycaemia using Glycated haemoglobin test as against 100% using fasting glucose test. Interprofessional Collaborative care, involving physicians, pharmacists, patients and other health care providers, as well as point-of-care Glycated haemoglobin testing are recommended to ensure rational medication prescribing and improved care outcomes.

Keywords:- *Prescription Pattern, Antidiabetes, Glycated Haemoglobin, Type 2Diabetes, Nigeria.*

I. INTRODUCTION

The prevalence of Diabetes mellitus (DM) is growing exponentially across the globe, with figures rising from 285 million in 2009 to 463 million in 2019 [1]. This number is projected to hit 578 million and 700 million by 2030 and 2045.

[2]. Furthermore, 79% of adults (20-79 years) with diabetes live in low- and middle-income countries (LMICs), including Africa, with majority located in Sub Saharan Africa (SSA) [1]. According to a 2018 meta-analysis, the pooled mean prevalence of diabetes in Nigeria was approximately 5.8%, with the highest burden (9.8%) observed in the oil-rich South-South and lowest (3.0%) in North- West region of the country [3]. This represent a 3.6% increase over the 1997 national survey, which reported a 2.2% prevalence of DM in Nigeria [4].

Type 2 diabetes mellitus (T2DM) accounts for over 90% of all cases of diabetes worldwide, being accelerated by rapid, unplanned urbanization, sedentary lifestyle, physical inactivity, aging population and increased obesity in many LMICs like Nigeria [1,3]. There are atleast 6 classes

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of oral antidiabetes agents (OAAs) currently used in the management of T2DM, viz: biguanides (BGs), sulphonylureas (SUs), thiazolidindiones (TZDs), alpha glucosidase inhibitors (α-GIs), dipeptidyl peptidase-4 inhibitors (DPPIs-4) and meglitinides, while injectable, such as insulin, amylin analogs and glucagon-like peptide-1 receptor agonists are also used where and when necessary [5]. It is however, very worrisome that despite the myriad of antidiabetic medications, most people living with T2DM do not attain consistent optimal glycaemic control [6-8]. The prevalence of poor glycaemic control in Nigeria ranges from 46% to 70.7% [9- 16], with the highest prevalence reported in a retrospective audit of 308 out- patients attending clinic at a tertiary facility in South-West [14] and the lowest in South- South region.

Although, fasting blood glucose (FBG) test, random blood glucose (RBG) test, A1C test and 2 hours post prandial or oral glucose tolerance test (OGTT) are all recommended for diagnosis [17,18], A1C is preferred over the others because epidemiological data have shown that it provide average blood glucose status for the past 8 to 12 weeks, making it more suitable for monitoring long term glycaemic control, screening individuals at high risk of diabetes and predicting the risk of developing chronic complications [19,20]. The emergence of A1C as a better index of glycaemic control in clinical trials in the 1980's [21], with supporting data from the Diabetes Control and Complications Trials (DCCT) and United Kingdom Prospective Diabetes Study in the 90's [22,23], completely changed the paradigm in diabetes management [20]. Moreover, detection of chronic uncontrolled glycaemia among diabetic populations, early identification of prediabetic individuals and patients at risk of developing diabetic complications will guide physicians in making prompt, informed, evidence-based decisions with regards to patient management. The use of A1C in DM patients is very common in high income countries (HICs) [24], while reverse is the case in resource-limited settings [9,11,14]. Furthermore, most studies conducted in Nigeria were retrospective, while some included both type 1and type 2 diabetic patients and thereby liable to selection and information bias. This study is therefore aimed to prospectively describe prescribing pattern and assess baseline glycaemic control using A1C test in patients with uncontrolled T2DM (FBG ≥ 7mmol/L) in a resource-limited setting.

II. METHODS

➢ *Study Setting, Design and Population*

This was a prospective, cross sectional, observational study conducted between December 2017 and May, 2018 at the diabetic clinic in Abubakar Tafawa Balewa University Teaching Hospital, Bauchi North-East Nigeria. The tertiary health facility has over 700 bed space and serves as a referral centre to other tertiary, secondary and primary health institutions within the state and beyond. The diabetic clinic is operated once every week, with approximately 100 to 120 patients receiving care from healthcare providers. A total of 206 type 2 diabetic patients with FBG ≥ 7mmol/L [14] were purposively selected, but only 200 subjects with regular clinic attendance, 18 years or older, diagnosed of diabetes for more than 6 months and signed written informed consent form were recruited for the study. Patients with Pregnancy-induced diabetes, those who have suffered amputation and taking haematinic medication(s) were excluded, to rule out false positive results.

➢ *Sampling Procedure and Sample Size Determination*

Patients with fasting blood glucose ≥7mmol/L were purposively recruited until the calculated study sample size was obtained. The sample size was determined as 187, using excel sample size calculator and the Cochran formula for population less than 10,000 [25]. With the addition of 10% attrition, a total of 206 subjects were expected to participate in the study, but the final number of patients was 200, representing 97.1% participation. Six 6 patients were declined based on the study inclusion/exclusion criteria.

➢ *Data Collection*

Patients with FBG ≥7mmol/L were invited by the research Pharmacist for interaction and those who accepted to sign informed consent form were recruited and interviewed. Socio-demographic characteristics including age, gender, marital status, level of education, occupational status, level of physical activity, alcohol consumption level and smoking status were collected using a researcher-administered proforma for data collection, Glycated haemoglobin test was conducted by the research Pharmacist using a Clover A1C Analyser™ (EuroMedix), based on a 4µl sample of capillary blood from the finger prick of individual subjects. Weight and height of patients were taken using weighing scale and stadiometre and body mass index (BMI) was computed by dividing weight in kilogramme (kg) over height in metre squared (m^2) [26], while blood pressure of subjects was measured using sphygmomanometer and stethoscope. Other information collected include family history of diabetes, duration of diabetes, comorbid conditions and prescribed medications.

➢ *Ethical Considerations*

The health research and ethics committee of the hospital approved the study proposal, with reference number: (REC No. 08/10/2017). Confidentiality of patient's information was ensured by assigning unique identification number to each participant in the study.

➢ *Statistical Analysis*

Patients' socio-demographic and clinical characteristics were presented using descriptive analysis, with Continuous data reported in mean and median depending on the items' distribution, while categorical variable were expressed in frequencies and proportions using Statistical package for social sciences (SPSS) Version 20.0 (IBM Corp, Armonk, New York, USA). Univariate analysis was employed to explore factors associated with poor glycaemic control (A1C ≥ 7%)

III. RESULTS

Of the 200 eligible participants, 135 (67.5%) were female and majority (165, 82.5%) were 40 years or older, with mean age of 50±11 years. Most (173, 86.5%) were married, about half (47%) had no formal education, 62% did no paid job, majority (96.5%) either do not drink alcohol or drink occasionally, 81% engaged in low physical activity and slightly above 50% had family history of diabetes (Table 1).

Characteristics	Categories	Frequency (n)	Percent (%)
Gender	Female	135	67.5
	Male	65	32.5
Age (years)	<40	35	17.5
	≥40	165	82.5
Age (years ±SD)*	Mean	50±11	
Marital Status	Single	27	13.5
	Married	173	86.5
Educational Status	No Former Education	94	47.0
	Primary Education	27	13.5
	Secondary Education	38	19.0
	Tertiary Education	41	20.5
Occupation	Unskilled Worker	32	16.0
	Skilled Worker	42	21.0
	Student	2	1.0
	No Paid Worker	124	62.0
Alcohol Consumption	Occasional Drinker	193	96.5
	Light Drinker	5	2.5
	Heavy Drinker	2	1.0
Physical Activity	Low	162	81.0
	Moderate	36	18.0
	Regular	2	1.0
Family History of Diabetes	Absent	66	33.0
	Present	103	51.5
	Not Sure	31	15.5

Table 1:- Socio- Demographic of Participants (n = 200)
***** SD –Standard Deviation

In table 2, about half (49%) of the participants have had diabetes for 5 to 10 years, with mean BMI of 26.89±5.24 Kg/m^2. Majority (136, 68%) were overweight and obese, 146 (73.0%) had high blood pressure, 145 (72.5%) were dyslipidaemic, with a mean fasting blood glucose of 10.62±3.62 for all recruited patients. The assessment of A1C revealed that 92(46%) had less than 7% A1C, while slightly more than half (108, 54%) were uncontrolled (A1C ≥ 7%).

Characteristics	Categories	Frequency (n)	Percent (%)
Duration of Diabetes (years)	<5	76	38.0
	5-10	98	49.0
	>10	26	13.0
	Median	6 (0.7–23 years)*	
Body Mass Index (BMI)	Mean	26.89±5.24	
BMI category	Under Weight	8	4.0
	Normal Weight	56	28.0
	Over Weight	87	43.5
	Obese	49	24.5
Hypertension	Absent	54	27.0
	Present	146	73.0
Dyslipidaemia	Absent	55	27.5
	Present	145	72.5
Fasting Blood Glucose(mmol/L)	Mean	10.62±3.62	
Glycated Haemoglobin A1C (%)	Uncontrolled FPG Mean Controlled (< 7)	200 7.4±1.592	100.0 46.0
	Uncontrolled (≥ 7)	108	54.0
* Range; FBG: Fasting blood glucose			

Table 2: Clinical Characteristics of Participants (n = 200)

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The figure below represent the pattern of antidiabetes agent prescribed in the research setting (Figure 1). Metformin was the most prescribed agent (183, 91.5%), closely followed by sulphonylureas (glibenclamide - 49%, glimepiride – 19.5% and glclazide – 4%), while pioglitazone, insulin and fixed-dose combination of Metformin and Sitagliptin were used in 63 subjects (31.5%), 24 (12%) and 10 (5%) respectively.

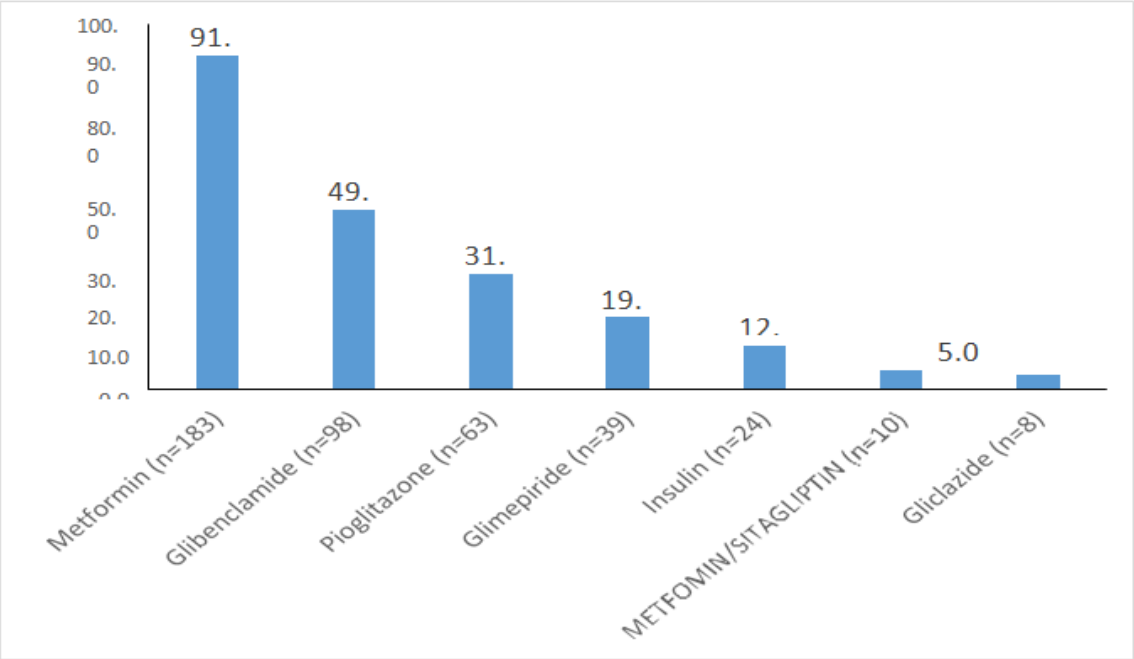

Fig 1:- Distribution of Antidiabetic Agents

In figure 2, 132 (66%) participants used blood pressure lowering agents while only 11 (5.5%) had anti lipidaemic prescription. The most prescribed blood pressure medication was lisinopril (111, 55.5%), while amlodipine and nifedipine (calcium channel blocker) were prescribed in 81 subjects (40.5%). Thirteen patients also received losartan (angiotensin receptor blocker), while only 1 (0.5%) had atenolol.

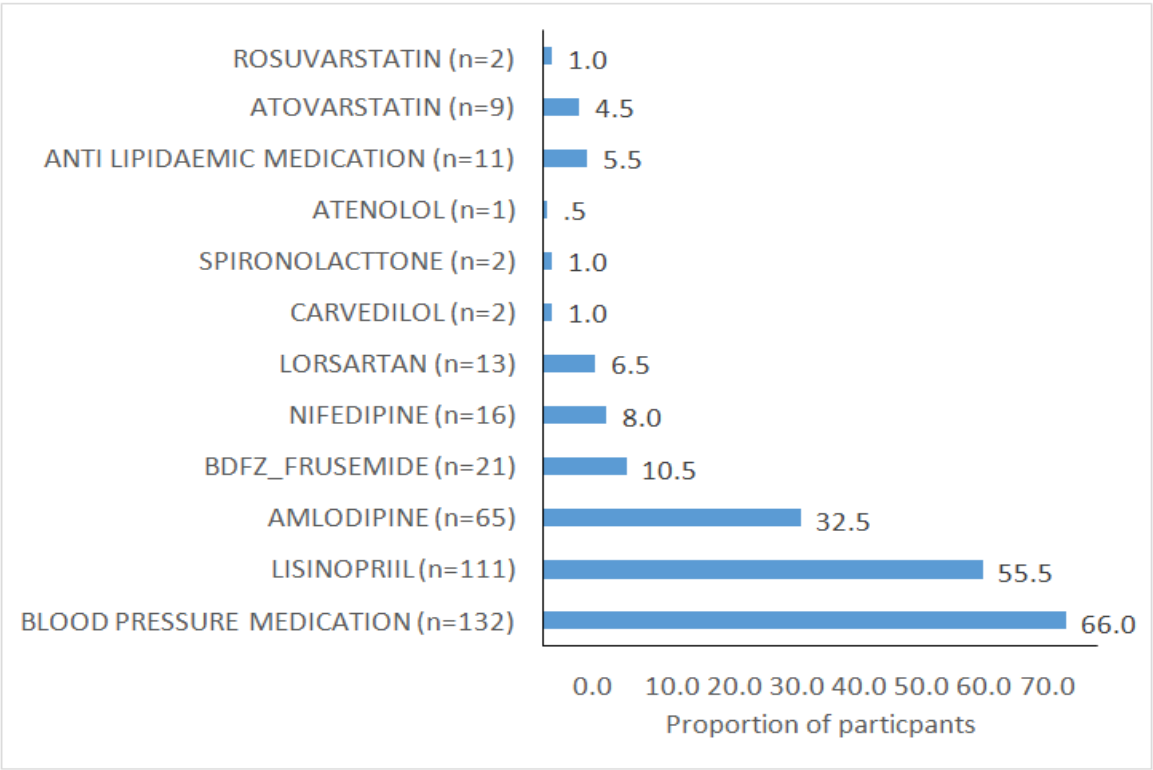

Fig 2:- Distribution of anti lipidaemic and antihypertensive agents used in the management of patients

The assessment of socio-demographic Characteristics showed that none was significantly associated ($P > 0.05$) to poor glycaemic control (Table 3).

		AIC <7%	AIC ≥7%	Chi-square (P value)
Gender	Female	50 (40.65)	73 (59.35)	1.68 (0.2)
	Male	30 (50.85)	29 (49.15)	
Age (years)	<40	15 (45.45)	18 (54.55)	0.53 (0.91)
	40-49	26 (47.27)	29 (52.73)	
	50-59	24 (42.11)	33 (57.89)	
	4.00	15 (40.54)	22 (59.46)	
Education	No Formal Education	44 (49.44)	45 (50.56)	2.77 (0.43)
	Primary	11 (44)	14 (56)	
	Secondary	10 (33.33)	20 (66.67)	
	Tertiary	15 (39.47)	23 (60.53)	
Occupation	Unskilled worker	11 (37.93)	18 (62.07)	0.87 (0.83)
	Skilled worker	16 (41.03)	23 (58.97)	
	Student	1 (50)	1 (50)	
	No paid worker	52 (46.43)	60 (53.57)	
Alcohol	Occasional/non-drinker	78 (44.32)	98 (55.68)	0.62 (0.73)
	Light drinker	1 (25)	3 (75)	
	Heavy drinker	1 (50)	1 (50)	
Activity	Low activity	67 (44.97)	82 (55.03)	0.44 (0.8)
	Moderate activity	12 (38.71)	19 (61.29)	
	High activity	1 (50)	1 (50)	
Duration	<5	34 (50.75)	33 (49.25)	1.99 (0.37)
	5-10	36 (40)	54 (60)	
	>10	10 (40)	15 (60)	
BMI status	Under weight	2 (33.33)	4 (66.67)	0.6 (0.89)
	Normal weight	22 (43.14)	29 (56.86)	
	Over weight	34 (43.04)	45 (56.96)	
	Obesity	22 (47.83)	24 (52.17)	
Hypertension	Absent	23 (46)	27 (54)	0.117 (0.73)
	Present	57 (43.18)	75 (56.82)	
Dyslipidaemia	Absent	26 (50)	26 (50)	1.08 (0.3)
	Present	54 (41.54)	76 (58.46)	
Overweight	Absent	47 (45.63)	56 (54.37)	0.27 (0.6)
	Present	33 (41.77)	46 (58.23)	
Obesity	Absent	60 (45.45)	72 (54.55)	0.438 (0.51)
	Present	20 (40)	30 (60)	

Table 3: Factor Associated with Uncontrolled Blood Sugar

IV. DISCUSSION

Appropriate medication education and counselling by Pharmacists and the use of A1C test results will provide prescribers, patients and indeed all caregivers with basic information required to monitor long term glycaemic control and ensure achievement of desired treatment outcomes in patients with T2DM. In a cross-sectional, prospective, observational survey of 200 patients with T2DM, it was observed that majority of the sampled population were female. Similar female-to-male ratio was observed in previous studies in Nigeria [27- 30], but not consistent with others conducted in Tanzania, India and Saudi Arabia [31-33]. The reason for having more high proportion of female in this study may be attributed to the fact that females visit public health facilities than male [34] and the high prevalence of obesity and insulin resistance is reported among female [35].

Similarly, mean±SD age of 50±11 years reported in the current study is consistent with previous figures (48.99±9.2 years; 46.5±12.5 years) obtained in Nigeria [36], but lower than results from the Netherlands (67 years), Spain (60.5±12.8 years) and India (56.9±12.55 years) [37-39]. The variance may be explained by documented evidence that 45 to 50 years represent the peak incidence age range for diabetes in Nigeria and ageing as a major risk factor for the development of the disease [40,41]. A mean BMI of 26.89±5.24 Kg/m^2 and 68% of overweight and obese patients in the studied population is corroborative of result obtained in an Indian study [32] and a testimonial of the fact that only few participants engaged in regular physical activities. This study demonstrated a substantially high prevalence of hypertension and dyslipidaemia, which in

agreement with the result of a case- controlled Lebanese study, conducted in 2019. The study observed that hypertension and dyslipidaemia were present in 78.3% and 65.8% patients with T2DM [42]. Many studies outside Nigeria also reported prevalence of hypertension ranging from 58.4 to 72%, while dyslipidaemia occurred in up to 60% of patients [43-45]. Previous studies in different parts of African and Nigerian reported lower prevalence of hypertension between 30% and 54% [46- 49], but this is changing as demonstrated in a 2019 study conducted in Enugu state, Nigeria which found the prevalence of hypertension among diabetic patients to be as high as 74%. Similarly, in a multi- country Sub-Saharan African study, involving 2,784 T2DM patients, Ekoru and colleagues established that the most common comorbidities among participants were hypertension (71%; 95% Cl 89-73), hyperlipidaemia (34%; 95% Cl 32-36), and obesity (27%; 95% Cl 25-29) [50]. The observed high prevalence of hypertension (73%), dyslipidaemia (72.5%) and overweight/obesity (68%) in the current study may be partly attributed to low physical activity, poor glycaemic control and the adopted study design (using A1C measure on patients already certified uncontrolled by FBG test). Moreover, studies have shown that T2DM patients are more likely to have hypertension, which may even occur at the point of diagnosis of T2DM [51-53], while T2DM, obesity, dyslipidaemia and hypertension are regarded as components of metabolic syndrome, with an overlapping aetiology and pathophysiology [50,54].

Baseline assessment of participants classified all 200 patients to have uncontrolled glucose (FBG ≥7mmol/L), while the glycated haemoglobin test indicated that 46% out of the same population had controlled glycaemia (A1C <7%). This clearly demonstrate the need to encourage the use of A1C testing for glucose monitoring in patients with T2DM. Although, the use of A1C is almost non- existent in most developing Countries [55], it is regarded as a better index for monitoring chronic glycaemic control and predicting risk of developing complications [20,21,23]. Moreover, FBG is substantially affected by daily blood glucose fluctuations and highly subjective, making it an unreliable indicator [56], as observed in this study. However, the combination of both A1C and FBG has been recommended for patients with ≥5.55mmol/L FBG [57]. This variation in the proportion of patients with uncontrolled FBG and A1C (100% vs 54%) is a reason for great concern, as the FBG results could have erroneously influenced management decision, including change of medication, dose increase or addition of new medication.

Rational prescribing of oral antidiabetic medication is required to ensure optimal care outcomes in patients with T2DM. Biguanide (Metformin) and sulphonylureas (Glibenclamide and Glimepiride, Gliclazide) were the most prescribed medications, closely followed by Thiazolidinedione (pioglitazone). The result is consistent with most studies conducted among diabetic patients in Nigeria and other parts of the world [5,29,31,33,58,59]. Insulin was prescribed in 12% of studied participants while 5% were prescribed fixed-dose combination (FDC) of Sitagliptin/Metformin. Expectedly, the same scenario was reported in other studies [60,61], since individual in this category (T2DM) are not insulin dependent and the low prescription of FDC may be attributed to high cost and lack of dosage flexibility. Contrary to our findings, few studies have shown increased prescribing of insulin-based therapy in 32.2% to 43.6% participants [29,32] and this may be related to declined pancreatic function in T2DM patients. Hypertension was the most common comorbidity in the studied population and thus antihypertensive agents were widely prescribed, with angiotensin converting enzyme inhibitors/angiotensin receptor blockers (Lisinopril/Losartan) being the most prescribed blood lowering medication, followed by calcium channel blockers (Amlodipine and Nifedipine) and diuretics (Bendrofluazide, Furosemide and Spironolactone). This pattern was also reported in previous studies within and outside country [29, 31], but not supported for use in black hypertension [23,62,63].

The low prescribing of antilipidaemic agents (Rosuvastatin 1% and Atorvastatin 4.5%) was inconsistent with documented evidence demonstrated by large-scale randomized controlled trials and observational studies [64], as well as recommendations provided by the American Diabetes Association [65,66]. This may be related to cost or ignorance of the guideline for statin prescription in T2DM patients with multiple risk factor [20].

Although, chi square analyses failed to establish an association between sociodemographic characteristics and uncontrolled glycaemia in this population, it is however reported in literature that gender, duration of diabetes and comorbidity are part of factors responsible for poor glycaemic control in patients with T2DM [10,68,69].

V. CONCLUSION

The prescribing pattern for antidiabetic agents was consistent with recommended guidelines while prescription of antihypertensive and antilipidaemic agents were not. Contrary to the FBG results at baseline, 46% of patients earlier regarded as having poor glucose control (FBG ≥ 7mmol/L) were found to be normoglycaemic based on A1C test. Thus, Pharmacists should work with prescribers to ensure rational prescribing, especially in diabetic patients with comorbidities and the use of Glycated haemoglobin test is recommended in addition to FBG test, to ensure effective monitoring of glycaemic control, prediction of complications and informed decision-making by prescribers.

Conflict of Interest: Authors declare no conflict of interest

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