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Original Research

Effect of number and type of antidiabetes medications on adherence and glycemia of ambulatory type 2 diabetes patients in southwestern Nigeria

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ABSTRACT*

Objective: To determine the influence of number and type of antidiabetes medications on adherence and glycemia of ambulatory type 2 diabetes patients in southwestern Nigeria.

Methods: A cross-sectional study using pre-tested structured questionnaire among 176 consented patients recruited from the endocrinology clinics of two teaching hospitals between November, 2010 and January, 2011; and a retrospective review of case notes of the cohort for details of prescribed medications and blood glucose values. Descriptive statistics were used to summarize the data. Tests of proportions were evaluated using Chi-square or Fisher's exact test as appropriate. The differences in mean fasting blood glucose (FBG) between and among categorical variables were compared using student t-test and ANOVA respectively, with $p<0.05$ considered significant.

Results: Mean number of prescribed medications was 4.6±1.4. Almost two thirds 103 (60.6%) were placed on >4 medications. Adherence was better among patients on >4 medications compared to those on ≤4 medications (p=0.05). However, patients on >4 medications were mostly older adults (>60 years of age), and they were in the majority (66.7%) who had tertiary education compared to 33.3% of those on ≤4 medications who had tertiary education (p=0.02). Adherence rates to antidiabetes medications were in the ranking of oral antidiabetes medications (OAM) alone (50.0%) > insulin plus OAM (44.0%) > insulin alone (41.7%) with no significant difference (p=0.77). There was a significant difference in mean FBG among patients on >4 medications (172.1 ±61.1mg/dL) versus (198.8 ±83.8mg/dL) among those on ≤4 medications (p=0.02).

Conclusion: Prescribing more than four medications is linked to improved adherence and glycemic outcome. However, age and educational background of patients are important factors that need to be considered when prescribing multiple medications for type 2 diabetes.

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Keywords: Medication Adherence; Blood Glucose; Polypharmacy; Health Knowledge, Attitudes, Practice; Diabetes Mellitus, Type 2; Nigeria

EFECTO DEL NÚMERO Y TIPO DE ANTIDIABÉTICOS EN LA ADHERENCIA Y LA GLUCEMIA DE PACIENTES AMBULATORIOS CON DIABETES TIPO 2 N EL SUROESTE DE NIGERIA

RESUMEN

Objetivo: Determinarla influencia del número y tipo de medicamentos antidiabéticos en la adherencia y la glucemia de pacientes con diabetes tipo 2 en el suroeste de Nigeria.

Métodos: Estudio transversal utilizando un cuestionario pre-estructurado en 176 pacientes que aceptaron, reclutados en la clínica de endocrinología de dos hospitales Universitarios entre noviembre 2010 y enero 2011; y revisión retrospectiva de las notas clínicas de la cohorte para recopilar los detalles de medicamentos prescritos y valores de glucemia. Se utilizó estadística descriptiva para presentar los datos. Las proporciones se analizaron usando test chi-cuadrado o pruebas exactas de Fischer cuando fue apropiado. La diferencia entre las medias de glucemia en ayuno (FBG) se compararon usando t-test y ANOVA, considerando significativos $p<0,05$.

Resultados: La media de medicamentos prescritos fue de 4,6±1,4. Casi dos tercios, 103 (60,6%), tenían >4 medicamentos. La adherencia era mejor entre los pacientes con >4 medicamentos comparados con los de ≤4 medicamentos (p=0,05). Sin embargo, los pacientes con >4 medicamentos eran mayoritariamente adultos mayores (>60 años) y en su mayoría (66,7%) tenían educación terciaria, comparado con el 33,3% de los de ≤4 medicamentos con educación terciaria (p=0,02). Las tasas de adherencia a medicamentos antidiabéticos estaban en el margen de los antidiabéticos orales solos (AOS) (50,0%) > insulina más AOS (44,0%) > insulina sola (41,7%) sin diferencias significativas p=0,77). Hubo diferencia significativa en la FBG entre los pacientes con >4 medicamentos contra los de ≤4 (172.1±61.1mg/dL vs. 198.8±83.8mg/dL, respectivamente. p=0,02).

Conclusión: Prescribir más de cuatro medicamentos está asociado con una mejoría de la adherencia y de resultados de la glucemia. Sin

embargo, la edad y la escolaridad son factores importantes que deben considerarse cuando se prescriben medicamentos para la diabetes tipo 2.

Palabras clave: Cumplimiento de la Medicación; Glucemia; Polimedicación; Conocimientos, Actitudes y Práctica en Salud; Diabetes Mellitus Tipo 2; Nigeria

INTRODUCTION

Non-adherence to prescribed antidiabetes regimens has been identified as the most challenging aspect of diabetes control which continues to be a problem for healthcare providers, and a major concern for public health.[1-5] Diabetes mellitus is a chronic disease with increasing prevalence and socioeconomic burden.[6-8] The rising scourge of type 2 diabetes has been attributed to population growth, aging, urbanization and increasing rate of obesity and physical inactivity.[8-10] The multiple variables (medication, diet and lifestyle modifications) to be considered in diabetes management might also have an influence on the increasing incidence of non-adherence among patients.[11]

Numerous studies[5,12-19] have shown that poor adherence to medication is largely responsible for patient's failure to achieve and maintain adequate glycemic control. However, optimal glycemic control is necessary in ensuring good diabetes outcome and reduction in the risk of complications as well as morbidity and mortality of type 2 diabetes.[17,20-24] The reasons for non-adherence to prescribed medications among patients with chronic illness including type 2 diabetes are varied.[25,26] The factors predisposing to low adherence rates include multiple and complex drug regimens, financial constraints, delayed consequences of stopping medication, ambulatory treatment and advanced age.[27,28]

The consensus is that number of medications prescribed for a patient is inversely correlated with adherence to treatment regimen.[29-31] However, possible reduction in adherence with multiple medications has been cited as an important issue among patients with type 2 diabetes who are expected to take more than one medication to control hyperglycemia and the associated metabolic risk factors of hypertension and dyslipidemia which are common comorbid among diabetes patients.[31-33] Nonetheless, adherence research among patients on chronic medications including type 2 diabetes is still a challenge[34] especially in developing countries like Nigeria, and it remains unclear whether number and type of prescribed antidiabetes medications affect patients' adherence.

This study is therefore aimed at determining the influence of number of (antidiabetes and adjunctive) and type of prescribed antidiabetes (oral, insulin, or both) medications on adherence and glycemia of ambulatory patients with type 2 diabetes in southwestern Nigeria.

METHODS

This study was carried out at the endocrinology outpatient clinics of the University College Hospital (UCH), Ibadan and the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, both located in southwestern Nigeria. UCH is a 900-bed tertiary teaching hospital and affiliated with University of Ibadan; OAUTHC is a 600-bed tertiary hospital and affiliated with Obafemi Awolowo University. The two teaching hospitals have endocrinologist-managed diabetes clinics where different categories of ambulatory and institutionalized patients within and outside the region receive treatment. Ethical clearance and approval for the study was obtained from the joint University of Ibadan/University College Hospital Health Research and Ethics Committee.

The study consisted of two phases. A prospective cross-sectional study using pre-tested structured questionnaire among type 2 diabetes patients recruited from the endocrinology outpatient clinics of the hospitals between 15th November, 2010 and 16th January, 2011; and a retrospective review of case notes of the cohort for details of prescribed medications and blood glucose values.

Adult patients with type 2 diabetes who had been on antidiabetes medications for more than three months prior to the time of study were recruited. This is to ensure patient's familiarization with antidiabetes medications. Eligible patients also had average of fasting blood glucose (FBG) values for the two most recent consecutive measurements >110 mg/dL so as to ensure that patients with FBG above the United Kingdom Prospective Diabetes Study (UKPDS)[23,35] recommended blood glucose goals (FBG ≤108 mg/dL) were enrolled. All patients with type 1 diabetes, and type 2 diabetes patients who were unconscious or who declined participation were excluded.

Representativeness of the study sample was assured by calculating the target sample size based on assumptions of 5% statistical significance, and 95% confidence level with an estimated population of 340 patients for the eight weeks study period obtained from the average number of ambulatory type 2 diabetes patients (40 to 45 per week) who regularly attended the diabetes clinic of the hospitals. Based on these assumptions, a target sample size of approximately 185 was computed using a sample size calculator (www.surveysystem.com/sscal.html).[36]

Eligible patients were approached for participation while they were waiting to see the physician on each diabetes clinic days. Objectives of the study were explained to patients individually, after which an informed written consent was obtained from each patient to signify their willingness to participate in the study. Elderly patients were assisted by the caregivers who accompanied them to the hospital, while clarifications were made for patients who did not understand English Language by the principal investigator. Only patients who gave voluntary informed written consent for participation were enrolled. Participation was voluntary and patients

were assured of their anonymity and confidentiality of responses. An average of twenty-three patients fulfills the study inclusion criteria on each clinic days (Mondays for UCH; and Thursdays for OAUTHC).

The questionnaire for the study was assessed for clarity and validity of content by two consultant endocrinologists and two pharmacists who are scholar in diabetes mellitus. A pre-test of the sampling and recruitment procedures was done among fifteen randomly selected, recently diagnosed (<3-month) patients with type 2 diabetes chosen from the University College Hospital. Based on the feedback from the pre-test and validity assessment, some questions were rephrased to eliminate ambiguity. Questions which were initially designed in closed-ended dichotomous "Yes/No" response options were reframed as open-ended questions with relevant prompts to guide patients and ensure clarification of intention.

The questionnaire was divided into three sections: section A obtained information on socio-demographic data including age, sex, occupation, educational status, and marital status. Section B clarified information on duration of diagnosis, family history of diabetes, symptoms experienced at onset of the diabetes, prescribed medications (antidiabetes and adjunctive) and other medications used by patients. Section C was a modified Morisky Adherence Predictor Scale (MMAPS)[37] containing 4-item question administered in dichotomous "Yes/No" response options. The MMAPS is a validated self-reported adherence measure and is part of the World Health Organization Case Management Adherence Guideline Assessment Tools (CMAG)[4,38] commonly used to assess patient's adherence to therapy. In this study, a 'Yes' response to the item-statement on the scale was assigned a score of 'one' and 'No' response assigned a score of "zero". Thus, adherence was defined as 'No' response to all the 4-item questions on the MMAPS or a total score of 'zero'. Based on distribution of scores to patients' responses on the scale, binary variables using categorization of a total score of <1 for adherent and a total score of ≥1 for non-adherent status were developed.

Patient's extent of commitment to medication-taking was also assessed using a self-reported medication adherence score (SRMAS) with numerical rating scale ranging from 'one' (low commitment) to 'ten' (total or complete commitment). A binary categorization of SRMAS utilizing a cut-off of ≥8 for adherent and <8 for non-adherent was developed based on distribution of the data and previous studies.[37,39]

The questionnaires which took about 20 minutes to complete were administered to patients by the principal investigator on every diabetes clinic days of the hospitals. The retrospective data from the case notes of participants were retrieved using a pre-piloted data collection form. Information captured from the case notes included details of prescribed antidiabetes and adjunctive medications for the two most recent appointments with respect to medication name, dosage regimen, as well as the ancillary information written on the prescription to guide appropriate use of antidiabetes medications. Mean FBG value for the two most recent consecutive measurements was also retrieved in order to ascertain the extent of glycemic control among the patients. In this study, the total number of prescribed medications per contact with physician was categorized into binary variables viz >4 versus ≤4 medications (as cut-off) to indicate polypharmacy and non-polypharmacy prescriptions respectively. This classification was based on various definitions of polypharmacy from previous studies[40-42] which ranges from two medications to more than four.

Data were sorted, coded and entered into Predictive Analytics Software (PASW) for Windows (version 17.0.). Descriptive statistics including frequency and mean ±standard deviation were used to summarize the data. Associations between medication adherence assessed by MMAPS and relevant categorical variables including socio-demographic characteristics, duration of diagnosis in categories, number of prescribed medications in binary variables, and type of antidiabetes medications were evaluated using Chi-square or Fisher's exact test as appropriate. One-way analysis of variance (ANOVA) was used to compare the difference in mean FBG among patients who were placed on different types of antidiabetes medications. The difference in mean FBG for patients on >4 medications versus ≤4 medications, as well as adherent and non-adherent status was compared using student t-test. The priori level for statistical significance was set at $p<0.05$.

RESULTS

Of the 185 patients who were approached for participation, a total of 176 (95.1%) consented to participate from the two hospitals including 113 (64.2%) from UCH, and 63 (35.8%) from OAUTHC. One hundred and eight (61.4%) were females and 68 (38.6%) were males. The mean age for patients was 60.2 ±10.2 years. Mean duration of diagnosis was 6.3 ±5.6 years. Details of the socio-demographic characteristics and relevant clinical parameters for patients are shown in Table 1. Fifty-six (31.8%) had family history of diabetes including mother alone, 18 (32.1%); father alone, 15 (26.8%); both parents, 6 (10.7%); immediate and secondary family member such as siblings and uncles 17 (30.4%). The remainder 120 (68.2%) did not have a known family relation who had diabetes mellitus.

The mean number of prescribed medications per contact with physician was 4.6 ±1.4. Almost two thirds 103 (60.6%) of the patients were placed on more than four medications while 67 (39.4%) were placed on ≤4 medications. Patients on >4 medications were mostly older adults (above 60 years of age), and were in the majority, 26 (66.7%); who had post-secondary or tertiary education compared to those on ≤4 medications who were mostly younger adults (≤60 years) and who were in a smaller proportion 13 (33.3%) possessing post-secondary or tertiary education (chi square=10.55, p=0.02).

Table 1. Socio-demographic characteristics and relevant clinical parameters for patients

Variables	Frequency	Percent
Age (year) (n =176)		
30-40	7	4.0
41-50	26	14.8
51-60	53	30.1
61-70	62	35.2
Above 70	28	15.9
Sex (n = 176)		
Male	68	38.6
Female	108	61.4
Education qualification (n=176)		
No formal education	54	30.7
Primary	40	22.7
Secondary	43	24.4
Tertiary	39	22.2
Occupation (n =176)		
Trading	70	39.8
Retiree	37	21.0
Civil servant	28	15.9
Professionals	23	13.1
Unemployed	10	5.7
Artisan	8	4.5
Marital status (n = 176)		
Married	152	86.4
Widowed	24	13.6
Single	0	0.0
Divorcee	0	0.0
Type of antidiabetes medications (n =170)		
Oral antidiabetes medication (OAM) alone	130	76.5
Insulin plus OAM	26	15.3
Insulin alone	14	8.2
Number of prescribed medications (170)		
>4 medications	103	60.6
≤ 4 medications	67	39.4
Duration of diagnosis (year) (n =176)		
3 months to < 1 year	10	5.7
1-10	133	75.6
11-20	27	15.3
Above 20	6	3.4

Numbers may not add up to 176 for type of antidiabetes medications and number of prescribed medications because of the respondents who neither had medication regimen documented in their case notes nor had it reported in the prospective data collection tool; n = number; OAM = Oral antidiabetes medications

Responses to MMAPS showed that 78 (48.8%) were adherent with previous medications, while 82 (51.2%) were adjudged non-adherent (Table 2). Also, the mean SRMAS was 7.3 ±1.7. Relationship between number of prescribed medications and medication adherence (MMAPS) indicated that patients on >4 medications were more committed to medication-taking, 53 (55.2%); compared to patients on ≤4 medications, 24 (39.3%); with p=0.05. Also, adherence rates to prescribed antidiabetes medications were in the ranking of oral antidiabetes medications (OAM) alone (50.0%) > insulin combined with OAM (44.0%) > insulin regimen alone (41.7%) with no significant difference (p=0.77). Details of the association between medication adherence assessed by MMAPS and relevant categorical variables are shown in Table 3. Adherent patients had reduced mean FBG of 181.7 ±75.6 mg/dL compared to non-adherent counterparts (185.7 ±71.5 mg/dL) with no significant difference (t=-0.342, p=0.73). However, there was a significant difference in mean FBG value among

Table 2. Responses to Modified Morisky Adherence Predictor Scale (n = 160)

Question	Number (%)	
Response (score coding)	Yes (1)	No (0)
1. Do you sometimes forget to take your medications?	26 (16.3)	134 (83.3)
2. Do you sometimes not being careful with the way you take your medications?	71 (44.4)	89 (55.6)
3. When you feel better, do you sometimes stop taking your medications?	16 (10.0)	144 (90.0)
4. Sometimes if you feel worse when you take your medication(s), do you stop taking them?	18 (11.3)	142 (88.8)

Distribution of total scores	Total (%)
0	78 (48.8)
1	41 (25.6)
2	33 (20.6)
3	5 (3.1)
4	3 (1.9)

Cut-offs	Number (%)	Category
< 1	78 (48.8)	Adherent
≥ 1	82 (51.2)	Non-adherent

Only respondents who completely responded to all the 4-item questions were considered as valid respondents for classification into the binary variables

Table 3. Association between medication adherence (MMAPS) and relevant categorical variables

Variables	Adherent N (%)	Non-adherent N (%)	p-values
Age (year)			0.03**
30 – 40	2 (60.0)	3 (40.0)	
41- 50	6 (24.0)	19 (76.0)	
51 – 60	23 (48.9)	24 (51.1)	
61-70	28 (49.1)	29 (50.9)	
Above 70	18 (69.2)	8 (30.8)	
Sex			0.09*
Male	34 (57.6)	25 (42.4)	
Female	44 (43.6)	57 (56.4)	
Educational qualification			0.63*
No formal education	24 (48.0)	26 (52.0)	
Primary	14 (40.0)	21 (60.0)	
Secondary	22 (53.7)	19 (46.3)	
Tertiary	18 (52.9)	16 (47.1)	
Occupation			0.26**
Trading	26 (41.3)	37 (58.7)	
Retiree	24 (66.7)	12 (33.3)	
Civil servant	11 (45.8)	13 (54.2)	
Professionals	10 (50.0)	10 (50.0)	
Unemployed	4 (40.0)	6 (60.0)	
Artisans	3 (42.9)	4 (57.1)	
Marital status			0.32*
Married	69 (50.4)	68 (49.6)	
Widowed	9 (39.1)	14 (60.9)	
Type of antidiabetes medications			0.77*
Oral antidiabetes alone (OAM)	60 (50.0)	60 (50.0)	
Insulin plus OAM	11(44.0)	14 (56.0)	
Insulin alone	5 (41.7)	7 (58.3)	
Number of prescribed medications			0.05*
>4 medications	53 (55.2)	43 (44.8)	
≤ 4 medications	24 (39.3)	37 (60.7)	
Duration of diagnosis (year)			0.97**
3 months to < 1 year	4 (50.0)	4 (50.0)	
1 -10	60 (49.6)	61 (50.4)	
11-20	12 (46.2)	14 (53.8)	
Above 20	2 (40.0)	3 (60.0)	

** = Fisher's exact test; * = Chi-square test; Level of statistical significant p <0.05; MMAPS = Modified Morisky Adherence Predictor Scale.
Numbers may not add up to 160 for type of antidiabetes medications and number of prescribed medications because of the three valid respondents to MMAPS but who neither had medication regimen documented in their case notes nor had it reported in the prospective data collection tool.

patients who were placed on >4 medications (172.1 ±61.1 mg/dL) compared to those on ≤4 medications (198.8 ±83.8 mg/dL) (t=2.398, p=0.02). Also, there was a significant difference in mean FBG value among patients on OAM alone (174.3 ±62.9 mg/dL), insulin alone (204.4 ±86.5 mg/dL), and insulin combined with OAM (212.8 ±95.2 mg/dL) (F=3.936, p=0.02). The details of prescribed antidiabetes medications are shown in Table 4. Majority, 109 (69.9%) were on two-OAM combination, 31 (19.9%) on three-OAM combination, and 16 (10.3%) on a single OAM. Summarily, metformin was the most widely prescribed oral antidiabetes medications either singly, fixed dose or in co-administered combination 152 (97.4%). Of the cohorts who were prescribed antidiabetes medications, 28 (16.5%) had the pertinent ancillary information written on their prescriptions, while 142 (83.5%) had their prescriptions written without the supplementary information to ensure appropriate medication-taking in relation to the time of meal. Also, the details of prescribed and non-prescribed adjunctive medications for patients are shown in Table 5. Different classes of antihypertensive medications (54.8%) constituted the majority of prescribed adjunctive medications, while herbal concoctions (38.0%) were the most common non-prescribed medicines used by patients.

DISCUSSION

In the present study, majority of patients were placed on more than four medications per contact with physician which probably supported studies that reported multi-drug regimens as a natural consequence of providing evidence-based care to patients with type 2 diabetes.[29,32,43,44] Typically, more than one medication is required to control hyperglycemia and the associated metabolic risk factors of hypertension and hyperlipidemia which are common comorbid among diabetes patients.[31,32]

Interestingly, patients on more than four medications had improved adherence compared to those on four medications or less which is in contrast to most studies which demonstrated that the number of medications prescribed for a patient is inversely correlated with adherence to treatment regimen.[29-31] However, this finding should be considered in line with the fact that many of the patients on >4 medications were older adults (above 60 years of age) and were those in the majority who had tertiary education compared to patients on ≤4 medications who were mostly younger adults (≤60 years) and were in a smaller proportion with tertiary education. Nonetheless, this finding, especially with respect to multiple medications (polypharmacy) among the older adults

Table 4. Type and pattern of antidiabetes medications prescribed for patients

Type of antidiabetes medications (n =170)	Frequency	Percent
Oral antidiabetes medications (OAM) alone	130	76.5
Insulin + OAM	26	15.3
Insulin alone	14	8.2
Single OAM prescription		
Metformin	14	9.0
Glimepiride	2	1.3
Glibenclamide	0	0
Gliclazide	0	0
Pioglitazone or Rosiglitazone	0	0
Voglibose or Acarbose	0	0
2- OAM combination		
Glyburide/Metformin (Fixed)	2	1.3
Glimepiride/Metformin (Fixed)	2	1.3
Pioglitazone/Metformin (Fixed)	13	8.4
Glibenclamide + Metformin (Nonfixed/co-administered)	52	33.4
Glimepiride + Metformin (Nonfixed/co-administered)	37	23.9
Glimepiride + Pioglitazone (Nonfixed/co-administered)	2	1.2
Gliclazide + Metformin (Nonfixed/co-administered)	1	0.6
3- OAM combination		
Glimepiride + Metformin + Pioglitazone	20	12.9
Glibenclamide + Metformin +Pioglitazone	11	7.1
Neutral Protamine Hagedon (NPH)	20	50.0
Premixed/Mixtard insulin	11	27.5
NPH + Regular insulin	9	22.5

OAM= Oral antidiabetes medications, NPH= Neutral Protamine Hagedon

with type 2 diabetes, is consistent with many other studies.[45,46] Elderly diabetes patients are usually at high risk of co-existing medical conditions which may necessitate for multiple medications in order to manage hyperglycemia and the associated comorbid illness.[32,45] Also, improved adherence among older adults who are on multiple medications is in agreement with previous studies which reported better adherence to oral antidiabetes medications[47] and lifestyle program in the elderly adults with type 2 diabetes compared to younger age group.[48,49] Older adults with type 2 diabetes are perhaps making efforts to preserve quality of life as well as preventing the occurrence of diabetes-related complications[50], thus may wish to ensure better commitment to medication-taking and other treatment recommendations.

Also of note was the fact that a substantial proportion of patients on >4 medications had post-secondary or tertiary education which might perhaps positively influence patients to better adherence. Adequate literacy levels among patients[51] may facilitate better comprehension of the treatment regimens as well as encouraging better appreciation of diabetes treatment plans which is necessary to ensure sustained improvement in adherence with subsequent better glycemic outcome. Prescribers who are directly involved in diabetes care should therefore take cognizance of these findings when prescribing multiple medications for type 2 diabetes in routine clinical practice. In addition, improved adherence that was noted among patients on >4 medications compared to those on ≤4 medication is consistent with findings of Grant *et al*. (2003)[43] which reported that contrary to other patients' population, diabetes patients do not have a reduction in adherence to their medical regimen when multiple medications are prescribed. It may therefore be partly suggested that healthcare provider who are directly involve in diabetes care should not necessarily be discouraged in prescribing multiple medications for patients with type 2 diabetes as long as the prescribed medications are appropriate for patients' medical conditions and rational with respect to cost and therapeutic efficacy. This is especially important considering the fact that multiple medications constitute a well-recognized trend in a comprehensive approach to the management of type 2 diabetes.[32]

It is noted that patients on different combinations of oral antidiabetes medication alone recorded better adherence rates compared to those on insulin regimen alone. This is consistent with previous studies on adherence to medications among diabetes patients where average adherence to oral antidiabetes medications was reported to range from 36% to 93%[34], while estimate of adherence to insulin injection regimens varies from 20% to 80%.[52,53] Although, the possible explanations for the low adherence rates among patients on insulin injection regimens may vary across studies, the general consensus may be linked to patients' dislike for daily insulin injection[54,55] probably because of the perceived painful nature of the injection or the unfounded fear linked to insulin as a regimen that may be continued for a lifetime once it is initiated. Nonetheless, patients with type 2 diabetes who might be considered as candidate for insulin therapy may need to be informed of the reason for including insulin in their regimen and they should be educated on the importance of continuing adherence to insulin regimen so as to consistently ensure optimal glycemic control. In this study, a sizeable proportion of antidiabetes prescriptions were written without the necessary supplementary information to ensure appropriate medication-taking with respect to the time of meal. This information is essential as an additional instruction that will guarantee appropriate medication dispensing by pharmacist, as well as ensuring provision of a suitable and purposeful counseling to ascertain the correct use of

Table 5. Summary of prescribed and non-prescribed adjunctive medications used by patients

Medication	Frequency	Percent
Prescribed Adjunctive with antidiabetes Medication (n =371)		
Low dose aspirin (75mg)	107	28.8
Angiotensin converting enzyme inhibitors (ACEI)	96	25.9
Calcium channel blockers	56	15.1
Statins	32	8.6
Multivitamin containing Thiamine, Pyridoxine, Cyanocobalamin, plus Diclofenac	16	3.8
Hydrochlorothiazide/amiloride	14	3.8
alpha- methyldopa	14	3.5
Angiotensin receptor blockers (ARBs)	13	4.3
Amytriptilline	6	1.6
S(-) amilodipine	6	1.6
Dypridamole	4	1.1
Carbamazepine	2	0.5
Pregabalin	1	0.3
Multivitamin containing Alpha Lipoic Acid, Lutein and Vanadium	1	0.3
Beta blockers	1	0.3
Amilodipine/Valsartan	1	0.3
Antibiotics	1	0.3
Non-prescribed medicines used by patients (n = 213)		
Herbal concoctions	81	38.0
Analgesic	74	34.7
Antimalarials	29	13.6
Antibiotics	15	7.1
Multivitamins	8	3.8
Mixed over-the-counter (OTC) medicines	4	1.9
Antifungal	2	0.9

prescribed medicines by the patients. Provision of insufficient information and instruction(s) by healthcare provider may perhaps implying that patient's non-adherence may partly be the failure or inability of the provider to fortify patients with complete instructions necessary to ensure maximal therapeutic benefit. Adibe *et al*. (2009)[56] also reported that 74.7% prescriptions were written with no instruction on how the medications were to be taken. Prescribers who may be directly involved in diabetes care are therefore enjoined to always ensure that the prescriptions for antidiabetes medications are written with highlights of relevant information and instruction(s) to guarantee appropriate dispensing of medicines that will consistently ensure optimal therapeutic benefit for patients. Healthcare provider should also strive to probe for medication non-adherence at every encounter with patients, and efforts should be made to ensure patients' continuous commitment to medication-taking as prescribed. Interestingly, patients on more than four medications had reduced and hence better fasting blood glucose value compared to those on four medications or less. Also, adherent patients had reduced and improved glycemic values than their non-adherent counterparts implying that if patients were more committed to medication-taking, glycemic outcome will be better.

The presence of high number of prescriptions for antihypertensive as adjunctive medications for the patients is also expected since hypertension is the most common comorbid disease among diabetes patients.[31,33,57] The concomitant use of herbal concoctions (38.0%) alongside the antidiabetes medications among the patients is also noteworthy. Yusuff *et al*. (2008)[57] had reported self-medication with herbal medicine (13.8%) among ambulatory diabetes patients. The increased use of herbal concoctions among patients is a call for concern among healthcare providers. Although, some of the herbal remedies may contain active ingredients with blood glucose lowering effects, irrational use of herbal concoction with allopathic medicine may needs to be discouraged.

This study is limited by the fact that medication adherence was assessed by self-report measures which might be associated with some shortcomings. Patients may tend to over report good adherence or under report poor adherence, or they may simply not know their current adherence status. Also, there may be the likelihood of recall bias among the patients which may result in non-response for some item-statement in the data collection tool. However, it is known that there is no gold standard method for assessing adherence.[5,53,58] Self-report measure using non-threatening and non-judgmental questions has been described as a reliable tool to assess medication-taking behaviour of patients.[59,60] Also, the incomplete documentation of the prescribed regimen in the case notes of some patients constitutes a limitation worthy of mentioning. Though, the overall response rate among the patients is considerable to ensure better representation.

The non-availability of glycated hemoglobin (HbA1c) test as a measure to assess the glycemic control may be another limitation of this study. HbA1c test might have been a better objective measure. The relatively high cost for HbA1c test (approximately USD12.5 to 18.8) in the hospitals might have accounted for physician's reluctance to recommend the test for diabetes patients who are already making out-of-pocket payments for their treatment. Nonetheless, fasting blood glucose is the most common blood glucose test routinely prescribed for diabetes patients in these hospitals and assessment of patients' glycemic status by physician is usually based on the value of this test.

CONCLUSIONS

Prescribing more than four medications for the cohorts is linked to improved adherence and glycemic outcome. However, age and educational background of patients are important factors that need to be considered when prescribing multiple medications for type 2 diabetes as these factors may influence patient's adherence to multiple medications. Healthcare provider should therefore take cognizance of these findings in routine clinical practice.

In addition, patients on different combination of oral antidiabetes medications recorded better adherence rates and had improved mean fasting blood glucose value compared to those on insulin regimen alone suggesting the need for continuing encouragement and support for type 2 diabetes patients on insulin regimen so as to ensure better glycemic control. Nonetheless, prescribers who are directly involved in diabetes care should always ensure that prescriptions for antidiabetes medication are written with highlights of relevant ancillary information and instruction(s) that will guarantee appropriate medication dispensing by pharmacist, as well as ensuring the correct use of the prescribed medicines by patients, so as to optimized the therapeutic benefit.

CONFLICT OF INTEREST

None to declare by the authors.

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