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RETRACTED ARTICLE: Antidiabetic medication adherence and associated factors among patients in Botswana; implications for the future

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ABSTRACT

Background: Diabetes mellitus (DM) is a major global public health problem. Lack of adherence to medication causes suboptimal glycemic control increasing complication rates, costs and mortality. The objective of the study was to determine current antidiabetic medication adherence in Botswana and assess associated factors so as to direct potential future interventions.

Materials and methods: A cross-sectional study among 376 randomly selected diabetic patients attending a leading clinic in Gaborone, Botswana. Eight item Morisky Medication adherence questionnaire was used to assess antidiabetic medication adherence. A structured questionnaire was also used to collect information on factors influencing adherence including age, gender, education, type and duration of diabetes, treatment, complications and HIV status. Data were entered and analyzed using STATA Version 14, and logistic regression performed.

Results: Over forty percent (41.8%) of patients were non-adherent to antidiabetic medications. Studied sociodemographic characteristics and clinical variables did not affect adherence. HIV positive status was associated with a statistically significant better adherence at multivariate analysis.

Conclusion: Adherence to antidiabetic medication was found to be suboptimal in a setting where medicines are provided free of charge. Only HIV positivity was found to be significantly associated with better adherence, probably due to effect of greater psychosocial support and counselling as part of HIV treatment. There is a need to carry out studies to further improve understanding of factors associated with medication adherence that are pertinent to Botswana and similar settings given the growing prevalence of diabetes.

1. Introduction

Diabetic mellitus (DM) is a metabolic disorder, characterized by elevated blood glucose levels. It is of growing public health importance.[1] The prevalence of diabetes was estimated to increase from 171 million in 2000 to 366 million by the year 2030.[2] However, recent data from the International Diabetes Federation (IDF) suggest that previous estimates have already been exceeded, with a prevalence of 415 million by 2015 and estimated to reach 642 million by 2040.[3] The World Health Organization (WHO) also estimated that there were 422 million adults living with DM in

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2014, 8.5% of the adult population.[1] Global estimates further show that the rise in the prevalence of DM is unevenly distributed with over 70% of people with DM likely to live in developing countries, particularly sub-Saharan Africa, a region already heavily burdened by communicable diseases[4–9] as well as non-communicable diseases such as hypertension.[10,11] DM accounted for 1.5 million deaths in 2012 and rising.[1]

There is currently scarcity of data regarding the burden of DM in Botswana. However, according to the International Disease Federation, there were 52,000 documented diabetic patients (approximate prevalence of 2.4%) in 2015 in Botswana.[3] Data from the STEPS survey conducted by the WHO in 2007 documented that 34.7% and 38.7% of the population of Botswana performed low physical activity and were overweight respectively[12]; both variables being components of the metabolic syndrome leading to Type 2 diabetes (T2DM). This suggests that the burden of DM in Botswana may be higher than current estimates. It is well recognized that various forms of DM peculiar to sub-Saharan Africa exist, ranging from Type 1 and Type 2 DM, and malnutrition-related diabetes to ketosis-prone diabetes. However, T2DM is by far the most common type of diabetes, accounting for 90% of all cases.[13,14] T2DM occurrence is attributed to both modifiable and non-modifiable factors including but not limited to social and cultural behaviors, lack of physical activity, dietary habits, urbanization and ageing.[15,16] Patients with DM have increased morbidity and mortality[17–22] because of associated conditions as a result of the complications of DM. These range from cardiovascular diseases, neuropathy, nephropathy, and bacteremia to tuberculosis.[23–26]

The management of DM requires a multifaceted approach with a focus on dietary modification, physical exercise and pharmacotherapy.[27,28] Good adherence to treatment strategies is crucial for the successful management of chronic asymptomatic conditions such as hypercholesterolemia and hypertension.[29–33] For DM specifically, a combined approach of diet control, physical exercise and medication helps achieve sufficient glycemic control and avoids related short-term and long-term complications.[34–38] Good control of blood pressure and regular use of statins helps reduce cardio-vascular events and deaths.[39,40] However, the WHO estimates that only half of patients with chronic diseases are medication adherent.[41] Most of previous studies on adherence to antidiabetic medications have shown low adherence patterns to both pharmacotherapy and other aspects of diabetic care.[33,42–45]

Various factors are associated with non-adherence to medication in DM patients, which can be categorized as patient centered, therapy-related or healthcare system related.[46,47] Patient-centered factors include sociodemographic (age, gender and educational level) factors, psychological factors including motivation towards therapy taking, patient-prescriber relationship and patient knowledge.[42,48,49] Therapy-related factors include route, type and duration of treatment, complexity of treatment especially as patients may be on multiple medicines, cost of medication especially if co-payment is an issue and adverse effects.[50–55] Healthcare system factors include availability and accessibility of health care, and the health provider-patient interactions.[56]

Despite the fact that many studies have been performed globally on adherence to antidiabetic medicines, and the majority have showed varied non-adherence from low to high,[28] we felt it was justified to undertake a study in Botswana, as each community has its own culture and lifestyle that may affect adherence in a different way.[57] This is especially the case in Botswana with its high prevalence of HIV at over 22% of the adult population, with higher rates especially among women.[58] At one stage, nearly 50% of women aged 30–34 years had HIV[59]; however, rates are now decreasing among the young.[58] High prevalence rates are also seen in other African countries, with higher rates generally among women than men.[60,61] This is important as this will appreciably enhance the pill burden in patients with both DM and HIV.

This study was conducted to determine the magnitude of antidiabetic medication adherence and assess associated factors among both patients with Type 1 and Type 2 DM in a tertiary diabetic clinic in Gaborone including those with HIV. If there were concerns with medication adherence in this specialized setting, this would reflect concerns generally throughout Botswana. The findings may also be of interest to other African countries with high prevalence rates of HIV and growing rates of DM to help improve their future management of these patients.

2. Materials and methods

2.1. Study design and setting

This was a cross-sectional study conducted at Block 6 clinic, a tertiary clinic specializing in the treatment of patients with both Type 1 and Type 2 DM. Block B clinic is situated in Gaborone, the capital city of Botswana, with a population of approximately 200,000. The clinic offers various services to over estimated 3000 diabetic patients. Services include physician consultations, health education, eye and foot screening and the issuing of medicines. Medicines are provided free-of-charge so co-payment is not an issue affecting medication adherence.[62,63] On average 1800–2000 diabetic patients visit the clinic monthly for various reasons, of which an average of 1400 patient visits are physician consultations.

2.2. Study population

A total of 376 patients were randomly selected over the course of two months from 21st July 2015 to 21st September 2015. At the time of data collection, approximately 70 patients attended the clinic each day. *Inclusion criteria*: All patients above the age of 21 years who attended the clinic on working days (Monday to Friday) and who consented to participate in the study. *Exclusion criteria*: Patients with decision impaired illnesses such as mental illness, including schizophrenia, bipolar disorder and dementia, were excluded from the study along with those who refused to take part.

2.3. Sample size

Sample size was calculated using the formula for cross-sectional study using a prevalence of non-adherence to chronic medication of 67%[64,65] with standard score of 95% confidence level and margin of error of 5% giving a minimum sample size of 340 patients.

2.4. Data collection

Data were collected by two research assistants, who were qualified nurses, and trained in interview techniques prior to the study. A list of patients attending the clinic was obtained from the nurses doing vital signs, and a coin was tossed for the first 10 patients on the list to randomly obtain the first patient for each day of data collection. From there, every 5th patient was subsequently approached for consent to participate in the study. In case of refusal, either tossing the coin was repeated or a subsequent 5th patient was approached, without affecting the prior order, to ensure a random sample. About 8–10 patients were recruited on each week day of recruitment. A structured questionnaire, which was pre-tested, was used to obtain information on the socio-demographic characteristics, as well as factors affecting

medication adherence. Self-reported adherence to antidiabetic medication was determined during the interview using the Morisky 8-Item Medication Adherence Questionnaire (Box 1). All questions, except for the last question, were answered with a yes/no response, with corresponding 1 and 0 value. Overall adherence to medication was categorized based on patients' responses, according to the following scores: >2 = low adherence; 1 or 2 = medium adherence; 0 = high adherence.[66–68]

Box 1 Morisky 8-Item Medication Adherence Questionnaire[67]

- Do you sometimes forget to take your medicine? (Y = 1; N = 0)
- People sometimes miss taking their medicines for reasons other than forgetting. Thinking over the past 2 weeks, were there any days when you did not take your medicine? (Y = 1; N = 0)
- Have you ever cut back or stopped taking your medicine without telling your doctor because you felt worse when you took it? (Y = 1; N = 0)
- When you travel or leave home, do you sometimes forget to bring along your medicine? (Y = 1; N = 0)
- Did you take all your medicines yesterday?(Y = 0; N = 1)
- When you feel like your symptoms are under control, do you sometimes stop taking your medicine? (Y = 1; N = 0)
- Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan? (Y = 1; N = 0)
- How often do you have difficulty remembering to take all your medicine? (A = 0; B–E = 1 where A. Never/rarely; B. Once in a while; C. Sometimes; D. Usually; E. All the time).

Clinical characteristics, past medical history and history of documented diabetic complications were obtained from patients' charts. Further information on the patients' history was obtained from outpatient charts. Results of previous laboratory investigations (undertaken within six months of the index visit) such as glycated haemoglobin were obtained from the Integrated Patients Management System (IPMS). As regards the HIV status, patients were categorized as either HIV negative/-positive/-unknown according to their response of being tested with evidence of documentation in the past year or known HIV seropositive results recorded in the IPMS.

Physical examination of patients by clinic staff is undertaken routinely. This involves measuring weight, using a calibrated weighing scale and entering the data onto the charts. The height of each patient taking part was measured by research assistants using calibrated height scale to enable calculations of the Body Mass Index (weight in kg/height in m^2).

Patients' ages were recorded as whole numbers, e.g. if a patient was 50 years and 9 months, the age would be recorded as 50 years.

2.5. Data management and analysis

Data were entered and analyzed using STATA Version 14. To assess any associations, both univariate and multivariate logistic regression with odds ratios (OR) and 95% confidence interval (CI) were performed. Medication adherence was dichotomized as either adherent (Morisky score = 0/high adherence) or non-adherent (Morisky score ≥1/low and medium adherence). The dichotomization in this study was according to previous studies that used Morisky scale and categorized any score above zero as non-adherent.[69–71] A p-value of less than 0.05 was considered statistically significant.

3. Ethical considerations

Ethical clearance to conduct the study was obtained from the University of Botswana Ethics Committee and the Institutional Review Board (IRB) as well as the Ethics Committee at Princess Marina Hospital. Ethical clearance was also secured from the Botswana Ministry of Health Research Unit. All patients provided written informed consent for participation.

4. Results

4.1. Baseline socio-demographic characteristics

A total of 376 patients were interviewed after excluding 4 patients who refused informed consent. The majority of patients were female (69.1%). The mean age of patients was 56.5 (SD: 13.7) years with a median duration of DM of 5.0 years. Most of the study participants were either overweight or obese accounting for 29.2% and 50.0% respectively (Table 1).

4.2. Clinical and medication characteristics of study participants

Most of the interviewed patients were T2DM, accounting for 353 of the 376 patients (93.9%). As regards the duration of diagnosed diabetes, nearly half of the patients (46.8%) had been diagnosed less than 5 years ago. Over 80% of patients were either only on oral hypoglycemic agents or on a combination of oral hypoglycemic agents and insulin. The majority (81.8%) of patients had diabetic complications documented in their outpatients'

Table 1
Sociodemographic characteristics of the study participants (n = 376).

Characteristic	n (%)
Sex	
Female	260 (69.1)
Male	116 (30.9)
Age	
<36	32 (8.5)
36–50	78 (20.7)
51–65	163 (43.4)
≥66	103 (27.4)
Age, mean (SD)	56.5 (13.7)
Education level	
No formal school	70 (18.6)
Less than primary school	78 (20.7)
Primary school completed	103 (27.4)
Secondary school completed	77 (20.5)
College/University completed	42 (11.2)
Post-graduate degree	6 (1.6)
Marital status	
Never married	102 (27.1)
Currently married	155 (41.2)
Separated	2 (0.5)
Divorced	13 (3.5)
Widowed	74 (19.7)
Cohabiting	30 (8.0)
BMI, median (IQR)	
Underweight	5 (1.5)
Normal weight	65 (19.3)
Overweight	98 (29.2)
Obese	168 (50)

SD: Standard deviation.

Table 2
Clinical and medication characteristics of study participants (n = 376).

Clinical and medication characteristics	n (%)
Type of diabetes mellitus	
Type 1	23 (6.1)
Type 2	353 (93.9)
Duration of diabetes	
<5 years	176 (46.8)
5–10 years	89 (23.7)
>10 years	93 (24.7)
Missing	18 (4.8)
Modality of treatment for diabetes	
Oral hypoglycemic agents (OHA)	224 (59.6)
Insulin	51 (13.6)
Both OHA and insulin	101 (26.8)
Number of OHA currently in use	
One	164 (43.6)
Two	161 (42.8)
Missing	51 (13.6)
Diabetic complications	
No	65 (17.3)
Yes	311 (82.7)
Diabetic complications (multiple responses)	
Eye complications-retinopathy	142 (37.4)
Skin complications with or without itching	133 (35.0)
Postural hypotension	116 (30.5)
Palpitations	113 (29.7)
Gastroparesis	77 (20.3)
Erectile dysfunction	59 (15.5)
Neuropathy	55 (14.5)
Heart failure	32 (8.4)
Diabetic foot/hand with or without ulcer	23 (6.1)
Kidney complications-nephropathy	18 (4.7)
Stroke	3 (0.8)
HIV status	
Positive	38 (10.1)
Negative	234 (62.2)
Unknown	104 (27.7)

Table 3
Prevalence of adherence to antidiabetic medication according to Morisky scale (n = 376).

Adherence category (Morisky score)	n (%)
High adherence (0)	219 (58.2)
Medium adherence (1–2)	91 (24.2)
Low adherence (>2)	66 (17.6)

charts, despite their duration of diagnosed diabetes being less than 5 years. Nearly two thirds (62.2%) of patients were HIV negative and for 27.7% the HIV-status was unknown (Table 2).

4.3. Prevalence of antidiabetic medication adherence

The prevalence of high adherence to antidiabetic medication according to the Morisky scale was 58.2%. Medium and low adherence was 24.2% and 17.6% respectively accounting for 41.8% of non-adherent group (Table 3).

4.4. Factors associated with antidiabetic adherence

Several factors, including sociodemographic characteristics (age, gender, educational level and marital status) and clinical and medication characteristics (HIV status, type of diabetes, duration of diabetes and modality of treatment) were analyzed to determine any association with adherence to antidiabetic medication. For this purpose as mentioned, patients were categorized as either adherent (Morisky score = 0/high adherence) or non-adherent (Morisky score ≥1/low and medium adherence).

For all the studied factors, only HIV-positive status was associated with high antidiabetic medication adherence; 30/38 (78.9%) of HIV-positive patients were adherent to antidiabetic medication compared to 122/234 (52.1%) (p-value = 0.017, AOR = 0.31, 95% CI = 0.13–0.74) (Table 4).

4.5. Association between antidiabetic medication adherence and glycemic control

Overall, the analysis of the extent of antidiabetic medication adherence to glycemic control from using glycated haemoglobin (HbA1c levels) revealed no statistically significant association (p-value = 0.09; COR = 1.45; 95% CI = 0.94–2.23). The association between HIV positive status and better antidiabetic medication was still significant in multivariate analysis (Table 5).

5. Discussion

The duration of diagnosed diabetes was less than 5 years for nearly half of the patients in this study, however; over 80% of patients had documented complications in their charts. This implies either the possibility of late diagnosis, calling for an increase in screening programmes in the community especially given the likelihood of the high prevalence rates of diabetes in Botswana; alternatively poor adherence to combined treatment approaches, including diet, exercise and medicines. Screening programs to diagnose diabetes mellitus earlier will help reduce both microvascular and macrovascular complications as well as associated costs.[34,72,73]

Overall, adherence to antidiabetic medication was found to be suboptimal with only 57.6% of patients demonstrating high adherence (Table 3). This is higher though than in a Nigerian study using the same instrument which reported only 40.6% of patients with high medication adherence.[74] While other studies have shown costs, i.e. patient co-payments, to significantly affect adherence to antidiabetic medication,[50,55,75] the same cannot be said for Botswana as medication for the treatment of DM are provided free of charge. However, this rate of adherence was low compared to other studies undertaken in Nigeria (72.5%),[76] as we; as Uganda (71%)[55] and Tanzania (71.2%).[50] The reason for the differences seen may partly be explained by the different methodologies used to estimate adherence rates in the various studies. These studies typically used patients' recall on adherence or pill counts. However, we feel that the use of the Morisky scale is justified in our study to estimate adherence as this methodology is well validated and has been used widely.[77] In any event, our findings mean more educational and other input needs to be undertaken in the clinics to improve adherence rates in Botswana.

Interestingly in our study, high adherence to diabetes medicines was not significantly associated with better glycemic control, which is similar though to other studies.[50,78,79] However, it is important to point out that only antidiabetic medication adherence was studied and not other factors including physical exercise and diet, in addition to HIV medication.[80–82]

Other studies have also shown contrasting results on factors affecting adherence to antidiabetic medication, with factors ranging from demographic characteristics such as age, gender and level of education[55,83–85] to clinical and medication factors such as duration of diagnosed diabetes, modality of treatment and complexity of treatment.[40] The findings of our study (Table 4) did not reveal any association to any of these commonly studied variables. This may again reflect different methodologies and settings, and needs further investigation.

Patients with an HIV-positive status in this study were found to be more adherent than those with an HIV-negative or –unknown

Table 4
The relationship between sociodemographic, clinical, and other characteristics on adherence to antidiabetic medication.

Characteristics	Adherent[a]	Non-adherent[a]	Crude OR (95% CI)	p-Value
Age group				0.43
<36	24	8	1 (Ref)	
36–50	41	37	2.72 (1.82–9.04)	
51–65	96	67	2.21 (0.64–7.66)	
>66	54	49	2.31 (0.62–8.62)	
Sex				0.50
Male	71	45	1 (Ref)	
Female	144	116	1.18 (0.73–1.93)	
Education level				0.16
No/primary	148	103	1 (Ref)	
Secondary or higher	67	58	1.47 (0.86–2.50)	
Marital status				0.73
Married/cohabiting	105	80	1 (Ref)	
Single/separated/divorced/widowed	110	81	1.08 (0.69–1.69)	
HIV status				0.01
Negative	122	112	1 (Ref)	
Positive	30	8	0.29 (0.12–0.69)	
Unknown	66	38	0.68 (0.41–1.41)	
Type of diabetes				0.56
Type 1	17	6	1 (Ref)	
Type 2	198	155	0.63 (0.14–2.91)	
Diabetes duration				0.92
<5 years	114	64	1 (Ref)	
5–10 years	50	41	1.53 (0.89–2.65)	
>10 years	47	46	1.83 (1.02–3.28)	
Modality of treatment				0.28
OHA	127	97	1 (Ref)	
Insulin	38	13	0.24 (0.05–1.18)	
Both OHA and Insulin	57	44	0.46 (0.11–1.86)	

Note: 4 patients with no Morisky score results excluded from analysis.
[a] Adherent: Morisky score = 0/high adherence; Non-adherent: Morisky score ≥1/low and medium adherence.

Table 5
Logistic regression output showing factors associated with antidiabetic medication adherence.

	Adjusted OR (95% CI)	p-Value
HIV status		0.007
Negative	1 (Ref)	
Positive	0.29 (0.13–0.67)	
Unknown	0.68 (0.43–1.09)	

status. HIV care and services are well developed within Botswana's health care system. A patient in a diabetes clinic in Botswana was previously overheard, saying in Setswana (local language), "*Go ka bo go ne go le botoka go nna le HIV gona le bolwetse jwa sukiri*", and when translated to English, *"It would have been better if I had HIV instead of diabetes."*.[86] These words imply that diabetic patients may feel they are not cared for as well as their HIV positive counterparts. Screening for diabetes does not take place routinely; hence patients with diabetes are often diagnosed and come to the attention of specialist clinics only when they have already developed complications.[84] This will be explored further in future research in view of the growing prevalence of diabetes in Botswana, the need to ensure high adherence with prescribed treatment approaches, and the fact that our study revealed a positive association between HIV-positive status and better antidiabetic medication adherence (Table 5). Some of the 'unknowns' (Table 5) are also likely to be HIV positive in view of the prevalence in Botswana.[58] This phenomenon may possibly be explained by the fact that HIV positive patients receive counseling sessions and psychosocial support to enhance their antiretroviral medication adherence. As a result, also improving antidiabetic medication adherence, despite an appreciably increased pill burden. This will also be the subject of future research projects.

6. Study limitations

Our findings should be interpreted with caution. Firstly, we only conducted the study in one centre in Botswana. However, this was a leading clinic in Botswana and if poor adherence rates were seen here, the situation may be worse in other centres.

We also did not include psychosocial factors in our questionnaire. We acknowledge that other published studies have shown the role of factors including language, health literacy, social support, cultural factors and stigma, which can contribute to low adherence.[57] This will be investigated further in future studies.

Our study also only included aspects of pharmacotherapy. The importance of the other two components of diabetes care, namely physical exercise and dietary modifications, cannot be over stated in their role to enhance glycemic control and improve the outcome of patients with DM.

However, we do believe that this first study on antidiabetic medication adherence in Botswana including patients with concomitant HIV, and will encourage further research to improve future patient management in Botswana, given the current low adherence rates and high numbers of patients with DM, having complications early in their disease state.

7. Conclusion

About two in every five patients was non-adherent to antidiabetic medication. This is quite a significant number especially in this specialist clinic in Botswana where medicines are provided monthly at no cost to the patients. Only HIV-positive status was found to be significantly associated with better medication adherence, probably due to the effect of greater patient support and counseling offered at HIV clinics, despite appreciably increasing

the pill burden. This has important implications for improved management of patients with DM in Botswana in the future and will be the subject of further research along with exploring psychosocial factors associated with medication adherence that are pertinent to the Botswana setting. There is also a need for greater screening of patients to identify patients earlier to reduce complication rates.

Conflicts of interest

The authors declare they have no conflicts of interest and all the authors have read and approved the final submitted version.

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