Original Article

Adherence to Oral Hypoglycemic Drugs among Type 2 Diabetic Patients in a Resource-Poor Setting

Abstract

Objective: Diabetes mellitus is a growing public health problem in many countries including Ghana. Adherence to drugs, especially among patients with type 2 diabetes mellitus (T2DM) is often poor is some resource-poor settings. The objective of this study was to assess adherence to oral hypoglycemic drugs and factors that affect adherence among patients with T2DM in the Volta Region of Ghana. **Methods:** The study was cross-sectional and conducted among 400 patients with T2DM attending diabetic clinics at 4 randomly selected hospitals in the Volta Region of Ghana between January 10 and March 30, 2015. Patients were interviewed using a structured questionnaire and other data collection tools to determine the commonest self-reported reason(s) for nonadherence. Adherence was assessed using the 8-item Morisky Medication Adherence Scale. Multivariate analysis was performed between adherence and statistically significant patient variables. **Results:** Adherence to oral hypoglycemic drugs among T2DM patients was 47.75%. The odds of adherence with fasting blood glucose between 1 and 6 mmol/L was approximately two-fold (adjusted odd ratio [aOR] =1.92, confidence interval [CI]: 1.11–3.32) versus the odds of having fasting blood glucose of above 10 mmol/L. The odds of adherence among patients with tertiary education was approximately three-fold (aOR = 3.01 CI: 1.44–6.269) versus patients with no formal education. The commonest self-reported reason for nonadherence was forgetfulness. **Conclusion:** Adherence to oral hypoglycemic drugs among T2DM patients in the current study was sub-optimal. Therefore, in such settings, management of T2DM must include strategies to identify nonadherent patients, and regular patient education and counseling.

Keywords: *Adherence, oral hypoglycemic drugs, resource-poor setting, type 2 diabetes mellitus*

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Introduction

Diabetes mellitus (DM) is a metabolic disorder characterized by impaired insulin-mediated glucose disposal as a result of absence of insulin, or the inability of the human body to respond to insulin.[1] DM is ranked as the seventh leading cause of death worldwide.[2,3] DM, if left untreated or poorly controlled, is a major cause of morbidity and mortality. This is mostly due to macrovascular and microvascular complications associated with the disease.[4,5] DM is also known to adversely affect the quality of life of patients.[6,7] DM is a growing problem in sub-Saharan Africa, as there has been an appreciable change in diet and lifestyle of indigenes, Ghana inclusive.[8-10] In Ghana, the prevalence of DM according to International Diabetes Federation data as of 2013 was 3.35%.[11] Furthermore, the prevalence of especially type 2 diabetes mellitus (T2DM) in African countries appears to be on the rise.[12]

Management of DM includes pharmacotherapy. Some of the pharmacotherapeutic approaches include the use of oral hypoglycemic (antidiabetic) drugs, exogenous insulins, and lipid lowering drugs.[13] A major challenge to the management of DM is nonadherence to therapy. This is highly prevalent in patients with T2DM, and has been linked with an increase in morbidity, mortality, and healthcare costs.[14-16] On the average, 50% of new medication users will fail to adhere to at least 80% of prescribed drugs during the first year of therapy.[17,18] A systematic review of drugs for DM found that patients adherence ranged between 36% and 93%,[14] with some being as low as 23%.[19] Overall, the World Health Organization (WHO) estimates adherence among patients suffering from chronic diseases to be around 50% in developed countries, and much

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lower in developing or resource-poor countries.[20] Studies have also shown that, there is an association between poor adherence to medications indicated for chronic diseases and health resource utilization.[21]

There have been several studies which have explored adherence to oral hypoglycemic medications among diabetic patients with varying results. Some factors found to be associated with nonadherence to oral hypoglycemic medication include financial difficulties, forgetfulness, level of education of patients, existing diabetes complications, among others.[16,17,19] One major impact of nonadherence to antidiabetic medications is increased costs to families especially in most African countries where healthcare costs are borne by patients.[16] In Ghana, there is paucity of data on adherence to diabetic treatment especially in rural areas where the population is generally poor, and with less access to health care. Furthermore, most of adherence to oral hypoglycemic drugs among T2DM patients have been carried out in developed countries, leaving a gap in knowledge about the prevalence and factors that may be associated with adherence to diabetes treatment in resource-poor settings.

This study, therefore, sought to evaluate adherence to oral hypoglycemic agents among T2DM patients in the Volta Region of Ghana, and possible impact on glycemic control. Data from this study would inform policymakers, health managers, and health workers: with a future need of designing interventions that will improve patient adherence.

Methods

Study design and setting

This was a cross-sectional study among T2DM patients who reported to 4 district/municipal hospitals in the Volta Region of Ghana between January 10, 2015, and March 30, 2015. The study was conducted in Government Hospitals which operated diabetic clinics. The 4 hospitals were Ho Municipal Hospital and Hohoe Municipal Hospital (representing Northern Volta), and Keta Municipal Hospital and Ketu South District Hospital (representing Southern Volta).

Volta Region of Ghana (as it was called before the creation of new regions in Ghana in February 2019), could be divided into two geographical sectors: Northern and Southern Volta. Volta Region was one of Ghana's ten administrative regions. The region's capital was Ho and had an estimated regional area of 20,570 km_2. The population of the Region as of the year 2000 was 1,635,421. In the 2010 population census, a population of 2,118,252 was reported, and this represented 8.6% of the total population of Ghana.

Sampling and sample size calculation

Prevalence of nonadherence to oral anti-diabetic therapy among adults was estimated as 40% based on a similar study conducted in ambulatory patients with T2DM in a healthcare setting in Southwestern Nigeria.[22] The level of significance and margin of error were set as 0.05% and 5% respectively. This gave a minimum sample size of 368. The sample size was increased to 400 to account for 10% nonrespondents.

Study population

T2DM patients were included in this study if they were aged 18 years and above after initially giving informed consent. Patients were randomly sampled from Ho Municipal Hospital (n = 200), Keta Municipal Hospital (n = 100), Hohoe Municipal Hospital (n = 50) and Ketu South Municipal Hospital (n = 50). Differences in sample size per hospital were based on respective average total attendance per month per hospital. Patients who did not consent to be part of the study were excluded.

Data collection

Questionnaires were administered by trained pharmacists and pharmacist technicians in all the 4 study centers. Data collected included social demographics, adherence to oral hypoglycemic agents and clinical parameters (obtained from hospital records). Clinical parameters included comorbidity (whether patients had hypertension, etc.) or complications of T2DM (e.g., neuropathy). The questionnaire used, the 8-item Morisky Medication Adherence Scale (MMAS-8) consisted of 7 dichotomous questions and a 5-point Likert scale questions. Questionnaires were pretested among 10 T2DM patients (at Ho Municipal Hospital).

To ensure privacy, respondents were individually interviewed in counseling rooms at all 4 study sites. Patients were also assured of confidentiality before interview process.

Data analysis

Data generated from the questionnaires were analyzed using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 21 software. Descriptive statistical analysis was used for demographic data. For level of adherence, patients were classified as adherent if the MMAS-8 score obtained was between 6 and 8, and nonadherent if the MMAS-8 score obtained was <6.[23]

Cross-tabulation was subsequently performed to assess relationship between socio-demographic characteristics, as well as clinical characteristics and adherence score of patients. A multivariate analysis was subsequently done to predict adherence in statistically significant independent variables obtained after cross-tabulation. This was done by determining odd ratios at a 95% confidence interval (CI).

Ethical issues

The study was approved by Administrations of selected government hospitals under the Ghana Health Service.

Written informed consent was obtained from all study participants. Data were kept securely locked at all times and was only accessible to researchers.

Results

Sociodemographic characteristics of patients

Of the 400 patients interviewed, about two-third were females and about 50% middle-aged (41–60 years). More than half of the respondents were married, and most had some form of formal education (with approximately one-third having had a middle school/junior high school education). The majority of interviewed patients were employed: with about 50% being self-employed and about 25% being unemployed. A summary of demographic data of respondents is shown in Table 1a. Almost all of the patients (99.3%) were National Health Insurance Scheme holders. About 80% of the patients had no social history of taking neither alcohol nor smoking. Other sociodemographic information are shown in Table 1b.

Clinical characteristics of patients

Clinical data showed that about 40% of T2DM patients were on oral hypoglycemic agents for about 3–6. Only about 12% of the patients had been on oral hypoglycemic agents for more than 10 years. Hypertension was the commonest (63.7%) co-morbid condition among patients, whilst the presence of diabetic neuropathy (4.5%) resulted in an increase in the total number of oral drugs to be taken by patients. About seven out of ten patients had their medications prescribed for just 1 month duration after hospital visit. In addition, about half of the patients (n = 209; 52.3%) recorded a MMAS-8 score of <6 and hence were classified as nonadherent to their treatment regimen. A summary of clinical characteristics of respondents is shown in Table 2a. Additional clinical characteristics of respondents is shown in Table 2b. Furthermore, fasting blood glucose level of patients on day of interview is also shown in Table 3.

The commonest self-reported reason for nonadherence was forgetfulness (30.87%), followed by a combination of forgetfulness and the side effects of the medication. A summary of reasons for nonadherence is shown in Figure 1.

Multivariate analysis between adherence and selected characteristics of respondents

Cross-tabulation of independent variables against adherence gave statistically significant

Table 1a: Sociodemographic characteristics of patients and level of adherence (n=400)

Sociodemographic characteristics	Total, n (%)	Adherence level of respondents		P[a]
		Nonadherent, n (%)	Adherent, n (%)	
Gender				
Male	112 (28.0)	50 (23.9)	62 (32.5)	0.058
Female	288 (72.0)	159 (76.1)	129 (67.5)	
Age (years)				
Young group (18-40)	34 (8.5)	14 (6.7)	20 (10.4)	0.056
Middle age (41-60)	200 (50.0)	116 (55.5)	84 (43.9)	
Elderly (>60)	166 (41.5)	79 (37.8)	87 (45.5)	
Marital status				
Married	236 (59.0)	128 (61.2)	108 (56.5)	0.109
Not married	83 (20.8)	35 (16.7)	48 (25.1)	
Separated/divorced/widowed	81 (20.3)	46 (22.0)	35 (18.3)	
Educational status				
Primary/elementary	90 (22.5)	50 (23.9)	40 (20.9)	0.002
Middle school/junior high	139 (34.8)	64 (30.6)	75 (39.2)	
Senior high/vocational	27 (6.8)	19 (9.1)	8 (4.2)	
Tertiary	60 (15.0)	22 (10.5)	38 (19.9)	
No formal education	84 (21.0)	54 (25.8)	30 (15.7)	
Employment status				
Unemployed	108 (27.0)	55 (26.4)	53 (27.7)	0.545
Employed	58 (14.5)	29 (13.9)	29 (15.2)	
Self-employed	195 (48.8)	108 (51.6)	87 (45.5)	
Retired	39 (9.8)	17 (8.1)	22 (11.5)	
Religion				
Christian	357 (89.3)	187 (89.5)	170 (89.0)	0.332
Muslim	7 (1.8)	2 (0.9)	5 (2.6)	
Traditional	32 (8.0)	19 (9.1)	13 (6.8)	
Others	4 (1.0)	1 (0.5)	3 (1.5)	

[a]P value from Chi-square

Table 1b: Other sociodemographic characteristics of respondents and adherence (*n*=400)

Sociodemographics characteristic	Total, *n* (%)	Adherence level of respondents		*P*[a]
		Nonadherent, *n* (%)	Adherent, *n* (%)	
Social status				
Smoking	17 (4.3)	10 (4.8)	7 (3.7)	0.044
Alcohol	39 (9.8)	25 (12.0)	14 (7.3)	
Both	5 (1.3)	0 (0.00)	5 (2.6)	
None	339 (84.8)	174 (83.2)	165 (86.4)	
NHIS registration status				
NHIS registrant	397 (99.3)	207 (99.0%)	190 (99.5)	0.616
Non-NHIS registrant	3 (0.8)	2 (1.0)	1 (0.5)	

[a]*P* value from Chi-square. NHIS: National Health Insurance Scheme

Table 2a: Clinical characteristics of respondents at the 4 study sites (*n*=400)

Clinical characteristic	Total (*n*=400), *n* (%)	Adherence level of respondents		*P*[a]
		Nonadherent (*n*=209), *n* (%)	Adherent (*n*=191), *n* (%)	
Number of years of being on oral hypoglycemic medication since diagnosis (years)				
<1-2	87 (21.8)	35 (16.7)	52 (27.2)	0.03
3-6	174 (43.5)	92 (44.1)	82 (42.9)	
7-10	88 (22.0)	55 (26.3)	33 (17.3)	
>10	51 (12.8)	27 (12.9)	24 (12.6)	
Number of oral hypoglycemic drugs prescribed at last attendance				
1	50 (12.5)	24 (11.5)	26 (13.6)	0.198
2	215 (53.8)	106 (50.7)	109 (57.1)	
3	135 (33.7)	79 (37.8)	56 (29.3)	
Number of oral hypoglycemic drugs prescribed that were unavailable at hospital pharmacy at last attendance				
0	304 (76.0)	172 (82.3)	132 (69.1)	0.005
1	81 (20.3)	33 (15.8)	48 (25.1)	
2	15 (3.7)	4 (1.9)	11 (5.8)	
Presence of chronic comorbid condition at last attendance				
Yes	317 (79.3)	170 (81.3)	147 (77.0)	0.281
No	83 (20.7)	39 (18.7)	44 (23.0)	
Chronic comorbid condition presented with diabetes at last attendance				
Hypertension	255 (63.7)	132 (63.2)	123 (64.4)	0.338
Diabetes neuropathy	18 (4.5)	13 (6.2)	5 (2.6)	
Hypertension + neuropathy + retinopathy	16 (4.0)	10 (4.8)	6 (3.1)	
Hypertension + neuropathy	7 (1.8)	2 (1.0)	5 (2.6)	
Other co-morbid condition	18 (4.5)	10 (4.7)	8 (2.6)	
No co-morbid condition	86 (21.5)	41 (19.6)	45 (23.6)	

[a]*P* value from Chi-square

association ($P < 0.05$) with a number of variables. The variables were: number of years patients had been on their oral hypoglycemic medicines, alcohol/smoking social history status, educational status, fasting blood glucose on the day of interview, and the number of oral hypoglycemic drugs prescribed.

However, multivariate logistic regression controlling for all variables as possible confounders found that alcohol, smoking, and number of years patients were on their oral hypoglycemic agents did not retain their statistical significance [Table 4]. The variables that retained their significance after the multivariate analysis were the fasting blood glucose level recorded on the day of interview, educational status and the number of oral hypoglycemic agents prescribed but unavailable (out of stock) at the pharmacy. The multivariate analysis also revealed that, the odds of adherence was approximately 2-fold in respondents with fasting blood glucose of between 1

Table 2b: Other clinical characteristics of respondents at the 4 study sites (*n*=400)

Clinical characteristic	Total (*n*=400), *n* (%)	Adherence level of respondents		*P*[a]
		Nonadherent (*n*=209), *n* (%)	Adherent (*n*=191), *n* (%)	
Total medications prescribed for diabetes and comorbid conditions				
1-2	99 (24.8)	45 (21.5)	54 (28.3)	0.256
3-4	269 (67.3)	148 (70.8)	121 (63.4)	
≥5	32 (8.0)	16 (7.7)	16 (8.4)	
Duration of oral hypoglycemic agents prescribed at last attendance (months)				
1	281 (70.3)	151 (72.2)	130 (68.1)	0.407
2	118 (29.5)	58 (27.8)	60 (31.4)	
3	1 (0.3)	0 (0.0)	1 (0.5)	
Type of oral hypoglycemic agents prescribed at last attendance				
Metformin	34 (8.5)	19 (9.1)	15 (7.9)	0.547
Glibenclamide	16 (4.0)	7 (3.4)	9 (4.7)	
Metformin + glibenclamide	167 (41.8)	86 (41.1)	81 (42.4)	
Metformin + glimepiride	37 (9.2)	19 (9.1)	18 (9.4)	
Metformin + gliclazide	18 (4.5)	9 (4.3)	9 (4.7)	
Metformin + glibenclamide + pioglitazone	32 (8.0)	22 (10.5)	10 (5.2)	
Metformin + glimepiride + pioglitazone	13 (3.3)	8 (3.8)	5 (2.6)	
Metformin + gliclazide + pioglitazone	73 (18.3)	36 (17.2)	37 (19.4)	
Others	10 (2.5)	3 (1.4)	7 (3.7)	
Number of oral hypoglycemic agents prescribed at maximum dose				
0	243 (60.7)	120 (57.4)	123 (64.4)	0.197
1	72 (18.0)	42 (20.1)	30 (15.7)	
2	82 (20.5)	44 (21.1)	38 (19.9)	
3	3 (0.8)	3 (1.4)	0 (0.0)	

[a]*P* value from Chi-square

Table 3: Fasting blood glucose level of respondents taken on day of interviews (*n*=400)

Characteristic	Total (*n*=400), *n* (%)	Adherence level of respondents		*P*[a]
		Nonadherent, *n* (%)	Adherent, *n* (%)	
Fasting blood glucose checked on day of attendance (mmol/L)				
1-6	120 (30.0)	50 (23.9)	70 (36.6)	0.02
7-10	158 (39.5)	91 (43.5)	67 (35.1)	
>10	122 (30.5)	68 (32.6)	54 (29.3)	

[a]*P* value from Chi-square

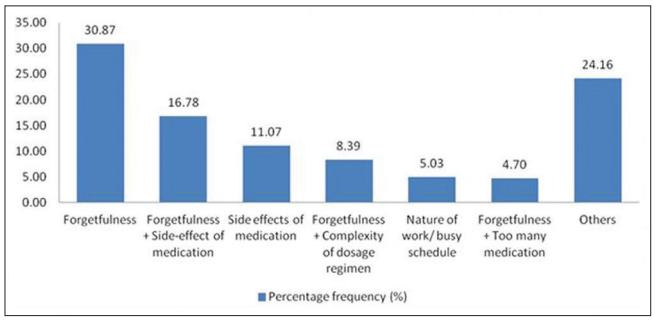

Figure 1: Self-reported reasons for nonadherence to oral hypoglycemic agents among respondents (*n* = 400)

and 6 mmol/L as compared to those with fasting blood glucose >10 mmol/L (adjusted odd ratio [aOR] =1.92, CI: 1.11–3.319). The aOR obtained was also statistically significant with $P < 0.05$ and a narrow CI.

Furthermore, patients who did not receive all their prescribed medication at their facility had relatively higher odds of adherence [Table 4]. Patients who had at least one drug prescribed but not dispensed had approximately two-fold odds of adherence (odd ratio = 1.99, CI: 1.19–3.33).

The multivariate analysis also showed that educational status had statistically significant association with adherence. From the bivariate analysis, respondents who had middle school/junior high education had approximately two-fold odds of increased adherence compared to those with no formal education, but the ratio reduced

Table 4: Predictors of adherence to oral hypoglycemic agents from logistic regression model[a]

Patient characteristics	cOR (95% CI)	aOR (95% CI)
Number of years on drugs since diagnosis		
<1-2	1.858 (0.917-3.767)	1.869 (0.883-3.955)
3-6	1.094 (0.579-2.068)	1.073 (0.544-2.115)
7-10	0.759 (0.374-1.538)	0.805 (0.379-1.710)
>10 (*r*)	1	1
Number of drugs prescribed that were unavailable at hospital pharmacy at last attendance		
1	1.895 (1.152-3.118)*	1.734 (1.008-2.984)*
2	3.583 (1.116-11.507)*	3.726 (1.071-12.961)*
0 (*r*)	1	1
Fasting blood glucose checked on day of attendance to clinic (mmol/L)		
1-6	1.763 (1.059-2.934)*	1.920 (1.110-3.319)*
7-10	0.927 (0.576-1.493)	1.004 (0.597-1.686)
>10 (*r*)	1	1
Educational status		
Primary/elementary	1.44 (0.782-2.650)	1.16 (0.604-2.224)
Middle school/junior high	2.109 (1.208-3.682)**	1.89 (1.029-3.460)*
Senior high/vocational	0.758 (0.296-1.938)	0.61 (0.222-1.656)
Tertiary	3.109 (1.561-6.193)**	3.01 (1.445-6.269)**
No formal education (*r*)	1	1
Social status		
Smoking	0.738 (0.275-1.985)	0.52 (0.179-1.518)
Alcohol	0.591 (0.297-1.175)	0.48 (0.227-1.025)
Both	1703591652	1237943851
None (*r*)	1	1

[a]*P<0.05, **P<0.01, figures without asterix are not statistically significant; *r*: Represents reference category; cOR (95% CI): Unadjusted odds ratio from simple logistics regression with a 95% confidence interval, aOR (95% CI): Adjusted odds ratio from a multiple logistics regression (all variables were included in the model), model summary; −2 log likelihood=336.461; Cox and Snell R^2=0.077; Nagelkerke R^2=0.127; **P* value significant at <0.05. aOR: Adjusted odd ratio; CI: Confidence interval

after adjusting for confounders. The odds of adherence among tertiary education respondents was approximately three-fold (aOR = 2.888, CI: 1.394–5.982) compared to those with no formal education, and this value was similar to the crude odds ratio indicating the absence of confounding effect.

Discussion

In this study, we assessed adherence and factors that affect adherence among T2DM patients on oral hypoglycemic agents in the Volta Region of Ghana. Our data showed that adherence to oral hypoglycemic agents among our study population was 47.7%. This percentage is similar to overall adherence rates reported by the WHO for patients with chronic conditions.[20] Adherence to oral hypoglycemic agents in the current study was similar to a 6-month cross-sectional study conducted among 7 primary clinics in Malaysia.[24] However, our finding was marginally lower than the 51.3% observed in a similar study conducted in Ethiopia,[25] but higher than a 40.1% reported in Nigeria.[26] The differences observed could be due to differences in study settings and adherence scales used. It is noteworthy that, self-reported measurement of adherence has the tendency of overestimating adherence. Since interviews were conducted in a healthcare facility, patients may tend to report higher levels of adherence in order to please healthcare provider or to avoid criticism.

In the current study, variables that retained their significance after the multivariate analysis were educational status, fasting blood glucose level recorded on the day of interview and the number of oral hypoglycemic agents prescribed but not dispensed at the pharmacy of visited clinic. Generally, level of adherence to drugs is known to increase with increasing level of education.[24-26] An important barrier to adherence is the inability of a patient to understand instructions for taking medication. Patients' beliefs are also known to be a strong predictor of adherence. Whilst we did not investigate this in our study, we believe that education has the tendency to positively influence ones beliefs.

In the current study, adherence was higher in patients with fasting blood glucose level between 1 and 6 mmol/L. This is similar to findings from a systematic review which concluded that better adherence to oral hypoglycemic agents tended to be associated with improved glycemic control.[27] Data from the current study showed that only 30% of the respondents had adequate glycemic control (1–6 mmol/L). It is noteworthy that lack of appropriate therapy may be one of the reasons patients fail to reach recommended therapeutic targets, hence, the

need for continuous patient follow-up and drug regimen modification, if need be.

Data from current study showed that forgetfulness was the highest self-reported reason for nonadherence to oral hypoglycemic agents. The second highest self-reported reason for non-adherence was a combination of forgetfulness and side-effects of medication. This is consistent with findings in other studies that reported forgetfulness as the main reason for nonadherence to therapy.[28] Whilst lack of oral hypoglycemic agents in stock was reported as a key barrier for adherence to oral hypoglycemic agents,[28] our study showed that patients who had one or two undispensed medication(s) due to unavailability were more adherent than those who received all their medications. Our study, however, did not probe to find out whether these patients obtained drugs elsewhere.

Forgetfulness has been identified as one of the major contributors to nonadherence to antidiabetic medication.[28,29] To address this short-fall, there is need for regular follow-up visits, counseling sessions involving a family member, and even patient group campaigns. Healthcare workers home visits are likely to significantly improve adherence to antidiabetic medication, improve glycemic control and overall health outcomes. Furthermore, mobile technology for sending reminders have demonstrated improved medication adherence among people with HIV.[30]

We acknowledge that a limitation of our study is the use of self-reported data which has the tendency to overestimate adherence due to recall challenges and patient bias. However, research has suggested that validated self-report questionnaires provide a reasonably accurate estimate of adherence.[23] We are also aware that a preferred indicator for glycemic control is the glycated hemoglobin. However, our study used fasting blood glucose, which is an equally good indicator of glycemic control. In addition, our study sites were diabetic clinics which were government facilities providing free service and medication to National Health Insurance holders, conditions which may not exist in some resource-poor settings. Nevertheless, we believe our findings are relevant and reflect what pertains in a number of resource-poor settings.

Conclusion

Adherence to oral hypoglycemic drugs among respondents with T2DM was found to be 47.75%. The commonest self-reported reason for nonadherence was forgetfulness. Adherence to treatment regimen was significantly associated with fasting blood glucose level, educational status, and availability of prescribed medication at health facility. Therefore, in such settings, management of T2DM must include strategies to identify nonadherent patients, and regular patient education and counseling.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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