

Frequency and predictors of suboptimal glycemic control in an African diabetic population

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Background: Persistent suboptimal glycemic control is invariably associated with onset and progression of acute and chronic diabetic complications in diabetic patients. In Uganda, studies documenting the magnitude and predictors of suboptimal glycemic control in adult ambulatory diabetic patients are limited. This study aimed at determining the frequency and predictors of suboptimal glycemic control in adult diabetic patients attending three urban outpatient diabetic clinics in Uganda.

Methods: In this hospital-based cross-sectional study, eligible ambulatory adult diabetic patients attending outpatient diabetic clinics of three urban hospitals were consecutively enrolled over 11 months. Suboptimal glycemic control was defined as glycosylated hemoglobin (HbA_{1c}) level $\geq 7\%$. Multivariable analysis was applied to determine the predictors.

Results: The mean age of the study participants was 52.2 \pm 14.4 years, and the majority of them were females (283, 66.9%). The median (interquartile range) HbA_{1c} level was 9% (6.8%–12.4%). Suboptimal glycemic control was noted in 311 study participants, accounting for 73.52% of the participants. HbA_{1c} levels of 7%–8%, 8.1%–9.9%, and $\geq 10\%$ were noted in 56 (13.24%), 76 (17.97%), and 179 (42.32%) study participants, respectively. The documented predictors of suboptimal glycemic control were metformin monotherapy (odds ratio: 0.36, 95% confidence interval: 0.21–0.63, $p < 0.005$) and insulin therapy (odds ratio: 2.41, 95% confidence interval: 1.41–4.12, $p = 0.001$).

Conclusion: Suboptimal glycemic control was highly prevalent in this study population with an association to metformin monotherapy and insulin therapy. Strategies aimed at improving glycemic control in diabetes care in Uganda should be enhanced.

Keywords: suboptimal glycemic control, frequency, predictors, Africa, Uganda

Introduction

Acute diabetic complications such as diabetic ketoacidosis and chronic micro- and macrovascular diabetic complications and their associated adverse outcomes are intimately related to suboptimal glycemic control in clinical practice. Each 1% reduction in the mean glycosylated hemoglobin (HbA_{1c}) has been shown to be associated with reduction in risk of 21% for deaths related to diabetes, 14% for myocardial infarction, and 37% for microvascular complications.¹ Despite this unequivocal clinical evidence that underscores the value of optimal glycemic control among diabetic patients, studies from sub-Saharan Africa and other regions of the world still document that majority of the patients in clinical care do not attain the recommended glycemic targets.^{2–4} This ultimately translates to increased risk of onset and progression of the fatal diabetic complications, hence increasing morbidity and mortality.

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Due to the economic growth and ensuing rapid urbanization, there is a demonstrable growing trend of diabetes mellitus (DM) and other noncommunicable diseases in Uganda. Several published community-based cross-sectional studies performed in different regions of rural and semi-urban Uganda have reported different prevalence of DM ranging from 0.4% to 9%.⁵⁻⁸ The disparity in the reported prevalence could probably be explained by the differences in the study diagnostic methods. A recently concluded representative national survey on the burden of noncommunicable diseases in Uganda using the standardized World Health Organization's stepwise approach reported a low prevalence of DM of 1.4%, which is also lower than the International Diabetes Federation 2014 estimate of 4.4%.^{9,10}

Despite this growing trend of DM in Uganda, studies assessing the levels of glycemic control and related factors among adult diabetic patients are limited. The objective of this study was to determine the frequency of suboptimal glycemic control and its related factors among adult diabetic patients attending outpatients' diabetic clinics at three urban hospitals in Kampala, the capital city of Uganda. This information obtained will be integral in influencing evidence-based policy formulation and implementation in the national and institutional diabetes management programs.

Study methods

Study design, setting, and selection criteria

This was a cross-sectional study performed between September 2014 and July 2015 in three outpatient diabetic clinics of Mulago National Referral and Teaching Hospital, a public hospital where health services are offered at no charge, and at Mengo Hospital and Our Lady of Consolata Hospital Kisubi, which are not-for-profit, faith-based hospitals where health services are offered at subsidized fees. All these hospitals manage an adult diabetes clinic at least once weekly.

At each center, patients aged ≥ 18 years with a diagnosis of diabetes confirmed by a general practitioner or physician using fasting blood glucose levels, an oral glucose tolerance test, HbA_{1c}, or random blood sugar level in the presence of symptoms of diabetes and having been receiving care for at least a minimum of 6 months were enrolled consecutively until the desired sample size was attained. All eligible patients offered written informed consent prior to being enrolled into the study.

Data collection

Using a pretested questionnaire, information about the study participants' sociodemographic characteristics, preexisting

medical conditions (coexisting hypertension and HIV), type of diabetes, age at diagnosis of DM, duration since diagnosis, and drug history were collected. All participants underwent standard anthropometric measurements to calculate the body mass index (BMI), and blood pressure (BP) was also measured. A fasting venous blood sample was obtained from each study participant after consent for determination of the HbA_{1c} levels and to perform a fasting lipid profile. The analysis was done at each center using a full automated COBAS® integra 400 (Roche Diagnostics GmbH, Indianapolis, IN, USA) machine.

Statistical analysis

Data were entered into Microsoft Excel database, and Stata software (College Station, TX, USA), version 12.1 was used for all statistical analysis. Patient characteristics were reported as frequency and percentage for categorical variables, mean and standard deviation for the normally distributed continuous variables, and median and interquartile range (IQR) for continuous variables that were not normally distributed.

The 2015 American Diabetes Association (ADA) guidelines of standards of care of diabetes care were used to define suboptimal glycemic control as HbA_{1c} levels $\geq 7\%$. Other components of optimal diabetes care were also defined as follows: optimal BP $< 140/90$ mmHg, optimal low-density lipoprotein cholesterol ≤ 2.6 mmol/L, high-density lipoprotein cholesterol ≥ 1 mmol/L for men and ≥ 1.3 mmol/L for women, triglyceride ≤ 1.7 mmol/L, and total cholesterol concentrations ≤ 5 mmol/L.¹¹ Proportions of participants with HbA_{1c} levels of $< 7\%$, $7\% - 8\%$, $8.1\% - 9.9\%$, and $\geq 10\%$ were analyzed. In addition, we also analyzed the proportion of participants with: 1) optimal BP, glycemic, and lipid control; 2) optimal BP and glycemic control; 3) optimal BP and lipid control; and 4) optimal lipid and glycemic control.

To determine associations between the different sociodemographic, clinical, and laboratory factors and suboptimal glycemic control, bivariate analyses using χ^2 test were performed. Multivariate analysis was then performed to identify the independent predictors. A *p*-value of < 0.05 and confidence intervals (CIs) not including 1 were considered to be statistically significant.

Ethics approval

This study was approved by the ethics review board of Makerere University College of Health Sciences, Mengo Hospital, and Our Lady of Consolata Hospital Kisubi.

Results

Sociodemographic and clinical characteristics of the study participants

The mean age of the study participants was 52.2 ± 14.4 years, with majority being females (283, 66.9%). Most of the study participants were educated to a primary or lower level of education (165, 39%) and were urban dwellers (288, 67.9%). A low prevalence of smoking (2.35%) was reported among the study participants.

Type 2 DM diagnosed using clinical criterion was the most common type of DM in this study population, accounting for 86.87% of the cases. Hypertension as a comorbidity and a family history of DM were also frequently seen, accounting for 68.87% and 62.26% of the participants, respectively. This study population had a relatively short duration of diabetes (median duration [IQR]: 4.5 [2–10] years) and a young age at diagnosis (median duration [IQR]: 47 [37–55] years). With regard to glycemic therapy, majority were on a combination of oral hypoglycemic therapy and conservative approach (236, 56.66%). Insulin therapy either as monotherapy or in combination with metformin was used in 188 (44.34%) participants (Table 1).

Table 1 Sociodemographic, clinical, and laboratory characteristics of the study participants

Variable	N (%)
Age in years, median (IQR)	53 (43.5–62)
Gender, n (%)	
Male	140 (33.02)
Female	284 (66.98)
Education level, n (%)	
None	38 (8.96)
Primary	165 (38.92)
Secondary	141 (33.25)
Tertiary	79 (18.63)
Occupation, n (%)	
Employed	212 (50)
Unemployed	212 (50)
Marital status, n (%)	
Married	259 (61.08)
Cohabiting	10 (2.36)
Single	47 (11.08)
Divorced	41 (9.67)
Widow/widowed	67 (15.80)
Place of residence	
Rural	136 (32.08)
Urban	288 (67.92)
Study site	
Government	199 (46.82)
Private	226 (53.18)
Smoking	
Yes	10 (2.35)
No	415 (97.65)

(Continued)

Table 1 (Continued)

Variable	N (%)
Known HT	
Yes	292 (68.87)
No	132 (31.13)
HIV coexistent	
Yes	17 (4.00)
No	408 (96.00)
FH-DM	
Yes	264 (62.26)
No	160 (37.74)
Type of DM	
Type 1 DM	55 (13.13)
Type 2 DM	364 (86.87)
Drug history	
Diet alone	3 (0.71)
Metformin alone	79 (18.59)
Met + SU	127 (29.88)
Met + SU + TZD	16 (3.76)
Met + Incretins	8 (1.88)
Insulin alone/+Met	188 (44.34)
Statins	89 (20.94)
Variable	Median (IQR), N=425
Age at diagnosis, years	47 (37–55)
Duration with DM, years	4.5 (2–10)
BMI, kg/m ²	27 (23–30.6)
HbA _{1c} (%)	9 (6.8–12.4)
LDLC, mmol/L	2.9 (2.3–3.84)
HDLC, mmol/L	1.19 (0.9–1.42)
TC, mmol/L	4.82 (4.1–5.71)
TGL, mmol/L	1.6 (1.23–2.2)
SBP, mmHg	139 (124–155)
DBP, mmHg	80 (73–91)

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Abbreviations: IQR, interquartile range; DM, diabetes mellitus; HT, hypertension; FH, family history; SU, sulfonylureas; Met, metformin; Pio, pioglitazone; BMI, body mass index; HbA_{1c}, glycated hemoglobin; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; TC, total cholesterol; TGL, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; TZD, thiazolidinediones.

Glycemic, BP, and lipid control among the study participants

Of the study participants enrolled, results of 423 participants were complete, and so these were used to analyze the extent of glycemic, BP, and lipid control. The median HbA_{1c} was 9 (6.8–12.4) %. Only 112 (26.48%) of the study participants had optimal glycemic control as defined by the 2015 ADA guidelines of diabetes management (ie, <7%). Majority of the participants had suboptimal glycemic control, defined as HbA_{1c} $\geq 7\%$ (311, 73.52%).

Considering other components of diabetes care, a very small proportion of the study participants had optimal glycemic, lipid, and BP control collectively (9, 2.1%). Optimal glycemic and BP control, glycemic and lipid control, and lipid

Table 2 Extent of glycemic, BP, and lipid control among the study participants (n=423)

HbA _{1c} (%)	N (%)
<7	112 (26.48)
7–8	56 (13.24)
8.1–9.9	76 (17.97)
≥10	179 (42.32)
All L (LDLC, HDLC, TC, TGL collectively), BP, HbA _{1c} normal	9 (2.1)
HbA _{1c} -BP normal	59 (13.9)
HbA _{1c} -L normal	15 (3.6)
L-BP normal	27 (6.4)

Abbreviations: L, lipid profile; HbA_{1c}, glycated hemoglobin; BP, blood pressure; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; TC, total cholesterol; TGL, triglycerides.

plus BP control were documented in only 13.9%, 3.6%, and 6.4% of the participants, respectively (Table 2).

Sociodemographic, clinical, and laboratory characteristics of the study participants at bivariate analysis

At bivariate analysis, metformin monotherapy ($p<0.005$), use of insulin therapy either as monotherapy or in combination with metformin ($p<0.005$), and systolic BP ($p=0.01$) were statistically significant. There was a trend toward significance for age of the study participants ($p=0.052$). Table 3

Table 3 Bivariate analysis of sociodemographic and clinical characteristics associated with suboptimal glycemic control

Characteristic	HbA _{1c} ≥7%, n (%)	HbA _{1c} <7%, n (%)	OR (95% CI)	p-value
Age, years				
≤40	30 (20.69)	82 (29.50)	0.62 (0.39–1.01)	0.052
>40	115 (79.31)	196 (73.52)		
Gender				
Male	41 (29.50)	98 (0.50)	0.79 (0.51–1.25)	0.325
Female	71 (25.00)	213 (75.00)		
Type of hospital				
Government	56 (28.14)	143 (71.86)	0.85 (0.55–1.31)	0.466
Private	56 (25)	168 (75)		
Place of residence				
Rural	28 (20.74)	107 (79.26)	1.57 (0.96–2.57)	0.067
Urban	84 (29.17)	204 (70.83)		
Smoking				
Smoker	3 (30.00)	7 (73.00)	0.84 (0.21–3.30)	0.799
Nonsmoker	109 (26.39)	304 (73.61)		
Coexisting HT				
Yes	78 (26.71)	214 (73.29)	0.96 (0.60–1.54)	0.870
No	34 (25.95)	97 (74.05)		
DM type				
Type 1 DM	13 (23.64)	42 (76.36)	1.21 (0.62–2.35)	0.571
Type 2 DM	99 (27.27)	264 (72.73)		
Family history of DM				
Yes	70 (26.52)	194 (73.48)	0.99 (0.64–1.55)	0.982

(Continued)

Table 3 (Continued)

Characteristic	HbA _{1c} ≥7%, n (%)	HbA _{1c} <7%, n (%)	OR (95% CI)	p-value
No	42 (26.42)	117 (73.58)		
HIV comorbidity				
Yes	5 (29.41)	12 (70.59)	0.86 (0.30–2.50)	0.780
No	107 (26.35)	299 (73.65)		
Median years with DM				
≤10	89 (27.55)	234 (72.45)	1.27(0.75–2.16)	0.368
>10	23 (23.00)	77 (77.00)		
BP, mmHg				
≤140/90	55 (23.81)	176 (76.19)	0.74 (0.48–1.14)	0.173
>140/90	57 (29.69)	135 (70.31)		
BMI, kg/m ²				
≤25	44 (26.83)	120 (73.17)	1	1
25.1–29	23 (21.90)	82 (78.10)	1.31 (0.73–2.33)	0.363
≥30	42 (30.43)	96 (69.57)	0.84 (0.51–1.38)	0.489
Glucose-lowering therapy, n (%)				
Metformin alone	41 (52.56)	37 (47.44)	0.23 (0.14–0.40)	<0.005
Met + SU	34 (26.77)	93 (73.23)	0.98 (0.61–1.57)	0.929
Incretins + Met	1 (12.50)	7 (87.50)	2.56 (0.31–21.10)	0.366
Met + SU + TZD	6 (37.50)	10 (62.50)	0.59 (0.21–1.66)	1.309
Insulin alone/+ Met	27 (14.36)	161 (85.64)	3.38 (2.04–5.59)	<0.005
On statin therapy, n (%)	26 (29.21)	63 (70.79)	0.84 (0.500–1.41)	0.511
LDLC, mmol/L				
≤2.6	45 (29.22)	109 (70.78)	1.26 (0.80–1.97)	0.32
>2.6	64 (24.71)	195 (75.29)		
HDLC, mmol/L				
<1	33 (26.61)	76 (26.39)	1.01 (0.62–1.63)	0.962
≥1	76 (26.39)	212 (73.61)		
TC, mmol/L				
≤5	64 (27.95)	165 (72.05)	1.19 (0.76–1.85)	0.443
>5	45 (24.59)	138 (75.41)		
TGL, mmol/L				
≤1.7	65 (27.78)	169 (72.22)	1.18 (0.76–1.84)	0.466
>1.7	44 (24.58)	135 (75.42)		
Non-HDLc, mmol/L				
<3.4	49 (29.52)	117 (70.48)	1.29 (0.83–2.02)	0.248
≥3.4	60 (24.39)	186 (75.61)		
TC/HDLC ratio				
<4.5	68 (29.06)	166 (70.94)	1.37(0.87–2.15)	0.170
≥4.5	41 (23.03)	137 (76.97)		
SBP, mmHg				
<140	45 (21.03)	169 (78.97)	0.56 (0.36–0.88)	0.01
≥140	67 (32.06)	142 (67.94)		
DBP, mmHg				
<90	72 (26.37)	201 (73.63)	0.99 (0.63–1.55)	0.948
≥90	40 (26.67)	110 (73.33)		

Abbreviations: OR, odds ratio; CI, confidence interval; DM, diabetes mellitus; BP, blood pressure; HT, hypertension; FH, family history; SU, sulfonylureas; Met, metformin; BMI, body mass index; HbA_{1c}, glycated hemoglobin; LDLc, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; TC, total cholesterol; TGL, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure; TZD, thiazolidinediones.

Table 4 Independent predictors of suboptimal glycaemic control on multivariable analysis

Variable	Unadjusted		Adjusted analysis	
	OR (95% CI)	p-Value	OR (95% CI)	p-Value
Place of residence	1.57 (0.96–2.57)	0.067	0.64 (0.38–1.07)	0.089
Metformin monotherapy	0.23 (0.14–0.40)	0.000	0.36 (0.21–0.63)	<0.005
Insulin therapy ^a	3.38 (2.04–5.59)	0.000	2.41 (1.41–4.12)	0.001

Note: ^aEither in monotherapy or in combination with metformin.

Abbreviations: OR, odds ratio; CI, confidence interval.

summarizes the sociodemographic, clinical, and laboratory characteristics of the study participants in association with suboptimal glycaemic control at bivariable analysis.

Independent predictors of suboptimal glycaemic control at multivariate analysis

The documented predictors of suboptimal glycaemic control were only glucose-lowering therapies, ie, metformin monotherapy (odds ratio [OR]: 0.36, 95% CI: 0.21–0.63, $p < 0.005$) and insulin therapy (OR: 2.41, 95% CI: 1.41–4.12, $p = 0.001$). Place of residence of the study participants was not statistically significant after multivariate analysis (OR: 0.64, 95% CI: 0.38–1.07, $p = 0.089$) (Table 4).

Discussion

This study documents a high prevalence of suboptimal glycaemic control among this ambulatory Ugandan adult diabetic population. The identified independent predictors of suboptimal glycaemic control were only glucose-lowering therapies, ie, metformin monotherapy and insulin therapy.

Comparable high frequencies of suboptimal glycaemic control have been reported in several studies performed in Africa and other developing countries. In the largest sub-Saharan African study assessing the quality of diabetes care in 2,352 type 2 DM patients, the mean HbA_{1c} was 8.2%±2.4%, with 71% of the patients having suboptimal HbA_{1c}, defined as levels >6.5%.² Other similar studies in Ethiopia, South Africa, and Uganda have documented frequencies of suboptimal glycaemic control to be between 64.7% and 79.2%.^{12–15} In another large study of 1,179 diabetic patients from Eastern Europe, Asia, Latin America, and Africa called the International Diabetes Mellitus Practice Study (IDMPS), suboptimal glycaemic control defined as HbA_{1c} greater than 7% was noted in 75% of the patients.¹⁶

The probable reasons to explain these high proportions of patients with suboptimal glycaemic control in our developing countries, as demonstrated in some of the studies, include lack of access to HbA_{1c} monitoring, inequitable access to diabetes medication, delay, and fear to initiate and optimize

insulin therapy among health care workers, low levels of patient education, and, generally, knowledge gaps in diabetes management among the health care workers.^{2,14–16}

Independent predictors of suboptimal glycaemic control

The two identified independent predictors were metformin monotherapy and insulin therapy. Metformin monotherapy was noted to have a protective effect against suboptimal glycaemic control in our study. Similarly in the IDMPS, among patients on oral glucose-lowering therapy, the use of fewer oral therapies was associated with attainment of optimal glycaemic goals in all the regions studied.¹⁶ Fewer medications in clinical practice generally tend to improve patient drug adherence and compliance, hence resulting in better treatment outcomes. Metformin monotherapy in clinical practice might reflect mild severity or early disease with easy attainment of glycaemic goals.

Insulin therapy was noted to increase the odds of suboptimal glycaemic control. This has also been reported in similar studies from Ethiopia and Brazil.^{12,17} However, poor glycaemic control cannot be directly attributed to insulin therapy per se. In diabetes care, there is an observed clinical inertia, which can be defined as the failure to initiate, establish appropriate targets, and optimize treatment so as to achieve treatment goals with regard to insulin therapy.¹⁸ This could be due to the physician's lack of knowledge and experience with insulin use and the patient's fear of insulin-induced hypoglycemia and weight gain. There is also hesitancy among patients to accept insulin treatment due to fear of pain of injections, cost, hypoglycemia, and weight gain. Insulin use is, thus, reserved for only patients with severe disease or for patients later in the disease course and for those that have failed to reach glycaemic goals despite very high doses of oral glucose-lowering drugs.

Study limitations

Due to the small sample size and cross-sectional nature of the study as well as its performance in an urban hospital setting, we cannot establish temporal relationships and also generalize to the entire adult diabetic population seeking care in Uganda.

Conclusion and recommendations

Suboptimal glycaemic control is a highly prevalent finding among adult diabetic patients affecting about seven in ten patients. Metformin monotherapy and insulin therapy either in monotherapy or in combination with metformin were observed to be independent predictors of suboptimal glycaemic control. There is an imperative need to improve optimal glycaemic management in adult diabetic patients.

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Disclosure

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