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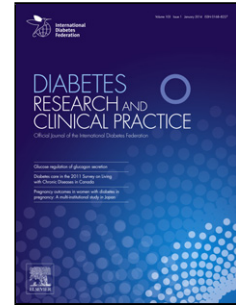
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1 **Poor glycaemic control in type 2 diabetes in the South of the Sahara: the issue of limited**
2 **access to an HbA1c test.**

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1 **Abstract**

2

3 *Background:* - Management of type 2 diabetes remains a challenge in Africa. The objective of
4 this study was to evaluate the prevalence and predictors of poor glyceemic control in patients
5 with type 2 diabetes living in sub-Saharan.

6 *Patients and methods:* - This was a cross-sectional study involving 1267 people (61%
7 women) with type 2 diabetes (mean age 58 years) recruited across health facilities in
8 Cameroon and Guinea. Predictors of poor glyceemic control (HbA1c $\geq 7.0\%$ (53 mmol/mol))
9 were investigated via logistic regressions.

10 *Results:* - The mean body mass index was 27.4 ± 5.8 kg/m², and 74% of patients had poor
11 glyceemic control. Predictors of poor glyceemic control in multivariable regression models were
12 recruitment in Guinea [odd ratio: 2.91 (95% confidence interval 2.07 to 4.11)], age <65 years
13 [1.40 (1.04 to 1.88)], diabetes duration ≥ 3 years [2.36 (1.74 to 3.21)], treatment with: oral
14 glucose control agents [3.46 (2.28 to 5.26)], insulin alone or with oral glucose control agents
15 [7.74 (4.70 to 12.74)] and absence of a previous HbA1c measurement in Guinea [2.96 (1.30 to
16 6.75)].

17 *Conclusion:* - Poor control of blood glucose is common in patients with type 2 diabetes in
18 these two countries. Limited access to HbA1c appears to be a key factor associated with poor
19 glyceemic control in Guinea, and should be addressed by health policies targeting
20 improvement in the outcomes of diabetes care.

21

22 *Keywords:* Type 2 diabetes, glyceemic control, sub-Saharan Africa

23

1 **1. Introduction**

2

3 Type 2 diabetes is a common and rapidly growing chronic non-communicable disease
4 worldwide [1], including in sub-Saharan Africa [2]. The long-term microvascular and
5 macrovascular complications of diabetes are responsible for significant morbidity and
6 mortality. The growing population of people in need of care for diabetes is a challenge for
7 low-income countries where non-communicable diseases are adding to the burden of
8 communicable diseases [3].

9 Several large clinical trials have demonstrated the beneficial effect of glycemic
10 control on the development of long-term complications of diabetes [4]. Despite this evidence,
11 a high proportion of patients with diabetes remains poorly controlled [5]. This is the case in
12 Africa where a large number of people with diabetes do not reach the recommended HbA1c
13 targets [6]. The difficulties to achieve an appropriate glycemic control in developing countries
14 are likely due to a limited access to adequate health services, poor education level, reduced
15 access to medical education and a lack of monitoring of glucose control. The magnitude of
16 poor glycemic control in patients with type 2 diabetes in Africa has not been extensively
17 investigated, nor have the predictors of poor glycemic control received greater attention in
18 this setting.

19 The main aim of this study was to determine the prevalence and investigate the
20 predictors of poor glycemic control in patients with type 2 diabetes across outpatient diabetes
21 clinics in Cameroon and Guinea. We specifically investigated whether prior measures of
22 HbA1c affect subsequent glycemic control.

23

2. Population and methods

2.1 Source of data

Patients with type 2 diabetes included in the current study were recruited and examined as part of the baseline evaluation of the project "Improving access to HbA1c in sub-Saharan Africa", which has been described previously [7]. In brief, data were collected over a one year period between 2009 and 2010 and included demographics, history of diabetes, blood pressure and anthropometric measurements, fasting blood glucose and glycated haemoglobin (HbA1c).

2.2 Study sites and population

Patients were recruited in 10 diabetes management centers including six regional centers in Cameroon (a Central African country with 18 million inhabitants) and four regional centers in Guinea (a West African country with 10 million inhabitants). The centres were either university hospitals (UH) where patients were seen by endocrinologists or regional hospitals (RH) where patients were seen by general physicians or diabetologists. Prior to the study "Improving access to HbA1c in sub-Saharan Africa", these centers monitored metabolic control of patients with fasting capillary blood glucose. The study protocol was approved by the Ethics Committees of the Ministries of Public Health in Cameroon and Guinea.

Participants were informed of the purpose of the study and signed an informed consent.

Between August 2009 and October 2010, 1349 patients with type 1 or type 2 diabetes were selected at outpatient visits. The inclusion criteria were: being diagnosed with diabetes since at least one year and being 16 years of age or older. For the current analyses, patients with missing data on the duration of diabetes and age were excluded ($n = 17$), as well as those with type 1 diabetes ($n = 65$). Thus, data from 1267 patients with type 2 diabetes were analysed.

2.3 Measurements and operational definition

In this study, HbA1c was measured in a capillary blood sample by spectrophotometry using the Biorad® IN2IT devices [8,9]. A good glycemic control was defined as HbA1c $<7.0\%$ (<53 mmol/mol) [10].

The following data were collected: country of recruitment, health facility (University or Regional hospital), gender (Female or Male), age (dichotomized into <65 or ≥ 65 years), marital status (married, single), level of education (Illiterate, \leq High school, $>$ High school), employment (employed or unemployed), duration of diabetes (grouped as 1-2 and ≥ 3 years),

1 treatment of diabetes (categorized as diet only, oral glucose control agents alone, insulin alone
2 or with oral glucose control agents), self-monitoring of blood glucose (yes or no), waist and
3 hip circumferences. Among the 350 subjects who were treated with insulin, information about
4 the number of injections per day was available for 262 patients who were grouped as 1 and 2-
5 3 injections per day. The socioeconomic status was based on the employment status and level
6 of education. The body mass index (BMI) was calculated using Quetelet's index (weight /
7 height²) and expressed in kilograms per meters square (kg/m²) and was further dichotomized
8 into <25 and ≥25 kg/m².

9 The American Diabetes Association definition of hypertension was applied: i.e.
10 systolic/diastolic blood pressure ≥ 130/80 mmHg or antihypertensive treatment [10]. The
11 patients were classified for hypertension status as normal, unknown hypertension, known
12 hypertension with treatment and known hypertension without treatment.

13

14 *2.4 Statistical analysis*

15 Data are presented as mean ± SD or as [median (quartile 1, quartile 3)] for continuous
16 variables and as count (%) for categorical variables. The Pearson correlation coefficient was
17 used to measure the continuous association between HbA1c and fasting glucose. Patients
18 from Cameroon and Guinea were combined for the analysis the predictors of poor glycemic
19 control.

20 Predictors with $p \leq 0.30$ in univariable analysis were entered into a multivariable
21 logistic regression models, and factors associated with poor glycemic control retained from
22 backward selections. Interaction terms were tested and those significant at $p < 0.10$ were
23 added to the final model. Odds ratios and 95% confidence intervals were calculated and a
24 value of $p < 0.05$ was considered statistically significant. The quality of the final model was
25 verified by the Hosmer and Lemeshow fit test and the area under receiver operating
26 characteristic curve. Analyses used SAS software (version 9.3, SAS Institute, Cary, NC).

27

1 3. Results

3 3.1 Characteristics of the study population

4 The characteristics of the 1267 patients with type 2 diabetes included in the study are
5 presented in Table 1; 60% were from Cameroon; 54% were followed in university hospitals;
6 30% were illiterate. The mean duration of diabetes was 7.6 ± 6.3 years [median 6 years (25th-
7 75th percentiles: 3-10)]. The mean age was 58.4 ± 10.5 years [median 58 years (52- 65)]. They
8 were mostly treated with an oral oral glucose control agents alone (62% overall, 66% in
9 Cameroon and 56% in Guinea). Among patients who were receiving insulin, the information
10 of number of injections per day was available for 262. Most of them (90.1%) had two or three
11 injections per day. In all 39% of patients reported that they self-monitored their blood
12 glucose, more frequently in Guinea (42%) than in Cameroon (38%). Only 21% had had a
13 previous determination of HbA1c prior to the study. The mean body mass index (BMI) was
14 27.4 ± 5.8 kg/m², which was significantly higher in Cameroon (28.6 ± 6.2 kg/m²) than in
15 Guinea (25.5 ± 4.7 kg/m²); $p < 0.001$. Among the 962 subjects (76%) with hypertension, only
16 42% were on antihypertensive therapy at inclusion.

18 3.2 Glycemic and blood pressure control

19 Among the 1267 patients, 939 (74%) had an HbA1c $\geq 7.0\%$ (≥ 53 mmol/mol) of whom 388
20 (41%) had an HbA1c $\geq 10.0\%$ (≥ 86 mmol/mol) (Table 2). The frequency of poor glycemic
21 control was 74% overall and significantly higher in Guinea (84%) than in Cameroon (68%);
22 $p < 0.001$. The average HbA1c was $8.9 \pm 2.5\%$ (74 ± 4 mmol/mol) and fasting glucose
23 averaged 9.4 ± 4.3 mmol/L. HbA1c and fasting glucose were significantly and positively
24 correlated with each other ($r = 0.68$, $p < 0.001$). A blood pressure below 130 / 80 mmHg was
25 observed in only 250 subjects (20%) and only 75 (6%) patients had both glycemia and blood
26 pressure values below the recommended thresholds.

28 3.3 Univariable predictors of poor glycemic control

29 Demographic factors significantly associated with poor glycemic control were:
30 recruitment in Guinea [odds ratio: 2.52 (95% confidence interval: 1.89 to 3.34)] and age
31 under 65 years [1.33 (1.01 to 1.75)]. Diabetes was more likely to be poorly controlled among
32 those with little education [1.53 (1.13 to 2.07)] (Table 2). Compared to the patients with
33 <high school, those with \geq high school were the most likely to have poor glycemic control
34 even though this did not reach statistical significance. Clinical and behavioural factors

1 associated with poor glycemic control were the presence of high diastolic blood pressure
2 [1.39 (1.07 to 1.80)], absence of previous measures of HbA1c [1.68 (1.25 to 2.25)], diabetes
3 duration ≥ 3 years [2.61 (1.97 to 3.47)], treatment with oral glucose control agents [2.55 (1.75
4 to 3.72)], insulin alone or with oral glucose control agents [6.25 (3.94 to 9.91)]. Those who
5 had two or more insulin injections per day had a significantly higher odds ratio of having a
6 poor glycemic control [OR: 2.98; 95% CI: (1.14 to 7.75)] than those with one injection per
7 day. Normal weight (BMI < 25 kg/m²) was also associated with poor glycemic control [1.43
8 (1.09 to 1.88)].

9

10 *3.4 Multivariable predictors poor glycemic control*

11 The variables significantly associated with poor glycemic control based on a threshold
12 of $p < 0.30$ in univariate models, were entered altogether in the same multivariable model.
13 Then backward selection procedures were applied to retain the final predictors (Table 3). Of
14 all the interactions terms tested, only the interaction between country and previous
15 measurement of HbA1c ($p = 0.06$) was significant and was therefore added to the final model
16 which included: recruitment in Guinea [2.91 (2.07 to 4.11)], age < 65 years [1.40 (1.04 to
17 1.88)], diabetes duration ≥ 3 years [2.36 (1.74 to 3.20)], treatment with oral glucose control
18 agents alone [3.46 (2.28 to 5.26)], insulin alone or with oral glucose control agents [7.74 (4.70
19 to 12.74)] and no previous measurement of HbA1c in Guinea [2.96 (1.30 to 6.75)]. The level
20 of education, the body mass index, the diastolic blood pressure and the number of insulin
21 injections were not significantly related to the glycemic control in the multivariate model.

22 The Hosmer and Lemeshow chi-square statistic for the final multivariable model was
23 1.50 ($p = 0.98$); and the area under the ROC curve was 73%.

24

1 4. Discussion

2 This study has revealed that three out of four patients with type 2 diabetes in the
3 participating centres in two Sub-Saharan African countries (Cameroon and Guinea), had poor
4 glycaemic control and only 6% were at target control levels for glycaemia and blood pressure
5 values. On average, the diagnosed duration of diabetes was eight years at enrolment in the
6 study. Recruitment in Guinea, younger age, longer duration of diabetes, treatment with oral
7 glucose control agents with or without insulin, and lack of previous HbA1c measures were the
8 main predictors of poor glycaemic control.

9 High frequencies of poor glycaemic control for type 2 diabetes, defined by HbA1c
10 thresholds of 6.5% (48 mmol/mol) or 7.0% (53 mmol/mol), have been reported across regions
11 around the world. In "The International Diabetes Mellitus Practice Study" (IDMPS) [11],
12 conducted in low-income countries, the frequency of poor glycaemic control in type 2 diabetes
13 ranged from 63% in Asia to 64% in Eastern Europe and Latin America. In the "Diabcare
14 Africa study" [6] conducted across six African countries, the prevalence of HbA1c $\geq 6.5\%$
15 (≥ 48 mmol/mol) was 71%.

16 After adjusting for the others variables the level of education was not associated with
17 poor glycaemic control. Our result in terms of level of education was similar to that reported in
18 Michigan [12]. However, a low level of education was associated with poor glycaemic control
19 in Jordan [13] and in Mexican Americas in the United States [14].

20 Our study confirmed that a longer duration of diabetes is significantly associated with
21 poor glycaemic control [15,16], as observed in the natural history of the disease. Furthermore,
22 among patients with longstanding diabetes, those with normal BMI were more likely to have
23 poor glycaemic control, possibly reflecting the effect of weight loss in the context of poor
24 glycaemic control [17]. We also found young age to be associated with poor glycaemic control,
25 in line with some reports in the literature [18–20] but not all [15,21]. Treatment with oral
26 glucose lowering agents or insulin was associated with poorer glycaemic control, most likely
27 reflecting the phenomenon of reverse causality, i.e. more intensive treatment being required
28 by the presence of elevated glycaemia. A poor glycaemic control was more frequently
29 observed among patients who were treated with drugs (oral agents and / or insulin), but more
30 so in those who were treated with insulin (alone or in combination with oral drugs). Some
31 studies [22,23] have reported a link between poor glycaemic control and treatment with a
32 combination of oral glucose lowering agents and insulin. These results may reflect a delay in
33 the introduction of insulin in the treatment of patients with poor glycaemic control [4,24] but
34 also to the intensification of insulin therapy with insufficient insulin doses.

1 Affordable access to HbA1c measurements for people with diabetes remain a
2 challenge in developing countries [25], which may affect the quality of care and explain the
3 correlation found in our study lack of access to HbA1c and poor glycemc control in Guinea.
4 Indeed, HbA1c measurement is the cornerstone in strategies for initiating and intensifying
5 treatments for people with diabetes [26]. Availability of HbA1c has been associated with
6 improved glycemc control [27], both by positively affecting the attitude of healthcare
7 providers [28], and improving adherence to treatments in patients.
8 The cross-sectional nature of this study limits inferences about causality of relationships
9 between the predictors identified in the study and poor diabetes control in our sample. This
10 study is also limited by the lack of information on physical activity, psychological status, and
11 compliance to treatment, other factors that may influence glycemc control and the outcomes
12 of diabetes care.

13 In conclusion, the percentage of patients with poor glycemc control is as high in
14 Cameroon and Guinea as has been reported in a number of other countries. Limited access to
15 HbA1c monitoring appears to be a contributing factor. These findings suggest that increased
16 access to an HbA1c test could be an important step in health policies to improve glycemc
17 control in patients with type 2 diabetes from Sub Sahara Africa.

18

19 **Conflict of interest statement**

20

21 None

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2

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6

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11

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35

1 **Table 1:** Characteristic (mean \pm SD or n (%)) of the 1267 type 2 diabetes patients from
 2 Cameroon and Guinea.
 3

	Total (N=1267)	Cameroon (n=766)	Guinea (n=501)
Age (years)	58.4 (\pm 10.5)	58.7 (\pm 10.7)	57.8 (\pm 10.1)
Monitoring site: University Hospital	688 (54%)	380 (50%)	308 (61%)
Women	775 (61%)	461 (60%)	314 (63%)
Married	881 (70%)	499 (65%)	382 (76%)
Unemployed	612 (48%)	383 (50%)	229 (46%)
Level of education			
Illiterate	378 (30%)	162 (21%)	216 (43%)
\leq High school	678 (53%)	500 (65%)	178 (36%)
$>$ High school	211 (17%)	104 (14%)	107 (21%)
Treatment of diabetes			
Diet only	130 (10%)	53 (7%)	77 (15%)
oral glucose control agents alone	787 (62%)	509 (66%)	278 (56%)
insulin alone or with oral glucose control agents	350 (28%)	204 (27%)	146 (29%)
Number insulin injections per day (n=262)	1.9 (\pm 0.3)	1.9 (\pm 0.4)	1.9 (\pm 0.3)
Diabetes duration (years)	7.6 (\pm 6.3)	7.5 (\pm 6.5)	7.8 (\pm 5.9)
Previous measurement of HbA1c	266 (21%)	232 (30%)	34 (7%)
Self-monitoring of blood glucose	498 (39%)	289 (38%)	209 (42%)
Known hypertension	962 (76%)	534 (70%)	428 (85%)
Hip (cm)	101 (\pm 11.4)	102 (\pm 11.8)	99.6 (\pm 10.7)
Waist (cm)	94.8 (\pm 13)	96.2 (\pm 14.1)	92.7 (\pm 10.6)
Body mass index (kg/m ²)	27.4 (\pm 5.8)	28.6 (\pm 6.2)	25.6 (\pm 4.7)

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1 **Table 2:** Odds ratios for factors associated with poor diabetes control (HbA1c $\geq 7\%$) in type 2
 2 diabetes patients in Cameroon and Guinea
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		HbA1c < 7% (n=328)	HbA1c $\geq 7\%$ (n=939)	OR non adjusted (95% CI)	
Country	Cameroon	248 (32%)	518 (68%)	Ref	-
	Guinea	80 (16%)	421 (84%)	2.52	1.89-3.34
Monitoring site	University Hospital	171 (25%)	517 (75%)	Ref	-
	Regional Hospital	157 (27%)	422 (73%)	0.89	0.69-1.14
Age	≥ 65 years	102 (30.0%)	238 (70.0%)	Ref	-
	< 65 years	226 (24.4%)	701 (75.6%)	1.33	1.01-1.75
Sex	Man	138 (28%)	355 (72%)	Ref	-
	Woman	190 (24%)	584 (75%)	1.19	0.93-1.54
Marital status (Married)	No	101 (26%)	285 (74%)	Ref	-
	Yes	227 (26%)	654 (74%)	1.02	0.78-1.34
Employment	Unemployed	169 (28%)	443 (72%)	Ref	-
	Employed	159 (24%)	496 (76%)	1.19	0.92-1.53
Level of education	Illiterate	78 (20.6%)	300 (79.4%)	1.53	1.13-2.07
	\leq High school	193 (28.5%)	485 (71.5%)	Ref	-
	>High school	57 (27.0%)	154 (73.0%)	1.07	0.76-1.52
Treatment of diabetes	Diet only	64 (49.2%)	66 (50.8%)	Ref	-
	oral glucose control agents alone	217 (27.6%)	570 (72.4%)	2.55	1.75- 3.72
	insulin alone or with oral glucose control agents	47 (13.4%)	303 (86.6%)	6.25	3.94-9.91
Number injections per day (n=262)	1	7 (26.9%)	19 (73.1%)	Ref	-
	2-3	26 (11.0%)	210 (89.0%)	2.98	1.14 - 7.75
Duration of diabetes	<1-3 years	114 (41.8%)	159 (58.2%)	Ref	-
	≥ 3 years	214 (21.5%)	780 (78.5%)	2.61	1.97-3.47
Previous measurement of HbA1c	Yes	91 (34.2%)	175 (65.8%)	Ref	-
	No	237 (23.7%)	764 (76.3%)	1.68	1.25-2.25
Self-monitoring of blood glucose	Yes	132 (26.5%)	366 (73.5%)	Ref	-
	No	196 (25.5%)	573 (74.5%)	1.05	0.82-1.36
Body mass index	≥ 25 kg/m ²	231 (28.3%)	586 (71.7%)	Ref	-
	<25 kg/m ²	97 (21.6%)	353 (78.4%)	1.43	1.09-1.88
Hypertension	unknown hypertension	86 (28.2%)	219 (71.8%)	Ref	-
	known hypertension treated	103 (25.6%)	300 (74.4%)	1.14	0.82-1.59
	known hypertension without treatment	139 (24.9%)	420 (75.1%)	1.19	0.87-1.63
Blood pressure systolic ≥ 130 mmHg	No	100 (28.3%)	254 (71.7%)	Ref	-
	Yes	228 (25.0%)	685 (75.0%)	1.18	0.89-1.56
Blood pressure diastolic ≥ 80 mmHg	No	135 (30.1%)	314 (69.9%)	Ref	-
	Yes	193 (23.6%)	625 (76.4%)	1.39	1.07-1.80

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1 **Table 3:** Odds ratios (95% confidence intervals) of factors associated independently with
 2 poor glycaemic control (HbA1c \geq 7%) in type 2 diabetes patients in Cameroon and Guinea
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	OR (95% CI) without interaction term	OR (95% CI) with interaction term
Country (Guinea)	2.62 (1.90 -3.61)	2.91 (2.07 - 4.11)
Age (<65 years)	1.39 (1.03 -1.88)	1.40 (1.04 - 1.88)
Duration of diabetes (\geq 3 years)	2.36 (1.74 -3.20)	2.36 (1.74 - 3.21)
Treatment of diabetes		
oral glucose control agents alone	3.38 (2.23 -5.12)	3.46 (2.28 - 5.26)
insulin alone or with oral glucose control agents	7.60 (4.62 -12.48)	7.74 (4.70 - 12.74)
Previous measurement of HbA1c (none)	1.43 (1.04 -1.98)	
No previous measurement of HbA1c in Guinea		2.96 (1.30 - 6.75)
No previous measurement of HbA1c in Cameroon		1.28 (0.91 - 1.81)

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