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Importance of the Glycated Hemoglobin Assay in Congolese Women with Polycystic Ovary Syndrome: A Case-Control Study in Kinshasa, DR Congo

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Abstract

Context: Polycystic ovary syndrome (PCOS) is considered a syndrome related to the metabolic syndrome with a high risk for developing diabetes mellitus. The evaluation of the glycated hemoglobin (HbA1c) seems to be an interesting tool to detect states of hyperglycemia that may be associated with this syndrome and to understand her pathophysiology. Aims: The purposes of this study are to determine the profile of HbA1c in Congolese women with PCOS, to determine the frequency of states of hyperglycemia and to assess the impact of this marker on clinical signs on this syndrome. Material and methods: This is a case-control study of 130 Congolese subfertile women; 65 with a diagnosis of PCOS and 65 others without PCOS. This is conducted from June 2016 to June 2019 among Congolese women of childbearing age.

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All these women were recruited at the subfertility outpatient clinic of the University Hospital of UNIKIN as well of the YANGA medical centers in Kinshasa, Democratic Republic of Congo. Sickle cell disease was excluded as also the cases of anemia. HbA1c was assayed via the immunoturbidimetric method and the results interpreted according to the ADA recommendations with a pathological cut-off point ≥ 6.5%. Results: Mean hemoglobin was 11.6 ± 1.2 g/dl (11.5 ± 1.1 g/dl vs. 11.8 ± 1.4 g/dl, $P = 0.568$). The proportion of diabetics was 1.6% (1.6% vs. 1.5%, $P = 0.74$). Higher HbA1c values were noted in the PCOS group compared to the control group (7.3% ± 2.1% vs. 5.6% ± 0.6%, $P < 0.001$). The multivariate analysis showed a strong correlation between elevated HbA1c levels and PCOS (OR 14.79 (CI 5.43 - 40.32), $P < 0.001$). In the PCOS group, higher HbA1c values were significantly correlated with a higher socio-economic status (OR 3.38 (1.67 - 8.47), $P = 0.018$) and with obesity (OR 3.48 IC (1.31 - 7.13) $P = 0.029$). A perfect, positive and significant linear correlation was found between HbA1c and fasting blood glucose (r = 0.807). 60% of women in the PCOS group had pathological values of HbA1c (≥6.5%) compared to 7.7% in the control group ($P < 0.001$). Oligomenorrhea was found more significantly in patients with pathological HbA1c values (≥6.5%) compared to those with values < 6.5% ($P = 0.003$). Conclusion: This study found that in our population 60% of women with PCOS had states of hyperglycemia, demanding systematic screening of glucose metabolism disorders in women with this syndrome.

Keywords

PCOS, HbA1c, Subfertility, Congolese Women

1. Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy observed in women of childbearing age. It affects about 3% to 22% of women worldwide and is one of the leading causes of subfertility by anovulation [1] [2]. Although its pathophysiology isn't still well known, diet seems to play an important role in the genesis of this affection. Numerous studies have shown that hyperglycemic states, even apart from proven diabetes, would be a risk factor for the occurrence of this syndrome by complex mechanisms [3] [4] [5]. A high percentage of affected women have abnormalities of carbohydrate metabolism [6]. The prevalence of insulin resistance in affected women varies between 30% and 60% [7] [8]. Carbohydrate intolerance is found in 20% to 40% of slim women and in 70% of obese women with this condition [9]. Compared with a healthy woman, their risk of developing diabetes mellitus in the next 30 years is markedly increased (2.3% vs. 15%) [10].

In these days, the PCOS is considered a syndrome related to the metabolic syndrome for which the Rotterdam conference recommended a systematic screening of carbohydrate tolerance disorders and states of hyperglycemia. In

this regard, the American Diabetes Association (ADA) has approved since 2010 the use of glycated hemoglobin (HbA1c) as a tool for routine screening of these disorders [11] [12]. The choice made for HbA1c is justified by the fact that it is not affected by daily blood glucose and reflects the state of plasma glucose during the 2 to 3 months preceding the measurement. In addition, some studies have shown a direct correlation between elevated HbA1c levels and PCOS complications, providing evidence that HbA1c could itself play a potential role in the onset of PCOS [13]-[19]. Thus, the evaluation of the level of HbA1c in patients with PCOS is a useful and indispensable approach to on the one hand understand the mechanisms of occurrence of this syndrome and on the other hand to detect states of hyperglycemia that are there frequently associated.

The present study aims to determine the profile of HbA1c in Congolese women with PCOS versus healthy women, in order to assess the frequency of states of hyperglycemia that may be associated with this syndrome and to establish the relationship between this marker and the clinical expressions of this syndrome.

2. Materials and Method

This is a case-control study conducted from June 2016 to June 2019 among Congolese women of childbearing age. All these women were recruited at the subfertility outpatient clinic of the University Hospital of UNIKIN as well of the YANGA medical centers in Kinshasa, Democratic Republic of Congo. The sampling is probabilistic exhaustive, simple random. Its size is calculated by the following formula: $n \geq 2\ (Z\alpha + Z1\text{-}\beta) \times p\ (1 - p)/(Po - P1)^2$ where n = size of the sample; zα = coefficient of confidence (95%); Z1-β = Power of the test; P = Overall prevalence of at-risk and no-risk; Po = Prevalence; P1 = the non-event. In total130 women divided into two groups: 65 cases of PCOS and 65 non PCOS, paired for age.

The cases were women of childbearing age with PCOS diagnosed according to the criteria of the Rotterdam Conference [20] [21] in whom an HbA1c test was performed and Controls were women with an age equal to that of the preceding included person with a gynecological problem other than PCOS and in whom the HbA1c test was performed. All these women were recruited at the subfertility outpatient clinic of the University Hospital of UNIKIN as well of the YANGA medical centers in Kinshasa, Democratic Republic of Congo and they gave a written or oral informed consent to participate in the study.

Women with other causes of dys- or anovulation (hyperprolactinemia, dysthyroidism …), women with ovarian or adrenal tumors and women with a documented infertility due to uterine (synechiae), tubal, central cause or male causes were excluded.

The socio-demographic and clinical data of these women were collected by clinical examination.

Assays of biological markers were carried out in the clinical biology laboratory of the General Reference Hospital of Kinshasa. The search for sickle cell disease

in these women was done using the SICKLE SCAN device in order to exclude this hemoglobinopathy, common in our environment [22] [23] and whose influence on the HbA1c value is well documented [24]. The fasting glucose assay was performed using a ACCU-CHEK blood glucose meter. A level above 110 mg/dl was considered abnormal.

The determination of glycated hemoglobin was performed by the immunoturbidimetric technique using the biochemistry analyzer COBAS C11. The results obtained were interpreted according to the recommendations of the American Diabetes Association. A value of ≥6.5% was considered as a pathological cut-off [25] [26].

3. Statistics Processing and Analysis Statistics

3.1. Data Analysis

The database being constituted, the analyzes were carried out with SPSS software version 22.0.

3.2. Statistical Analyzes

The statistics used to describe the variables were the means ± standard deviation for continuous quantitative variables with symmetric distribution. The qualitative variables have been described as absolute frequency (n) and/or relative (%). For the analyzes, the comparison of the means was carried out using Student's t-test. Pearson's Chi-square or Fisher's exact test, as the case may be, was applied to compare the proportions.

The linear regression test was applied to verify the correlation between HbA1c and blood glucose, the linear regression coefficient in simple analysis was calculated to evaluate the association between HbA1c and blood glucose.

Logistic regression was used to identify factors associated with elevated HbA1c. Only variables significantly associated with elevated HbA1c in univariate analysis were tested in multivariate analysis. Adjusted Odds-ratios (ORs) and their 95% confidence intervals (CIs) and p-values were derived from the final models. For all tests used, $P < 0.05$ was the statistical significance level.

4. Results

In total, 130 women were part of this study among them, 65 with PCOS and 65 others without PCOS. They were paired for age.

The socio-demographic characteristics of these women are shown in **Table 1**. The average age of these women was 34.0 ± 6.0 years. There is a predominance of young women in the group of women with PCOS compared to the control group (32.7 ± 5.6 years vs. 35.3 ± 6.2 years, $P = 0.036$).

The results in **Table 2** show that obesity was found mainly in women with POCS compared to those in the control group ($P = 0.004$).

Table 3 shows the clinical characteristics of the patients in the study population. It is noted that oligomenorrhea and acnee were the most found signs in

Table 1. Distribution according to socio-demographic characteristics.

Variables	All n = 130	PCOS n = 65	Controls n = 65	*P*
Age (years)	34.0 ± 6.0	32.7 ± 5.6	35.3 ± 6.2	**0.036**
≤30	34 (26.2)	22 (33.8)	12 (18.5)	
>30	96 (73.8)	43 (66.2)	53 (81.5)	
Civil Status				0.823
Maried	108 (83.1)	52 (80.0)	56 (86.2)	
Single	8 (6.2)	5 (7.7)	3 (4.6)	
Divorcee	8 (6.2)	5 (7.7)	3 (4.6)	
Free union	6 (4.6)	3 (4.6)	3 (4.6)	
Socio-economic level				0.138
Low	9 (6.9)	3 (4.6)	6 (9.2)	
Midle	109 (83.8)	53 (81.5)	56 (86.2)	
High	12 (9.2)	9 (13.8)	3 (4.6)	

Data are expressed as mean ± standard deviation or absolute and relative frequency in % between brackets.

Table 2. Distribution according to medical history.

Antecedents	All n = 130	PCOS n = 65	Controls n = 65	*P*
Overweight	16 (12.3)	11 (16.9)	5 (7.7)	0.090
Obesity	11 (8.5)	10 (15.4)	1 (1.5)	**0.004**
Hypertension	19 (14.6)	7 (10.8)	12 (18.5)	0.160
Diabetes	2 (1.5)	1 (1.5)	1 (1.5)	0.752
Alcoholism	11 (8.5)	7 (10.8)	4 (6.2)	0.265

Data are expressed as absolute and relative frequency in % between brackets.

Table 3. Distribution according to clinical characteristics.

Variables	All n = 130	PCOS n = 65	Controls n = 65	*P*
Amenorrhea	5 (3.8)	3 (4.6)	2 (3.1)	0.500
oligomenorrhea	25 (19.2)	17 (26.2)	8 (12.3)	**0.037**
Dysmenorrhea	19 (14.6)	11 (16.9)	8 (12.3)	0.310
Pregnancy loss	13 (10.0)	4 (6.2)	9 (13.8)	0.121
metrorrhagia	4 (3.1)	4 (6.2)	0 (0.0)	-
obesity android	17 (13.1)	11 (16.9)	6 (9.2)	0.149
Hirsutism	14 (10.8)	10 (15.4)	4 (6.2)	0.055
Hoarsely	2 (1.5)	0 (0.0)	2 (3.1)	-
baldness	2 (1.5)	0 (0.0)	2 (3.1)	-
Acnee	10 (7.7)	8 (12.3)	2 (3.1)	0.048

The data are expressed as absolute and relative frequency in % between brackets.

patients with POCS compared to controls ($P = 0.037$ and 0.048).

Biological endpoint values in women with PCOS and in controls are shown in Table 4. The mean hemoglobin levels were 11.6 ± 1.2 g (11.5 ± 1.1 g vs. 11.8 ± 1.4, $P = 0.568$) and the mean fasting glucose levels were 95.5 ± 11.1 mg/dl (96.9 ± 12.1 mg/dl vs. 94.2 ± 9.8 mg/dl, $P = 0.156$). No difference was noted by comparing the two groups according to the hemoglobin electrophoresis of subjects ($P = 0.50$).

However, this table shows that women with PCOS had higher HbA1c levels compared to women in the control group ($P < 0.001$).

Figure 1 shows a perfect, positive and significant linear correlation between HbA1C and fasting glucose. This correlation is 81% (r = 0.807).

The majority of patients had a fasting blood glucose level below 110 mg/dl as shown in Table 5 and no clinical parameters were significantly associated with the blood glucose value.

Table 4. Breakdown according to para-clinical examinations.

Variables	All n = 130	PCOS n = 65	Controls n = 65	*P*
Hemoglobin	11.6 ± 1.2	11.5 ± 1.1	11.8 ± 1.4	0.568
<12 g/dl	27 (65.9)	20 (66.7)	7 (63.6)	
≥12 g/dl	14 (34.1)	10 (33.3)	4 (36.4)	
Hemoglobin Electrophoresis				0.500
AA	127 (97.7)	63 (96.9)	64 (98.5)	
AS	3 (2.3)	2 (3.1)	1 (1.5)	
HbA1c	6.4 ± 1.7	7.3 ± 2.1	5.6 ± 0.6	**<0.001**
Fasting blood glucose	95.5 ± 11.1	96.9 ± 12.1	94.2 ± 9.8	0.156

Data are expressed as mean ± standard deviation or absolute and relative frequency in % between brackets.

Table 5. Glycemia by clinical characteristics.

Variables	<110 mg/dL n = 115	≥110 mg/dL n = 15	*P*
Alcohol	9 (7.8)	2 (13.3)	0.370
Over weight	11 (9.6)	5 (33.3)	0.021
Obesity	17 (14.8)	2 (13.3)	0.620
Obesity android	12 (10.4)	5 (33.3)	0.028
Amenorrhea	5 (4.3)	0 (0.0)	-
oligomenorrhea	21 (18.3)	4 (26.7)	0.318
Dysmenorrhea	15 (13.0)	4 (26.7)	0.154
Metrorragia	4 (3.5)	0 (0.0)	-
Hirsutism	11 (9.6)	3 (20.0)	0.206
Hoarsely	2 (1.7)	0 (0.0)	-
Alopécia	2 (1.7)	0 (0.0)	-
Acne	8 (7.0)	2 (13.3)	0.324

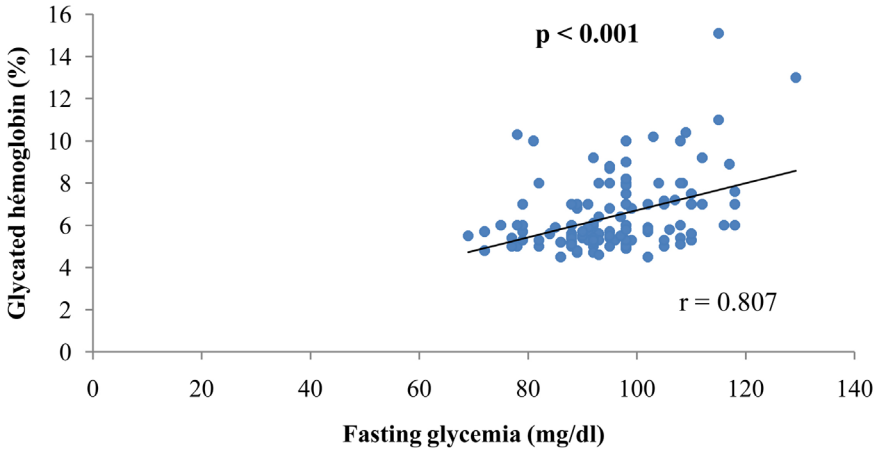

Figure 1. Simple linear correlation between fasting glycemia and HbA1c.

The proportion of women with pathological HbA1c values (≥6.5%) is given in Figure 2. It is noted that 33.8% of women in the study population had pathological values for glycated hemoglobin.

As shown in Figure 3, compared to women in the control group, women with PCOS predominantly had pathological HbA1c values ≥ 6.5% (60% vs. 7.7%, $P < 0.001$).

In relation to the socio-economic level of patients, Figure 4 shows that pathological values of HbA1c (≥6.5%) were found in 58% of women with a high socio-economic level. This proportion was higher than that found in women of average socio-economic (33%) and low socio-economic level (11.1%). This difference is significant ($P = 0.036$).

The results in Table 6 show that pathological values of HbA1c ≥ 6.5% were mainly found in women with risk factors for insulin resistance, especially in women with obesity, overweight and android obesity ($P = 0.035$, 0.044 and 0.046). More pathological HbA1c values were also observed in women with oligomenorrhea ($P = 0.003$).

Among women with PCOS, pathological values of HbA1c ≥ 6.5 were mainly found in those with alcoholismantecedent ($P = 0.014$), overweight ($P = 0.009$), android obesity ($P = 0.009$), dysmenorrhea ($P = 0.027$) and oligomenorrhea ($P = 0.009$). Although oligomenorrhea and dysmenorrhea are common in women with PCOS, Table 7 also shows that these two clinical signs were also found in the few women of the control group with pathological HbA1c values.

As shown in Table 8, the multivariate analysis showed a strong correlation between high HbA1c levels and having PCOS (OR 14.79 (CI 5.43 - 40.32), $P < 0.001$). High HbA1c levels also significantly correlate with a high socioeconomic level (OR 3.38 (1.67 - 8.47), $P = 0.018$) and with obesity (OR 3.48 IC (1.31 - 7.13) $P = 0.029$).

5. Discussion

1) Prevalence of PCOS

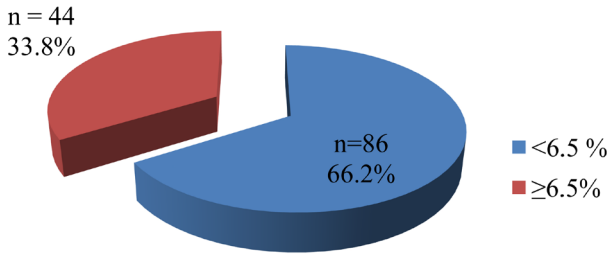

Figure 2. Frequency of pathological HbA1c values in the study population.

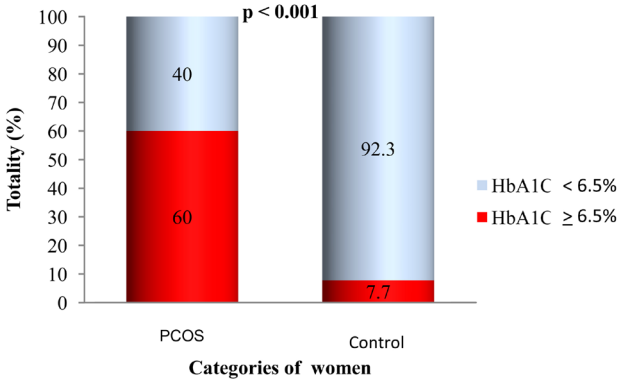

Figure 3. Pathological values of HbA1c according to the control case.

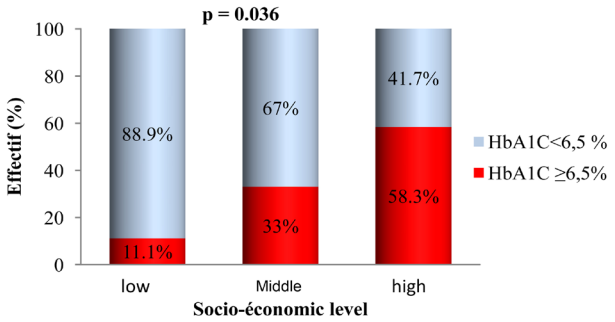

Figure 4. Pathological values of HbA1c by women's socioeconomic status.

The prevalence of PCOS is estimated to be between 3% and 22% in the population of women who consult for subfertility [1] [20] [27] [28]. It varies, however, according to the criteria used to define the disease. We found a prevalence of 21% using the clinical and ultrasound criteria set by the Rotterdam Consensus. According to these criteria, the ultrasound associated with the clinic confirms the diagnosis of SOMPK in 92% of women [21]. In a study conducted in the same city with women also consulting for subfertility, Mboloko E. *et al*. [28] found a prevalence of 22.2%. Similar results have been published by Mbuyamba N.K.L. *et al*. [27] who noted a prevalence of 23.6% among Congolese infertile couples living in Mbuji-Mayi. In the study by Goldzieher W.J. *et al*. [29] with 1079 cases of PCOS from 167 different publications worldwide, it was noted that

Table 6. Clinical and biological characteristics according to HbA1c.

Variables	HbA1c < 6.5% n = 86	HbA1c ≥ 6.5% n = 44	*P*
Alcohol	5 (5.8)	6 (13.6)	0.120
Over weight	7 (8.1)	9 (20.5)	**0.044**
Obesity	4 (4.7)	7 (15.9)	**0.035**
Hypertension	13 (15.1)	6 (13.6)	0.523
Diabetes	0 (0.0)	2 (4.5)	-
Amnorrhea	2 (2.3)	3 (6.8)	0.214
Oligomenorrhea	10 (11.6)	15 (34.1)	**0.003**
Dysmenorrhea	9 (10.5)	10 (22.7)	0.056
Pregnancy loss	8 (9.3)	5 (11.4)	0.465
Metrorragia	2 (2.3)	2 (4.5)	0.417
Obesity android	8 (9.3)	9 (20.5)	**0.046**
Hirsutism	7 (8.1)	7 (15.9)	0.146
Hoarsely	2 (2.3)	0 (0.0)	-
baldness	2 (2.3)	0 (0.0)	-
Acna	6 (7.0)	4 (9.1)	0.455
Hemoglobin			0.466
<12 g/dl	9 (69.2)	18 (62.1)	
≥12 g/dl	4 (30.8)	11 (37.9)	

The data are expressed as absolute and relative frequency in % between brackets.

Table 7. Clinical characteristics according to HbA1c by comparison group (PCOS and controls).

Variables	SOMPK. n = 65			Pas SOMPK. n = 65		
	HbA1 < 6.5 n = 26	HbA1 ≥ 6.5 n = 39	*P*	HbA1 < 6.5 n = 60	HbA1 ≥ 6.5 n = 5	*P*
Alcohol	1 (3.8)	6 (15.4)	**0.014**	4 (6.7)	0 (0.0)	-
Over weight	2 (7.7)	9 (23.1)	**0.009**	5 (8.3)	0 (0.0)	-
Obesity	5 (23.8)	3 (27.3)	0.575	1 (16.1)	0 (0.0)	
Obesity android	2 (7.7)	9 (23.1)	**0.009**	6 (10.0)	0 (0.0)	-
Hypertension	3 (11.5)	4 (10.3)	0,587	10 (16.7)	2 (40.0)	0.144
Amenorrhea	0 (0.0)	3 (7.7)	-	2 (3.3)	0 (0.0)	-
Oligomenorrhea	4 (15.4)	13 (33.3)	**0.009**	6 (10.0)	2 (40.0)	**0.011**
Dysmenorrhea	3 (11.5)	8 (20.5)	**0.027**	6 (10.0)	2 (40.0)	**0.011**
Pregnancy loss	1 (3.8)	3 (7.7)	0.472	7 (11.7)	2 (40.0)	0.113
Metrorragia	2 (7.7)	2 (5.1)	0.528	--	--	-
Hirsutism	4 (15.4)	6 (15.4)	0.631	3 (5.0)	1 (20.0)	0.280
Hoarsely	-	-	-	2 (3.3)	0 (0.0)	-
baldness	-	-	-	2 (3.3)	0 (0.0)	-
Acnee	4 (15.4)	4 (10.3)	0.402	2 (3.3)	0 (0.0)	-

Table 8. Risk factors associated with HbA1c.

Factors	Univariate analysis		Multivariate analysis	
	P	OR (IC95)	*P*	ORa (IC95)
Status				
Controls		1		1
PCOS	**<0.001**	16.25 (6.09 - 43.35)	**<0.001**	14.79 (5.43 - 40.32)
Socio-economic level				
Midle		1		1
High	**0.029**	3.04 (1.12 - 8.25)	**0.018**	3.38 (1.67 - 8.47)
Obesity				
No		1		1
Yes	**0.012**	3.68 (1.02 - 13.35)	**0.029**	3.48 (1.31 - 7.13)
Over Weight				
No		1		1
Yes	**0.012**	2.38 (1.80 - 7.06)	0.419	1.74 (0.45 - 6.66)

74% of the patients involved consulted for subfertility, making PCOS, the leading cause of anovulation infertility.

2) Anthropometric parameters of patients with PCOS

Our study confirms that obesity was statistically significantly more common in patients with PCOS compared to controls (15.4% vs. 1.5%, $P = 0.004$). Many studies have shown that PCOS is frequently associated with overweight or obesity as a factor in insulin resistance. Such an association is found in 30% to 80% of patients in American studies [30] [31]. In the study by Mboloko E. *et al*. [28], it was noted 26% of obese patients among those with PCOS. The difference in frequency observed in these studies could well be explained by the sampling used but also the mode of feeding that differs according to ethnic groups. The results of our study show that the majority of patients with PCOS had a BMI within the norms. Our results corroborate those published by other authors who note in their series a large number of slim women with this syndrome. In a study of a population of Turkish women with PCOS, Seda A. *et al*. [32] note that women with BMI < 25 kg/m^2 are more affected by this syndrome and have very high levels of LH and LH/FSH ratio than women with a BMI > 30 kg/m^2. Such observation reflects the fact that obesity is not in itself the cause of PCOS, but rather an aggravating factor.

3) Profile of glycated hemoglobin (HbA1c) in Congolese with PCOS

The results of many studies show that a high percentage of women with PCOS have abnormalities in carbohydrate metabolism. The prevalence of insulin resistance varies between 30% and 60% depending on the studies and the techniques used to assess it [33]. An intolerance to carbohydrates would be found in 20% to 40% of slim women and in 70% of obese women with PCOS with a high risk of developing diabetes mellitus [9].

During this study, glycosylated hemoglobin was measured in patients with PCOS and controls by immunoturbidimetric technique using COBAS C11 and the results obtained were interpreted according to the recommendations of the American Diabetes Association with a pathological threshold value ≥ 6.5% [25] [26].

The mean hemoglobin level in all our patients was 11.6 ± 1.2 g/dl (11.5 ± 1.1 g/dl vs 11.8 ± 1.4 g/dl, $P = 0.568$) excluding any case of anemia. The proportion of diabetics in the study population was 1.6% (1.6% vs. 1.5%, $P = 0.74$). In order to avoid misunderstandings related to the shortening of the duration of red blood cells, we conducted a search and exclusion of patients with sickle cell disease, the most common hemoglobinopathy in our populations [22] [23]. The studies by Arlène S. *et al*. [24] as well by many other authors indicate that HbA1c is not a reliable indicator in the search for carbohydrate tolerance disorders in subjects with sickle cell disease.

We noted in this study a perfect linear correlation, positive and between the HbA1c values obtained and the fasting glucose (r = 0.807). Patients with PCOS had higher HbA1c values compared to control patients (7.3% ± 2.1% vs 5.6% ± 0.6%, $P < 0.001$). Multi-variate analysis showed a strong correlation between elevated HbA1C levels and the diagnosis of PCOS (OR 14.79 (CI 5.43 - 40.32), $P < 0.001$). Although very few studies have reported the prevalence of abnormal HbA1c levels in patients with PCOS, previous studies have shown that an increase in HbA1c was observed in 40% of Brazilian women with PCOS [34] and in 38% of Korean patients with PCOS [35]. Interestingly, in this latest Korean study, 20% of non-obese patients with PCOS had elevated HbA1c levels compared to only 6% of obese patients with PCOS. Similar observations have been made in other studies that have shown very high levels of HBA1c in women with PCOS [36] [37] [38]. In the study by Jin J.K. *et al*. [35], it was noted that a woman's chances of having high levels of HbA1C are 6.7 times higher if she suffers from PCOS, suggesting that the PCOS may itself be associated with an abnormal status of HbA1C which plays an important role in its clinical expression and in the occurrence of complications. In a study in Congolese women with PCOS, Mbuyamba N.K.L. *et al*. [27] note a very high risk of developing PCOS in the presence of a high standard of living (RR = 2.03, 95% CI: 1.73 - 2.38, $P = 0.00$). However, no mention was made of the determinants of this association. We noted in this study that high HbA1c levels in women with PCOS were significantly correlated at a high socioeconomic level (OR 3.38 (1.67 - 8.47), $P = 0.018$) and obesity (OR 3.48 IC (1.31 - 7.13) $P = 0.029$). The results of the studies of Jayesh S. *et al*. [39], Masafumi K. *et al*. [40] and Jain M. *et al*. [41] note a positive linear correlation between lipidemia and HbA1C. We also noted in this study that women with PCOS who had a history of alcoholism had pathological HbA1C values compared to those who did not have this history of alcoholism. In their studies Zhang J. *et al*. [42], Medeiros I.C. *et al*. [43], Rutkowska A.Z. *et al*. [44], note that alcohol consumption is associated with an increased risk of de-

veloping PCOS by more complex mechanisms.

4) Frequency of hyperglycemia in Congolese patients with PCOS

Since 2010, the American Diabetes Association (ADA) has approved the use of glycated hemoglobin as a useful tool to diagnose diabetes and pre diabetes. The Hb1Ac cut-off value for the diagnosis of diabetes is ≥6.5% and for pre-diabetes is 5.7% - 6.4% [25] [26]. These reference values were also adopted to diagnose these conditions in women with PCOS [29]. The frequency of pathological HbA1c values (≥6.5%) noted during this study was 38.2% for both groups. This frequency was higher (60%) in patients with PCOS compared to 7.7% in those in the control group ($p < 0.001$). The proportion of women with pathological HbA1c values was higher among those with higher socioeconomic status than among those with a low socioeconomic status (58% vs. 11.1%) ($P = 0.036$). A perfect, positive and significant linear correlation was found between HbA1c and fasting blood glucose ($r = 0.807$), establishing that 60% of women with SOMPK in our series had presented states of hyperglycemia probably as part of the metabolic syndrome. A systematic search for these states of hyperglycaemia would be essential for women with this syndrome in our environment. The results of studies show that the prevalence of metabolic syndrome in women with PCOS is between 34% and 46% according to the studies [5] [20] [45] [46] [47] [48]. In the study by Alessandra G. *et al*. [47], there was a significantly higher prevalence of diabetes mellitus in women with PCOS compared to healthy women of the same age (39.3% vs. 5.8%).

5) HbA1C and clinical expression of PCOS in Congolese

The results of our study show that oligomenorrhea and acnee were the two clinical signs that stood out very significantly in women with PCOS compared to those in the control group ($P = 0.037$ and 0.048). These signs, which reflect dysovulation and hyperandrogenism, are part of the diagnostic criteria of PCOS [29]. Oligomenorrhea was found more significantly in patients with pathological HbA1c values (≥6.5%) compared to those with values < 6.5% ($P = 0.003$). The results obtained from the study of Iván C-R *et al*. [48] show that in diabetics and non-diabetics, any 1% increase in the absolute HbA1c concentration influences the clinical expression of the underlying pathology and is associated with an increased risk of cardiovascular disease. In the study by Jin J.K. *et al*. [35], it was noted that a woman's chances of having high levels of HbA1c is 6.7 times higher if she suffers from PCOS suggesting that the PCOS may itself be associated with an abnormal status of HbA1c which plays an important role in its clinical expression and in the occurrence of complications. Niels H.I.H. *et al*. [13] report that elevated levels of HbA1c are associated with high testosterone concentrations and low concentrations of inhibin A, leading to anovulation and female infertility. Oluboyo A.O. *et al*. [49] noted in their study that elevated HbA1c levels were associated with increased estradiol levels and decreased levels of FSH, L.H., and prolactin resulting in menstrual cycle disturbances, anovulation and infertility. Kelly C.C. *et al*. [50] were the first to show that inflammation played a

crucial role in the onset of PCOS. High concentrations of inflammatory markers including C-reactive proteins, tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), IL-18, monocyte chemoattractant protein-1 (MCP-1) have been found in patients with PCOS and would play an important role in the pathogenesis of this condition [51] [52]. The results of studies by Shuqian L. [53], Wu T. [54], and Sushma B. J. [55] show that elevated levels of HbAIc are associated with high concentrations of inflammation markers. The Mortada R study [56] also shows that HbA1c is a potential and reliable marker of inflammation in patients with PCOS. More recently studies have demonstrated the role played by HbA1c through AGEs (AGE Advanced glycation end-products) in the onset of PCOS. AGEs are a diverse group of reactive molecules that are formed endogenously non-enzymatically from the intermediate and irreversible glycation products of which HbA1c is a part. The accumulation of AGEs in ovarian tissues induces cellular oxidative stress and promotes inflammation thereby increasing the vulnerability of ovarian tissues to the occurrence of lesions [18] [19] [57] [58]. The proteins modified by the interaction between AGEs and their receptors RAGEs are expressed in the human ovarian tissue and are responsible for the alterations of the enzymes of collagen synthesis. These alterations are likely to lead to excessive deposition of collagen in the ovarian tissue and crosslinking phenomenon at the base of dysovulation and anovulation noted in this syndrome. More recently there has been a significant negative correlation between elevated levels of HbA1c and AGEs with the number of ovarian follicles and the level of antimullerianhormon, which would be the basis of infertility [59].

This study is the first performed in women with PCOS in our community. Its strength results from the fact that It has discovered that the majority of patients with PCOS in our environment have hyperglycemic disorders often unrecognized. This leads to a systematic search for diabetes mellitus in these patients by appropriate tests. The results obtained are consistent with those published by many authors. However, some weaknesses should be noted among them the fact that we used a weak sampling, but also the non-achievement of the test of oralhyperglycemiain patients having pathological values of HbA1c to look for the prevalence of diabetes mellitus and possibly offer support. We recommend subsequent similar studies on large samples to validate these results and to investigate the prevalence of diabetes mellitus in these women with this syndrome.

6. Conclusion

We conducted a study to determine the profile of HbA1c in Congolese women with PCOS in order to determine the frequency of hyperglycemia states in these women and to assess the impact of this marker on the clinical signs of this syndrome. The results obtained show that 60% of Congolese women with this syndrome have pathological HbA1C values that are also associated with oligomenorrhea, a major symptom of dysovulation in this syndrome. These results have led us to recommend a systematic screening of carbohydrate disorders in pa-

tients with this syndrome in our environment. However, the limitations of this study prompt us to recommend that further studies be conducted on a large sample of patients for validation of the results obtained.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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