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Glycated Haemoglobin Determination in the Biological Follow-Up of Diabetic Subjects Admitted to the Endocrinology Department of the CNHU-HKM of Cotonou

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Abstract

Introduction: One of the biological markers for monitoring glycaemic control in diabetic patients is glycated protein. The definition of a reference method to improve the accuracy of measurement tools is necessary. The aim of our study was to assess the glycemic control of diabetic patients based on glycated hemoglobin. **Patients and Method:** This is a descriptive cross-sectional study conducted in April 2021 at the national university hospital center (CNHU-HKM) of Cotonou. All patients who consulted during the period and who gave their consent were included. After collecting the blood samples according to the classical standards of the pre-analytical phase, we measured the blood glucose level and the HbA1c. **Results:** The mean blood glucose level of the patients was 1.52 ± 0.16 g/L with extremes of 0.80 g/L and 3.5 g/L. The mean HbA1c proportion was 8.39% ± 0.60% with a minimum and maximum value of 5.40% and 16% respectively. We also noted that the mean body mass index (BMI) of the patients was 28.61 ± 1.46 Kg/m^2 with extremes of 17.50 Kg/m^2 and 46.02 Kg/m^2. Oral anti diabetic and hygienic-dietary measures were used by 44 patients (80%) and hygienic-dietary measures (HDM) only used by 9.09%. A frequency of 87.53% of patients had at least one degenerative complication. Retinopathy was the most observed degenerative disease (36.36%) followed by cardiovascular disease (25.45%). **Conclusion:** This study showed that there is a poor correlation between fasting blood glucose and glycated haemoglobin levels, which could be due to several biological and clinical reasons. It also showed that despite the respect of hygienic dietary measures and a well conducted treatment, it is difficult to obtain a satisfactory glycemic balance in obese patients.

Keywords

Glycemia, Glycated Haemoglobin, Diabetes, Benin

1. Introduction

The prevalence of diabetes is steadily increasing everywhere, particularly in middle-income countries. According to the World Health Organization (WHO), diabetes is one of the leading causes of death in the world, along with hypertension, with 422 million people worldwide affected by diabetes [1]. Chronic diseases are long-term, stable or progressive conditions that cannot be cured permanently but whose progression or at least symptoms can usually be controlled. They require medical follow-up and lifestyle changes. For several decades, the diagnostic criteria for diabetes have been based on blood glucose values such as fasting blood glucose or glucose tolerance test (GTT). In 2010, the American Diabetes Association (ADA) approved the use of glycated haemoglobin as a diagnostic tool for diabetes and pre-diabetes based on the recommendations of an international expert panel including representatives from the ADA, the International Diabetes Federation (IDF) and the European Association for the Study of Diabetes (EADS) [2]. Glycated haemoglobin has thus become an essential parameter for monitoring the diabetic patient. Its measurement is now used to reveal the patient's level of glycaemic control during the 2 - 3 months prior to testing and to estimate the risk of developing complications, particularly microvascular ones, in the longer term [3]. The treatment of diabetes requires the long-term maintenance of blood glucose levels as close to normal as possible in order to limit the risk of long-term vascular complications. A simple fasting blood glucose measurement gives an indication of the immediate past of a patient's condition (the previous few hours) but does not necessarily provide a true picture of the patient's blood glucose regulation. For this reason, the researchers chose glycated haemoglobin (HbA1c) as a method for monitoring and diagnosing diabetes [4]. This study is part of the evaluation of the diagnostic performance of glycated haemoglobin in the biological monitoring of diabetic subjects.

2. Study Method

This is a descriptive cross-sectional study in which glycated haemoglobin and blood glucose levels are assessed for monitoring glycaemic control in diabetic subjects. It involved 55 diabetic patients followed during one month in April 2021 in Endocrinology at the CNHU HKM. A previously established survey form, including elements related to the disease as well as therapeutic education, was used. The inclusion criteria were all type 1 and type 2 diabetics with or without degenerative complications followed at the endocrinology department of the CNHU-HKM of Cotonou. All pregnant women were excluded from this study. The variables studied were socio-demographic: age, sex, level of education; clinical: type of diabetes, duration of diabetes, diabetic heredity in the family and complications of diabetes; biological: glycated haemoglobin (HbA1c) level, blood glucose level; patient therapy: compliance with hygienic-dietary measures (HDM), insulin therapy and ADO. The quality and reliability of laboratory results are important for good patient management. The reliability of laboratory results does not only depend on the correct analytical technique, but also on the proper preparation of the samples before the analytical phase. Biological analyses are carried out on samples taken from patients under strict conditions because, in biochemistry as in other biological specialities, the constituents to be measured or characterised must not undergo any qualitative or quantitative change. In the quality assurance system, the pre-analytical practices condition the success of the other phases because they make it possible to obtain the sample that will be analysed. It is imperative that the subject is fasting at the time of collection. Data entry and statistical analysis were performed using EPI INFO software version 7.2.1.0 and Microsoft Excel 2013. The Student's t test of superiority of means was also used to assess the difference between the different groups. This difference is statistically significant if $p < 0.05$. Quantitative variables were expressed as mean ± standard deviation and qualitative variables as percentage. The threshold of significance was $p < 0.05$.

3. Results

3.1. Socio-Demographics Characteristics

The analysis of the results shows a clear predominance of diabetes in the female (60%) compared to the male (40%).

The mean age of the patients was 56.34 ± 2.58 years. The majority of patients are over 40 years old (93%).

The majority of patients have had diabetes for more than 5 years (58.18%).

3.2. Clinical Characteristics

BMI

The mean BMI of the patients was 28.61 ± 1.46 Kg/m^2 with the extremes of 17.50 Kg/m^2 and 46.02 Kg/m^2. In total, 74.55% of the patients were overweight/obesity.

Acute complications of diabetes (Table 1)

Hypoglycaemia is the most common complication.

Chronic complications of diabetes (Table 2)

Retinopathy is the most common degenerative disease followed by cardiovascular disease.

Distribution according to the therapy followed

Oral anti diabetic and hygienic-dietary measures were used by 44 patients (80%) and hygienic-dietary measures only used by 9.09%.

Relation between fasting blood glucose and HbA1c (Table 3)

The mean blood glucose level of the patients was 1.52 ± 0.16 g/L with extremes of 0.80 g/L and 3.5 g/L. The mean HbA1c proportion was 8.39% ± 0.60% with a minimum and maximum value of 5.40% and 16% respectively.

The Pearson test (r = 0.01) shows that there is a correlation, but of low intensity, between HbA1c values and fasting blood glucose levels since the existence of this link is supported by the significance level (p = 0.03).

Relation between HbA1c and different complications (Table 4)

There was a statistically significant association between HbA1C levels and cardiovascular outcomes (p = 0.03).

Relation between HbA1c and therapy (Table 5)

A statistically significant association between HbA1c and the HDM + ADO treatment combination (p = 0.006) was found.

Table 1. Distribution of patients according to acute complications.

Acute complications of diabetes	Workforce	Percentages (%)
Hypoglycemia	08	14.55
Acido ketosis	05	9.26
Hyperosmolar hyperglycaemia	00	00.00
Lactic acidosis	00	00.00
No acute complications	43	76.36

Table 2. Distribution of patients according to degenerative complications of diabetes.

Degenerative complications of diabetes	Workforce	Percentages (%)
Retinopathy	20	36.36
Nephropathy	08	14.81
Cardiovascular disease	14	25.45
Podiatric impairment	06	10.91
No complications	23	41.81

Table 3. Correlation between fasting blood glucose and HbA1c.

Average	Correlation coefficient	p-value
Fasting blood glucose	1.52 ± 0.16	0.01*
HbA1c	8.39 ± 0.60	0.03*

Table 4. Association between HbA1c and different complications in diabetics.

Complications of diabetes	HbA1c level		p-value	OR	IC 95% OR
	<7%	≥7%			
Hypoglycemia					
NO	18	29	0.23	1	
YES	1	7		0.23	0.02 - 2.02

Continued

Acido ketosis					
NO	17	32	0.52	1	
YES	2	3		1.25	0.19 - 8.25
Retinopathy					
NO	12	23	0.95	1	
YES	7	13		1.03	0.32 - 3.27
Nephropathy					
NO	15	31	0.43	1	
YES	4	4		2.06	0.45 - 9.41
Cardiovascular diseases					
NO	11	30	0.03*	1	
YES	8	6		3.63	1.02 - 12.87
Foot problems					
NO	18	31	0.6	1	
YES	1	5		0.45	0.07 - 2.81

Table 5. Correlation between HbA1c and therapy.

Ongoing therapy	HbA1c level		p-value	OR	IC 95% OR
	<7%	≥7%			
MHD alone	4	1		1	
MHD + ADO	15	29	0.006*	2.34	1.28 - 4.27
MHD + ADO + insulin	0	6		6.32	3.12 - 14.1

4. Discussion

Our study involved fifty-five (55) patients followed at the CNHU-HKM of Cotonou, all of whom had type 2 diabetes with a predominance of women (60%). This female predominance was also found by Djrolo *et al.* [5] in Cotonou (62.1%). (68%) but differs from that obtained by Makulo *et al.* [6] where it was noted that men were more represented (53.04%) than women (46.96%). This could be explained by the fact that women have a low physical activity and a diet rich in lipids generating obesity. The average BMI of the patients was 28.61 ± 1.46 kg/m^2 with extremes of 17.50 kg/m^2 and 46.02 kg/m^2 and 74.55% of the patients were overweight. This result is lower than that obtained (86.8%) by Kaké *et al.* [7] in Malabo (Equatorial Guinea). The traditional practices of walking and physical work have been replaced by motorised transport and sedentary activities, particularly in urban areas. The obesity observed in black African patients is due on the one hand to a diet rich in cereals and starchy foods and on the other hand to socio-cultural factors showing it as a sign of social ease and well-being, especially for women (Oniankitan *et al.*) [8]. This obesity of the woman is a reason for the husband's appreciation.

The majority of patients had a diabetic course of less than 5 years (41.82%). This result is similar to that of Kéita [9] (42.85%) in Mali. This could be explained by the fact that T2DM is probably discovered incidentally (systematic assessment) in our series (61.81%). Contrary to our results, Cissé [10], Touré [11] and Diakité [12] in Mali all found that the main mode of discovery was poliuro-polydypsic syndrome (PPS). Secondary level patients (43.64%) were the most represented, followed by higher level patients (41.82%). This observation is probably due to the fact that the study was conducted in an urban environment (Cotonou). The average age of the patients was 56.34 ± 2.58 years. This average is close to that of Taleb *et al.* [13] in Lebanon (56.4 ± 11 years) and that of Yameogo *et al.* [14] (58.2 ± 9.2 years) in Senegal. Patients older than 40 years were in the majority in our study (92.73%). This result is supported by that obtained by Razzouki [15] in Marrakech where the majority of diabetics are over 50 years old. This high number of people older than 40 years could be justified by the silent character of T2DM evolution but also by its frequency which increases clearly with age, justifying the name given to T2DM: *Mature diabetes*.

Of our 55 patients, 44 (80%) were simultaneously subjected to the combination of MHD + ADO treatment and only 09.09% to hygienic-dietary measures. This could be explained by the fact that in the majority of cases, the diabetic patient consults in a state of hyperglycaemia where only hygienic-dietary measures such as a balanced diet will not give the expected results, *i.e.* an HbA1c lower than 7%. In our study, 87.53% of the patients had at least one degenerative complication with retinopathy the most common degenerative disease (36.36%) followed by cardiovascular disease (25.45%). This figure is higher than what Razzouki [15] reported (33.84% retinopathy) and Assavedo (17.5%) in Parakou [16]. This frequency is similar to that reported by Djrolo [5] in Cotonou (36.6%). The consequences of diabetes can be serious for health and can lead to retinal dysfunction, hence retinopathy. As for acute complications, 13 patients presented with them. Hypoglycaemia was the most common complication (14.55%). It could be said that this rate of hypoglycaemia is a direct consequence of the treatment.

The mean blood glucose level of the patients was 1.52 ± 0.16 g/L with extremes of 0.80 g/L and 3.5 g/L. The mean HbA1C proportion was 8.39% ± 0.60% with a minimum and maximum value of 5.40% and 16% respectively. These results are similar to those of Lotfi *et al.* in 2010 in Morocco (8.5% ± 2.6% for glycosylated haemoglobin and 1.5 g/L ± 1.3 for mean blood glucose). These results show that these patients are not balanced. This could be due to ignorance of the consequences of diabetes, non-compliance with treatment and HDMs and other diseases. This study showed that there is a poor correlation between fasting blood glucose and HbA1c levels which could be due to several reasons both biological and clinical. Firstly, it could be explained by the fact that fasting blood glucose is a snapshot of the glycaemic state whereas glycated haemoglobin is a reflection of the average blood glucose (postprandial and fasting blood glucose) over a period of 02 to 03 months. Secondly, this discrepancy between HbA1c and fasting blood glucose can be easily explained in the clinical context by the fact that some patients do not implement dietary measures until a few days before the fasting blood glucose test. In fact, following dietary measures for a few days is sufficient to rapidly and favourably modify fasting blood glucose levels. On the other hand, the glycated haemoglobin level, which incorporates chronic exposure over a period of three months, can only be improved if the dietary hygiene measures are respected over the three months, which justifies normal fasting blood glucose levels concomitant with a high HbA1c level Nonnotte [17]. Finally, certain comorbidities are also at the origin of this observed discordance. Any shortening of the life span of red blood cells (haemolysis, hypersplenism, acute or chronic bleeding) will lead to a loss of red blood cells chronically exposed to glycaemia, which will be replaced by virgin reticulocytes (without contact with glycaemia), thus inducing a lowering of the HbA1c level, whereas these comorbidities have no influence on fasting glycaemia Procopiou [18]. In sum, this study has shown that there is no relationship between fasting blood glucose and HbA1c and therefore an extrapolation from fasting blood glucose to HbA1c is not possible and vice versa.

Our study has also shown that despite the respect of hygienic and dietary measures and a well conducted treatment, it is difficult to obtain a satisfactory glycemic balance in obese patients. These results are corroborated by the work *of* Zighari *et al.* [19] and Antuna-Puente *et al.* [20] who showed that fasting blood glucose and HbA1c levels were higher in obese diabetic patients than in normo-weighted patients. The elevation of these two glycaemic parameters is explained by adipocyte secretion of adipokines responsible for insulin resistance Antuna-Puente *et al.* [20].

In our study population, there was a statistically significant association between HbA1c and cardiovascular disease ($p = 0.03$). Specifically, the presence of cardiovascular disease in patients increases the chance or risk of HbA1c elevation above 7% (OR = 3.63). Cardiovascular disease is therefore a risk factor for HbA1c elevation in our patients. In our cohort, we observed a statistically significant association between HbA1c and the combination of MHD+ADO treatment ($p = 0.006$). In the medium and long term, the aim of treatment is to maintain optimal glycaemic control with ADOs associated with MHD and to prevent chronic complications by treating associated comorbidities (hypertension, dyslipidaemia, smoking cessation, overweight and sedentary lifestyle).

In our study, there was no significant association between HbA1c and the duration of diabetes, in contrast to a significant number of international studies that found an association between HbA1c and the duration of diabetes.

5. Conclusion

Diabetes, a chronic disease, is a real health challenge and is the subject of growing concern. Moreover, poorly controlled diabetes leads to several complications, which are either acute metabolic, infectious, or degenerative. It is therefore necessary to opt for an adequate method of diabetes monitoring and diagnosis. The value of HbA1c as a retrospective marker of glycaemic control in the diabetic patient is well established and its interpretation is simple in terms of diabetic complications. This biomarker can be recommended as an objective criterion in the diagnosis and treatment of diabetes mellitus. However, caution should be exercised when interpreting HbA1c results in these patients and other means of assessing glycaemic control should not be neglected.

Conflicts of Interest

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

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