



## Biochemical and Hematological Profiles of Type 2 Diabetics Living with HIV in Ivory Coast

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### ABSTRACT

The objective of this study was to determine the biochemical and hematological profiles of type 2 diabetic patients living with HIV. A total of 260 participants including 100 HIV positive and 160 HIV negative diabetics participated. Blood samples were obtained by venipuncture of the elbow crease. They were used to obtain plasma and serum. Serum was used for the determination of creatinine, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, magnesium, phosphorus, urea, and cystatin C, while plasma was used to measure the level of glycated hemoglobin, blood sugar and perform blood count. The respective values of magnesium and phosphorus of DM/HIV+ ( $22.64 \pm 5.72$ ;  $39.49 \pm 9.66$  mg/l) were significantly ( $p=0.000$ ;  $<0.05$ ) higher than those of DM/HIV- ( $20.11 \pm 4.63$ ;  $35.81 \pm 4.51$  mg/l). The hematological parameters such as red blood cells, hemoglobin, hematocrit, lymphocytes, and basophils of DM/HIV+ were significantly lower than those of DM/HIV-. The GMV, MCHR, and platelets of HIV-positive patients were significantly higher than those of HIV patients.

**Keywords:** Biochemical and hematological profiles, Type 2 diabetes mellitus, HIV

### INTRODUCTION

Diabetes is becoming a major health problem in Africa. Type 2 diabetes (T2DM) is the most prevalent and its prevalence is increasing rapidly [1]. Like other regions of the world, sub-Saharan Africa is experiencing an increasing prevalence of diabetes as is the case with other non-communicable diseases [2]. Furthermore, several infectious diseases such as HIV are highly prevalent in sub-Saharan Africa with 25.7 million people living with HIV and its corollaries of co-infection or association with non-communicable diseases such as diabetes, high blood pressure [3]. At the same time, there are cardio-metabolic complications attributable to HIV itself and its treatment [4]. People Living with HIV (PLHIV) are dying from non-AIDS-related conditions, including type 2 diabetes and Chronic Kidney Disease (CKD) [5]. Diabetes is associated with abnormalities in carbohydrate, fat, and protein metabolism. Chronic exposure to hyperglycemia can lead to dysfunction and failure of various organs, particularly the eyes, kidneys, nerves, heart, and blood vessels [6]. Several studies have reported an increase in the prevalence and incidence of metabolic disorders such as impaired glucose tolerance and diabetes mellitus in HIV-infected individuals [7,8]. This increase is up to fourfold in HIV-infected people exposed to antiretroviral therapy [9,10].

People with type 2 diabetes are at increased risk of myocardial infarction, stroke, and hematological disease [11]. In type 2 diabetes, hyperglycemia disrupts hematological parameters and, is associated with well-known risk factors, which can lead to degenerative complications. Furthermore, Alterations in these hematological parameters are closely associated with glycated hemoglobin (HbA1c) levels and some of these parameters are associated with complications

in people with diabetes [12]. The objective of this study was to determine the biochemical and hematological profiles in type 2 diabetic patients living with HIV.

## MATERIAL AND METHODS

### Study Population

The study population consisted of two groups of individuals, HIV-positive diabetics (DM/HIV+) and HIV-uninfected diabetics (DM/HIV-). The selection of patients was based on the analysis of medical records in two main centers: the Abidjan Antidiabetic Centre (CADA) and the NGO Ruban Rouge, which is an NGO fighting against HIV/AIDS. A total of 260 participants consisting of 100 diabetics living with HIV and 160 Type 2 diabetics not infected with HIV were selected for the study.

### Inclusion and No n-Inclusion Criteria

The study concerned type 2 diabetics living or not with HIV, aged over 15 years.

Type 1 diabetics, pregnant women, and children under 15 years of age, carriers of pathologies such as malaria, tuberculosis, and hepatitis were not included.

The other information was completed with a questionnaire at the interview of the patients after they had given their free and informed consent. The data collected included socio-demographic characteristics, information on HIV infection (age of diagnosis and type of HIV), diabetes (age of diagnosis, therapy, micro- and macro-angiopathic complications), and the presence of comorbidity.

### Ethical Approval and Consent

The study was conducted after approval from the National Ethics Committee for Life Sciences and Health of Ivory Coast (CNESVS). All participants signed an informed consent form before the implementation of the study.

### Blood Samples

Blood samples were taken from fasting subjects by venipuncture at the crease of the elbow. They have been used to obtain plasma and serum for the determination of biochemical and hematological parameters. A volume of 5 ml of blood was drawn into dry tubes without anticoagulant and centrifuged at 3000 rpm for 15 minutes. The collected serum was used for the determination of creatinine, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, magnesium, phosphorus, urea, and cystatin C. Blood collected in tubes EDTA was used for glycosylated hemoglobin, and complete blood counts, while blood obtained in fluoride tubes was used to measuring fasting blood glucose.

### Determination of Biochemical and Haematological Parameters

Biochemical parameters such as Blood glucose, creatinine, total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, magnesium, phosphorus, urea, uric acid were measured by Cobas® c311 automated assays using specific Cobas® c311 reagents from Roche Diagnostics as well as the immunoassay of HbA1c using Roche Cobas C311 monoclonal antibody-based reagents. Cystatin C was determined by immunoturbidimetry using the RANDOX CYS4004 kit (UK). The principle is based on the formation of a latex agglutination complex that forms between cystatin C and latex particles. The reading was taken at 570 nm with a spectrophotometer.

The determination of hematological parameters was performed with the SYSMEX 1800i hematological analyzer using the combined system technique of independent variation and flow cytometry [13].

### Data Analysis

Data were entered and analyzed using SPSS software version 20 (IBM Corporation, Armonk, NY, USA). Data were reported as the mean and standard deviation for continuous variables, and as frequency and percentages for categorical variables. Means for continuous variables were compared using a t-test for equality of means, 95% CI of the difference. A p-value < 0.05 was considered statistically significant.

## RESULTS

## Epidemiological Analysis of the Study Population

Table 1 shows the characteristics of the study population consisting of 260 diabetic patients, 100 of whom were HIV-infected and 160 uninfected. The number of women (154 or 59.2%) was higher than that of men (106 or 40.8%). The average age of the whole population was  $48.72 \pm 12.50$  years with an average weight of  $72.11 \pm 15.20$  Kg. However, the mean age of HIV-positive diabetics ( $45.14 \pm 12.68$  years) was significantly lower ( $p < 0.05$ ) than that of HIV-negative diabetics ( $50.96 \pm 11.88$  years). The population was generally overweight with a mean BMI of  $26.18 \pm 5.36$  kg/m<sup>2</sup>. However, the mean BMI of HIV-negative diabetics ( $27.06 \pm 4.76$ ) was significantly higher ( $p < 0.001$ ) than that of HIV-positive diabetics ( $24.78 \pm 5.97$ ). There was no significant difference ( $p = 0.209$ ;  $> 0.05$ ) between the diabetes durations in the two groups.

Table 1 Characteristics of the study population

Parameters	DM/HIV-	DM/HIV+	Total	p-value
N	160	100	260 (100%)	Sig. p<0.05
<b>Ages (years)</b>				
18-28	2 (1.3%)	13 (13%)	15 (5.8%)	
29-38	22 (13.8%)	14 (14%)	36 (13.8%)	
39-48	40 (25%)	29 (29%)	69 (26.5%)	
49-58	46 (28.7%)	30 (30%)	76 (29.2%)	
59 and over	50 (31.3%)	14 (14%)	64 (24.6%)	
Average	$50.96 \pm 11.88$	$45.14 \pm 12.68$	$48.72 \pm 12.50$	0.000
<b>Gender</b>				
Men	78 (48.8%)	28 (28%)	106 (40.8%)	
Women	82 (51.2%)	72 (72%)	154 (59.2%)	
Weight (Kg)	$75.49 \pm 14.41$	$66.71 \pm 14.95$	$72.11 \pm 15.20$	0.000
Size (m)	$1.67 \pm 0.08$	$1.63 \pm 0.07$	$1.65 \pm 0.08$	0.000
<b>BMI Kg/m<sup>2</sup></b>				
18-25	102 (63.7%)	55 (55%)	157 (60.4%)	
25-30	43 (26.9%)	23 (23%)	66 (25.4%)	
> 30	15 (9.4%)	22 (22%)	37 (14.2%)	
Average	$27.06 \pm 4.76$	$24.78 \pm 5.97$	$26.18 \pm 5.36$	0.001
<b>Duration of diabetes</b>				
>5years	121 (75.6%)	63 (63%)	184 (70.8%)	
5-10years	23 (14.4%)	28 (28%)	51 (19.6%)	
>10years	16 (10%)	9 (9%)	25 (9.6%)	
Average	$5.11 \pm 5.30$	$4.36 \pm 3.31$	$4.82 \pm 4.64$	0.209
<b>Duration of HIV</b>				
<3years		79 (70%)		
3-5 years		17 (17%)		
>5years		4 (4%)		
Average		$3.37 \pm 2.58$		

According to Table 2, women (72%) were more infected than men (28%). HIV1 infection (69%) predominates over HIV2 infection (31%). The reference values of the measured parameters are given in Table 3.

Table 2 Distribution of the HIV-positive diabetic population according to HIV type and gender

Type of HIV	Gender of participants		
	Male	Woman	Total
HIV1	19 (19%)	50 (50%)	69 (69%)
HIV2	9 (9%)	22 (22%)	31 (31%)
Total	28 (28%)	72 (72%)	100 (100%)

Table 3 Reference values of the measured parameters

Biochemical parameters	References values	hematological parameters	References values
GLY (g/l)	0.75-1.10	GB (10 <sup>3</sup> /μL)	H:4.66; F:4-5.4
HBA1c (%)	4-6	GR (10 <sup>6</sup> /μL)	4.1-5.5
Creat (mg/l)	6-11	HB (g/dl)	H:13-18; F:12-16
UREE (g/L)	0.18-0.45	HTC (%)	H :40-52 ; F :37-48
CYST C (mg/l)	0.57-1.05	VGM (fL)	80-95
CHOL-T (g/l)	1.06-2.50	TCMH (pg)	27-31
HDL-C (g/l)	0.26-0.70	CCMC (g/dl)	32-36
LDL-C (g/l)	0.4-1.60	PLAQ (10 <sup>3</sup> /μL)	150-450
TRIGLY (g/l)	0.3-1.20	PNN (10 <sup>3</sup> /μL)	1.5-7.5
Mag (mg/l)	17-23	Lympho(10 <sup>3</sup> /μL)	1.5-4.0
Cal (mg/L)	80-105	Mono(10 <sup>3</sup> /μL)	0.1-1.0
Phosp (mg/l)	25-56	PNE(10 <sup>3</sup> /μL)	0-0.5
		PNB(10 <sup>3</sup> /μL)	0-0,05

Table 4 shows the values of the biochemical parameters. Indeed, the mean blood glucose values in the two groups (HIV- =1.64 ± 0.87 g/l; HIV+ =1.48 ± 0.81 g/l) are not significantly different (p=0.137). However, these values and that of the total population (1.58 ± 0.85 g/l) are greater than the value of the upper limit of the reference interval (0.75 to 1.10 g/l) for glycemia. In addition, as for blood glucose, the mean glycated hemoglobin values of the two groups were statistically not different (HIV- =8.13 ± 2.96%; HIV+ =7.75 ± 2.25%) (Table 5) and that of the total population (7.98 ± 2.71%) were above the reference value range (4%-6%). Apart from blood sugar and HBA1c, the values of the other biochemical parameters measured in the two groups remained within their normal range. However, only the respective values of Magnesium and phosphorus in DM/HIV+ (22.64 ± 5.72; 39.49 ± 9.66 mg/l) were significantly (p=0.000; <0.05) higher than those in DM/HIV- (20.11 ± 4.63; 35.81 ± 4.51mg/l) (Table 5).

Table 4 Distribution of biochemical parameters

Parameters	DM/HIV- n=160	DM/HIV+ n=100	Total N=260
GLY (g/l)	1.64 ± 0.87	1.48 ± 0.81	1.58 ± 0.85
HBA1c (%)	8.13 ± 2.96	7.75 ± 2.25	7.98 ± 2.71
Creat (mg/l)	8.6 ± 2.11	8.99 ± 3.68	8.79 ± 2.82
UREE (g/L)	0.26 ± 0.07	0.26 ± 0.13	0.26 ± 0.10
CYST C (mg/l)	0.72 ± 0.44	0.66 ± 0.38	0.69 ± 0.42
CHOL-T (g/l)	1.93 ± 0.59	1.99 ± 0.42	1.95 ± 0.53
HDL-C (g/l)	0.28 ± 0.13	0.25 ± 0.13	0.27 ± 0.13
LDL-C (g/l)	1.40 ± 0.57	1.47 ± 0.44	1.43 ± 0.53

TRIGLY (g/l)	1.21 ± 0.49	1.29 ± 0.62	1.24 ± 0.54
Mag (mg/l)	20.11 ± 4.63	22.64 ± 5.72	21.08 ± 5.22
Cal (mg/L)	91.94 ± 6.56	90.93 ± 6.56	91.55 ± 6.56
Phosp (mg/l)	35.81 ± 4.51	39.49 ± 9.66	37.22 ± 7.17

Table 5 t-test for equality of means, 95% confidence interval

Biochemical parameters	Anova p<0.05	Haematological parameters	t-test p<0.05
GLY (g/l)	0.137	GB (10 <sup>3</sup> /μL)	0.553
HBA1c (%)	0.271	GR (10 <sup>6</sup> /μL)	0.000
Creat (mg/l)	0.368	HB (g/dl)	0.000
UREE (g/L)	0.979	HTC (%)	0.000
CYST C (mg/l)	0.255	VGM (fL)	0.012
CHOL-T (g/l)	0.471	TCMH (pg)	0.004
HDL-C (g/l)	0.062	CCMC (g/dl)	0.502
LDL-C (g/l)	0.298	PLAQ (10 <sup>3</sup> /μL)	0.003
TRIGLY (g/l)	0.221	PNN (10 <sup>3</sup> /μL)	0.47
Mag (mg/l)	0	Lympho(10 <sup>3</sup> /μL)	0.023
Cal (mg/L)	0.228	Mono(10 <sup>3</sup> /μL)	0.988
Phosp (mg/l)	0	PNE(10 <sup>3</sup> /μL)	0.778
		PNB(10 <sup>3</sup> /μL)	0.019

The analysis of the hematological profile shown in Table 6 shows that most parameters are within the reference values for the whole population. However, the averages of red blood cells, hemoglobin, hematocrit, lymphocyte count, basophil count, and number in DM/HIV+ were significantly lower than those in DM/HIV- (Table 5). On the other hand, the values of other parameters such as mean corpuscular volume, mean corpuscular hemoglobin content, number of blood platelets in DM/HIV+ were significantly higher than those of DM/HIV- (Table 5).

Table 6 Distribution of hematological parameters in the study population

Parameters	DT2HIV-	DT2HIV+	Total
	n=160	n=100	N=260
GB (10 <sup>3</sup> /μL)	5.25 ± 1.42	5.14 ± 1.64	5.21 ± 1.50
GR (10 <sup>6</sup> /μL)	4.70 ± 0.55	4.10 ± 0.53	4.47 ± 0.61
HB (g/dl)	M: 13.81 ± 1.40	M: 12.48 ± 1.52	12.71 ± 1.50
	W: 12.62 ± 0.97	W: 11.71 ± 1.32	
	T: 13.20 ± 1.33	T: 11.92 ± 1.42	
HTC (%)	39.30 ± 3.65	35.30 ± 3.92	37.76 ± 4.22
VGM (fL)	84.11 ± 7.25	86.53 ± 8.00	85.04 ± 7.63
TCMH (pg)	28.23 ± 2.50	29.24 ± 3.07	28.62 ± 2.77
CCMC (g/dl)	33.61 ± 1.85	33.76 ± 1.28	33.67 ± 1.65
PLAQ (10 <sup>3</sup> /μL)	245.35 ± 64.48	282.08 ± 133.10	259.48 ± 98.21
PNN (10 <sup>3</sup> /μL)	2.35 ± 0.89	2.45 ± 1.41	2.39 ± 1.12
Lympho(10 <sup>3</sup> /μL)	2.25 ± 0.72	2.05 ± .63	2.18 ± 0.69
Mono(10 <sup>3</sup> /μL)	0.46 ± 0.18	0.46 ± 0.20	0.46 ± 0.19
PNE(10 <sup>3</sup> /μL)	0.14 ± 0.13	0.13 ± 0.13	0.14 ± 0.13
PNB(10 <sup>3</sup> /μL)	0.02 ± 0.01	0.01 ± 0.01	0.02 ± 0.01

## DISCUSSION

In our study, the mean age of HIV-positive diabetics was  $45.14 \pm 12.68$  years. These results corroborate data from studies in other countries. In the study by Lozes, et al., patients in the 25-45 years age group were the most affected by HIV and constituted 70.7% [14]. Another study conducted in Togo showed the same age group to be most affected by the infection, with a percentage of 83.7% [14,15]. This age group corresponds to that of maximum sexual activity exposing to the risks of transmission of sexually transmitted infections. The predominance of heterosexual transmission in tropical regions, particularly in sub-Saharan Africa, may explain the prevalence of the disease in this age group [14,16]. In all these studies, women were the most represented, as in our study where HIV-infected diabetic women represented 72%. This female predominance was reported by Boyvin, et al. in Côte d'Ivoire where HIV1 patients were the majority (95.38%) [17]. Our study reported 69% of HIV1 cases, 50% of which were female. In Congo Brazzaville, ELIRA Dokekias, et al. reported a female predominance of 68.2% [18,19]. Diabetes mellitus encompasses a heterogeneous group of disorders characterized by hyperglycemia associated with multiple disorders, including metabolic, cellular, and blood disorders leading to vascular complications [20]. HIV infection and diabetes mellitus represent a cluster of life-threatening chronic diseases. As in HIV-uninfected diabetics, the biochemical profile of diabetics living with HIV showed some disturbances. We noted an increase in blood glucose and poor glycaemic control expressed by a glycated hemoglobin level above 7%. These findings corroborate those of Kims, et al. and Henry, et al. [21,22]. A study from South Africa showed that about 85.23% of diabetic patients living with HIV had suboptimal glycaemic control. There are multiple risk factors for the occurrence of diabetes and poorly controlled blood glucose in PLHIV. These include antiretroviral drugs, HIV itself, multiple opportunistic infections, which will increase oxidative stress, insulin resistance, lipodystrophy, non-comprehensive clinical care for diabetic patients only, and diabetic patients living with HIV [23-27]. Traoré et al also showed that the majority of patients in their study (73.1%) considered diabetes as a second health problem [8]. The higher number of drugs with the risk of interactions that this represents and an overly trivialized perception of diabetes may also explain this aspect.

HIV, on the other hand, destroys the immune system in infected individuals, leading to metabolic disturbances, including lipid disorders [28]. An increase in triglycerides in HIV-infected subjects was found in our study as in typical cases of diabetes. Sagna, et al. also reported triglyceride values above the normal range [28] as in several other studies carried out in HIV-infected individuals, because during T2DM, quantitative and qualitative lipid abnormalities are observed [29,30]. The main quantitative abnormalities are hypertriglyceridemia and decreased HDL-Cholesterol (HDL-C) [31]. Although statistically insignificant, HDL-C values of HIV+ DMs were lower than those of HIV- DMs. In the study by Abebe, et al., the majority of HIV and AIDS patients had at least one lipid profile abnormality that can label them as having dyslipidemia [32]. Similarly, another study shows that the natural course of HIV infection is characterized by a reduction in HDL-cholesterol [33]. On the other hand, the pathophysiological mechanisms during HIV involve two major disturbances, namely insulin resistance of adipose tissue due to lipodystrophy and a decrease in adiponectin. These two alterations lead to poor use of glucose by the muscles and a decrease in the penetration of fatty acids into the mitochondria preventing their oxidation. This leads to the synthesis of Very Low-Density Lipoproteins (VLDL) and thus the accumulation of Triglycerides (TG) in muscle and liver [8]. Triglyceride and HDL-C abnormalities, which are referred to as atherogenic dyslipidemia, are characteristic of diabetes and cause macrovascular and microvascular complications [34]. Although the majority of hematological parameters in diabetics were within the reference values, we observed some abnormalities. In type 2 diabetes, hyperglycemia disturbs hematological parameters and, is associated with risk factors, which may lead to degenerative complications. The mean Hgb and hematocrit values in T2DM/HIV+ patients were significantly lower than those in uninfected diabetics. In general, the relatively low hemoglobin level in T2DM patients is because the heme (protein) part of hemoglobin is subject to glycation and is affected by the duration and level of hyperglycemia in these patients. Excess glucose reacts with hemoglobin to form glycosylated hemoglobin so that the total hemoglobin level is decreased [35]. Since in PLWHIV- the hemoglobin level is higher, we believe that the decrease in hemoglobin in PLWHIV+ is due to HIV. Indeed, anemia is the most common hematological abnormality in human immunodeficiency virus (HIV)-positive patients and a significant predictor of its progression to AIDS or death [36]. In Africa, several studies have reported high frequencies of anemia in people living with HIV. For example, Diallo, et al. obtained a prevalence of 78.9% in Mali against, 92.2% reported by Malyangu, et al. in Zimbabwe, Boyvin in Côte d'Ivoire, and many others [17,37,38].

## CONCLUSION

In conclusion, these data show that HIV-positive diabetic subjects have the same biochemical disturbances as uninfected diabetics. Poor glycaemic control was observed in both groups. The hematological profile of diabetics living with HIV was the most disturbed.

## DECLARATIONS

### Conflicts of Interest

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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