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The Association between Glomerular Filtration Rate, Cardiometabolic Risk, and HbA1c Levels among Outpatients with Type 2 Diabetes Mellitus in Mopti

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Abstract

Type 2 diabetes mellitus (T2DM) outpatients, characterized by hyperglycemia, present challenges in managing glycemic control by glycated hemoglobin (HbA1c) and its connection to cardiometabolic and renal complications. These complications exacerbate insulin resistance, thereby affecting the reliability of HbA1c. There is a need for integrated management strategies to improve cardiovascular and renal outcomes of T2DM outpatients. This cross-sectional study investigates the link between HbA1c levels and both cardiometabolic and renal risk factors in T2DM outpatients. Univariate and multivariate analyses were conducted using linear regression within the generalized linear model (GLM) framework, applying a predefined HbA1c threshold of ≥7% (53 mmol/mol) as the cut-off of the dependent variable. Factors with no effect were eliminated by using an analysis of variance (ANOVA) test. The median of HbA1c was 7.4% [5.6% - 10.1%]. Multivariate analysis with continuous biological variables showed that fasting plasma glucose (FPG): OR, 1.4 (95% CI [1.2 - 1.7], $p < 0.001$); total cholesterol (TC): OR, 13.2 (95% CI [2.8 - 85.7], $p = 0.002$); estimated glomerular filtration rate chronic kidney disease epidemiology 2021 (eGFR-CKD-EPI 2021) creatinine-based formula: OR, 1.0

(95% CI [1.0 - 1.1], $p = 0.03$) and estimated glomerular filtration rate modification of diet in renal disease (eGFR-MDRD): OR, 1.0 (95% CI [1.0 - 1.0], $p = 0.03$) were positively associated with the likelihood of HbA1c ≥ 7%. In contrast, atherogenic index (AI): OR, 0.4 (95% CI [0.1 - 1.2], $p = 0.11$), body mass index (BMI) (18.5 - 25 Kg/m^2): OR, 0.1 (95% CI [0.0 - 0.8], $p = 0.052$) and HDL cholesterol (HDL-C): OR, 0.0 (95% CI [0.0 - 0.5], $p = 0.03$) were negatively associated with HbA1c, but AI association was not significant. Categorical biological variables multivariate analysis highlighted that BMI (18.5 - 25 Kg/m^2): OR, 0.1 (95% CI [0.0 - 0.6], $p = 0.03$), FPG (<7.15 mmol/L): OR, 0.1 (95% CI [0.0 - 0.2], $p < 0.001$) and Na^+ (135 - 145 mmol/L): OR, 0.2 (95% CI [0.1 - 0.9], $p = 0.03$) were negatively associated with HbA1c ≥ 7%. Our findings highlight that the management of outpatients with T2DM requires a more holistic approach than merely evaluating HbA1c levels. Thus, it is essential to implement comprehensive strategies addressing cardiometabolic and renal factors that influence HbA1c variability.

Keywords

Cardiometabolic and Renal Risk Factors, HbA1c, Type 2 Diabetes Mellitus

1. Introduction

Diabetes mellitus (DM) encompasses a range of metabolic disorders characterized by elevated fasting plasma glucose (FPG) levels due to issues with insulin secretion, its action, or both. The chronic high FPG in DM leads to prolonged damage and dysfunction, particularly affecting the heart, kidneys, eyes, blood vessels, and nerves. The underlying cause of the metabolic irregularities in carbohydrates, fats, and proteins relates to inadequate insulin action on target tissues. From a nosological perspective, it encompasses types 1 and 2 DM (T2DM), other specific types of DM, and gestational DM (GDM). Unlike type 1 DM, which stems from an autoimmune disorder leading to a gradual decrease in β-cell insulin production, T2DM is more commonly associated with insulin resistance and metabolic syndrome [1]. The chances of developing T2DM increase with factors such as age, obesity, and a sedentary lifestyle. Symptoms, as observed in type 1, often present in a non-specific manner, and diagnosis may be delayed for several years after onset, frequently being established only once complications have arisen. T2DM, influenced by genetic factors, can be prevented or delayed by a healthy diet, exercise, maintaining a normal weight, and not smoking. People with the disease can control their blood sugar with oral antidiabetic medications, regular monitoring, and an adequate lifestyle to avoid complications [2]. In its 2009 report, the International Expert Committee recommends the use of glycated hemoglobin (HbA1c) to diagnose DM [3]. DM diagnosis relies on the criteria of HbA1c or plasma glucose (PG) levels, which include fasting plasma glucose (FPG), the 2-hour PG from a 75 g oral glucose tolerance test (OGTT), or random glucose values paired with

classic hyperglycemic symptoms. HbA1c reflects the average blood glucose throughout the last 8 to 12 weeks [4]. A diagnosis of DM is made if the HbA1c level is at least 6.5% (or 48 mmol/mol). However, PG homeostasis relies on multifactorial processes such as regulatory hormones, dietary intake, and physical activity. Moreover, HbA1c is also suggested to have many interfering factors that cause discordance between FPG and HbA1c [1]. T2DM, characterized by hyperglycemia, presents challenges in managing glycemic control by HbA1c and its connection to cardiometabolic and renal complications.

Cardiometabolic syndrome worsens insulin resistance and elevates HbA1c, while renal dysfunction both impairs HbA1c reliability and is aggravated by hyperglycemia, increasing the risk of end-stage renal disease (ESRD). Managing HbA1c improves renal outcomes, highlighting the need for integrated management strategies [5]. Therefore, it is of paramount importance to know the link between HbA1c levels and cardiometabolic risk factors to improve the management of diabetic patients. This study aimed to investigate the relationships between HbA1c levels and both cardiometabolic and renal complications during the follow-up of T2DM outpatients.

2. Materials and Methods

2.1. Study Design and Population

This was a cross-sectional study conducted between April 1, 2023 and May 31, 2024, with consecutive recruitment, using qualitative and quantitative methods. The qualitative study was carried out through semi-structured interviews to collect specific information defined in the survey form. The study population was defined as outpatients with T2DM aged 18 years and older, attending the Medicine Department of Hôpital Sominé DOLO in Mopti (HSD-M). Each T2DM outpatient underwent a physical examination and a semi-structured interview to assess sociodemographic, behavioral, clinical, and biological variables. Only subjects in the stationary phase who visited the Medicine Department were included in this study. Patients presenting with diabetic emergencies, those without written informed consent, or those who did not meet the study criteria were not included.

2.2. Sample Size

The sample size was computed using Schwartz's formula: $n = (Z^2 * p * (1 - p)) / d^2$, where: n = required sample size, Z = standard normal deviate corresponding to the desired confidence level (1.96 for 95% confidence), p = expected prevalence or proportion, d = margin of error (precision). This formula was applied to determine the minimum number of participants to ensure adequate statistical power. With a margin of error of 5% and a confidence level of 95%, and based on a 7% prevalence of T2DM, based on a study conducted in 16 West African countries [6], the minimum sample size n = 100 outpatients was required for this study.

2.3. Clinical and Biological Variables Assessed

Qualitative data were collected through semi-structured interviews during the doctor's visit to gather behavioral and sociodemographic data (education level, occupation, tobacco or alcohol consumption) from participants relevant to the research question. Clinical data were also determined during physical examination, including gender, age, weight, height, waist circumference, blood pressure, cardiac syndrome, medication, personal and family medical history, impact on organs, eye impairment, and presence of infection. The following biochemical parameters were measured in all participants: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), direct low-density lipoprotein cholesterol (LDL-C), creatinine, uric acid (UA), fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), and blood ionogram. Standardized enzymatic methods were applied according to the manufacturer's instructions. The atherogenic index (AI), calculated with Castelli's Risk Index I (CRI-I), defined as the ratio of total cholesterol to HDL cholesterol: AI = TC / HDL-C, was used to assess cardiovascular risk. The clinical cut-offs were set at ≥ 4.5 for men and ≥ 4.0 for women, above which the risk of cardiovascular events is considered elevated.

2.4. Sample Collection and Handling

Blood samples were collected by venipuncture at the elbow crease using the Vacutainer system after 8 to 12 hours of fasting. Approximately 4 mL of whole blood was collected using heparinized, ethylenediaminetetraacetic acid (EDTA), and fluoride tubes from all included subjects. All tubes, except the EDTA tube, were centrifuged at 1500 g for 5 minutes, and plasma was separated into Eppendor™ Safe-Lock 2.0 mL tubes (Hamburg, Germany). The biological variables such as FPG, HbA1c, TC, HDL-C, LDL-C, UA, creatinine, TG, sodium, potassium, and chloride were assessed and used to evaluate cardiometabolic risk factors and their association with HbA1c. The Cobas c311™ analyzer (Roche Diagnostics GmbH, Germany) was used for the measurement of biological variables.

2.5. Quality Control

PreciControl ClinChem Multi 1 (4 × 5 mL; Ref 05947626190), HbA1c Control (4 × 1.0 mL; Ref 06380204190), and ISETROL (1 × 10 mL; Ref 03112888180) levels 1 - 3 were used for the quality control (QC). QC was monitored by using the Levey-Jennings plot and Westgard's six-sigma rules.

2.6. Data Management

Data were collected on survey sheets, entered into Excel, and then analyzed with R version 4.4. The Shapiro-Wilk test was used to assess the normality of continuous variables. Categorical variables were compared using Pearson's chi-square or Fisher's exact test, and the Wilcoxon-Mann-Whitney test was used to compare continuous variables. Continuous variables were presented as median with first and third quartiles (Q1 and Q3), while categorical variables were presented as per-

centage with confidence interval. The body mass index (BMI) was calculated as the ratio of weight to squared height: (Weight (kg))/(Height (m)^2). The estimated glomerular filtration rate (eGFR) was computed using two validated equations: CKD-EPI 2021 creatinine-based formula (Chronic Kidney Disease Epidemiology 2021):

eGFR-CKD-EPI 2021 = 142 × min(Scr/K, 1)$^{\alpha}$ × max(Scr/K, 1)$^{-1.200}$ × 0.9938$^{\text{Age}}$ × (1.012 if female).

MDRD formula (Modification of Diet in Renal Disease, 4 variables):

eGFR-MDRD = 175 × (Scr)$^{-1.154}$ × (Age)$^{-0.203}$ × (0.742 if female) × (1.212 if Black)

Where Scr = serum creatinine (mg/dL), Age = years, K = 0.7 for females, K = 0.9 for males, $\alpha = -0.241$ for females, $\alpha = -0.302$ for males.

Univariate analyses were first conducted using linear regression within the generalized linear model (GLM) framework, applying a predefined HbA1c threshold of ≥ 7% (53 mmol/mol) as the dependent variable cut-off. For each independent variable X_i, the univariate model was expressed as: HbA1c = $\beta_0 + \beta_1 X_i + \varepsilon$. All the independent variables were first entered into multivariate regression models of the form: HbA1c = $\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots + \beta_n X_n + \varepsilon$. To determine the contribution of each factor, analysis of variance (ANOVA) was performed using the following test statistic: $F = MS\_between/MS\_within$. Only independent variables with a statistically significant effect ($p < 0.05$) were retained in the final model, thereby identifying independent predictors of HbA1c variation.

3. Results

Out of the 100 T2DM outpatients, the FPG median was 9.4 [6.7 - 13.4] mmol/L. The medians of lipid variables were as follows: 4.1 [3.2 - 5.0] mmol/L, 0.94 [0.9 - 1.3] mmol/L, 2.8 [2.2 - 3.6] mmol/L, and 1.4 [1.0 - 1.8] mmol/L for TC, HDL-C, LDL-C, and TG, respectively. The plasma UA median was 211.2 [160.6 - 275.2] μmol/L. The eGFRs were 107.3 [81.3 - 121.3] mL/min/1.73 m^2, and 106.5 [83.7 - 131.4] mL/min/1.73 m^2 for eGFR-CKD-EPI 2021 and eGFR-MDRD, respectively. Plasma electrolytes medians were as follows: 135.0 [134.0 - 136.2] mmol/L, 3.7 [3.3 - 4.3] mmol/L, and 106.0 [99.7 - 109.0] mmol/L for Na^+, K^+, and Cl^-, respectively. When expressed in the Diabetes Control and Complications Trial/National Glycohemoglobin Standardization Program (DCCT/NGSP) units, the median of HbA1c was 7.4% [5.6 - 10.1%], or in International Federation of Clinical Chemistry (IFCC) units, 57.4 [38.2 - 87.2] mmol/mol as shown in Table 1.

Univariate analysis of clinical, demographic, and behavioral variables at the HbA1c ≥ 53 mmol/mol (≥7%) cutoff showed that the atherogenic index (AI) was significantly elevated in subjects with HbA1c ≥ 7% compared to those with HbA1c < 7%: (3.94 [3.41 - 5.46] vs 3.54 [2.66 - 4.17], $p = 0.01$). Conversely, blurred vision was negatively associated with HbA1c: (19 [42%] vs 13 [24%], $p = 0.05$). The other clinical, demographic, and behavioral variables showed no significant differences as shown in Table 2.

Continuous biological variables such as FPG and total TC levels were positively associated with the likelihood of HbA1c ≥ 7%. FPG values were (7.2 [5.0 - 9.9] vs 11.0 [7.7 - 17.6] mmol/L, $p < 0.001$), and TC values were (3.63 [2.80 - 4.41] vs 4.61 [3.44 - 5.32] mmol/L, $p = 0.002$) in univariate analysis. The other continuous biological variables were not significantly different as shown in Table 3.

Table 1. Descriptive statistics of biological variables.

Biological parameters	Measures of central tendency and dispersion						
	Min	1 Q	Median	Mean	3 Q	ET	Max
FPG (mmol/L)	2.2	6.7	9.4	11.0	13.4	6.4	33.3
TC (mmol/L)	1.8	3.2	4.1	4.2	5.0	1.3	8.9
HDL-C (mmol/L)	0.6	0.9	0.94	1.1	1.3	0.4	3.1
LDL-C (mmol/L)	1.0	2.2	2.8	3.0	3.6	1.1	6.7
TG (mmol/L)	0.2	1.0	1.4	1.6	1.8	1.0	6.9
Creatinine level (µmol/L)	17.7	61.9	70.7	94.4	90.6	131.4	1273
eDFG-CKD-EPI 2021	4.4	81.3	107.3	104.2	121.3	35.7	202.2
eDFG-MDRD	5.0	83.7	106.5	120.5	131.4	73.2	470.9
UA (µmol/L)	77.3	160.6	211.2	229.0	275.2	100.2	773.5
Natremia (mmol/L)	121.0	134.0	135.0	135.4	136.2	8.1	203.0
Kaliemia (mmol/L)	2.9	3.3	3.7	4.1	4.3	1.1	9.0
Chloremia (mmol/L)	88.0	99.7	106.0	104.6	109.0	9.0	164.0
HbA1c NGSP (%)	3.5	5.6	7.4	8.2	10.1	3.1	14.8
HbA1c IFCC (mmol/mol)	14.8	38.2	57.4	66.2	87.2	34.0	138.3

Table 2. Univariate analysis of clinical, sociodemographic, and behavioral parameters.

Independent variables	Dependent variable			
	HbA1c < 7% $N = 45$[1]	HbA1c ≥ 7% $N = 55$[1]	Total $N = 100$[1]	*p-value*[2]
Sex				
F	27 (60%)	31 (56%)	58 (58%)	0.7
M	18 (40%)	24 (44%)	42 (42%)	
BMI	24.8 (23.0 - 28.5)	25.8 (20.4 - 29.3)	25.2 (22.0 - 29.3)	>0.9
AI	3.54 (2.66 - 4.17)	3.94 (3.41 - 5.46)	3.71 (2.91 - 5.21)	0.01
Tobacco				
No	40 (89%)	52 (95%)	92 (92%)	0.5
Yes	5 (11%)	3 (5.5%)	8 (8.0%)	
Alcohol				
No	42 (93%)	55 (100%)	97 (97%)	0.9
Yes	3 (6.7%)	0 (0%)	3 (3.0%)	

Continued

Impact on organe				
No	40 (89%)	45 (82%)	85 (85%)	0.3
Yes	5 (11%)	10 (18%)	15 (15%)	
Blurred vision				
No	26 (58%)	42 (76%)	68 (68%)	0.05
Yes	19 (42%)	13 (24%)	32 (32%)	
Infection				
No	26 (58%)	39 (71%)	65 (65%)	0.2
Yes	19 (42%)	16 (29%)	35 (35%)	
Neuritis				
No	22 (49%)	30 (55%)	52 (52%)	0.6
Yes	23 (51%)	25 (45%)	48 (48%)	
Age	52 (45 - 58)	50 (34 - 58)	52 (38 - 58)	0.3

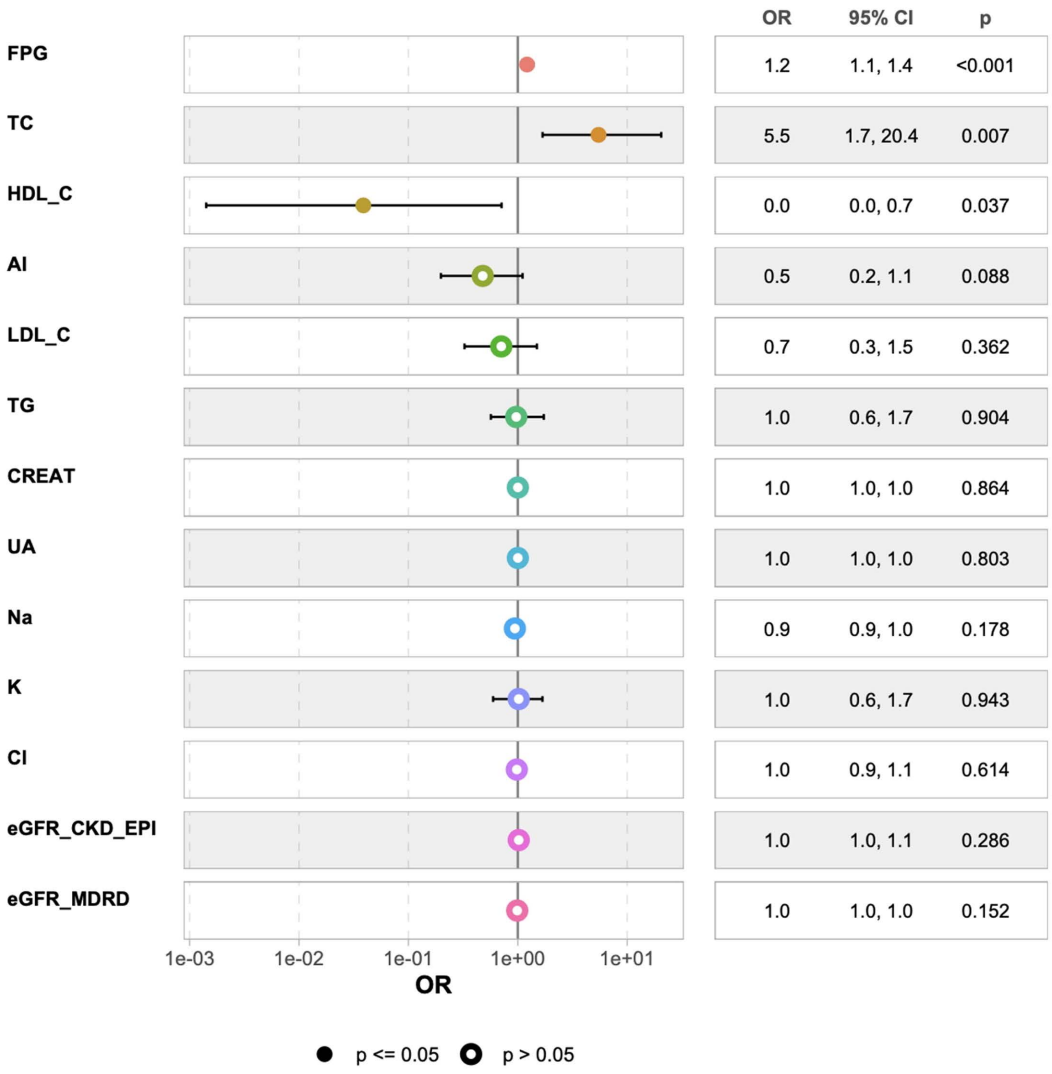
1: n (%); Median (Q1 - Q3); 2: Chi-square test of independence; Fisher's exact test; Wilcoxon-Mann-Whitney test.

Table 3. Univariate analysis of continuous biological variables.

Independent variables	Dependent variable			
	HbA1c < 7% $N = 45^1$	HbA1c ≥ 7% $N = 55^1$	Total $N = 100^1$	*p-value*[2]
FPG (mmol/L)	7.2 (5.0 - 9.9)	11.0 (7.7 - 17.6)	9.4 (6.6 - 13.5)	<0.001
TC (mmol/L)	3.63 (2.80 - 4.41)	4.61 (3.44 - 5.32)	4.15 (3.18 - 5.02)	0.002
HDL-C (mmol/L)	0.97 (0.78 - 1.18)	0.92 (0.91 - 1.34)	0.95 (0.88 - 1.34)	>0.9
LDL-C (mmol/L)	2.67 (2.07 - 3.51)	3.03 (2.43 - 3.71)	2.82 (2.24 - 3.65)	0.12
TG (mmol/L)	1.29 (0.97 - 1.81)	1.41 (1.06 - 1.76)	1.38 (1.05 - 1.80)	0.4
Creatinine (µmol/L)	71 (53 - 88)	71 (62 - 97)	71 (62 - 93)	0.4
UA (µmol/L)	190 (161 - 268)	238 (155 - 292)	211 (161 - 277)	0.5
Sodium (mmol/L)	135.0 (135.0 - 137.0)	135.0 (133.0 - 135.0)	135.0 (134.0 - 136.5)	0.11
Potassium (mmol/L)	3.70 (3.50 - 4.50)	3.90 (3.30 - 4.30)	3.75 (3.30 - 4.35)	0.9
Chlore (mmol/L)	106 (103 - 110)	106 (99 - 109)	106 (100 - 109)	0.2
eDFG-CKD-EPI 2021 (mL/min/1.73 m^2)	107 (84 - 120)	108 (79 - 125)	107 (81 - 122)	0.6
eDFG-MDRD (mL/min/1.73 m^2)	105 (85 - 134)	109 (81 - 125)	106 (84 - 132)	0.6

1: Median (Q1 - Q3); 2: Wilcoxon-Mann-Whitney test.

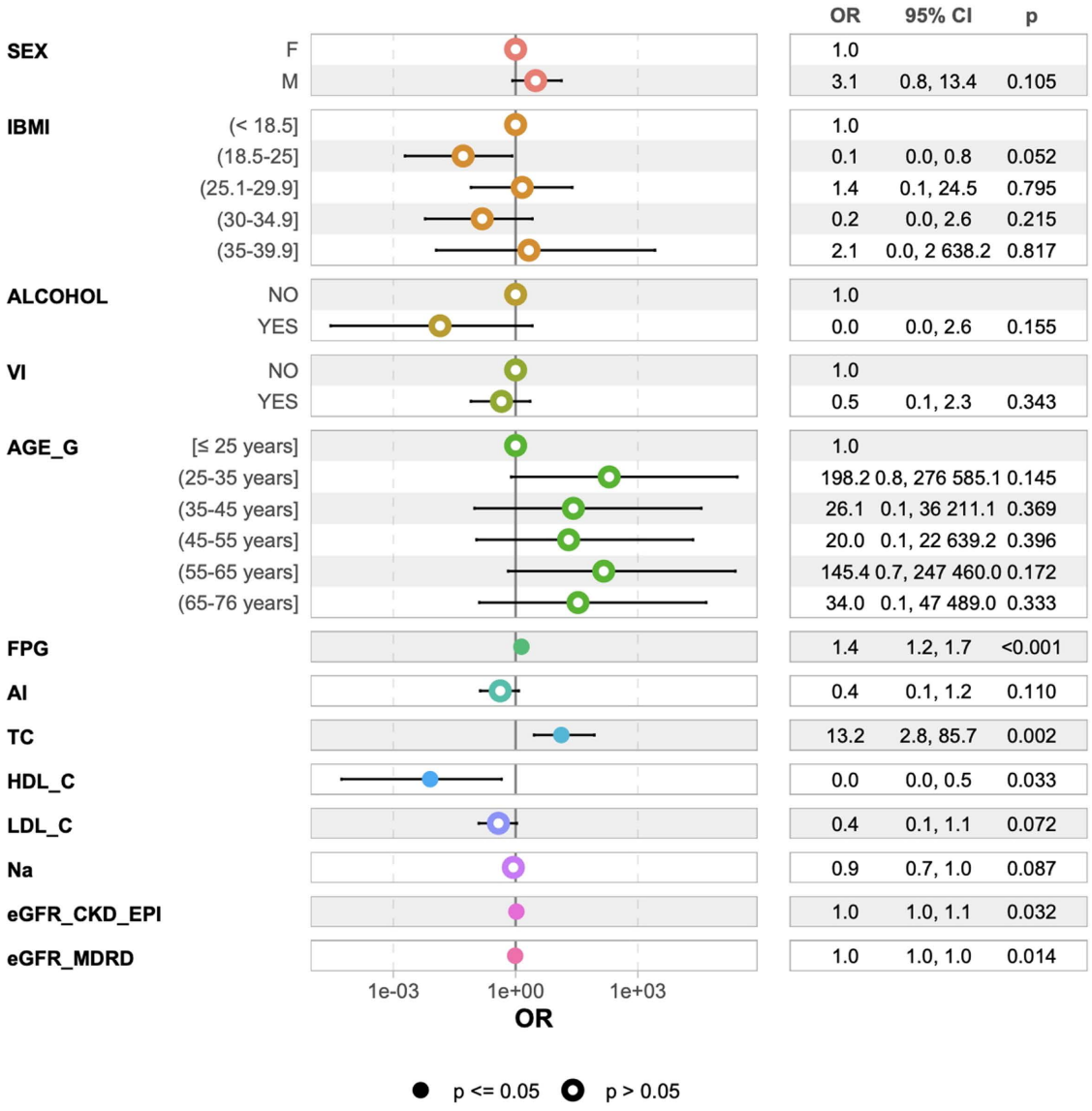
Multivariate analysis of continuous biological variables showed that FPG and TC were positively associated with HbA1c: OR, 1.2 (95% CI [1.1 - 1.4] mmol/L, $p < 0.001$); OR, 5.5 (95% CI [1.7 - 20.4] mmol/L, $p = 0.007$), respectively. In contrast, HDL-C was negatively associated with HbA1c: OR, 0.0 (95% CI [0.0 - 0.7] mmol/L, $p = 0.04$). The other continuous biological variables were not significantly associated with HbA1c in multivariate analysis as shown in Figure 1.



FPG = fasting plasma glucose, TC = total cholesterol, HDL-C = high density lipoprotein cholesterol, AI = Atherogenic index, LDL-C = low density lipoprotein cholesterol, TG = triglycerides, CREAT = creatinine, UA = Uric acid, Na = sodium, K = potassium, Cl = chloride level, eGFR_CKD_EPI = estimated of glomerular filtration rate chronic kidney disease epidemiology, eGFR_MDRD = estimated glomerular filtration rate modification of diet in renal disease.

Figure 1. Multivariate analysis of continuous biological variables.

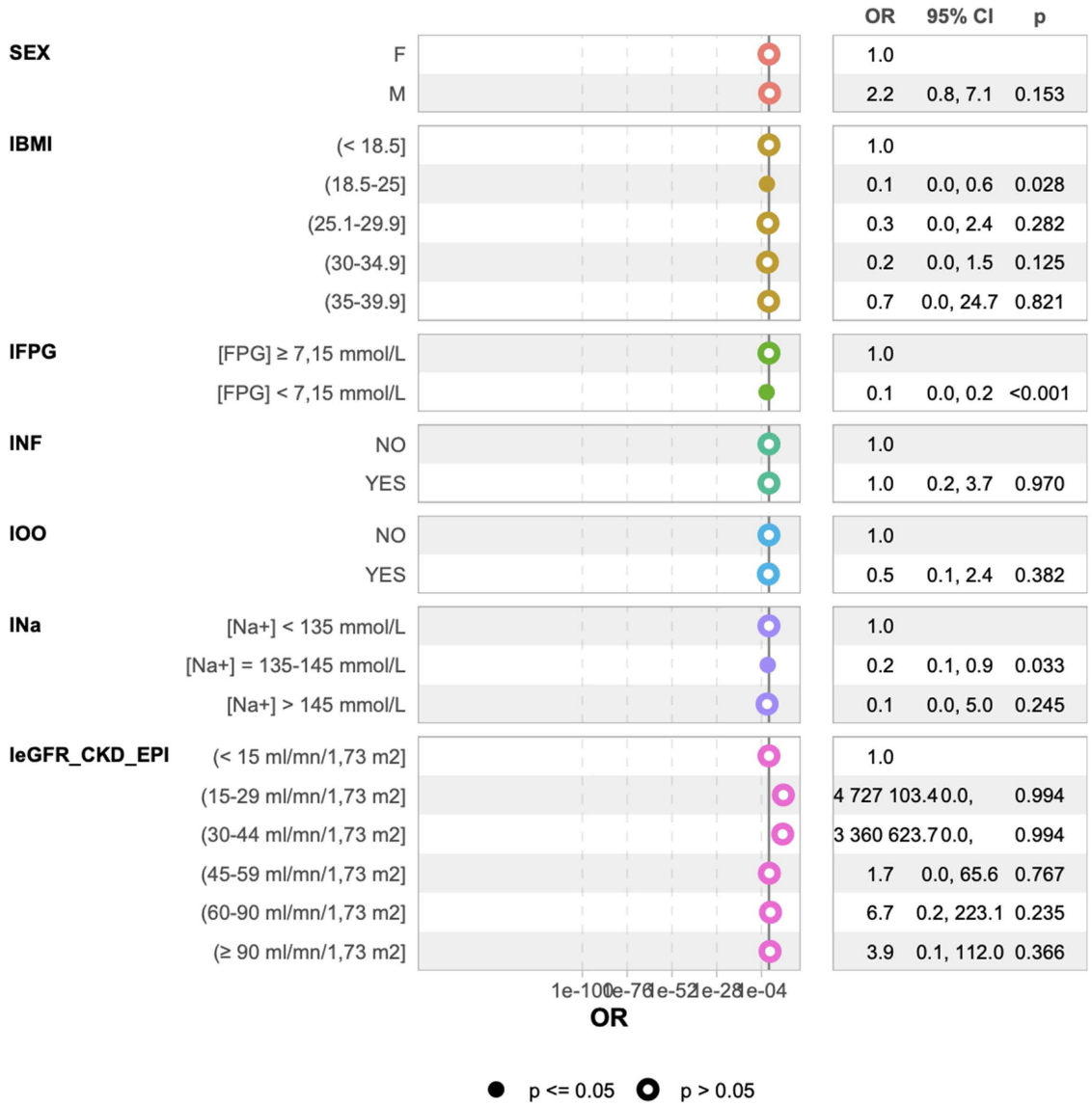
The multivariate analysis of continuous biological, categorical clinical, socio-demographic, and behavioral variables showed that FPG: OR, 1.4 (95% CI [1.2 - 1.7], $p < 0.001$), TC: OR, 13.2 (95% CI [2.8 - 85.7], $p = 0.002$), eGFR-CKD-EPI 2021 creatinine-based formula: OR, 1.0 (95% CI [1.0 - 1.1] $p = 0.03$), and eGFR-MDRD: OR, 1.0 (95% CI [1.0 - 1.0], $p = 0.03$) were positively associated with HbA1c ≥ 7%. In contrast, AI: OR, 0.4 (95% CI [0.1 - 1.2], $p = 0.11$), normal BMI (18.5 - 25 Kg/m^2): OR, 0.1 (95% CI [0.0 - 0.8], $p = 0.052$), and HDL-C: OR, 0.0 (95% CI [0.0 - 0.5], $p = 0.03$) were negatively associated with HbA1c, but the AI association was not significant. The other parameters did not show a significant association with HbA1c in this analysis as shown in Figure 2.



F = Female, M = Masculine, IBMI = Intervals of body mass index, VI = Vision impairment, AGE_G = Age groups, FPG = fasting plasma glucose, AI = Atherogenic index, TC = total cholesterol, HDL-C = high density lipoprotein cholesterol, LDL-C = low density lipoprotein cholesterol, Na = Sodium, eGFR_CKD-EPI = estimation of glomerular filtration rate chronic kidney disease epidemiology, eGFR_MDRD = estimation of glomerular filtration rate modification of diet in renal disease.

Figure 2. Multivariate analysis of continuous biological and categorical clinical, sociodemographic, and behavioral variables.

Finally, in a multivariate analysis of categorical biological variables and clinical, sociodemographic, and behavioral variables, normal interval of BMI (IBMI) (18.5 - 25 Kg/m^2): OR, 0.1 (95% CI [0.0 - 0.6], $p = 0.03$), normal FPG (<7.15 mmol/L): OR, 0.1 (95% CI [0.0 - 0.2], $p < 0.001$), and normal Na^+ (135 - 145 mmol/L): OR, 0.2 (95% CI [0.1 - 0.9], $p = 0.03$) were negatively associated with HbA1c ≥ 7%. The other parameters did not show significant differences with HbA1c ≥ 7% as shown in Figure 3.



F = Female, M = Masculine, IBMI = Intervals of body mass index, IFPG = interval fasting blood glucose, INF = Infection, IOO = impact on organs, Ina = intervals of Sodium, IeGFR-CKD-EPI = Intervals of estimated glomerular filtration rate calculated using the chronic kidney disease equation.

Figure 3. Multivariate analysis of categorical biological variables and, clinical, sociodemographic, and behavioral variables.

4. Discussion

Type 2 diabetes mellitus (T2DM) is a complex metabolic disorder marked by chronic hyperglycemia. Understanding the condition, which not only predisposes patients to numerous complications but also creates challenges in effective disease management, is of paramount importance. In particular, the interplay between glycemic control, measured by levels of HbA1c, and both cardiometabolic and renal complications is multifaceted. Out of 100 T2DM outpatients, the obesity proportions were 17% and 5% for grade I and grade II, respectively (Table 1). The

median FPG was 9.4 [6.7 - 13.4] mmol/L. The mean FPG level was 11 ± 6.4 mmol/L, with values ranging from 2.2 to 33.3 mmol/L. Our FPG mean was similar to that of Avignon A *et al.*, who found a mean FPG of 11.04 ± 2.72 mmol/L in poorly controlled type 2 diabetics (HbA1c ≥ 8.5%) [7]. In our study, the lower limit of FPG was 2.2 mmol/L. Hypoglycemia is common in T2DM, with 29.5% experiencing at least one symptomatic episode, often of iatrogenic origin, according to Mimouni *et al.* [8].

The management of T2DM requires a detailed understanding of the clinical parameters that influence long-term outcomes, particularly those related to cardiovascular and other cardiometabolic complications. HbA1c reflects the mean plasma glucose level over the preceding 8 - 12 weeks and is widely used for monitoring diabetes control. It therefore serves as a key biomarker for assessing long-term glycemic regulation and represents a critical indicator of cardiometabolic risk in T2DM patients. In the present study, the median HbA1c was 7.4% [5.6 - 10.1%] in DCCT/NGSP units and 57.4 [38.2 - 87.2] mmol/mol in IFCC units. Investigating the association between specific HbA1c thresholds and increased cardiometabolic risk remains essential for optimizing the clinical management of T2DM outpatients. In our study, 45% of the subjects were in glycemic control: HbA1c < 7%, whereas 55% were above the glycemic target: HbA1c ≥ 7%. Elevated HbA1c levels have been consistently linked to an increased risk of cardiovascular disease (CVD) as well as other complications, including heart failure and myocardial remodeling. Thus, the implications of HbA1c abnormalities extend beyond increased cardiovascular risk alone. In fact, elevated HbA1c is not only a marker of cardiovascular disease but also a predictor of structural and functional cardiac changes in T2DM outpatients. Li *et al.* demonstrated that higher HbA1c levels in patients with preserved ejection fraction were associated with increased extracellular volume and impaired left ventricular strain, findings that suggest early myocardial fibrosis and deformation [9]. These myocardial changes have been linked to a predisposition toward adverse cardiac remodeling and subsequent heart failure. Furthermore, an additional dimension of the risk associated with elevated HbA1c is mortality. A comprehensive analysis utilizing data from the UK Biobank and a Hong Kong SAR cohort reported that T2DM outpatients with HbA1c levels ≥ 9% had a significantly higher risk of all-cause mortality compared with their counterparts with HbA1c levels < 7% [10]. This observation reinforces the critical importance of stringent glycemic monitoring as a component of overall mortality risk management in T2DM.

In outpatient settings, monitoring HbA1c is a cornerstone of diabetes management. Numerous studies have highlighted its value not only in assessing long-term glycemic control but also in predicting future cardiometabolic events [11]. In addition, a cohort study conducted in Taiwan Region found that HbA1c levels of 7.5% or higher significantly increased the risks of cardiovascular disease and all-cause mortality [11]. Meanwhile, the UK Prospective Diabetes Study (UKPDS) showed that intensive glycemic control (achieving an HbA1c of 7.0% or lower)

reduces microvascular complications, although the effects on long-term macrovascular risk are less clear [12]. Such findings advocate for personalized HbA1c targets that take into account a patient's specific risk factors and overall health status [13].

A hospital-based cohort study from Taiwan Region, which included 126,079 T2DM patients, established that for each 1% increase in baseline HbA1c, there was a 5% higher hazard ratio for developing CVD [14]. This strong association indicates that even modest elevations in HbA1c can significantly impact cardiovascular risk. However, the relationship between glycemic control and cardiovascular outcomes is complex. Research has shown a U-shaped association whereby both high and extremely low HbA1c levels may adversely affect cardiovascular health. Patients with low (<6%) as well as high (>10%) HbA1c levels face an increased risk of heart failure [15]. This observation suggests that while hyperglycemia potentiates risk, overly aggressive glycemic control may also predispose patients to heart failure development, underscoring the need for an optimal glycemic target. These targets help guide treatment plans and ensure that the risk of cardiovascular complications is minimized [16] [17]. In our study, we used 7% as the cutoff of HbA1c to study the association between cardiometabolic risk factors and HbA1c in T2DM outpatients. The American Diabetes Association (ADA) has long set the diagnostic threshold for diabetes at an HbA1c level of 6.5% or higher [16]. However, determining an optimal HbA1c cutoff for predicting complications remains complex. A notable meta-analysis by Sattar *et al.* [17] indicated that in diabetic individuals, an HbA1c level above 9.0% is associated with a higher risk of cardiovascular events and all-cause mortality. Studies have provided insights into specific HbA1c cutoff values that correspond to an increased risk of cardiometabolic events. In the cohort from Taiwan Region, T2DM patients with a mean HbA1c greater than 8% faced more than a twofold increased risk of developing cardiovascular diseases compared to those with HbA1c levels below 7% [14]. This substantial increase in risk underscores the importance of maintaining HbA1c levels at sufficiently low levels to mitigate cardiovascular complications. However, given the U-shaped association between HbA1c and cardiovascular outcomes, as highlighted by Currie *et al.* [15], other research supports the view that both low (<6.5%) and high (>7.5%) HbA1c levels are associated with worsened clinical outcomes, particularly in T2DM patients with heart failure and reduced ejection fraction. Thus, the lowest risk of adverse events was observed in patients whose HbA1c levels ranged between 6.5% and 7.5% [18]. The so-called concept of a U-shaped relationship calls for clinicians to maintain HbA1c levels within a moderate range if they wish to reduce the cardiometabolic risk. The paradoxical increase in risk associated with low HbA1c levels may be attributed to the potential for hypoglycemic episodes, which themselves can contribute to adverse cardiovascular events [15]. Thus, a clinical consensus appears to emerge while excessively elevated HbA1c levels HbA1c (>8%) significantly increase cardiovascular risk, overly stringent glycemic control HbA1c (<6.5%) may likewise be harmful.

Consequently, an ideal target range for many T2DM outpatients, particularly those with established cardiovascular or heart failure status, appears to lie between 6.5% and 7.5%. Elevated HbA1c levels are linked to a higher likelihood of developing several cardiometabolic risk factors. Studies have demonstrated that patients with higher HbA1c values are more prone to experiencing hypertension. For instance, research by Hussein *et al.* [19] found a significant correlation between higher HbA1c levels and increased risk of developing high blood pressure during follow-up periods. According to the univariate analysis results, subjects with HbA1c ≥ 7% exhibited a significantly higher atherogenic index (AI) than those with levels < 7% (3.94 [3.41 - 5.46] vs 3.54 [2.66 - 4.17], 95% CI, $p = 0.01$). The findings were consistent with existing scientific literature. Notably, recent clinical strategies have placed significant emphasis on the relationship between HbA1c levels and the AI, which is calculated using the ratio of TC to HDL-C. The established HbA1c cutoff for optimal glycemic control is 7.0%, a target that plays an important role not only in preventing diabetes-related microvascular complications but also in modulating lipid profiles associated with cardiovascular health [4] [20]. Additionally, the clustering of risk factors such as abdominal obesity, dyslipidemia, and high blood pressure appears to be more common among individuals with elevated HbA1c. Okosun *et al.* [21] highlighted that the combination of these risk factors greatly increases the overall cardiometabolic risk in patients with type 2 diabetes. This observation highlights the critical importance of adopting a comprehensive approach when managing diabetes, which involves not only controlling blood glucose levels but also addressing the broader spectrum of cardiometabolic risks. It is also important to note that the relationship between HbA1c and mortality may follow a U-shaped curve, where both low (below 6.0% in non-diabetic individuals) and high levels of HbA1c are associated with increased mortality risks [17]. This further emphasizes the need to individualize goals and targets. While maintaining a lower HbA1c is beneficial in reducing the risk of complications, an excessively low HbA1c may present its own challenges, reinforcing the idea that treatment should be tailored to each patient's unique needs. Poor glycemic control, as reflected by higher HbA1c values, is associated with increased levels of TC and reduced HDL-C concentration. Consequently, an elevated AI is often observed, highlighting the dual challenge of managing both glycemia and lipid abnormalities in these patients [22]. Diabetic retinopathy (DR) remains one of the leading causes of vision impairment among patients with type 2 diabetes. Evidence from multiple clinical studies has demonstrated a strong relationship between glycemic control and the progression of DR [20]. There was a negative association between blurred vision and HbA1c levels, indicating that the proportion of individuals experiencing vision impairment was notably greater in those whose HbA1c was below 7% than in those whose levels were 7% or above, represented as 19 (42%) vs 13 (24%), $p = 0.05$. This unexpected outcome could be explained by the use of intensive treatment strategies intended to drastically lower HbA1c in patients who showed signs of DR complications. The UKPDS demon-

strated that intensive glycemia control with targets aiming around an HbA1c ≤ 6.5% can significantly reduce the risk of microvascular complications, including DR, compared to conventional treatment methods [23]. While the UKPDS primarily highlights the benefits of tighter glycemic control, it indirectly supports the notion that maintaining HbA1c below the 7% threshold is beneficial. The DCCT, although focused on type 1 diabetes, demonstrated that tight glycemic regulation with an HbA1c level near 6.0% significantly decreases the progression of DR compared to higher levels [24]. Another study named Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, designed to assess the effects of lowering HbA1c below 6.0% on cardiovascular outcomes, the ACCORD trial also underscored the complications associated with overly aggressive glycemic control, including severe hypoglycemia and a higher risk of mortality. This trial highlights the necessity of personalized treatment strategies, reinforcing that maintaining HbA1c levels around or below 7% may offer an optimal balance between risk reduction and safety [25]. Patients with HbA1c levels of 7% or higher may be at increased risk for these complications. However, it is important to note that aggressive efforts to lower HbA1c too rapidly can introduce their own risks, necessitating an individualized treatment approach [20]. Besides AI and vision impairment, the results of the univariate analysis demonstrated that there were no significant differences among the other clinical, demographic, and behavioral variables included in our study. T2DM is commonly accompanied by dyslipidemia, a disorder characterized by elevated TC, LDL-C and TG levels, as well as decreased HDL-C levels [20]. In univariate analysis, it was observed that continuous biological variables such as FPG and TC levels were positively associated with the likelihood of HbA1c levels ≥ 7% (95% CI 11.0 [7.7 - 17.6] vs 95% CI: 7.2 [5.0 - 9.9] mmol/L, $p < 0.001$) and (95% CI 4.61 [3.44 - 5.32] vs 95% CI: 3.63 [2.80 - 4.41] mmol/L, $p = 0.002$), respectively. This pattern was validated through a multivariate analysis of continuous biological variables, indicating that FPG and TC were positively associated with HbA1c, showing an odds ratio (OR),1.2 (95% CI [1.1 - 1.4], $p < 0.001$) and OR, 5.5 (95% CI [1.7 - 20.4] mmol/L, $p = 0.007$), respectively (**Figure 1**). Similarly, in multivariate analysis combining clinical, sociodemographic and continuous biological variables, FPG and TC confirmed their positive association with HbA1c: OR, 1.4 (95% CI [1.2 - 1.7], $p < 0.001$); and OR,13.2 (95% CI [2.8 - 85.7] mmol/L, $p = 0.002$), respectively. Conversely, in our series, HDL-C was found to have a negative association with HbA1c, with an OR, 0.0 (95% CI [0.0 - 0.5] mmol/L, $p = 0.04$). Numerous studies, like ours, have demonstrated a significant association between high HbA1c levels and lipid abnormalities. A study carried out in Jeddah, Saudi Arabia, with 988 patients suffering from T2DM, revealed a significant positive association between HbA1c levels and both TC and TG levels. The results indicate that deteriorating glycemic control, represented by HbA1c values exceeding 7%, leads to an aggravation of dyslipidemia [26]. Similarly, research from Morocco involving 505 T2DM patients showed that those with HbA1c levels > 7.0% had significantly higher FPG, TC, triglyceride levels,

and an increased AI when compared with patients maintaining HbA1c levels ≤ 7.0%. The authors conclude that their study highlighted the impact that poor glycemic control can negatively affect the lipid profile of patients [27]. In contrast, still in multivariate analysis concerning continuous biological variables, AI: OR, 0.5 (95% CI [0.2 - 1.1], $p = 0.09$) and HDL-C: OR, 0.0 (95% CI [0.0 - 0.7] mmol/L; $p = 0.04$) were negatively associated with HbA1c, but AI association was not significant. While both biomarkers (HbA1c and FPG) are essential for the diagnosis and monitoring of diabetes, they do not always produce matching results. Study involving more than 40,667 participants showed that based on FPG, 10.6% of the participants had pre-diabetes but this increased to 14.2% based on HbA1c (r = 0.86; $p < 0.001$). HbA1c had a sensitivity of 58.20% (95% CI [56.43 - 59.96]) and a specificity of 98.59% (95% CI [98.46 - 98.70]). The authors conclude that this lack of agreement highlights the necessity of employing both assessments in conjunction for a more complete understanding of a patient's glycemic status [28]. Other studies involving outpatients with T2DM have highlighted the discrepancies between HbA1c and FPG readings [29] [30]. In multivariate analysis combining clinical, sociodemographic, behavioral and continuous biological variables, normal BMI (18.5 - 25 Kg/m^2) showed a negative association: OR, 1.1 (95% CI [0.0 - 0.8]), but this association was not significant in the present study ($p = 0.052$). Unlike our study, a study from India with 142 T2DM patients found that HbA1c levels were directly correlated with BMI [31]. In contrast, eGFR-CKD-EPI 2021 formula: (OR = 1.0, 95% CI [1.0 - 1.1]; $p = 0.03$) and eGFR-MDRD: (OR = 1.0, 95% CI [1.0 - 1.0]; $p = 0.01$) were positively associated with HbA1c ≥ 7%. Moreover, a comprehensive analysis of United States (U.S) healthcare data from 2012 to 2019 demonstrated that as BMI increased, the mean HbA1c levels also rose, with a concomitant decrease in the proportion of individuals achieving the target HbA1c (<7%) [32]. This trend is further corroborated by a Japanese study, which observed that over 50% of T2DM patients in obesity classes I-IV had HbA1c levels ≥ 7% [33]. According to a cross-sectional study involving 200 T2DM patients, the association between BMI and HbA1c is not only apparent but also dose-dependent because of a positive correlation (r = 0.45, $p < 0.001$) between higher BMI and raised HbA1c levels [34]. Thus, obesity plays a critical role in exacerbating hyperglycemia in T2DM. Interventions such as decreasing body weight and bariatric surgery could help to improve insulin sensitivity and reduce HbA1c levels among overweight and obese individuals and thereby prevent T2DM complications [35] [36].

There is evidence that elevated HbA1c levels are consistently associated with adverse renal outcomes in T2DM patients. A prospective observational cohort study involving over 4000 patients demonstrated that each 1% increase in baseline HbA1c was associated with a significantly higher odds ratio of experiencing both a > 50% decline in eGFR: OR, 1.07 (95% CI [1.01 - 1.4], $p < 0.05$) and a rapid decline in renal function OR, 1.11 (95% CI [1.05 - 1.18], $p < 0.001$) [37]. Additionally, findings from the KoreaN cohort study for Outcome in patients With

Chronic Kidney Disease (KNOW-CKD) involving 707 patients with CKD stages G1 - G5 and T2DM revealed that higher HbA1c levels were associated with an increased risk of major adverse cardiovascular events (MACE) and all-cause mortality [38]. When compared with patients whose HbA1c was <7.0%, those with HbA1c levels between 7.0% - 7.9% and ≥8.0% experienced an OR, 1.59 (95% CI [1.01 - 2.49]) and 1.99 (95% CI [1.24 - 3.19]) times higher risk, respectively, for the composite outcome [38]. Another study involving 2599 T2DM patients highlighted the impact of HbA1c reduction on eGFR decline by finding that a reduction in HbA1c levels was significantly associated with a downward trend in eGFR decline independent of factors such as Urinary Albumin-to-Creatinine Ratio (UACR), diabetes duration, and hyperfiltration [39]. Finally, in a global multivariate analysis of categorical biological, clinical, sociodemographic, and behavioral variables, only normal BMI (18.5 - 25 Kg/m^2): OR, 0.1 (95% CI [0.0 - 0.6] Kg/m^2, $p < 0.03$), normal FPG (<7.15 mmol/L): OR, 0.1 (95% CI [0.0 - 0.2] mmol/L, $p < 0.001$), and normal Na^+ (135 - 145 mmol/L): OR, 0.2 (95% CI [0.1 - 0.9], $p = 0.03$) were negatively associated with HbA1c ≥ 7%. The other parameters did not show significant differences. The correlation between HbA1c levels and BMI was reported by an Indian study [31]. Uncontrolled hyperglycemia leads to osmotic diuresis, resulting in increased renal sodium excretion and subsequent reduction in serum sodium levels. A study identified a moderate negative correlation between serum sodium levels and HbA1c in T2DM patients who exhibited poor adherence to antidiabetic medications. According to their findings, higher HbA1c values were associated with lower sodium concentrations, suggesting that ineffective glycemic control could contribute to sodium imbalance [40]. The precise biological mechanisms underlying the association between natremia and HbA1c are not completely understood. One possibility is that hyperglycemia induces osmotic diuresis, thereby increasing renal sodium excretion and resulting in hyponatremia. This cascade not only alters the serum sodium levels but may also affect insulin secretion and its peripheral action, further exacerbating the glycemic control challenge [40]. These insights underscore the importance of comprehensive patient monitoring and suggest that correcting electrolyte disturbances may lead to improvements in glycemic control. However, further research is necessary to fully elucidate the underlying pathways and to develop targeted clinical interventions. Given that T2DM is a complex metabolic disorder characterized by insulin resistance, impaired insulin secretion, and chronic hyperglycemia, these metabolic disturbances significantly contribute to various cardiometabolic risk factors such as obesity, dyslipidemia, hypertension, and chronic inflammation, thereby increasing the risk of CVD [41].

This study has several limitations. First, its cross-sectional design precludes any causal inference regarding the observed associations. Second, the sampling was restricted to a single-center setting, which may limit the generalizability of the findings to broader populations. Finally, potential interferences with HbA1c measurement, such as anemia or the presence of hemoglobin variants, could not

be fully excluded and may have influenced the accuracy of HbA1c assessment. HbA1c measurement is highly dependent on preanalytical and pathological conditions, as well as the analytical methods used [1]. The critical factors, including sample collection, handling, storage, and quality control, were considered in our study. However, conditions that affect the lifespan of red blood cells (RBCs), such as hemolytic or iron-deficiency anemia, which may lead to falsely low or high HbA1c values, respectively, were not taken into account [42]. Furthermore, the presence of hemoglobin variants (HbS, HbC, HbD, and HbE) further complicates assay reliability by potentially interfering with the measurement process [43]. Additionally, various analytical methods are employed for determining HbA1c levels. We performed an immunoassay using monoclonal antibodies to specifically detect the Amadori product of hemoglobin glycation. Nevertheless, high-performance liquid chromatography (HPLC) is known for its ability to separate labile intermediates, thereby minimizing interferences that might be observed in other techniques [43].

5. Conclusion

The present study involved 100 active T2DM outpatients and aimed to evaluate the biological monitoring of patients, their association with glycated hemoglobin, and other sociodemographic, clinical, behavioral, and biological parameters. This study led us to the following conclusions: increased FPG, TC, and eGFR-CKD-EPI 2021 may positively reflect higher HbA1c levels in T2DM outpatients. Conversely, lower AI and HDL-C values, as well as normal BMI and normal plasma sodium levels, may indicate lower HbA1c levels in T2DM outpatients. HbA1c remains an effective tool for monitoring glycemic control in T2DM, essential for tracking disease progression, preventing acute complications, and delaying chronic complications. While it is essential for T2DM outpatients to have their HbA1c levels monitored regularly, at least three to four times a year, it is equally important to assess these results alongside other factors that can affect the fluctuations in these levels.

Authors Contributions

These authors contributed equally: Modibo Coulibaly, Djibril Mamadou Coulibaly, Moctar Bah, Djeneba Djiguiba, Klétigui Casimir Dembélé, Dramane Samaké, Lamine Sidibé, Adama Kondé, Aboubacar Sidiki Traoré, Moussa Diawara, Valentin Sagara, Soumaïla Touré, Boubacar Coulibaly, Boubacar Sidiki Ibrahim Dramé, Boubacar Tiétié Bissan, Yaya Goita, Seydou Sassou Coulibaly, Bakary Maiga, Kassoum Kayentao, and Amagana Dolo. C.M., C.D.M., and B.M. conceived and planned the study protocol and the experiments. C.M., B.M., and D.D. carried out the experiments. C.M. and D.D. contributed to sample preparation. C.M., C.D.M., and K.K. contributed to the interpretation of the results. C.M. and C.D.M. were involved in writing the manuscript. All authors provided critical feed-

back and helped shape the research, analysis, and manuscript. All authors have read and approved the final version of the manuscript.

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Ethical Approval and Consent to Participate

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. The study protocol received approval from the Faculty of Pharmacy, and institutional authorization was granted by the management of Hôpital Sominé DOLO de Mopti. No participant was enrolled without first having read and signed the informed consent form or having received an appropriate translation. All patient information was managed in compliance with biomedical research ethics, ensuring confidentiality through the coding and secure handling of sensitive data.

Data Availability and Statement

The datasets generated and/or analyzed during the current study are not publicly available due to confidentiality, ethical restrictions, and institutional data protection policies. However, they may be obtained from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflict of interest. All aspects of the study design, data collection, analysis, and interpretation, as well as the writing of the manuscript and the decision to publish the results, were conducted independently by the authors.

References

[1] ElSayed, N.A., Aleppo, G., Bannuru, R.R., Bruemmer, D., Collins, B.S., Ekhlaspour, L., *et al.* (2023) 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2024. *Diabetes Care*, **47**, S20-S42. https://doi.org/10.2337/dc24-s002

[2] Pearson, E.R. (2019) Type 2 Diabetes: A Multifaceted Disease. *Diabetologia*, **62**, 1107-1112. https://doi.org/10.1007/s00125-019-4909-y

[3] Gillett, M.J. (2009) International Expert Committee Report on the Role of the A1C Assay in the Diagnosis of Diabetes. *Diabetes Care*, **32**, 1327-1334. https://doi.org/10.2337/dc09-9033

[4] World Health Organization (2011) Use of Glycated Haemoglobin (HbA1C) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. World Health Organization. http://www.ncbi.nlm.nih.gov/books/NBK304267/

[5] Lee, C.L., Chen, C.H., Wu, M.J. and Tsai, S.F. (2020) The Variability of Glycated Hemoglobin Is Associated with Renal Function Decline in Patients with Type 2 Diabetes. *Therapeutic Advances in Chronic Disease*, **11**, 1-10. https://doi.org/10.1177/2040622319898370

[6] Sundufu, A.J., Bockarie, C.N. and Jacobsen, K.H. (2017) The Prevalence of Type 2 Diabetes in Urban Bo, Sierra Leone, and in the 16 Countries of the West Africa Region. *Diabetes/Metabolism Research and Reviews*, **33**, e2904. https://doi.org/10.1002/dmrr.2904

[7] Avignon, A., Radauceanu, A. and Monnier, L. (1997) Nonfasting Plasma Glucose Is a Better Marker of Diabetic Control than Fasting Plasma Glucose in Type 2 Diabetes. *Diabetes Care*, **20**, 1822-1826. https://doi.org/10.2337/diacare.20.12.1822

[8] Mimouni, S., Faraoun, K., Nouri, N. and Serouti, A. (2022) Fréquence de l'hypoglycémie chez les patients diabétiques de type 2 traités par insuline basale en Algérie (Hypo Study). *Médecine des Maladies Métaboliques*, **16**, 351-358. https://doi.org/10.1016/j.mmm.2022.04.005

[9] Li, Z., Han, D., Qi, T., Deng, J., Li, L., Gao, C., *et al.* (2023) Hemoglobin A1C in Type 2 Diabetes Mellitus Patients with Preserved Ejection Fraction Is an Independent Predictor of Left Ventricular Myocardial Deformation and Tissue Abnormalities. *BMC Cardiovascular Disorders*, **23**, Article No. 49. https://doi.org/10.1186/s12872-023-03082-5

[10] Wan, E.Y.F., Yu, E.Y.T., Mak, I.L., Youn, H.M., Chan, K.S., Chan, E.W.Y., *et al.* (2023) Diabetes with Poor-Control HbA1C Is Cardiovascular Disease "Risk Equivalent" for Mortality. *BMJ Open Diabetes Research & Care*, **11**, e003075. https://doi.org/10.1136/bmjdrc-2022-003075

[11] Chen, Y., Lin, Y., Chong, E., Chen, P., Chao, T., Chen, S., *et al.* (2015) The Impact of Diabetes Mellitus and Corresponding HbA1C Levels on the Future Risks of Cardiovascular Disease and Mortality: A Representative Cohort Study in Taiwan Region. *PLOS ONE*, **10**, e0123116. https://doi.org/10.1371/journal.pone.0123116

[12] Lau, C.S. and Aw, T.C. (2020) HbA1C in the Diagnosis and Management of Diabetes Mellitus: An Update. *Diabetes Updates*, **6**, 1-4. https://doi.org/10.15761/du.1000137

[13] Sandler, C.N. and McDonnell, M.E. (2016) The Role of Hemoglobin A1c in the Assessment of Diabetes and Cardiovascular Risk. *Cleveland Clinic Journal of Medicine*, **83**, S4-S10. https://doi.org/10.3949/ccjm.83.s1.02

[14] Chang, C., Chang, S. and Lin, Y. (2018) HbA1C as a Risk Factor for Cardiovascular Disease in Type 2 Diabetes Mellitus: A Hospital-Based Study in Taiwan Region. *Value in Health*, **21**, S36. https://doi.org/10.1016/j.jval.2018.07.273

[15] Parry, H.M., Deshmukh, H., Levin, D., Van Zuydam, N., Elder, D.H.J., Morris, A.D., *et al.* (2015) Both High and Low HbA1C Predict Incident Heart Failure in Type 2 Diabetes Mellitus. *Circulation*: *Heart Failure*, **8**, 236-242. https://doi.org/10.1161/circheartfailure.113.000920

[16] ADA (2018) 6. Glycemic Targets: Standards of Medical Care in Diabetes—2019. *Diabetes Care*, **42**, S61-S70. https://doi.org/10.2337/dc19-s006

[17] Sattar, N. and Preiss, D. (2017) Research Digest: More Cardiovascular Outcome Trials in Diabetes. *The Lancet Diabetes & Endocrinology*, **5**, 687. https://doi.org/10.1016/s2213-8587(17)30266-8

[18] Shi, K., Zhang, G., Fu, H., Li, X., Gao, Y., Shi, R., *et al.* (2024) Glycemic Control and Clinical Outcomes in Diabetic Patients with Heart Failure and Reduced Ejection Fraction: Insight from Ventricular Remodeling Using Cardiac MRI. *Cardiovascular*

Diabetology, **23**, Article No. 148. https://doi.org/10.1186/s12933-024-02243-w

[19] Hussein, A., Mahmoud, S.E., Awad, M.S. and Mahmoud, H.E.M. (2020) Assessment of Cardiovascular Risk Factors in Patients with Type 2 Diabetes in Upper Egypt Villages. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, **13**, 4737-4746. https://doi.org/10.2147/dmso.s282888

[20] ADA (2021) 6. Glycemic Targets: Standards of Medical Care in Diabetes—2022. *Diabetes Care*, **45**, S83-S96. https://doi.org/10.2337/dc22-s006

[21] Okosun, I.S., Annor, F., Dawodu, E.A. and Eriksen, M.P. (2014) Clustering of Cardiometabolic Risk Factors and Risk of Elevated HbA1C in Non-Hispanic White, Non-Hispanic Black and Mexican-American Adults with Type 2 Diabetes. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, **8**, 75-81. https://doi.org/10.1016/j.dsx.2014.04.026

[22] Saleh, J. (2015) Glycated Hemoglobin and Its Spinoffs: Cardiovascular Disease Markers or Risk Factors? *World Journal of Cardiology*, **7**, Article No. 449. https://doi.org/10.4330/wjc.v7.i8.449

[23] UKPDS (1998) Intensive Blood-Glucose Control with Sulphonylureas or Insulin Compared with Conventional Treatment and Risk of Complications in Patients with Type 2 Diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. *The Lancet*, **352**, 837-853.

[24] The Diabetes Control and Complications (DCCT) Research Group (1995) Effect of Intensive Therapy on the Development and Progression of Diabetic Nephropathy in the Diabetes Control and Complications Trial. *Kidney International*, **47**, 1703-1720. https://doi.org/10.1038/ki.1995.236

[25] ACCRSG, Gerstein, H.C., Miller, M.E., Byington, R.P., Goff, D.C., Bigger, J.T., *et al.* (2008) Effects of Intensive Glucose Lowering in Type 2 Diabetes. *The New England Journal of Medicine*, **358**, 2545-2559.

[26] Sharahili, A.Y., Mir, S.A., ALDosari, S., Manzar, M.D., Alshehri, B., Al Othaim, A., *et al.* (2023) Correlation of HbA1C Level with Lipid Profile in Type 2 Diabetes Mellitus Patients Visiting a Primary Healthcare Center in Jeddah City, Saudi Arabia: A Retrospective Cross-Sectional Study. *Diseases*, **11**, Article No. 154. https://doi.org/10.3390/diseases11040154

[27] El Alami, H., Haddou, I., Benaadi, G., Lkhider, M., Wakrim, L., Allali, M., *et al.* (2022) Prevalence of Dyslipidemia and the Relationship between HbA1C and Lipid Profile in Moroccan Patients with T2DM: A Cross-Sectional Study. *Pan African Medical Journal*, **43**, Article No. 86. https://doi.org/10.11604/pamj.2022.43.86.35898

[28] Abdul Murad, N.A., Abdullah, N., Kamaruddin, M.A., Abd Jalal, N., Ismail, N., Mhd Yusof, N.A., *et al.* (2021) Discordance between Fasting Plasma Glucose (FPG) and HbA1C in Diagnosing Diabetes and Pre-Diabetes in the Malaysian Cohort. *Journal of the ASEAN Federation of Endocrine Societies*, **36**, 127-132. https://doi.org/10.15605/jafes.036.02.02

[29] Poorirerngpoom, N., Ganokroj, P., Vorayingyong, A., Rattananupong, T., Pusavat, J. and Supasiri, T. (2023) Discrepancy in Diagnoses of Diabetes and Prediabetes Using Fasting Plasma Glucose and Glycosylated Hemoglobin and the Underdiagnosis by ICD-10 Coding: Data from a Tertiary Hospital in Thailand. *Frontiers in Public Health*, **11**, Article ID: 1322480. https://doi.org/10.3389/fpubh.2023.1322480

[30] Unwin, N., Howitt, C., Rose, A.M., Samuels, T.A., Hennis, A.J. and Hambleton, I.R. (2017) Prevalence and Phenotype of Diabetes and Prediabetes Using Fasting Glucose vs HbA1C in a Caribbean Population. *Journal of Global Health*, **7**, Article ID: 020407. https://doi.org/10.7189/jogh.07.020407

[31] Kidwai, S.S., Nageen, A., Bashir, F. and Ara, J. (2020) HbA1C—A Predictor of Dyslipidemia in Type 2 Diabetes Mellitus. *Pakistan Journal of Medical Sciences*, **36**, Article No. 1339. https://doi.org/10.12669/pjms.36.6.2000

[32] Boye, K.S., Lage, M.J., Shinde, S., Thieu, V. and Bae, J.P. (2021) Trends in HbA1C and Body Mass Index among Individuals with Type 2 Diabetes: Evidence from a US Database 2012-2019. *Diabetes Therapy*, **12**, 2077-2087. https://doi.org/10.1007/s13300-021-01084-0

[33] Hara, K., Hirase, T., Pathadka, S., Cai, Z., Sato, M., Ishida, N., *et al.* (2024) Trends of HbA1C and BMI in People with Type 2 Diabetes: A Japanese Claims-Based Study. *Diabetes Therapy*, **15**, 801-817. https://doi.org/10.1007/s13300-024-01543-4

[34] Deng, L., Jia, L., Wu, X. and Cheng, M. (2025) Association between Body Mass Index and Glycemic Control in Type 2 Diabetes Mellitus: A Cross-Sectional Study. *Diabetes, Metabolic Syndrome and Obesity*, **18**, 555-563. https://doi.org/10.2147/dmso.s508365

[35] Hu, S., Lin, C., Cai, X., Li, Z., Lv, F., Yang, W., *et al.* (2023) Trends in Baseline HbA1C and Body-Mass Index in Randomised Placebo-Controlled Trials of Type 2 Diabetes from 1987 to 2022: A Systematic Review and Meta-Analysis. *eClinicalMedicine*, **57**, Article ID: 101868. https://doi.org/10.1016/j.eclinm.2023.101868

[36] Zhou, K., Wolski, K., Malin, S.K., Aminian, A., Schauer, P.R., Bhatt, D.L., *et al.* (2019) Impact of Weight Loss Trajectory Following Randomization to Bariatric Surgery on Long-Term Diabetes Glycemic and Cardiometabolic Parameters. *Endocrine Practice*, **25**, 572-579. https://doi.org/10.4158/ep-2018-0522

[37] Torkamani, N., Churilov, L., Robbins, R., Jerums, G., Beik, V., Radcliffe, N., *et al.* (2020) Diabetes and Higher HbA1C Levels Are Independently Associated with Adverse Renal Outcomes in Inpatients Following Multiple Hospital Admissions. *Journal of Diabetes and its Complications*, **34**, Article ID: 107465. https://doi.org/10.1016/j.jdiacomp.2019.107465

[38] Heo, G.Y., Koh, H.B., Kim, H.W., Park, J.T., Yoo, T., Kang, S., *et al.* (2023) Glycemic Control and Adverse Clinical Outcomes in Patients with Chronic Kidney Disease and Type 2 Diabetes Mellitus: Results from KNOW-CKD. *Diabetes & Metabolism Journal*, **47**, 535-546. https://doi.org/10.4093/dmj.2022.0112

[39] An, L., Yu, Q., Chen, L., Tang, H., Liu, Y., Yuan, Q., *et al.* (2022) The Association between the Decline of eGFR and a Reduction of Hemoglobin A1c in Type 2 Diabetic Patients. *Frontiers in Endocrinology*, **12**, Article ID: 723720. https://doi.org/10.3389/fendo.2021.723720

[40] Lengeiya, F., Mathenge, S. and Ojola, P. (2024) Relationship between Electrolytes and Glycated Hemoglobin among Diabetic Patients with Poor Adherence to Antidiabetic Medications: A Cross-Sectional Study. *The Pan African Medical Journal*, **47**, Article No. 37. https://doi.org/10.11604/pamj.2024.47.37.41815

[41] Chakraborty, S., Verma, A., Garg, R., Singh, J. and Verma, H. (2023) Cardiometabolic Risk Factors Associated with Type 2 Diabetes Mellitus: A Mechanistic Insight. *Clinical Medicine Insights: Endocrinology and Diabetes*, **16**, 1-18. https://doi.org/10.1177/11795514231220780

[42] Eyth, E., Zubair, M. and Naik, R. (2025) Hemoglobin A1C. StatPearls Publishing. http://www.ncbi.nlm.nih.gov/books/NBK549816/

[43] Li, M., Ge, S., Shu, X., Wu, X., Liu, H., Xu, A., *et al.* (2024) Interference of Hemoglobin Variants with HbA1C Measurements by Six Commonly Used HbA1C Methods. *Laboratory Medicine*, **55**, 708-712. https://doi.org/10.1093/labmed/lmae034