Heliyon 7 (2021) e06139

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Inflammatory biomarkers and prediction of insulin resistance in Congolese adults

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ARTICLE INFO

Keywords:
Insulin resistance
HOMA-IR
Adiponectin
Tumor necrosis factor
Melanodermic

ABSTRACT

Several studies have shown that low levels of adiponectin (ADP) and high levels of alpha tumor necrosis factor (NFT) increase the risk or severity of many cardiometabolic diseases associated with insulin resistance. The main objective of this study was to evaluate the association between plasma adipokines and IR measured by HOMA-IR. The secondary objective was to determine the biomarker of the potential inflammation to predict IR in Congolese melanoderm subjects residing in Brazzaville. This cross-sectional study was conducted on 234 apparently healthy participants over the age of 18. Socio-demographic and clinical data were collected. Biological data, including the total ADP and NFT dosage, were measured using the ELISA method. Participants were categorized into two groups according to HOMA-IR $\geq$ 2.5. Univariate and multivariate logistic regression analyses were conducted to identify risk factors for insulin resistance. An optimized model was obtained after the logistic regression. The analysis of the receptor's operating characteristics (OCR) was performed to determine the optimal threshold value and diagnostic characteristics, as well as the area under the curve (ASC). ADP averages were significantly low (11.49 $\pm$ 7.61 ng/mL; P $<$ 0.001) while those of TNF were significantly higher (96.03 $\pm$ 44.09 pg/mL) in the HOMA-IR group $\geq$ 2.5. There was a positive and significant correlation (p $<$ 0.05) between BMI, TT, CRPhs, TNF and HOMA-IR. And a negative and significant correlation was noted between ADP and HOMA-IR (r = - 0.39; P $<$ 0.01). Similarly, a negative and significant correlation (p $<$ 0.01) was noted between BMI, TT, TNF, CRPhs and ADP. The optimal threshold value of the total ADP for predicting IR was 17.52 ng/mL with a sensitivity of 89% [IC 95% (0.83–0.95)], 56% specificity [IC 95% (0.47–0.65)] and a CSA of 0.76 [IC 95% (0.69–0.81)]. After logistic regression, the CSA of the optimized model was 0.84 [IC 95% (0.79–0.89)]. ADP can be used as a highly plausible IR prediction biomarker.

1. Introduction

The insulin resistance (IR) is a major component of metabolic disorders which concern a substantial fraction of the general population and is particularly prevalent in obese subjects [1, 2, 3, 4, 5, 6, 7]. The mechanism of IR is multifactorial, but factors such as the obesity and in particular the accumulation of visceral adipose tissue were involved [2, 8, 9, 10, 11, 12, 13]. Indeed, the adipose tissue is an active complex organ both endocrine and metabolic which releases adipokines such as the adiponectin (ADP) and tumor necrosis factor (TNFα) [8, 13, 14, 15, 16]. These adipokines are key regulators of glucose metabolism, fatty acid intake, and inflammation [2, 13, 17, 18, 19]. An imbalance between

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https://doi.org/10.1016/j.heliyon.2021.e06139
Received 11 November 2020; Received in revised form 18 January 2021; Accepted 25 January 2021

these adipokines in the bloodstream increases the risk or severity of many cardiometabolic diseases associated with IR such as type 2 diabetes, dyslipidemias, high blood pressure, etc. [2, 3, 10, 13, 20]. Therefore, the evaluation of these adipokines as biomarkers of IR within a population whose "epidemy" of obesity is increasing is necessary to enable early intervention and primary prevention of disease development cardiometabolic.

To date, the method of the clamp euglycemia hyperinsulinemic is the gold standard of the IR but can be performed only in specialized centres [4, 21]. Nevertheless, there are other methods such as the Insulin Resistance Homeostasis Model Assessment (HOMA-IR) which is a reliable technique for predicting IR [6, 22, 23]. Several investigators have reported the use of adipokines as potential biomarkers for the prediction of the IR and therefore the cardiometabolic risk [3, 4, 6, 14, 20, 24]. Indeed, previous studies reported that the TNFα is overexpressed in obesity and positively correlated with the IR [8, 12, 13, 14]. On the other hand other adipokines such as ADP are diminished and negatively correlated to obesity, the triglyceride levels, C-reactive protein (CRP) and the IR [2, 25]. The evaluation of adipokines has not been correlated with HOMA-IR in the prediction of IR in Brazzaville. It is in this perspective that we proposed to carry out this study, the main objective of which was to evaluate the association between the adipokines plasma and the IR measured by HOMA-IR. The secondary objective was to determine the potential biomarker to predict IR in Congolese melanoderma subjects residing in Brazzaville.

2. Participants and methods

2.1. Type and period of study

This was an analytical cross-sectional study that took place from February 14 to May 22, 2019.

2.2. Study framework

This study was carried out in the city of Brazzaville in the Republic of Congo (BZ/RC). The city of Brazzaville has a multi-ethnic population estimated at 1.838.348 inhabitants [23]. It is subdivided into nine (09) districts (Makélékélé, Bacongo, Poto-poto, Moungali, Ouenze, Talangai, Mfilou, Ndjiri and Madibou). Laboratory tests were carried out in Public Health National Laboratory and the National Reference Centre for Sickle Cell Disease in Brazzaville, Republic of Congo.

2.3. Study population

The study population was a probability sample from the general and eligible population of the city of Brazzaville according to the logigram (Figure 1). Participants were recruited from Catholic churches in the city of Brazzaville. The selection criteria required for inclusion: any person aged at least 18 years living in Brazzaville for at least 10 years, with informed consent. Were excluded all participants with a known DS, pregnancy, HIV/AIDS, renal failure, stroke, ischemic heart disease, heart failure, hemoglobinopathies and all participants under treatment lipid-lowering drugs, thyroid hormones, oral contraceptives.

2.4. Sample size

Given the lack of information on the prevalence and recurrence of malignant hemopathies, the size of the study was calculated according to the following formula: 4x (Za = 1.96 with 95 % CI) 2xp (= 0.50 as prevalence/recurrences) x [1-p]/(0.20 = extent) 2 = 192 and rounding 200 + 20% lost to follow-up = 240 required from a simple probabilistic sample.

2.5. Methods

2.5.1. Variables of interest

The participants were recruited from Catholic churches in the city of Brazzaville. The demographic characteristics including gender, age, height, weight and waist circumference were collected. The anthropometric measurements of the participants were obtained according to the criteria of the STEP program [26]. The height (in cm) was measured using a vertical rod (type SECA 220) to the nearest half a centimeter. The weight was measured using an electronic scale (type SECA 762), with an accuracy of 0,1kg. Waist circumference was measured at 0,1cm close to the end of a minimum breathing using a flexible tape graduated in millimeters placed on top of the iliac crest [27]. Body mass index (BMI) was calculated by dividing an individual's weight by the square of their height (kg/m^2) [28]. Participants were divided according to BMI models as general obesity (BMI ≥25) and non-obese (BMI <25). The waist circumference (TT) in cm (TT >94 for men and >80 for women) made it possible to identify participants with visceral abdominal obesity [29].

The values of blood pressure (BP) were obtained using a type of electronic sphygmomanometer (OMRON M3 Comfort) after which participants rested for at least 15 min in a sitting position. This measurement was repeated three times in a row to obtain average values of blood pressure. Hypertension was defined by the presence of systolic BP ≥ 130mmHg and/or diastolic BP ≥ 85 mmHg [29]. Metabolic syndrome (MetS) has been defined according to the International Diabetes Federation which requires the presence of at least any three of the following five abnormalities: elevated BP (systolic BP ≥ 130 and/or diastolic BP ≥ 85mmHg or antihypertensive treatment), HDL –c low (<1,0 mmol/L men, <1,3 mmol/L in women), TG high (≥1,7 mmol/L), fasting hyperglycemia (≥5,6 mmol/L or antidiabetic treatment), abdominal adiposity (TT ≥ 80 cm in women or ≥94 cm in men) [29].

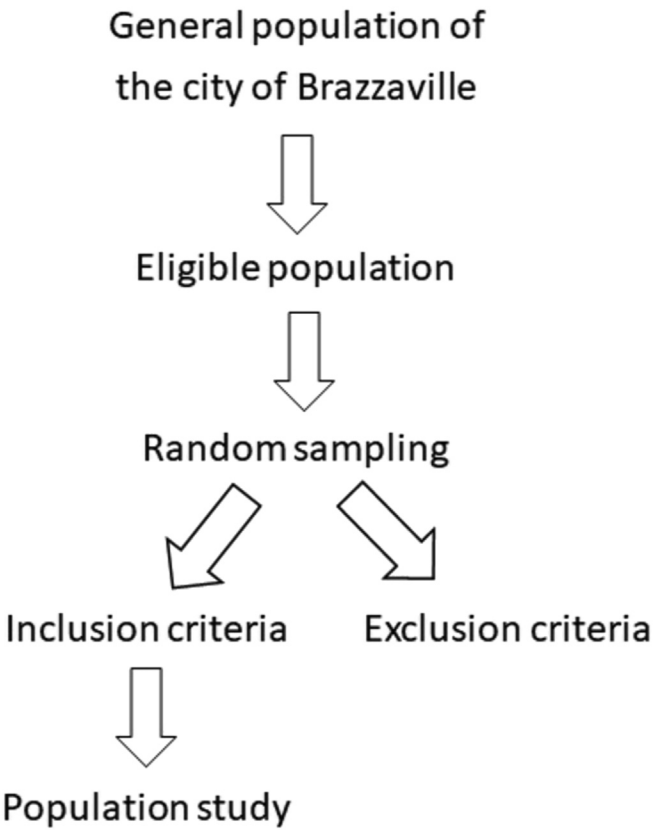

Figure 1. Flowchart showing the study logigram of the general population.

2.5.2. Blood collection and processing of blood samples

Blood samples were collected from participants by antecubital venepuncture in vacutainer tubes following at least 10 h of fasting. All samples were taken between 7.00 and 10.00 am. The blood samples were sent to the biochemistry laboratory. Plasma and serum were collected after a low speed centrifugation at 3000 rpm at 4 °C for 15 min and the supernatants were aliquoted. The determination of glucose, triglycerides (TG), cholesterol to high density lipoprotein (HDL-C) and insulin were made the same day of collection by the enzymatic colorimetric method using kits Cypress, Spain using a KENZA MAX type spectrophotometer. Insulin was tested by means of a COBAS e411 (Roche Diagnostics, Mannheim, Germany) using immunochemistry method with a detection interval between 0.200 to 1000 μU/mL. Part of the aliquots was stored at -80 °C for 3 months until the ADP, C-reactive protein and TNFα assays were performed. The assay of a high-sensitivity C-reactive protein (CRPHs) was realised using the COBAS c311 (Roche Diagnostics GmbH, Mannheim, Germany) according to the immunochemistry method with an interval of detection between 0.3 to 350 mg/L. The total ADP and TNFα were assayed by the immuno-enzymatic method linked to monoclonal antibodies by ELISA (enzyme-linked immunosorbent assay) (kit Fine Test, Wuhan Fine Biotech Co., Ltd.) with an interval of detection between 1.5 to 100 ng/mL for ADP and 15.6–1000 pg/mL for TNFα. To ensure the accuracy of the calibration, three reference pools were analyzed on both the COBAS e411, COBAS c311 and the spectrophotometer. These tests were calibrated according to the operating procedures. The manufacturers recommended quality control procedures for all biochemical tests were followed throughout the study. The method of reference used in this study to evaluate the IR was the HOMA-IR ≥ 2.5 [23], calculated as for following mule [Insulin (mμ/L)×Blood glucose (mmol/L)/22.5] [23].

2.5.3. Statistical analyzes

Quantitative variables were expressed on average ±standard deviation; these averages were compared by the Student t test. For qualitative variables, frequencies (n) and proportions (%) have been calculated. These frequencies were compared by Pearson's Independence Chi Square Test or Fisher's exact test when an expected number was less than 5. Univariate logistic regression analyses were conducted to identify risk factors for insulin resistance (HOMA-IR ≥ 2.5) at the alpha-5% threshold. Spearman's correlation test was used to test correlations between certain variables. The analysis of receptor operating characteristics (ROC) was performed to assess the area under the curve (ASC), the optimal threshold value determined with the Youden criteria and the diagnostic characteristics (sensitivity, specificity, positive predictive value, negative predictive value). Subsequently, all variables with a significant association with insulin resistance were used to perform a multivariate analysis (logistical regression). The model obtained with all of these variables was optimized by a step-by-step downward selection based on the Akaké criterion (AIC). The statistical analysis was carried out using the software R (Core Team) version 4.0. All of these tests were done at the threshold α 0.05.

2.5.4. Ethical consideration

All participants gave consent after receiving explanations concerning the purpose of the study. The study protocol was approved by the Health Sciences Research Ethics Committee (HSREC). The confidentiality of the information collected was respected and the results were given to the participants individually.

3. Results

Out of the random sample, the rate response was 97.5% (n = 234/240 eligible participants). The characteristics of the participants were classified according to the HOMA-IR using a cut-off value of 2.5.

3.1. Demographic characteristics of participants according to HOMA-IR

A total of 234 people participated in this study, of whom 44.44% (n = 104/234) were men and 55.56% (n = 130/234) were women, the sex ratio was 0.8. The average age of study population was distributed from 46.37 ± 13.75 years, with a median at 46 years, and extremes of 18 and 77 years, the interquartile was 30–56 years. A total of 43.6% (n = 102/234) participants had a HOMA-IR≥ 2.5. There were no significant differences (p > 0.05) between sex, age, socioeconomic status and HOMA-IR (Table 1).

3.2. Clinical characteristics of participants according to the HOMA-IR

The study population had a mean BMI of 26.60 ± 5.63 kg/m^2. Insulinist participants had averages of 28.93 ± 5.64 kg/m^2 and 97.11 ± 14.37 cm, respectively for BMI and TT. There was a significant difference between BMI, metabolic syndrome and HOMA-IR. There were no significant differences between waist circumference, high blood pressure, family history and HOMA-IR (Table 2).

3.3. Biological characteristics of participants according to the HOMA-IR

In the HOMA-IR group ≥2.5, there were average blood glucose, insulin, insulin, CRPhs, ADP and TNF, respectively, 1.23 ± 0.55 (g/L) 15.21 ± 4.57 (m/L), 17.28 ± 10.83 (mg/L), 11.49 ± 7.61 (ng/mL) and 96.03 ± 44.09 (pg/mL). All biomarkers were significantly associated with HOMA-IR (P < 0.001) (Table 3).

3.4. Correlations between certain variables

BMI, the TT, the CRPhs and the TNFα were positively correlated significantly to the HOMA-IR. Whereas ADP (r = -0.39; P = 0.01) and ADP/TNFα ratio (r = -0.27; P = 0.01) were negatively correlated. Moreover, negative and significant correlations were noted between BMI, TT, TNFα, CRPhs and ADP. However, a positive and significant correlation was found between TNFα and the CRPhs (Table 4).

Bivariate correlation analysis between each inflammatory biomarker and HOMA-IR in the presence of general obesity (Figure 2) and abdominal obesity (Figure 3) have been performed. In all scatter plots, there

Table 1. Demographic characteristics of participants according to the HOMA-IR.

	Women			Men		
	HOMA-IR < 2.5 n = 69 (52.27%)	HOMA-IR ≥2.5 n = 61 (59.8%)	p-value	HOMA-IR < 2.5 n = 63 (47.73%)	HOMA-IR ≥2.5 n = 41 (40.2%)	p-value
AGE GROUPS			0.062			0.234
<35 years	25 (36.2%)	11 (18.0%)		16 (25.4%)	6 (14.6%)	
35–54 years old	27 (39.1%)	33 (54.1%)		31 (49.2%)	19 (46.3%)	
>54 years old	17 (24.6%)	17 (27.9%)		16 (25.4%)	16 (39.0%)	
SOCIOECONOMIC LEVEL			0.125			0.695
Low	42 (60.9%)	28 (45.9%)		48 (76.2%)	29 (70.7%)	
Medium high	27 (39.1%)	33 (54.1%)		15 (23.8%)	12 (29.3%)	

Table 2. Clinical characteristics of participants according to the HOMA-IR.

	Women			Men		
	HOMA-IR <2.5 n = 69 (52.27%)	HOMA-IR ≥2.5 n = 61 (59.8%)	p-value	HOMA-IR <2.5 n = 63 (47.73%)	HOMA-IR ≥2.5 n = 41 (40.2%)	p-value
BMI (Kg/m^2)	25.8 ± 5.38	30.9 ± 5.64	<0.001	23.7 ± 4.19	26.2 ± 4.46	0.006
<25	35 (50.7%)	10 (16.4%)	<0.001	40 (63.5%)	20 (48.8%)	0.200
≥25	34 (49.3%)	51 (83.6%)		23 (36.5%)	21 (51.2%)	
Waist circumference (cm)	167 ± 9.28	163 ± 8.27	0.017	175 ± 7.74	172 ± 9.07	0.082
TT low	19 (27.5%)	7 (11.5%)	0.039	33 (52.4%)	21 (51.2%)	1.000
High TT	50 (72.5%)	54 (88.5%)		30 (47.6%)	20 (48.8%)	
HTA (mmHg)			0.954			0.229
No	28 (40.6%)	26 (42.6%)		35 (55.6%)	17 (41.5%)	
Yes	41 (59.4%)	35 (57.4%)		28 (44.4%)	24 (58.5%)	
Metabolic syndrome			<0.001			<0.001
No	49 (71.0%)	20 (32.8%)		52 (82.5%)	14 (34.1%)	
Yes	20 (29.0%)	41 (67.2%)		11 (17.5%)	27 (65.9%)	
Family history			0.347			0.303
No	25 (36.2%)	28 (45.9%)		21 (33.3%)	9 (22.0%)	
Yes	44 (63.8%)	33 (54.1%)		42 (66.7%)	32 (78.0%)	

Table 3. Biological characteristics of participants according to the HOMA-IR.

	Women			Men		
	HOMA-IR <2.5 n = 69 (52.27%)	HOMA-IR ≥2.5 n = 61 (59.8%)	p-value	HOMA-IR <25 n = 63 (47.73%)	HOMA-IR ≥2.5 n = 41 (40.2%)	p-value
GLY (g/L)	0,81 ± 0,15	1,21 ± 0,57	<0,001	0,87 ± 0,20	1,28 ± 0,54	<0,001
INSULINE (μU/mL)	8,26 ± 2,57	15,8 ± 4,33	<0,001	7,90 ± 2,77	14,4 ± 4,81	<0,001
HOMA, IR (U/L)	1,62 ± 0,43	4,52 ± 2,21	<0,001	1,64 ± 0,50	4,17 ± 1,57	<0,001
TG (g/L)	1,62 ± 0,43	4,52 ± 2,21	<0,001	1,64 ± 0,50	4,17 ± 1,57	<0,001
HDL-c (g/L)	1,40 ± 0,36	1,73 ± 0,35	<0,001	1,36 ± 0,43	1,77 ± 0,37	<0,001
TG/HDL (U/L)	1,86 ± 0,60	2,98 ± 0,71	<0,001	2,05 ± 0,59	3,32 ± 0,83	<0,001
CRPhs (mg/L)	0,78 ± 0,18	0,60 ± 0,15	<0,001	0,68 ± 0,16	0,55 ± 0,14	<0,001
ADP (ng/mL)	1,86 ± 0,60	2,98 ± 0,71	<0,001	2,05 ± 0,59	3,32 ± 0,83	<0,001
TNFα (pg/mL)	9,11 ± 7,51	16,5 ± 9,84	<0,001	11,2 ± 8,75	18,3 ± 12,2	0,002
ADP/TNFα (U/L)	29,9 ± 17,9	11,1 ± 6,27	<0,001	21,4 ± 15,3	12,5 ± 9,75	<0,001

were significant and negative correlations between ADP ($P < 0.001$), ADP/TNFα ratio ($P < 0.01$) and HOMA-IR. On the other hand, positive and significant correlations were noted between TNFα ($P < 0.001$), CRPhs ($P < 0.001$) and HOMA-IR.

3.5. Predictive value of insulin resistance by adiponectin

The optimal threshold value of the total ADP for predicting IR was 17.52 ng/mL. The ADP's assessment of the diagnostic characteristics of

Table 4. Correlations between certain variables.

Variables	BMI	TT	GLYC	INSULINE	HOMA-IR	CRPhs	ADP	TNF-α
GLYC	0.11	-0.00						
	[-0.02; 0.24]	[-0.13; 0.13]						
INSULINE	0.40**	0.28**	0.02					
	[0.28; 0.50]	[0.16; 0.40]	[-0.11; 0.14]					
HOMA-IR	0.35**	0.20**	0.67**	0.70**				
	[0.23; 0.46]	[0.07; 0.32]	[0.59; 0.73]	[0.63; 0.76]				
CRPhs	0.17**	0.11	0.28**	0.17**	0.28**			
	[0.04; 0.29]	[-0.02; 0.23]	[0.16; 0.40]	[0.04; 0.29]	[0.16; 0.40]			
ADP	-0.20**	-0.21**	-0.23**	-0.40**	-0.39**	-0.58**		
	[-0.32; -0.07]	[-0.33; -0.09]	[-0.35; -0.10]	[-0.50; -0.29]	[-0.49; -0.27]	[-0.66; -0.49]		
TNF-α	0.02	0.09	0.12	0.12	0.15*	0.47**	-0.48**	
	[-0.11; 0.15]	[-0.04; 0.22]	[-0.01; 0.24]	[-0.00; 0.25]	[0.03; 0.28]	[0.36; 0.56]	[-0.57; -0.38]	
ADP/TNF	-0.19**	-0.19**	-0.18**	-0.25**	-0.27**	-0.45**	0.75**	-0.39**
	[-0.31; -0.06]	[-0.31; -0.06]	[-0.31; -0.06]	[-0.36; -0.12]	[-0.38; -0.14]	[-0.55; -0.34]	[0.69; 0.80]	[-0.49; -0.27]

Note: Values in square brackets indicate the 95% confidence interval for each correlation. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014), * indicates $p < 0.05$, ** indicates $p < 0.01$.

insulin resistance at the specified threshold resulted in a sensitivity of 0.89% [IC 95% (0.83–0.95)] and a specificity of 56% [IC 95% (0.47–0.65)]. This optimal threshold value of the ADP was determined from the study of the ROC curve with a range below the curve (ASC) of 0.76 [IC 95% (0.69–0.81)].

3.6. Logistics analysis multivariate

Multivariate analysis verifying the hypothesis that inflammatory biomarkers were associated with IR even after adjustment for all other variables in the model found that low ADP concentrations are associated with HOMA-IR IR (OR 0.91 IC 95%: 0.89–0.94; $p < 0.001$) compared to other inflammatory biomarkers (Tables 5 and 6).

At the end of the multivariate regression, an analysis of the ROC curve (Figure 4) of the optimized model was carried out to determine its predictive capacity. The area below the curve (ASC) of the optimized model was 0.84 [IC 95% (0.79–0.89)] with 86% sensitivity [IC 95% (0.78–0.92)] and 66% specificity [IC 95% (0.57–0.74)].

4. Discussion

IR which characterizes type 2 diabetes mellitus and MetS is associated with a low-grade inflammatory state characterized by a decrease in anti-inflammatory adipokines such as ADP; but also of an increase in inflammatory markers such as CRPhs and pro-inflammatories such as TNFα which are known cardiovascular risk factors [4, 5, 12, 21]. The present study was able to document an association between HOMA-IR and serum adipokines concentrations. ADP has proved to be a potential predictive biomarker of IR for the Congolese population with optimal threshold value of 17.52 ng/mL. This is the first study that reported the association between HOMA-IR and inflammatory biomarkers in a black population living in Brazzaville, Republic of Congo.

Moreover, the results of this study showed that the levels of ADP and ratio ADP/TNFα were significantly lowered in the HOMA-IR group ≥2.5 compared to HOMA group <2.5. These results are consistent with previous studies that reported that hypoadiponectinemia was associated with an Increase in IR [8, 18, 20, 30]. In the present study, it was also noted that the mean concentrations of TNFα and CRPhs was significantly

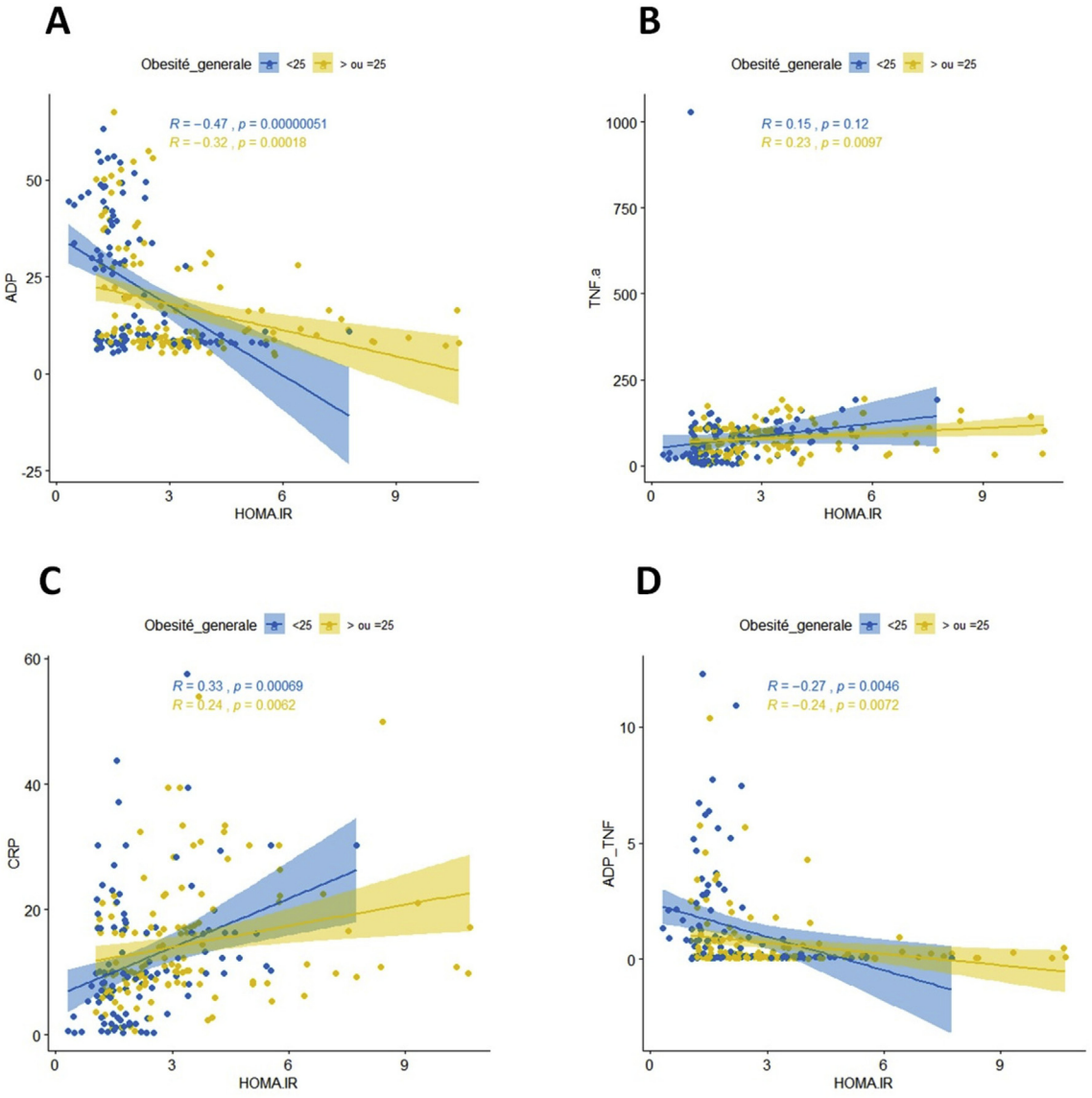

Figure 2. Bivariate correlations between HOMA-IR and inflammatory biomarkers as a function of general obesity: (A) correlation between HOMA-IR and ADP according to general obesity; (B) correlation between HOMA-IR and TNFα according to general obesity; (C) correlation between HOMA-IR and CRPhs according to general obesity; (D) correlation between HOMA-IR and ratio ADP/TNFα according to general obesity.

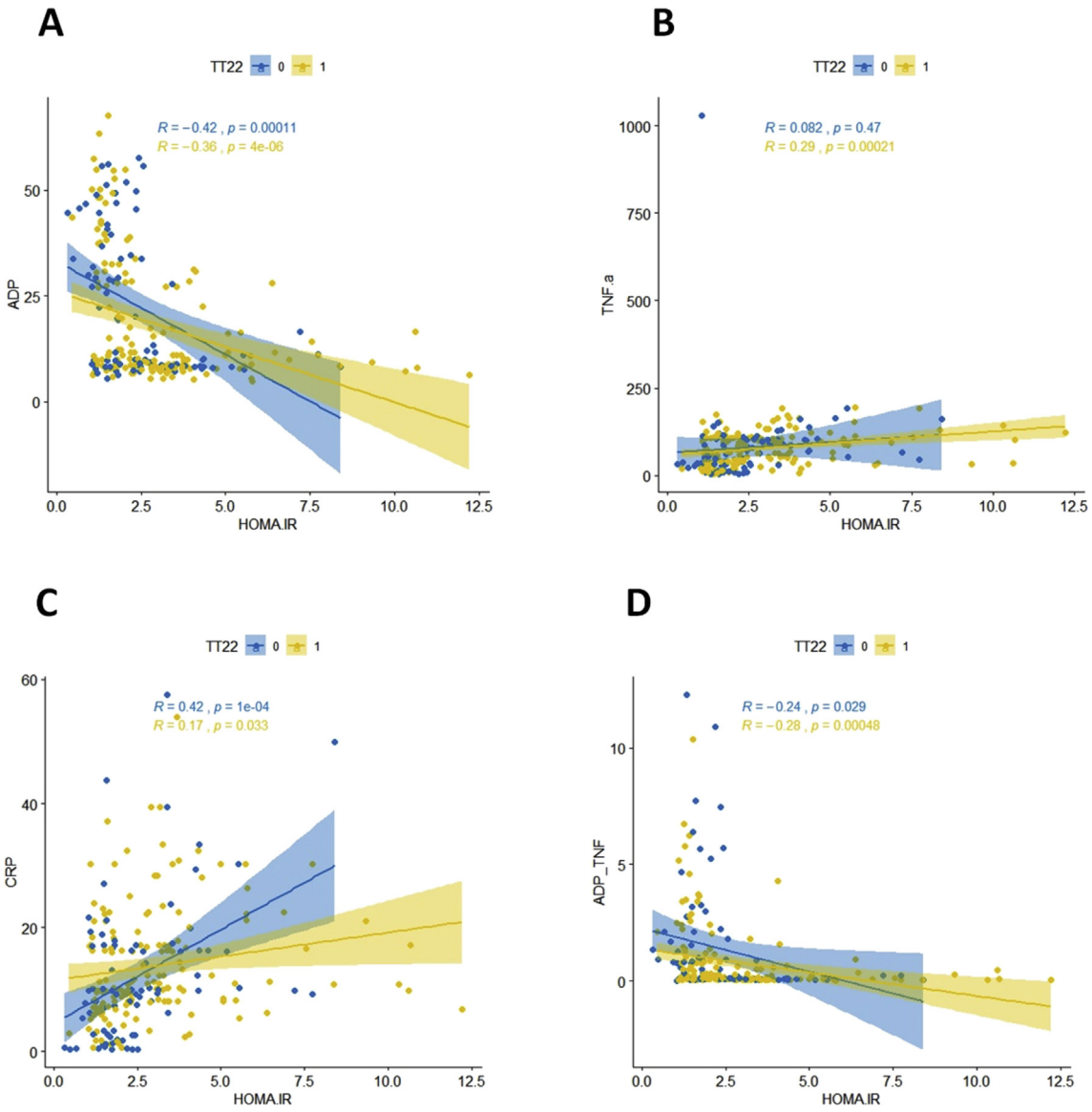

Figure 3. Correlations between HOMA-IR and inflammatory biomarkers as a function of Waist circumference: (A) correlation between HOMA-IR and ADP according of waist circumference; (B) correlation between HOMA-IR and TNFα according of waist circumference; (C) correlation between HOMA-IR and CRPhs according of waist circumference; (D) correlation between HOMA-IR and ratio ADP/TNFα according of waist circumference.

elevated in the group HOMA-IR ≥ 2.5. These results are consistent with those of other authors who have shown that systemic concentrations of TNFα and CRPhs were associated with IR and with obesity [2, 8, 12, 20, 21]. These results can be explained by the fact that ADP is an anti-inflammatory adipokine derived from adipocytes which helps to maintain the peripheral glucose and lipid homeostasis; it can also promote function and survival of beta cells [2, 8, 20, 31]. Contrary to ADP, TNFα is a pro inflammatory cytokine inducing either directly by an IR

Table 5. Analysis of logistic regression multivariate (Whole model).

Dependent: HOMA-IR		HOMA-IR < 2.5	HOMA-IR ≥ 2.5	Olds ratio (univariable)	Olds ratio (multivariable)
AGE (year)	Mean (SD)	44.5 ± 14.0	48.8 ± 13.0	1.02 (1.00–1.04) p = 0.018	1.02 (1.00–1.05) p = 0.074
BMI (Kg/m^2)					
<25		75 (56.82%)	30 (29.41%)	-	-
≥25		57 (43.18%)	72 (70.59%)	3.11 (1.80–5.39) p < 0.001	3.27 (1.60–6.90) p = 0.001
TT (cm)					
Low		52 (65.0%)	28 (27.45%)	-	-
High		80 (51.9%)	74 (72.55%)	1.69 (0.97–2.96) p = 0.057	0.45 (0.15–1.29) p = 0.146
CRPhs (mg/L)	Mean (SD)	10.1 ± 8.2	17.2 ± 10.8	1.09 (1.05–1.13) p < 0.001	1.03 (0.99–1.08) p = 0.138
ADP (ng/mL)	Mean (SD)	25.8 ± 17.2	11.4 ± 7.6	0.91 (0.89–0.94) p < 0.001	0.92 (0.88–0.95) p < 0.001)
TNFα (pg/mL)	Mean (SD)	65.2 ± 94.3	96.3 ± 43.9	1.01 (1.00–1.02) p = 0.001	1.00 (0.99–1.00) p = 0.429

Table 6. Logistic regression multivariate (Optimized model).

Dependent: HOMA-IR		HOMA-IR < 2.5	HOMA-IR ≥2.5	Olds ratio (univariable)	Olds ratio (multivariable)
AGE	Mean (SD)	44.5 ± 14.0	48.8 ± 13.0	1.02 (1.00–1.04) p = 0.018	1.02 (1.00–1.05) p = 0.060
BMI (Kg/m^2)					
<25		75 (71.4%)	30 (28.6%)	-	-
≥25		57 (44.2%)	72 (55.8%)	3.16 (1.84–5.51) p < 0.001	2.92 (1.58–5.50) p = 0.001
ADP	Mean (SD)	25.8 ± 17.2	11.4 ± 7.6	0.91 (0.89–0.94) p < 0.001	0.91 (0.88–0.94) p < 0.001

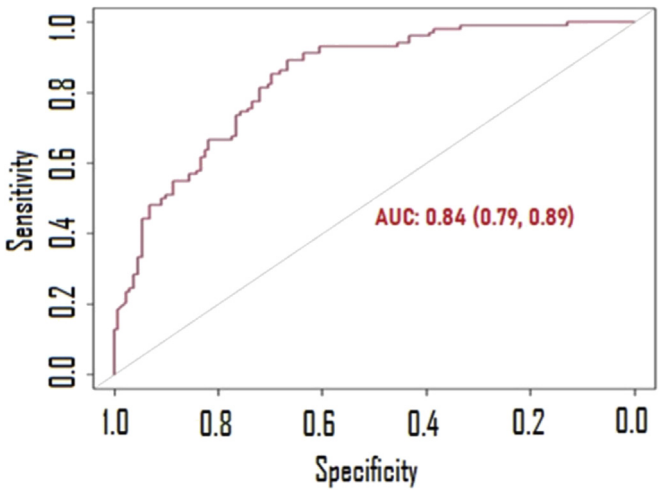

Figure 4. ASC ROC Curves of the optimized model.

phosphorylation of IRS-1 or indirectly by altering the differentiation of adipocyte and lipid metabolism which favors the lipolysis and the secretion of fatty acids thereby contributing to the increase in hepatic glucose production [14, 31]. It is the same for the CRPhs which is an inflammatory marker linked both to the IR, the metS and cardiovascular events and which appears to increase when the carbohydrate metabolism deteriorates [2, 8, 14].

Several studies have reported the reversed correlations between inflammatory biomarkers, some clinical markers and IR [3, 8, 16, 31]. The results of this study point in the same direction, Indeed, in the presence of general and abdominal obesity, positive correlations ($p < 0.05$) between the TNFα, the CRPhs and HOMA-IR have been reported. And conversely, negative correlations were found between ADP, the ADP/TNFα ratio and HOMA-IR. The results of this study also reported inverted and variable correlations between inflammatory biomarkers. In one hand, the levels of TNFα and CRPhs had negative and significant correlations with those of ADP. On the other hand, a positive and significant correlation was found between the levels of TNFα and CRPhs. These results are consistent with previous results [2, 3, 8, 12, 15, 30]. The latter can be explained by the fact that most cytokines have a common source, operate in loop and maintain an action mutual antagonist [2, 20]. Indeed, the ADP can significantly inhibit the expression of mRNA of TNFα in macrophages and can suppress the production of TNFα induced by lipopolysaccharides and vice versa, the TNFα is a potent inhibitor of the expression and secretion of the ADP gene in adipose tissue [14, 30, 31]. In addition, TNFα is a proinflammatory cytokine which can stimulate and direct the production of other cytokines such as IL-6, which in turn stimulates the production of CRP in the liver [8, 11]. Likewise, ADP directly decreases CRP and IL6 levels through dose-dependent reciprocal inhibition of TNFα [8, 30].

The results of the present study showed that ADP has good predictive characteristics of IR compared to CRP and TNFα. After analysis of the ROC curve, sensitivity, specificity and AUC showed that ADP is a powerful biomarker for predicting IR. Logistic regression multivariate, the risk IR was associated with a decrease in ADP levels. These results are in agreement with several studies [3, 32, 33]. Indeed, the ADP is a potent modulator of the action of insulin for its role in improving the insulin sensitivity of muscle cells and skeletal liver cells by stimulating oxidative mitochondrial fatty acids, glucose utilization and inhibiting gluconeogenesis [9, 31, 34]. It also increases phosphorylation-dependent protein kinase (AMPK) which causes an increase in insulin sensitivity, and therefore consumption of energy [17, 30, 33]. Factors which reduce the rate of ADP, such as obesity and especially abdominal obesity are associated with the IR [32]. As well, insulin can have a direct inhibitory effect on the expression of the ADP gene and infer concentrations [8].

The strength of this study relies on the representative size of our population to assess RI in a population at risk and on the use of standardized techniques for all measurements. However, studies expanded by adding other adipokines like leptin which could be an important adding factor in regression models.

5. Conclusion

The present study has demonstrated that the concentrations of adipokines and in particular ADP are closely related to IR. Significant correlation between clinical variables, metabolic and levels of ADP shows that ADP may be used an as a biomarker highly plausible for the prediction of IR.

Declarations

Author contribution statement

R. Eboka-Loumingou Sakou, B. Longo-Mbenza and M. Nkalla-Lambi: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

V. Tchokonte-Nana: Conceived and designed the experiments; Analyzed and interpreted the data; Wrote the paper.

E. Mokondjimobe, H. Monabeka, D. Moukassa and A. Abena: Performed the experiments; Contributed reagents, materials, analysis tools or data.

M. Tumchou: Contributed reagents, materials, analysis tools or data.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Acknowledgements

We would particularly like to thank the National Reference Center for Sickle Cell Disease and National Public Health Laboratory for the biochemical analyses, including all the field agents and all the people who participated in this study.

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