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The relationship between leptin-to-adiponectin ratio and HOMA-IR and metabolic syndrome in five African-origin populations

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OBJECTIVE: This cross-sectional study aims to assess the associations between serum leptin, adiponectin, leptin-to-adiponectin ratio (L/A ratio), and metabolic syndrome (MS) and HOMA-IR in five African-origin populations: Ghana, South Africa, Jamaica, Seychelles, and US.

METHODS: Clinical measures included serum glucose, insulin, adipokines, blood pressure and anthropometric measures. MS was determined using the Harmonized criteria. The final sample included 2087 adults.

RESULTS: After adjusting for age, sex, and fat mass, L/A ratio, unlike HOMA-IR, was significantly associated with MS across all sites ($p < 0.001$). Within sites, L/A ratio was only associated with MS and HOMA-IR in the US ($p < 0.001$) and South Africa ($p < 0.01$), respectively. Leptin was associated with MS in South Africa only ($p < 0.05$) but was significantly associated with HOMA-IR across all five sites and within the US ($p < 0.05$). Similarly, adiponectin was associated with HOMA-IR in South Africa ($p < 0.05$) and with MS across all five sites ($p < 0.001$) and within each site separately, except Ghana.

CONCLUSIONS: Our study suggests that individuals of the African diaspora in different geographical locations may differ in the determinants of MS. Future studies should investigate the determinants for the disparate relationships between MS, IS and adipokines across different African-origin populations.

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INTRODUCTION

Metabolic syndrome (MS) is characterized by a cluster of co-occurring risk factors and has been shown to increase the risk for cardiovascular disease (CVD), Type 2 diabetes (T2DM) [1], fatty liver disease [2], and certain cancers [3]. It is comprised of a combination of several factors including hypertension, hyperglycemia, dyslipidemia, and abdominal obesity [4]. While the exact etiology is not fully understood, MS is thought to be characterized by insulin resistance in conjunction with dysfunctional adipose tissue that secretes pro-inflammatory adipokines [5–8]. In fact, there is emerging evidence that points to the involvement of adipokines—mainly leptin and adiponectin—in the pathophysiology of increased adiposity, as well as in the development of oxidative stress and inflammation that characterize MS [9–13]. Specifically, a rise in circulating leptin levels [14] in tandem with a fall in adiponectin levels [15] is a hallmark of obesity and MS. Recently, the leptin-to-adiponectin ratio (L/A ratio) has been proposed as an index of adipose tissue dysfunction [16, 17], as well as a predictor of MS, such that a high ratio is associated with increased risk for MS [18, 19].

The epidemiologic transition is characterized by a shift in communicable to non-communicable diseases, that is thought to be the result of the worldwide increase in population-wide lifestyle changes along industrialization and globalizing markets worldwide [20]. Indeed, the increased reliance on inexpensive and ubiquitous ultra-processed foods, which accompany economic development, is an important cause of a global obesity pandemic [20], and thus the prevalence of MS has surged in many countries including sub-Saharan African countries [21]. A meta-analysis in 2020 that included 65 studies across 14 sub-Saharan African

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countries showed that the overall prevalence of MS ranged from 11.1% - 23.9% [22], which is similar to the MS prevalence in developed nations [23]. Despite this similar trend across nations, individuals of African-origin have been found to have unique metabolic abnormalities when compared to Caucasians [24, 25], such as (i) a dissociation of hypertension from insulin resistance [26, 27], (ii) a relatively favorable lipid profile in the context of increasing rates of cardiovascular disease [28], (iii) low levels of visceral adiposity in the context of insulin resistance [29], and (iv) a dissociation of insulin sensitivity and serum adiponectin [30].

In this study, we sought to assess the associations between serum levels of leptin and adiponectin as well as their ratio (L/A ratio) and MS and HOMA-IR. To the best of our knowledge, this is the first study to examine the determinants of MS and insulin resistance across five African-origin populations representing various degrees of economic development from Ghana, South Africa, Jamaica, Seychelles, and the United States (US).

METHODS

The Modeling the Epidemiologic Transition Study (METS) includes five cohorts of young adults (aged 25–45), who identified as African-origin. Briefly, between January 2010 and December 2011, 2506 men and women were recruited utilizing site-specific randomization methods, with about 500 at each of five locations: rural Ghana, peri-urban South Africa, urban Jamaica, mixed urban/rural Seychelles, and metropolitan Chicago, US. The selected study sites encompass a spectrum of socioeconomic development as measured by the UN Human Development Index (HDI) 2010: the US is designated "very high" HDI, Jamaica and Seychelles are designated "high" HDI, while South Africa is "middle" and Ghana is "low" HDI [31]. Participants with infectious conditions (e.g., HIV), pregnant and lactating women, and individuals who were unable to engage in physical activity were excluded. All measurements and laboratory techniques used in METS, as well as how the study size was arrived at, have been extensively outlined in a prior publication [32]. For this study, participants' baseline measures were cross-sectionally analyzed.

The METS protocol was approved by the Institutional Review Board of Loyola University Chicago (LU209537, Maywood, IL, US), the Board for Ethics and Clinical Research of the University of Lausanne (Lausanne, Switzerland), the National Research Ethics Committee of Seychelles, the Ethics Committee of the University of the West Indies (Kingston, Jamaica), the Health Sciences Faculty Research Ethics Committee of the University of Cape Town (Cape Town, South Africa), and the Committee on Human Research Publication and Ethics of Kwame Nkrumah University of Science and Technology (Kumasi, Ghana).

Anthropometric measures

The procedures used for measuring participants' heights (cm), weights (kg), waist circumferences (cm), and blood pressures (mmHg) were described in previous METS studies [33, 34]. Notably, the same model equipment was used at each of the 5 sites, with participants wearing light clothing and no shoes. Height and weight measurements were used to calculate body mass index (BMI) as kilograms per square meter (kg/m^2). Body composition was determined by bioelectrical impedance analysis (BIA, Quantum X, RJL Systems, MI, US) and a study specific equation which estimated body fat percentage, fat, and fat-free mass [35].

Biochemical measures

Fasting blood samples were drawn to assess serum insulin, glucose, triglycerides (TG), high density lipoprotein (HDL) cholesterol, leptin, and adiponectin. Measurement of fasting glucose was conducted at each collection site using the glucose oxidase method. Serum lipid assays were conducted at the Zentrum für Labormedizin, Leiter Klinische Chemie und Hämatologie (St. Gallen, Switzerland). Quantification of insulin, leptin, and adiponectin levels from all sites was performed at Loyola University Chicago (Linco Research, Inc., St. Charles, MO, US). L/A ratio was calculated by dividing the blood leptin concentration by the blood adiponectin concentration. HOMA-IR was calculated by multiplying the blood fasting insulin (μIU/mL) by the blood fasting glucose (mmol/L), then dividing by 22.5.

Assessment of cardiometabolic risk and metabolic syndrome within the study population

During the clinic visit, participants completed a brief health history which included questions regarding their current and past medications as well as any diagnosed metabolic disorders. For the current analysis, we defined metabolic syndrome using the Joint Interim Statement (JIS) Harmonized criteria [4]. According to the Harmonized definition, MS is defined as meeting three out of the five MS criteria: (1) waist circumference based on country of residence (US: ≥102 cm in men and ≥88 cm in women, sub-Saharan African countries: ≥94 cm in men and ≥80 cm in women); (2) elevated blood pressure (≥ 130/85 mm Hg) or receiving antihypertensive medication; (3) hypertriglyceridemia (≥ 150 mg/dL), or receiving lipid-lowering treatment; (4) low high density lipoprotein (HDL) cholesterol level (< 40 mg/dL in men and <50 mg/dL in women) or receiving treatment; and (5) elevated fasting plasma glucose (≥ 100 mg/dL) or receiving glucose-lowering treatment.

Statistical analyses

Clinical and metabolic characteristics of study participants were summarized using means ± standard deviations (SD) and proportions. One-Way ANOVA was used to test for statistically significant differences between means of participants' anthropometric measures. P-values were adjusted for all pairwise comparisons using the Bonferroni correction. Means of clinical and lab measurements were adjusted for age and fat mass using multiple linear regressions, and adjusted p-values were reported to denote significant differences between means. Kernel Density Plots were used to visualize the distribution of fat mass, L/A ratio, and HOMA-IR across the five sites. Multiple linear regressions and multiple logistic regressions were used to examine the associations between (i) leptin, adiponectin, L/A ratio and HOMA-IR, and (ii) leptin, adiponectin, L/A ratio and MS status, respectively, while controlling for age, sex, and free fat mass. An alpha of 0.05 was used to denote statistical significance. All statistical tests were done using IBM SPSS Statistics for macOS (Version 28) and RStudio (Version 2023).

RESULTS

A total of 2506 adults from Ghana, South Africa, Jamaica, Seychelles, and the US were recruited and consented into METS. After excluding those who had incomplete laboratory and anthropometric measurements, the final sample utilized for subsequent analyses included 2085 people (912 men and 1173 women), as shown in Fig. 1.

Clinical and metabolic characteristics of the study participants

Table 1 presents the main participant characteristics. The mean age of the participants ranged from 33.0 ± 6.0 years in South African women to 37.2 ± 5.6 years in Seychellois men. Overall, anthropometric adiposity measures such as BMI (kg/m^2), waist

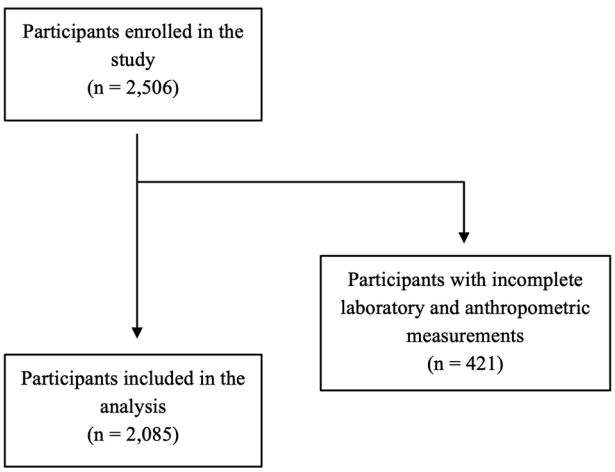

Fig. 1 Participants' flow diagram.

Table 1. Participant characteristics.

Males	Ghana N = 197	South Africa N = 226	Jamaica N = 152	Seychelles N = 107	US N = 230
Age	34.5 ± 6.8	33.7* ± 5.6	34.1 ± 6.0	37.2 ± 5.6	35.5 ± 6.2
Weight	63.8*** ± 8.9	65.5*** ± 13.7	72.2*** ± 14.4	80.9*** ± 16.8	93.5 ± 25.1
Height	169.1*** ± 6.6	170.9*** ± 6.3	175.8 ± 6.3	174.3* ± 5.8	176.6 ± 6.6
BMI	22.3*** ± 2.6	22.4*** ± 4.3	23.3*** ± 4.4	26.6*** ± 5.3	29.9 ± 7.7
Waist circumference	77.3*** ± 10.5	80.9*** ± 11.4	79.7*** ± 11.4	90.1*** ± 12.5	97.5 ± 21.9
Fat mass	10.8*** ± 5.2	14.9*** ± 8.4	15.1*** ± 8.7	21.0*** ± 10.4	29.8 ± 16.8
Females	**Ghana N = 279**	**South Africa N = 256**	**Jamaica N = 241**	**Seychelles N = 158**	**US N = 239**
Age	34.0 ± 6.7	33.0*** ± 6.0	34.7 ± 6.2	35.9 ± 6.2	35.1 ± 6.2
Weight	63.4*** ± 12.9	81.9*** ± 22.0	78.0*** ± 17.3	73.5*** ± 17.4	92.1 ± 24.7
Height	158.0*** ± 5.7	160.2*** ± 6.3	163.1 ± 6.5	161.2*** ± 6.9	163.7 ± 6.1
BMI	25.4*** ± 5.0	31.9** ± 8.1	29.3*** ± 6.5	28.3*** ± 6.3	34.3 ± 8.9
Waist circumference	84.1*** ± 12.3	96.9*** ± 16.3	91.8*** ± 13.6	88.8*** ± 12.5	102.5 ± 19.7
Fat mass	22.7*** ± 8.3	36.8*** ± 14.7	31.8*** ± 11.2	29.0*** ± 11.5	42.5 ± 16.7

Significantly different from US *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

circumference (cm), and fat mass (kg) were lowest in Ghana (men: 22.3 ± 2.6 kg/m^2, 77.3 ± 10.5 cm, 10.8 ± 5.2 kg, respectively; women: 25.4 ± 5.0 kg/m^2, 84.1 ± 12.3 cm, 22.7 ± 8.3 kg, respectively), and highest among the US participants (men: 29.9 ± 7.7 kg/m^2, 97.5 ± 21.9 cm, 29.8 ± 16.8 kg, respectively; women: 34.3 ± 8.9 kg/m^2, 102.5 ± 19.7 cm, 42.5 ± 16.7 kg, respectively), and generally higher among female participants.

Clinical laboratory measurements

Table 2 presents participants' metabolic and laboratory characteristics. The adipocytokines similarly followed a corresponding pattern, with Ghanaians having more favorable values of leptin, adiponectin, and their ratio (men: 2.81 ± 4.19 ng/mL, 7.59 ± 4.46 µg/mL, 0.81 ± 3.00, respectively; women: 18.6 ± 17.3 ng/mL, 10.6 ± 6.3 µg/mL, 2.53 ± 3.31, respectively) when compared to US participants (men: 12.1 ± 13.4 ng/mL, 7.64 ± 6.39 µg/mL, 3.00 ± 4.48, respectively; women: 42.6 ± 23.2 ng/mL, 8.51 ± 6.33 µg/mL, 9.08 ± 12.3, respectively), with women having higher values than men.

Cardiometabolic risk

Using the five features of metabolic syndrome, we were able to estimate cardiometabolic risk (Table 2). Overall, in men, Ghanaians presented with the most favorable profiles, compared to men from South Africa or the US, who had the least favorable metrics. For example serum HDL ranged from 44.8 ± 16.3 mg/dL in Ghana to 53.7 ± 19.8 mg/dL in South Africa; serum triglycerides ranged from 86.1 ± 42.2 mg/dL in Ghana to 94.9 ± 57.2 mg/dL in the US; systolic blood pressure ranged from 119.1 ± 13.2 mmHg in Ghana to 129.1 ± 17.3 mmHg in South Africa; diastolic blood pressure ranged from 68.5 ± 11.6 mmHg in Ghana to 81.3 ± 12.3 mmHg in the US; glucose ranged from 4.70 ± 0.74 mmol/L in South Africa to 5.98 ± 2.71 mmol/L in Seychelles; and waist circumference ranged from 77.3 ± 10.5 cm in Ghana to 97.5 ± 21.9 cm in the US. Similarly, among the women, Ghanaians as well as Jamaican women presented with the most favorable profiles compared to women from both South Africa and the US. For example serum HDL ranged from 46.2 ± 11.8 mg/dL in Jamaica to 51.8 ± 15.0 mg/dL in the US; serum triglycerides ranged from 65.9 ± 37.6 mg/dL in Seychelles to 96.6 ± 62.3 mg/dL in the US; systolic blood pressure ranged from 110.4 ± 15.3 mmHg in Ghana to 118.0 ± 18.2 mmHg in South Africa; diastolic blood pressure ranged from 66.2 ± 11.6 mmHg in Ghana to 79.4 ± 13.2 mmHg in the US; glucose ranged from 4.61 ± 1.63 mmol/L in South Africa to 5.61 ± 2.01 mmol/L in the US ; and waist circumference ranged from 84.1 ± 12.3 cm in Ghana to 102.5 ± 19.7 cm in the US.

US participants had the highest prevalence of MS, with 31.8% of US women and 27.8% of US men meeting the criteria for MS, compared to only 2.5% of Ghanian men and 6.5% of Ghanian women. Additionally, indices of insulin resistance such as HOMA-IR were also highest in US men and women, with mean values of 4.67 ± 3.88 and 5.45 ± 5.29, respectively. Correlating with the above data, the distribution of HOMA-IR, as well as fat mass and L/A ratio, is visualized in Fig. 2.

Relationship between adipocytokines and features of cardiometabolic risk

We next conducted multiple linear regression and multiple logistic regression analyses to study the associations between (1) leptin, adiponectin, L/A ratio and HOMA-IR, and (2) leptin, adiponectin, L/A ratio and MS status, respectively, while controlling for age, sex, and fat mass. Results of these regressions are shown in Tables 3, 4. Across all five sites, L/A ratio was significantly associated with MS status ($p < 0.001$) but not with HOMA-IR. Within sites, L/A ratio was a significant predictor for MS in the US only ($p < 0.001$) but was not associated with HOMA-IR in any of the sites. However, leptin was a significant predictor for HOMA-IR within the US ($p < 0.01$) and MS status within South Africa ($p < 0.05$). As for adiponectin, it was a significant predictor for HOMA-IR in South Africa ($p < 0.05$) and a predictor for MS status both across all five sites ($p < 0.001$) and within each site separately, except for Ghana.

DISCUSSION

This study aimed to assess the associations between serum levels of leptin and adiponectin, as well as their ratio, with MS and HOMA-IR across five population of African origin, providing insight on the effect of economic development on these associations. Our study is the first to explore the determinants of MS and HOMA-IR in a culturally diverse African-origin cohort representing populations at different stages of the epidemiologic transition.

We show that anthropometric measurements of adiposity exhibit site- and sex-specific differences and correspond to each site's stage of economic development. In total, women across all

Table 2. Clinical and metabolic characteristics of participants.

Males	Ghana N = 197	South Africa N = 226	Jamaica N = 152	Seychelles N = 107	US N = 230
Glucose (mmol/L)	5.61 ± 0.64	4.70*** ± 0.74	5.35 ± 0.50	5.98 ± 2.71	5.81 ± 1.60
Insulin (μIU/mL)	11.5*** ± 7.0	10.6*** ± 7.8	14.0 ± 7.5	12.3*** ± 7.6	17.5 ± 12.3
HOMA-IR	2.89*** ± 1.89	2.20*** ± 1.61	3.33** ± 1.87	3.19*** ± 2.09	4.67 ± 3.88
Leptin (ng/mL)	2.81** ± 4.19	5.34** ± 5.62	4.02 ± 5.96	5.90 ± 6.27	12.1 ± 13.4
Adiponectin (μg/mL)	7.59*** ± 4.46	12.6*** ± 6.2	8.05* ± 4.43	6.28*** ± 4.98	7.64 ± 6.39
L/A ratio	0.81** ± 3.00	0.64 ± 1.05	0.86 ± 1.84	1.64 ± 2.36	3.00 ± 4.48
HDL (mg/dL)	44.8*** ± 16.3	53.7 ± 19.8	47.1*** ± 12.7	47.9** ± 14.4	50.1 ± 15.0
Triglycerides (mg/dL)	86.1* ± 42.2	94.8** ± 60.0	70.5 ± 32.1	92.9 ± 58.9	94.9 ± 57.2
Systolic blood pressure	119.1*** ± 13.2	129.1** ± 17.3	120.9** ± 12.6	121.3*** ± 13.8	128.2 ± 14.6
Diastolic blood pressure	68.5*** ± 11.6	79.6** ± 13.3	70.8*** ± 11.0	73.9*** ± 11.0	81.3 ± 12.3
MS	5 (2.5%)	23 (10.2%)	12 (7.9%)	30 (28.0%)*	64 (27.8%)
Females	**Ghana N = 279**	**South Africa N = 256**	**Jamaica N = 241**	**Seychelles N = 158**	**US N = 239**
Glucose (mmol/L)	5.55 ± 0.70	4.61*** ± 1.63	5.03*** ± 0.50	5.33 ± 1.11	5.61 ± 2.01
Insulin (μIU/mL)	12.1*** ± 7.9	17.0*** ± 16.0	14.1*** ± 7.6	12.3*** ± 8.5	21.2 ± 16.4
HOMA-IR	2.99*** ± 2.03	3.46*** ± 3.44	3.17*** ± 1.78	2.93*** ± 2.16	5.45 ± 5.29
Leptin (ng/mL)	18.6* ± 17.3	36.0 ± 22.3	34.2* ± 20.2	23.2** ± 17.7	42.6 ± 23.2
Adiponectin (μg/mL)	10.6 ± 6.3	13.4*** ± 7.4	9.39 ± 5.01	8.57* ± 5.23	8.51 ± 6.33
L/A Ratio	2.53*** ± 3.31	4.02*** ± 4.10	5.49* ± 6.03	4.21** ± 5.03	9.08 ± 12.3
HDL (mg/dL)	47.5*** ± 13.2	46.2*** ± 16.6	46.2*** ± 11.8	48.2*** ± 12.0	51.8 ± 15.0
Triglycerides (mg/dL)	76.7 ± 34.8	76.1*** ± 37.4	74.4*** ± 38.6	65.9*** ± 37.6	96.6 ± 62.3
Systolic blood pressure	110.4*** ± 15.3	118.0 ± 18.2	115.3 ± 14.9	112.5*** ± 13.6	117.2 ± 16.1
Diastolic blood pressure	66.2*** ± 11.6	76.2 ± 11.7	72.0*** ± 11.5	72.0*** ± 10.8	79.4 ± 13.2
MS	18 (6.5%)***	52 (20.3%)	47 (19.5%)	40 (25.3%)	76 (31.8%)

Significantly different from US and adjusted for age and fat mass *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

sites had a higher BMI and fat mass compared to their male counterparts, and the US participants had significantly higher adiposity measures than the other sites. Higher adiposity tended to associate closely with a higher stage of economic development, apart from Seychellois women, who had lower BMI, fat mass, and weight compared to South African and Jamaican women. Interestingly, indices of glucose metabolism did not follow the trend of adiposity. This is consistent with the findings of Atiase et al. [36] who previously reported similar results for METS participants. The highest fasting levels of serum glucose and insulin were measured in Seychellois men and US women, respectively, while the lowest levels were in South African women and men, respectively. HOMA-IR was also highest in US women and lowest in South African men. On the other hand, adipokines followed an expected trend that tracked closely with adiposity. The US participants presented with a classic adipokine profile, known to correlate with higher levels of adiposity—high levels of leptin, low levels of adiponectin, and a high L/A ratio. The lowest levels of leptin were recorded in Ghanian men and women, while the highest adiponectin levels were recorded in South African men and women. In concordance with these leptin and adiponectin levels, the lowest L/A ratio was found in South African men and Ghanian women, reflecting the low levels of adiposity at both sites. Lipid profiles and blood pressure measurements were more variable and did not follow a defined trend. Interestingly, the South African participants presented with elevated blood pressure and higher levels of both triglycerides and HDL, which were similar to the US participants. We have previously reported on this phenomenon within our METS cohort [34, 37]. While the expectation is that a higher HDL level is associated with a more favorable cardiovascular risk profile, it is well-described that African Americans have a higher serum HDL and lower triglyceride levels despite having a higher prevalence of insulin resistance and adverse cardiovascular outcomes [38–40]. This has been termed "the lipid paradox" [41, 42]. Not surprisingly, the prevalence of MS tracked closely with adiposity measures and the stage of epidemiologic transition for each site, which adds to the extensive body of literature linking cardiometabolic risk to economic development [34, 43–48].

When exploring the relationship between adipokines and HOMA-IR and MS, it was found that these associations widely varied by site. Adiponectin was linearly associated with HOMA-IR only in South Africa, while leptin only showed that association in the US. In contrast, there was a statistically significant inverse relationship between adiponectin and MS both across and within all sites except for Ghana. However, the L/A ratio was associated with MS across the five sites and within the US, while leptin showed the same association only in South Africa. Our findings are in contrast to popular conceptions of the relationship between adipokines, insulin resistance, and MS. Indeed, studies involving individuals of African-origin have reported very weak or absent associations between intra-abdominal visceral fat content and insulin sensitivity [24]. This may explain why adipokines that directly reflect adiposity do not necessarily predict insulin resistance or MS. The inconsistent relationship between adipokines and MS and insulin resistance in our study population indicates that adipokine levels may not be a universally reliable clinical indicator for metabolic abnormalities across different

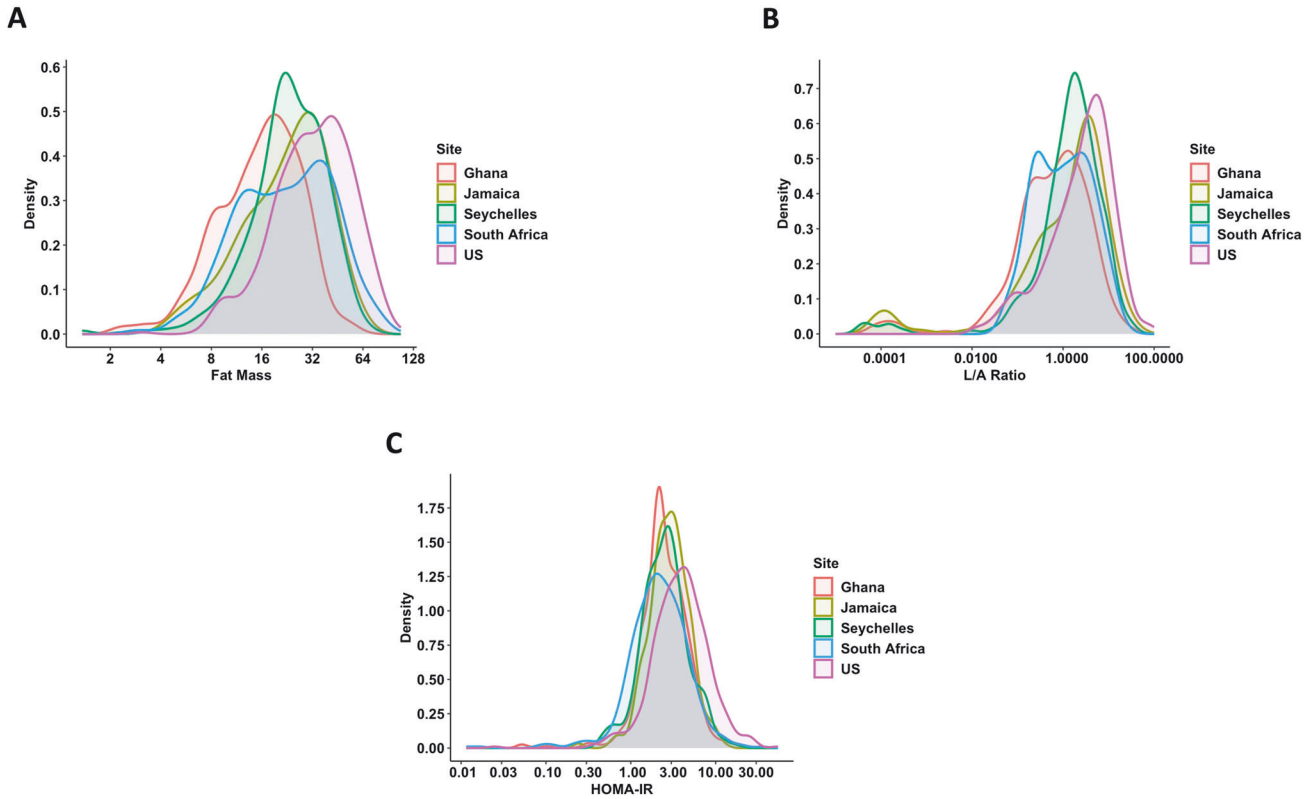

Fig. 2 Diagram explaining number of participants used in this analysis. Kernel density plots for: (**A**) fat mass (log_2 scale); (**B**) L/A ratio (log_{10} scale); and (**C**) HOMA-IR (log_{10} scale).

Table 3. Standardized regression coefficients examining the association of leptin, adiponectin, L/A ratio and HOMA-IR, adjusted for age, sex, and fat mass.

Model	L/A Ratio			Leptin			Adiponectin		
	β	95% CI	R^2	β	95% CI	R^2	β	95% CI	R^2
1. Ghana	−0.010	−0.07–0.06	0.004	0.091	−0.01–0.03	0.008	0.043	−0.02–0.05	0.006
2. South Africa	0.079	−0.03–0.16	0.068	−0.121	−0.04–0.01	0.069	−0.096	−0.08– −0.002*	0.073
3. Jamaica	0.123	0.00–0.08	0.016	0.001	−0.01–0.01	0.006	−0.102	−0.08–0.00	0.015
4. Seychelles	−0.050	−0.10–0.05	0.009	−0.094	−0.04–0.01	0.011	0.017	−0.05–0.06	0.008
5. US	0.018	−0.04–0.06	0.052	0.261	0.02–0.08**	0.072	−0.022	−0.08–0.05	0.053
6. All Sites	0.035	−0.01–0.04	0.094	0.070	0.00–0.02	0.095	−0.031	−0.04–0.01	0.094

*$p < 0.05$, **$p < 0.01$

populations. Our findings also suggest that individuals of the African diaspora residing in different geographical locations are metabolically diverse and may not be identical in the determinants of cardiometabolic syndrome. This suggests that perhaps a geographic lens should be used when interpreting these relationships.

Our study is not without limitations. The data reported in our study is cross-sectional, therefore, causality cannot be inferred from the relationships reported and no conclusions about the directionality of these relationships can be drawn. Secondly, data for other variables, such as hemoglobin A1c, educational and economic status, diet, physical activity, and tobacco or alcohol use, was not available for all participants and was therefore not included in the final analysis. Additionally, although our samples are representative of the participants' respective communities, they are not necessarily representative of each country as a whole, and hence caution should be exercised when generalizing the results of our study to countries in their totality.

CONCLUSION

In conclusion, our study found differing relationships between insulin resistance and metabolic risk and their possible determinants across five distinct populations of African-origin with considerably variable socioeconomic and health attributes. This prompts public health measures specific to each site and population. Our study suggests that individuals of the African diaspora residing in different geographical locations are metabolically diverse and may not be identical in the determinants of cardiometabolic syndrome. More studies are required to explore these relationships across different African populations and provide insight into the contribution of environmental and

Table 4. Odds ratios for metabolic syndrome status according to leptin, adiponectin, and L/A ratio by binary logistic regression, adjusted for age, sex, and fat mass.

Model	L/A Ratio			Leptin			Adiponectin		
	OR	95% CI	*p* value	OR	95% CI	*p* value	OR	95% CI	*p* value
1. Ghana	1.036	0.93–1.16	0.532	0.987	0.96–1.02	0.449	0.940	0.85–1.04	0.215
2. South Africa	1.062	0.98–1.15	0.153	0.979	0.96–0.99	0.035*	0.923	0.88–0.97	0.001**
3. Jamaica	0.991	0.94–1.05	0.765	0.989	0.97–1.01	0.268	0.895	0.83–0.97	0.004**
4. Seychelles	1.083	0.99–1.18	0.069	0.975	0.94–1.01	0.141	0.841	0.76–0.93	<0.001***
5. US	1.090	1.04–1.14	<0.001***	1.012	1.00–1.03	0.151	0.929	0.89–0.98	0.003**
6. All Sites	1.052	1.03–1.08	<0.001***	0.992	0.98–1.00	0.098	0.916	0.89–0.94	<0.001***

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

genetic factors in the development of cardiometabolic disease, as well as the clinical utility of adipokine levels in predicting metabolic abnormalities across different populations.

SUMMARY

What is already known about this subject?

- The leptin-to-adiponectin ratio (L/A ratio) has been proposed as an index of adipose tissue dysfunction, metabolic syndrome (MS), and insulin resistance.
- Individuals of African-origin have unique metabolic abnormalities when compared to Caucasians.

What are the new findings in your manuscript?

- The relationships between the L/A ratio and MS and insulin resistance differed across the five African-origin populations included in the study.

How might your results change the direction of research or the focus of clinical practice?

- Our results provide insight into the reliability of adipokine levels as a universal clinical indicator of metabolic abnormalities across different populations.

DATA AVAILABILITY

The data that support the findings of this study are available upon reasonable request. All data have been anonymized to protect the confidentiality of participants. For inquiries regarding data access, please contact corresponding author, Candice Choo-Kang.

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AUTHOR CONTRIBUTIONS

NS contributed to the conception, design of the study, data analysis, interpretation of the data, and drafting the manuscript. JJ contributed to the study's design, data analysis, and provided critical revisions to the manuscript. JZ, C.C-K, JZ, KB-A, TF, PB, EVL, WR, and WK, and YD were responsible for data acquisition and interpretation, edited the manuscript, and provided significant contributions to the interpretation of the results. BTL, LRD, and AL contributed to the conception of the study, provided oversight, and made substantial contributions to the manuscript's final approval. All authors reviewed and approved the final manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent was obtained from all participants. The METS protocol was approved by the Institutional Review Board of Loyola University Chicago (Maywood, IL, US), the Board for Ethics and Clinical Research of the University of Lausanne (Lausanne, Switzerland), the National Research Ethics Committee of Seychelles, the Ethics Committee of the University of the West Indies (Kingston, Jamaica), the Health Sciences Faculty Research Ethics Committee of the University of Cape Town (Cape Town, South Africa), and the Committee on Human Research Publication and Ethics of Kwame Nkrumah University of Science and Technology (Kumasi, Ghana). All methods were performed in accordance with the relevant guidelines and regulations.

ADDITIONAL INFORMATION

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