

# INSULIN RESISTANCE, BETA CELL FUNCTION AND CARDIOVASCULAR RISK FACTORS IN GHANAIS WITH VARYING DEGREES OF GLUCOSE TOLERANCE

**Objective:** Type 2 diabetes is characterized by beta cell dysfunction and insulin resistance (IR). The disease is associated with high rates of cardiovascular mortality and morbidity. Recently, the American Diabetes Association Expert Committee recommended the measurement of fasting glucose as a tool for screening and diagnosing diabetes, in order to identify patients with a mild form of the disease as well as to enhance the detection of undiagnosed type 2 diabetes. The significance of these criteria with respect to cardiovascular risk factors in native Ghanaians is unknown. The objectives of the present study were to examine the cardiovascular risk factors in a sample of native Ghanaians with varying degrees of glucose intolerance as defined by fasting glucose levels as specified by the ADA criteria.

**Research and Methods:** The population consisted of 200 indigenous Ghanaian subjects, age range 25–74 years, residing in the Accra metropolitan areas. Subjects were categorized using the fasting plasma glucose (FPG) alone as normal fasting glucose (NFG, FPG<110mg/dL), impaired fasting glucose (IFG, 110<FPG 126mg/dL), and diabetic (DM, FPG>126mg/dL). Anthropometric parameters (blood pressure, waist circumference and waist-hip circumference ratios) were measured in each subject. Levels of serum glucose, c-peptides and insulin were measured at baseline and after 2 hours of oral glucose challenge. Insulin resistance (HOMA-IR) and beta cell function (HOMA-%B) were assessed by homeostasis model assessment (HOMA). Levels of fasting serum cholesterol, high-density lipoprotein cholesterol (HDL-C), cholesterol, and triglycerides were measured in each subject.

**Results:** There were 181 subjects in the NFG category, 11 in the IFG category, and 8 newly diagnosed type 2 diabetic subjects. The mean age, BMI, waist circumference (WC), and WHR did not differ between the 3 groups. The mean fasting glucose and the corresponding 2-hour glucose levels rose with the worsening of glucose tolerance. Similarly, the means for serum fasting, post-challenge serum insulin, and c-peptide levels were significantly greater in the IFG and DM groups. Fasting serum cholesterol and high density lipoproteins did not differ statistically between the 3 groups. However, the means for serum triglycerides were greater in the IFG and DM groups when compared to the NFG group. The insulin resistance (IR) as assessed by HOMA was 2× and 4×

Albert G. B. Amoah, MBChB, FRCP;  
Dara P. Schuster, MD, FACE; Trudy Gaillard, MS, RN, CDE;  
Kwame Osei, MD, FACE, FACP

## INTRODUCTION

The occurrence of diabetes is increasing in all regions of the world<sup>1–13</sup> and is expected to double by 2025, with most sufferers residing in the developing world.<sup>1,2</sup> The complications associated with diabetes appear also to be increasing alongside the global pandemic.<sup>3–6</sup> Diabetes is fatal in the sub-Saharan region of Africa.<sup>14–17</sup> Cardiovascular diseases such as coronary artery disease, stroke, and heart failure are the main causes of death in individuals with diabetes in developed economies, accounting for nearly 80% of the deaths. Insulin resistance is the hallmark of type 2 diabetes<sup>18–22</sup> and cardiovascular diseases.<sup>23–26</sup> Insulin resistance with concomitant hyperinsulinemia precedes the development of IGT and type 2 diabetes by decades in sub-

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greater in the IFG (3.76) and DM (6.12) groups when compared with the NFG (1.82,  $P<.05$ ).

**Conclusions:** We have characterized the metabolic and anthropometric risk factors for CVD in native Ghanaians with varying degrees of glucose tolerance, as defined by the ADA criteria. We found that both IFG and DM were associated with beta cell dysfunction, insulin resistance, and elevated serum triglycerides. However, the well established cardiovascular risk factors, such as body mass index, body fat distribution, and blood pressure did not track with the increasing glucose intolerance in the native Ghanaians. We conclude that the Ghanaian patients with IFG and type 2 diabetes were non-obese and exhibited severe beta cell dysfunction, insulin resistance, and elevated triglycerides, but none of the other conventional risk factors, at the time of diagnosis. Future research should focus on the sequential changes in risk factors during development of cardiovascular diseases in native Ghanaians with varying degrees of glucose tolerance. (*Ethn Dis.* 2002;12[suppl3]:S3-10–S3-17)

Saharan Africans.<sup>27–28</sup> Limited data exists on the association between insulin resistance, hyperinsulinemia, and cardiovascular risk in Ghanaians. To research this association, we have used the frequently sampled intravenous glucose tolerance test (FSIGT) with minimal model method to assess insulin action in Ghanaian immigrants residing in the United States<sup>27</sup> as well as in Ghanaian subjects residing in their native country.<sup>28</sup> These studies have demonstrated that Ghanaian subjects manifest moderately severe insulin resistance at the initial diagnosis of impaired glucose tolerance and type 2 diabetes.<sup>29</sup> In addition, we have also demonstrated that non-diabetic, first-degree relatives of native Ghanaian patients with type 2 diabetes are more likely to manifest insulin resistance with compensatory hyperinsulinemia as compared to those without family history of diabetes.<sup>28</sup> However, none of our previous studies focused on the importance of insulin resistance and varying degrees of glucose tolerance on CVD risk factors in native Ghanaians.

We have recently reported that the rate of diabetes has increased from less

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From the Diabetes Research Laboratory, Department of Medicine and Therapeutics, University of Ghana Medical School, Accra, Ghana (AA); Division of Endocrinology and Metabolism; Department of Internal Medicine; The Ohio State University Hospitals; Columbus, Ohio.

Address correspondence and reprint requests to A.G.B. Amoah, MBChB(MD), FRCP, PhD; Diabetes Research Laboratory; Department of Medicine and Therapeutics; University of Ghana Medical School; Post Office Box 4236; Accra, Ghana; 233-21-671047 (tel/fax); agbamoah@hotmail.com

than 0.5% in 1950s to 6.4% in the Accra metropolitan area (Amoah ABG et al, personal communication). In a recent survey of 5,000 Ghanaians residing in the Accra metropolitan area, we also observed that the prevalence of high blood pressure (140/90 mm Hg) in Accra is now very high (28%). Moreover, during the past 2 decades, cardiovascular disease has continued to be a major cause of morbidity and mortality in Ghanaians with diabetes. Thus, it is imperative that we understand the relationship between insulin resistance, hyperinsulinemia, and cardiovascular risk factors in patients with varying degrees of glucose homeostasis in order to plan strategic prevention and intervention programs for diabetes and cardiovascular diseases.

Recently, Levitt et al<sup>29</sup> investigated the implications of the new American Diabetes Association (ADA), diagnostic criteria for diabetes, and categories of glucose intolerance in sub-Saharan Africans. The ADA stated that the use of the oral glucose tolerance test was still essential in these populations. Thus, the use of fasting plasma glucose as a major criterion for the diagnosis of diabetes was recommended because of simplicity, convenience, and reproducibility, but this test did not identify most patients with IGT and type 2 diabetes. However, the significance of the new category of impaired fasting glucose (IFG), introduced as a way of identifying individuals at risk for diabetes with respect to cardiovascular risk factors in sub-Saharan Africans, was not examined. Ghana is a tropical country in West Africa with a surface area of 238,533 km<sup>2</sup>. The 2000 population was 19.7 million, with a gross domestic product (GDP) of 7.4 billion US dollars, and a per capita GDP of 412 US dollars. The Accra metropolitan area has the largest urban population in the country, with 1.6 million.<sup>19</sup> We have recently characterized the insulin sensitivity index of Ghanaians with and without type 2 diabetes.<sup>28</sup> We demonstrated insulin resistance and hyperinsulinemia in non-diabetic first degree relatives of Ghanaians

with parental history of type 2 diabetes. Nevertheless, and to the best of our knowledge, the relationship between the new fasting diagnostic categories and insulin resistance, hyperinsulinemia, and cardiovascular risk factors have not been examined in native Ghanaians living in Ghana.

Therefore, the objectives of the present study were: 1) to characterize fasting glucose homeostasis in Ghanaian subjects; and 2) to examine the association of insulin sensitivity and cardiovascular risk factors, such as body mass index, body fat distribution, blood pressure, and lipids and lipoproteins with the categories of fasting glucose homeostasis. To this end, we measured fasting glucose, insulin sensitivity indices, beta cell function, and anthropometric and conventional risk factors for cardiovascular disease in 200 native Ghanaians living in the Accra metropolitan area who had not been previously diagnosed with diabetes or hypertension. The insulin resistance index was calculated using the homeostasis model assessment (HOMA) method,<sup>30</sup> which is more suitable and convenient, and less laborious for such epidemiologic studies than the gold standard: the euglycemic clamp<sup>31</sup> or frequently sampled intravenous glucose tolerance test.<sup>32</sup>

## SUBJECTS, METHODS, AND MATERIALS

### Subjects

The study population comprised 200 adults (aged 25–74 years), selected from a random community sample (cluster) from Ghana's Accra metropolitan area. The details of the design and sampling frame have been described elsewhere (Amoah AGB et al. Diabetes in Ghana: a community based study. *Diabetes Res Clin Pract.* In press.). Individuals with fasting plasma glucose  $\leq 3.5$  mol/L or who were taking exogenous insulin or anti-diabetic medication were excluded from the study. The subjects were non-

smokers with no previous diagnosis of hypertension or diabetes, and who were not taking medications that would interfere with the determination of insulin action, or with glucose and insulin responses. They were allowed their usual, relatively high-carbohydrate diet (ie, >250g carbohydrate per day) for the 3 days prior to testing.

### Study Protocol

After an overnight fast of 10–12 hours, anthropometric measurements were taken for subjects in light clothing and without shoes. Body weight was measured with a heavy duty Seca 770 floor digital scale (Seca, Hamburg, Germany) to the nearest 0.1 kg. Height was measured with a height stadiometer to the nearest 0.1 cm. Body mass index (BMI) was calculated from the weight and height measurements. Waist and hip girth were measured in duplicate with a non-elastic plastic measuring tape to the nearest 0.1 cm. The waist measurement was taken at the mid-point between the lower rib margin and the iliac crest at the end of gentle expiration. The hip girth was obtained at the level of the greater trochanter. The mean of the duplicate data was used to determine the waist girth and waist-to-hip circumference ratio (WHR). After at least 10 minutes of rest, 2 blood pressure readings were taken by trained nurses using a zero-centered sphygmomanometer.

The study was approved by the Ethical Review Committee of the University of Ghana Medical School and complied with the Helsinki Declaration of 1975 (revised in 1983) on human experimentation. Informed consent was obtained from all subjects.

### Metabolic Protocol

Fasting blood was drawn to ascertain levels of plasma glucose, serum cholesterol, triglycerides, high-density lipoprotein, insulin, and c-peptides. Each subject then ingested 75 grams of anhydrous glucose dissolved in 250 mL of water over a 2-minute period. Blood

samples were obtained after 2 hours for determination of plasma glucose, serum insulin, and c-peptide levels.

**Analytical Methods**

Serum triglyceride, cholesterol, and HDL-cholesterol levels were measured by enzymatic methods, and glucose level was measured by glucose oxidase (Randox Laboratories Limited, Crumlin, United Kingdom) on a chemistry auto-analyzer (Erba Smartlab, Mumbai, India). The inter-assay coefficients of variation for normal and elevated plasma glucose controls were 1.4% and 2.4%, respectively, the corresponding intra-assay coefficient of variation being 1.8% and 1.4%, respectively. The levels of serum insulin and c-peptides for each individual were determined by a standard double antibody radioimmunoassay technique with the sensitivity of the insulin assay being less than 2.5 uU/mL. Intra- and inter-assay coefficients of variation were 5% and 10%, respectively. The lower limit of the c-peptide assay was 0.20 nmol/mL and the intra- and inter-assay coefficients of variation, were 7% and 13%, respectively.

**Calculation and Statistical Analyses**

Results are expressed as mean ± standard error of the mean (SEM), unless otherwise stated. The subjects were divided into 3 groups, in accordance with the ADA fasting glucose criteria as described by Levitt et al<sup>29</sup> in their research among sub-Saharan Africans. Group 1 comprised: individuals with normal fasting glucose homeostasis (NFGH). These were defined as subjects with fasting serum glucose less than 6 mmol/L (FPG < 110 mg/dL). Group 2 contained: individuals with impaired fasting glucose (IFG); FSG > 6.0 mmol/L but FSG < 7.0 mmol/L (> 110 mg/dL, but < 126 mg/dL). Group 3 contained: type 2 diabetic patients (DM) FPG ≥ 7.0 mmol/L (≥ 126 mg/dL). High blood pressure was defined as ≥ 140/90 mm Hg in accor-

**Table 1. Clinical characteristics (mean and confidence interval) by fasting glycemic status in Ghanaians**

Parameters	NFG N = 181 M/F = 77/104	IFG N = 11 M/F = 6/5	Diabetes N = 8 M/F = 4/4	All Subjects N = 200 M/F = 87/113
Age (yrs)	40.7 (39.8–42.6)	43.8 (36.9–50.8)	48.8 (41.5–56.0)	41.2 (39.4–43.0)
BMI (kg/m <sup>2</sup> )	25.4 (24.7–26.1)	27.8 (24.5–31.1)	25.6 (24.8–26.2)	25.5 (24.9–26.2)
Waist (cm)	83.0 (81.2–84.7)	89.3 (80.5–98.0)	85.1 (80.5–89.7)	83.4 (81.7–85.0)
WHR	0.83 (0.82–0.85)	0.85 (0.78–0.92)	0.84 (0.83–0.85)	0.84 (0.83–0.85)
SBP (mm Hg)	128 (125–131)	128 (113–143)	140 (114–167)	128 (125–132)
DBP (mm Hg)	76 (74–78)	77 (68–87)	79 (67–91)	76 (75–78)

BMI = body mass index; WHR = waist to hip ratio; SBP = systolic BP; DBP = diastolic BP; NFG = normal fasting plasma glucose; IFG = impaired fasting glucose.

dance with the 1997 Joint National Committee criteria. HOMA insulin resistance (HOMA-IR) was calculated in accordance with the formula: fasting insulin (uU/mL) × fasting plasma glucose (mmol/L)/22.5. Beta cell function (HOMA %B) was determined using the formula: 20 × fasting insulin (uU/mL)/fasting glucose – 3.5.<sup>30</sup>

Unless indicated otherwise, the statistical package SPSS 10.0 for Windows (SPSS Inc, Chicago, Ill) was used for analyses. Multiple regression and correlation coefficients were calculated using least squares method. The unpaired two-tailed *t* test was used to compare means between 2 groups, and the one-way ANOVA was used to compare more than 2 groups of variables. Statistical significance was considered as probability value less than .05.

**RESULTS**

**Comparison of Clinical and Metabolic Data in Ghanaians with NGT, IFG and Type 2 Diabetes**

Table 1 shows the clinical and biochemical parameters of the 3 Ghanaian groups. The NFG group contained 181 subjects, the IFG had 11, and there

were 8 newly diagnosed type 2 diabetic patients in the DM group. The mean age, BMI, waist circumference, and WHR were not different among the NGT, IFG, and DM groups. Similarly, the systolic and diastolic blood pressures were not significantly different between the 3 groups. As expected, the median fasting serum glucose and the corresponding 2-hour glucose levels rose with the lessening of glucose tolerance. Similarly, the mean serum fasting and post-challenge insulin and c-peptide levels rose as the glucose tolerance worsened from NFG → IFG → type 2 diabetes. However, lipids and lipoprotein levels were not affected by fasting plasma glycemia. Insulin resistance as assessed by HOMA-IR was 2× and 4× greater in the IFG (3.76) and DM (6.12) groups, respectively, compared to the HOMA IR of the NFG (1.82, *P* < .05). The mean serum fasting cholesterol, and HDL-C, and levels were not significantly different among the 3 groups. However, the mean fasting levels of serum triglycerides were greater in those Ghanaians with IFG and type 2 diabetes.

**Comparing Ghanaian Patients with IFG and Type 2 Diabetes**

The mean demographic and anthropometric variables such as age, body fat

distribution, body weight, and body mass index did not differ between the 2 groups. Other than the HOMA-IR, which was significantly lower in the DM group vs the IFG group, the rest of the metabolic parameters did not differ significantly when examined in absolute terms. However, the mean serum insulin and c-peptide responses were inadequate for the prevailing glucose levels in the DM groups (Table 2).

**Partial Correlation of Fasting Plasma Glucose and Cardiovascular Risk Factors**

Table 3a shows the zero order and fourth order partial correlation of fasting plasma glucose and cardiovascular risk factors. Age, systolic blood pressure, and levels of serum triglycerides had the highest correlation with fasting plasma glucose. Generally, the relationship between fasting glucose and the metabolic parameters was weak (zero order partial correlation); the association became weaker still, when adjustments were made for age, BMI, waist girth, and WHR (fourth order partial correlation).

**Partial Correlation between Serum Insulin and Cardiovascular Risk Factors**

Table 3b shows the zero order and fourth order partial correlation of fasting serum insulin and cardiovascular risk factors. BMI, waist circumference, and level of serum triglycerides exhibited the highest correlation with fasting serum insulin. Weaker correlations were found between fasting insulin and the other risk factors. When adjustments were made for age, BMI, waist girth, and WHR (fourth order partials), the association of fasting insulin with the other risk factors became weaker still (fourth order correlation).

**Partial Correlation between HOMA-IR and Cardiovascular Risk Factors**

Table 3c shows the zero order and fourth order partial correlation between

**Table 2. Metabolic characteristics (mean and confidence intervals) by fasting glycaemic status in Ghanaians**

Parameters	NFG N = 181 M/F = 77/104	IFG N = 11 M/F = 6/5	Diabetes N = 8 M/F = 4/4	All Subjects N = 200 M/F = 87/113
FPG (mmol/l)	5.0 (5.0–5.1)	6.5 (6.4–6.7)	9.5 (7.5–11.5)*	5.3 (5.1–5.5)
2HPG (mmol/l)	6.5 (6.3–6.7)	8.6 (7.2–10.1)	12.9 (8.7–17.2)	6.9 (6.6–7.2)
Chol (mmol/l)	4.8 (4.5–5.0)	4.8 (3.9–5.7)	5.6 (4.5–6.7)†	4.8 (4.7–5.0)
Trig (mmol/l)	0.4 (0.42–0.48)	0.71 (0.41–1.01)	0.65 (0.33–0.97)*	0.47 (0.44–0.50)
HDL-C (mmol/l)	1.10 (1.02–1.17)	0.09 (0.62–0.96)	1.13 (1.01–1.15)†	1.08 (1.01–1.15)
FINSU (uU/ml)	8.02 (7.40–8.64)	12.87 (8.32–17.4)	14.55 (9.86–19.24)*	8.55 (7.89–9.20)
FC-pep (uU/ml)	1.10 (0.97–1.22)	1.66 (1.05–2.28)	1.86 (1.26–2.46)*	1.16 (1.04–1.28)
2HINS (uU/ml)	39.48 (34.92–44.04)	39.48 (24.33–54.63)	51.46 (43.97–58.96)†	39.98 (35.79–44.18)
2HC-pep (uU/ml)	4.50 (4.10–49.0)	7.02 (4.42–9.62)	6.09 (5.46–6.72)*	4.70 (4.31–5.10)
HOMA-IR	1.82 (1.67–1.97)	3.76 (2.41–5.12)	6.12 (3.61–8.63)*	2.10 (1.88–2.31)
HOMA-%BC	28.23 (25.85–30.60)	35.64 (22.06–49.22)	28.74 (17.20–40.30)†	28.66 (26.38–30.94)

\* P<.05.

† P>.05.

NFG = normal fasting plasma glucose; IFG = impaired fasting glucose; FPG = fasting plasma glucose; 2HPG = 2-hr plasma glucose; Trig = serum triglycerides; Chol = serum cholesterol; HDL-C = high density lipoprotein cholesterol; FINS = fasting serum insulin; FC-pep = fasting serum c-peptide; 2HINS = 2-hr serum insulin; 2HC-pep = 2-hr serum insulin.

HOMA-IR and cardiovascular risk factors. BMI, waist circumference, and serum triglycerides had the highest correlation with fasting serum insulin. Weaker correlations were found between HOMA-IR and the other risk factors. Adjustments for age and anthropometric indices rendered the correlations to weaker correlations (fourth order correlation) (Table 3c).

**Multiple Regression Analysis of Fasting Plasma Glucose and Cardiovascular Risk Factors**

Tables 4a–4c display the multiple regression model summaries for fasting plasma glucose, fasting insulin, and HOMA-IR and cardiovascular risk factors. Age, WHR, BMI, waist girth, and plasma lipids together could account for only 13% and 23% of the variance in

fasting plasma glucose and HOMA-IR, respectively.

**DISCUSSION**

In the present study, we found that beta cell function was only, moderately impaired in the IFG and mild type 2 diabetic subjects. The fasting levels of insulin and c-peptides were greater in the IFG and type 2 diabetic individuals. These findings are consistent with those found in other ethnic and racial populations, such as in Sub-Saharan Africans<sup>33–35</sup> and African Americans.<sup>36</sup> It should be noted that the relatively normal beta cell function was not entirely normal since these higher levels of fasting insulin and c-peptides occurred at the expense of higher serum glucose lev-

**Table 3a. Partial correlation of fasting plasma glucose level with cardiovascular risk factors**

	Correlation Coefficients (r)	
	Zero Order Partials	Fourth Order Partials
Age	0.227	
BMI	0.097	
Waist girth	0.142	
WHR	0.149	
DBP	0.183	0.095
SBP	0.250	0.155
Trig	0.279	0.231
Chol	0.122	0.074
HDL-C	0.010	-0.0002

**Table 3b. Partial correlation of fasting serum insulin with cardiovascular risk factors**

	Correlation Coefficients (r)	
	Zero Order Partials	Fourth Order Partials
Age	0.213*	
BMI	0.471*	
Waist girth	0.478*	
WHR	0.247*	
DBP	0.206*	-0.007†
SBP	0.226*	0.068†
Trig	0.373*	0.224*
Chol	0.270*	0.155*
HDL-C	0.042†	0.004†

\* P<.05.  
† P>.05.

**Table 3c. Partial correlation of insulin resistance index (HOMA-IR) with cardiovascular risk factors**

	Correlation Coefficients (r)	
	Zero Order Partials	Fourth Order Partials
Age	0.231*	
BMI	0.360*	
Waist girth	0.379*	
WHR	0.211†	
DBP	0.190*	0.012†
SBP	0.217*	0.066†
Trig	0.396*	0.282*
Chol	0.250*	0.153*
HDL-C	0.026†	-0.002†

\* P<.05.  
† P>.05.

els. In this regard, we have demonstrated that acute first phase insulin secretion is severely blunted in native and immigrant Ghanaian patients with impaired glucose tolerance (IGT) and type 2 diabetes.<sup>33</sup> Also Motala et al<sup>34</sup> found that IGT patients with lower 2-hour insulin secretion deteriorated to type 2 diabetes status. In a cross-sectional study, Ezenwaka et al<sup>37</sup> found lower acute first insulin secretion in non-diabetic, first degree relatives of patients with type 2 diabetes residing in Ibadan, Nigeria when compared to healthy controls without family history of diabetes. In addition, Mbanya et al<sup>13</sup> have reported that plasma insulin levels are lower 30 minutes after an oral glucose load in first-degree relatives of type 2 diabetic patients from Cameroon, when compared to age- and sex-matched healthy controls without a family history of di-

abetes. They found a 2-fold higher rate for both impaired glucose tolerance and type 2 diabetes among the offspring of diabetics, compared to the rates for the general population. In contrast, we have found that normal glucose tolerant, first-degree relatives of Ghanaian patients with type 2 diabetes manifest hyperinsulinemia after both oral and intravenous glucose challenges, as compared to the healthy controls.<sup>28</sup> These findings were similar to those of African Americans<sup>38</sup> and Afro-Caribbeans residing in the United Kingdom<sup>39</sup> and France.<sup>40</sup> We believe differences in obesity and body fat distribution, as well as different levels of physical activity or fitness, could partly explain the apparent discrepancies in beta cell function in these individuals of West African ances-

try. However, longitudinal metabolic studies among diverse SSA populations, similar to the study by Weyer et al<sup>21</sup> in Pima Indians, will be necessary in the future to address the discrepancies in beta cell function.

Insulin resistance (IR) is the hallmark of type 2 diabetes in the Western world.<sup>19-21,33,36</sup> IR is genetic and familial with an acquired component. It is now clear that race and ethnicity, independent of family history, also determine insulin resistance in several populations.<sup>41,42</sup> Recent studies have demonstrated that insulin resistance tracks with obesity in a given population.<sup>21,41</sup> IR, whether genetically inherited or acquired, could precipitate the development of IGT and type 2 diabetes in individuals susceptible to the disease.<sup>21,41</sup>

**Table 4a. Multiple regression model summary (dependent variable: fasting plasma glucose)**

Model	R	R <sup>2</sup>	Adjusted R <sup>2</sup>	Std Error	R <sup>2</sup> Change	F Change	df1	df2	Sig F Change	Dubin-Watson
1	.238*	.057	.036	1.124	.057	2.763	4	184	.029	
2	.282†	.080	.049	1.116	.023	2.281	2	182	.105	
3	.358‡	.128	.084	1.096	.048	3.299	3	179	.022	
4	.717§	.514	.487	.820	.386	141.349	1	178	.000	
5	.914	.836	.825	.478	.322	346.314	1	177	.000	2.062

\* Predictors: (Constant), WHR, BMI, Age, Waist.  
† Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP.  
‡ Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP, HDL-C, Trig, Chol.  
§ Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP, HDL-C, Trig, Chol, HOMA-IR.  
|| Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP, HDL-C, Trig, Chol, HOMA-IR, HOMABCF.

**Table 4b. Multiple regression model summary (dependent variable: fasting serum insulin)**

Model	R	R <sup>2</sup>	Adjusted R <sup>2</sup>	Std Error	R <sup>2</sup> Change	F Change	df1	df2	Sig F Change	Dubin-Watson
1	.496*	.246	.230	4.142	.246	15.894	4	195	.000	
2	.499†	.249	.226	4.153	.004	.465	2	193	.629	
3	.553‡	.306	.273	4.025	.057	5.188	3	190	.002	
4	.613§	.376	.343	3.827	.070	21.166	1	189	.000	1.749

\* Predictors: (Constant), WHR, BMI, AgE, Waist.

† Predictors: (Constant), WHR, BMI, AgE, Waist, DBP, SBP.

‡ Predictors: (Constant), WHR, BMI, AgE, Waist, DBP, SBP, HDL-C, Trig, Chol.

§ Predictors: (Constant), WHR, BMI, AgE, Waist, DBP, SBP, HDL-C, Trig, Chol, FPG.

Most importantly, insulin resistance, along with the resultant hyperinsulinemia, has been associated with increased cardiovascular risk and coronary artery disease and hypertension in several populations.<sup>23-26</sup> However, only limited data examining the associations between hyperinsulinemia, IR, and cardiovascular risk are available for the populations of sub-Saharan Africa. Because of the emergence of non-communicable diseases in developing African countries, research on the relationship and the potential pathogenetic role of IR in these various diseases among residents of sub-Saharan Africa is warranted.

In the present study, we found that the HOMA-IR progressively increased as the rate of glucose intolerance worsened. Note that increasing HOMA-IR signifies increasing insulin resistance in our Ghanaian populations. Indeed, compared to the normal fasting plasma glucose group, the impaired fasting glucose and diabetic groups were 2- and 4-fold more insulin resistant, respectively.

This is of great interest since the mean body weight, waist circumference, WHR, and BMI were not significantly different among the 3 groups. Since we did not assess intra-abdominal visceral fat content in our cross-sectional study of the Ghanaian population, we are uncertain whether the observed differences in HOMA-IR are related to differences in intra-abdominal fat in the 3 groups. Thus, prospective studies on the natural history of IR and glucose intolerance will be necessary to examine the proximate determinants of glucose intolerance in Ghanaians.

Lipid and lipoprotein abnormalities are very common in patients with impaired glucose tolerance and type 2 diabetes. Both insulin resistance as well as insulin deficiency play a role in the lipoprotein disorder found in patients with type 2 diabetes. While a large body of data has been accumulated to support the role of lipoprotein abnormalities in cardiovascular diseases in the Western and industrialized world, similar data

are scanty for the developing Sub-Saharan Africa. Typically, the most common lipid and lipoprotein disorders found in patients with IGT, type 2 diabetes, and/or insulin resistance syndrome, are high serum triglycerides and lower HDL-C levels. In the present study, we found that serum cholesterol, LDL-C cholesterol, levels of triglycerides, and HDL-C were all within normal limits. However, there was a tendency for serum triglycerides to increase along with the IR and glucose intolerance. This tendency was not seen in the HDL-C levels. We believe our population is unique since we studied non-obese, individuals with impaired fasting glycemia and mild type 2 diabetes. The present findings in Ghanaians with varying degrees of glucose intolerance extend, as well as confirm, the dissociation between IR and glucose intolerance and type 2 diabetes previously reported in African Americans<sup>43,44</sup> and Afro-Caribbeans.<sup>45</sup>

Hypertension has been found to be

**Table 4c. Multiple regression model summary (dependent variable: HOMA-IR)**

Model	R	R <sup>2</sup>	Adjusted R <sup>2</sup>	Std Error	R <sup>2</sup> Change	F Change	df1	df2	Sig F Change	Dubin-Watson
1	.391*	.153	.135	1.4	.153	8.309	4	184	.000	
2	.398†	.159	.131	1.4	.006	.627	2	182	.536	
3	.481‡	.231	.192	1.4	.072	5.594	3	179	.001	
4	.909§	.827	.817	0.7	.596	611.941	1	178	.000	
5	.987	.973	.972	0.3	.147	975.764	1	177	.000	1.774

\* Predictors: (Constant), WHR, BMI, Age, Waist.

† Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP.

‡ Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP, HDL-C, Trig, Chol.

§ Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP, HDL-C, Trig, Chol, FINS.

|| Predictors: (Constant), WHR, BMI, Age, Waist, DBP, SBP, HDL-C, Trig, Chol, FINS, HOMA-%BF.

a major risk factor for CVD and type 2 diabetes among several populations. Hypertension accounts for the increased morbidity and mortality in patients with type 2 diabetes. Indeed, hypertension is found in at least 50%–60% of patients with type 2 diabetes. The prevalence of hypertension in African Americans with type 2 diabetes approaches 80%, compared to 30% of non-diabetic African Americans. We have recently observed a very high rate (28.6%) of hypertension in Ghanaians residing in the Accra metropolitan area, and a prevalence of approximately 50% in our outpatient university diabetes clinic population. The etiology of hypertension in Ghanaians with and without diabetes and nephropathy remains uncertain. Therefore, we examined the relationship of fasting serum insulin and IR and blood pressure in our Ghanaian population with varying degrees of glucose tolerance. Surprisingly, we found no association of IR with blood pressure in our population. Indeed, as IR worsened with increasing glucose intolerance, both systolic and diastolic blood pressure remained normal in our non-obese Ghanaian populations. Although, the mechanism of the constellation of insulin resistance, hyperinsulinemia, glucose intolerance, and hypertension remains unknown, we are tempted to speculate that acquired and genetic factors as well as Westernization in developing sub-Saharan African countries could be involved.<sup>46–48</sup>

In summary, results of the present study demonstrate that both IFG and DM patients non-obese native Ghanaian patients are characterized by moderate to severe insulin resistance and beta cell dysfunction. However, these metabolic disparities in the 3 groups were not associated with concomitant abnormalities in blood pressure, metabolism of lipids and lipoproteins, or the clinical anthropometric parameters found in cardiovascular disease. These favorable lipoprotein profiles in the face of insulin resistance are similar to those reported

among diabetic and non-diabetic African Americans subjects. Because our present study in the Ghanaians was cross-sectional, we are unable to identify the risk factors for IFG, type 2 diabetes, cardiovascular disease in our native population. Thus, future longitudinal and prospective studies among the native Ghanaians should examine the predictors of impaired fasting glycemia, type 2 diabetes, and cardiovascular disease for further elucidation.

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*Data analysis and interpretation:* Amoah  
*Manuscript draft:* Amoah  
*Acquisition of funding:* Amoah  
*Administrative, technical, or material assistance:* Amoah  
*Supervision:* Amoah

**AUTHOR CONTRIBUTIONS**

*Design and concept of study:* Amoah  
*Acquisition of data:* Amoah