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**Waist circumference and obesity related abnormalities in French and Cameroonian adults: The role of urbanization and ethnicity**

**Running title:** Urbanization - ethnic effects on metabolic abnormalities.

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**ABSTRACT:**

**Objectives:** To evaluate the effect of urbanization and ethnicity on correlations between waist circumference (WC) and obesity related cardiovascular risk factors.

**Methods:** 1471 rural and urban Cameroonians, and 4185 French, from community based studies, aged  $\geq 25$  years, not treated for hypertension, diabetes and dyslipidemia participated to this study. Slopes of obesity related abnormalities with WC were compared using an interaction term between place of residence and WC.

**Results:** Women in urban Cameroon and men in France had significantly higher WC and BMI relative to their gender counterparts. Urban Cameroonians had higher abdominal adiposity, but lower BP and better metabolic profile than the French. WC was positively associated to all the obesity related abnormalities in the three sites except to FPG (both genders) and blood lipids (women) in rural Cameroon. A 5cm larger WC was associated with a higher increment among urban than rural Cameroonians for diastolic blood pressure (DBP) (women, 1.95/0.63mmHg; men, 2.56/1.44mmHg), HOMA-IR (women, 0.11/0.05), fasting plasma glucose (FPG) (men, 0.09/-0.01mmol/l) and triglycerides (women, 0.06/0.01mmol/l; men, 0.09/0.03mmol/l), all  $p < 0.05$ . A 5cm larger WC was associated with a higher increment among urban Cameroon than French people for DBP (women, 1.95/1.28mmHg,  $p < 0.01$ ; men, 2.56/1.49mmHg,  $p < 0.01$ ), but with a lower increment for HOMA-IR (women, 0.11/0.14,  $p < 0.05$ ), FPG (women, 0.05/0.09mmol/l), total cholesterol (women, 0.07/0.11mmol/l; men, 0.10/0.13mmol/l) and triglycerides (women, 0.06/0.11mmol/l; men, 0.09/0.13mmol/l) all  $p < 0.05$ .

**Conclusion:** Ethnicity and urbanization modify the association of WC with obesity related metabolic abnormalities. WC cut-off points derived from Caucasians may not be appropriate for black Sub-Saharan Africans.

**KEY WORDS:** Abdominal obesity, cardiovascular risk factors, ethnicity, urbanization, Sub-Saharan Africa.

**Abbreviations:** CVD, Cardiovascular diseases; D.E.S.I.R.: Données Epidémiologiques sur le Syndrome d'Insulino-Résistance; HOMA-IR: Homeostasis assessment model for insulin resistance; WC, waist circumference; DBP and SBP, Diastolic and systolic blood pressures

## **Introduction**

Fat accumulation is associated with numerous co-morbidities such as cardiovascular diseases (CVD), sleep disorders and gall bladder diseases.<sup>1-4</sup> For CVD, fat accumulation affects the risk of major outcomes, both directly and indirectly through its links with risk factors such as hypertension, type 2 diabetes, insulin resistance, lipid disorders and other metabolic and haematologic abnormalities.<sup>3, 5-8</sup> Because of this association, surrogate measures of fat accumulation, including body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR) have been used to predict related CVD risk in populations. Studies have suggested that WC may be a better anthropometric predictor of CVD risk than either BMI or WHR.<sup>9-11</sup> Indeed, WC is a surrogate measure of total body and abdominal fat accumulation, not accounted for by either BMI or WHR.<sup>8, 12</sup> WC is better correlated with visceral adipose tissue than are BMI or WHR, and is thus used as surrogate.<sup>13</sup> However, this correlation with WC varies significantly across ethnicities.<sup>14</sup>

Reports on ethnic differences in the association of WC with obesity related abnormalities are available for Caucasians, Asians and Black Americans, but not for Africans.<sup>15-17</sup> In spite of the high prevalence of obesity among populations from Sub-Saharan Africa,<sup>18-20</sup> obesity related metabolic abnormalities are reported at much lower frequencies than among populations from developed countries.<sup>21</sup> Genetic and environmental factors could explain these differences. Using data from Cameroon and France, we tested the hypothesis that the association of central obesity with a number of obesity related abnormalities is influenced by urbanization and ethnicity.

## **Methods and procedures**

### *Study populations*

The Cameroon study<sup>22, 23</sup> and the French D.E.S.I.R. (Données Epidémiologiques sur le Syndrome d'Insulino-Résistance) study<sup>24, 25</sup> are respectively population based and community based studies of type 2 diabetes and CVD risk factors, both initiated in 1994. The Cameroon 1994 study included 1986 Black African adults, 786 rural and 1160 urban subjects. The French study included 5212 adults, recruited from volunteers insured by the French Social Security System, which offers periodic health examinations free of charge to all affiliates.

Because the relationship between the studied risk factors of CVD and WC may be influenced by the duration of the factor existence and its treatment, subjects with physician diagnosis or specific treatment for hypertension, diabetes and dyslipidaemia were excluded from the analyses. Data on variables of interest were available for 1471 participants in Cameroon and 4185 in France. All individuals gave informed consent to participate. The studies were approved by relevant ethics committees in Cameroon and in France, and conformed to the principles outlined in the declaration of Helsinki.

### *Data collection and definition of variables*

Height, weight, waist and hip circumferences were measured by trained personnel as previously described.<sup>22-25</sup> BMI was computed as weight (kg)/height<sup>2</sup> (m)<sup>2</sup>. Waist to hip ratio (WHR) was the waist circumference divided by the hip circumference. Diastolic and systolic blood pressures (DBP and SBP) were measured on the right arm after at least 5 minutes of rest, with subjects in supine position, using a standard mercury sphygmomanometer and appropriate cuff sizes. Mean arterial pressure (MAP) was calculated as  $DBP + (SBP - DBP)/3$ . Venous blood samples were collected after an overnight fast of at least 12 hours for the determination of plasma glucose, insulin, total cholesterol and triglycerides. In Cameroon, samples for insulin determination were collected on ice, centrifuged immediately, separated

and stored at  $-70^{\circ}$  C until assayed. Fasting plasma glucose (FPG) was determined by the glucose-oxidase method using a spectrophotometer with external quality control on every 4<sup>th</sup> sample by a Cobas bio hexokinase fluorometric method. Plasma insulin was assayed at the Wellcome Laboratories, University of Newcastle Upon Tyne, by ELISA method using DAKO kits (Hersteller, UK). Serum cholesterol and triglycerides were measured by enzymatic colorimetric methods in the same laboratory. In France, samples were analyzed in laboratories participating in a national quality control program. Plasma glucose was assayed by the glucose oxidase method applied to fluoro-oxalated plasma using a Technicon RA 1000 (Bayer Diagnostics, France) or a KONA (Konelab, Evry, France). Serum insulin was centrally assayed at the Institut inter Régional pour la Santé by MIEA (Micro Particle Enzyme Immunoassay) with the IMX automated analyzer (Abbot, France). Serum cholesterol and triglycerides were determined with a DAX24 technique (Bayer Diagnostics, France) or with KONE (Konelab, Evry, France). Homeostasis assessment model for insulin resistance (HOMA-IR) was calculated as: Fasting plasma glucose (mmol/l) x Fasting plasma insulin ( $\mu$ U/ml)/22.5.

### **Statistical analyses**

STATA 8.02 (Statacorp., Texas, USA) was used for statistical analyses. All tests were two-sided and the significance level was  $p < 0.05$ . Data are presented as mean (standard deviation) and beta coefficients. HOMA-IR and fasting triglycerides were not normally distributed and were logarithmically transformed.

As there was not significant evidence of non linearity between WC and obesity related abnormalities, comparison of variables across places of residence used linear regression analyses, with and without adjustment for age. Regression analyses were used to characterize the associations between WC and SBP, DBP, MAP, fasting plasma glucose, HOMA-IR, total cholesterol and fasting triglycerides for the three places of residence. An interaction term

between gender and WC was used to test whether the effect of WC on obesity related abnormalities varied with gender. Comparison of slopes for obesity related abnormalities with WC across places of residence used appropriate contrasts for places of residence and an interaction term between place of residence and WC. The effect of urbanization was tested by comparing rural and urban Cameroon and the effect of ethnicity by comparing urban Cameroon and France. Adjustments were made for age to take into account the effect of age differences across places of residence on the studied parameters. To account for the effect of differences in hip circumference distribution according to gender and place of residence, the same analyses were performed using WHR instead of WC.

## Results

### *Characteristics of the study population*

For both genders, urban Cameroonians were younger than rural Cameroonians and the French people, and rural Cameroonian population is more heterogeneous for age (Table 1). Urban Cameroonian women had the highest mean values of weight, BMI, WC and hip circumference. Rural Cameroonian women had higher values of WHR than their urban Cameroonian counterpart or French women. In men, the lowest value of WHR was found in urban Cameroonians. Weight and WC of men increased from the rural to urban Cameroon and to France. Height and BMI of men was not significantly different in urban Cameroon and France. DBP, fasting total cholesterol and HOMA-IR increased in both genders from rural to urban Cameroon to France (Table 1).

After adjusting for age, the height of women was no longer significantly different across places of residence, and their WC was no longer significantly different in rural and urban Cameroon (data not shown); also, the DBP of men was no longer different in urban Cameroon and France.

### *Gender differences in anthropometry*

WC and BMI of women and men were not different in rural Cameroon (WC:  $p=0.056$ ; BMI:  $p=0.25$ ), were higher for women than for men in urban Cameroon (WC:  $p<0.03$ ; BMI:  $p<0.001$ ), and were lower for women than for men in France (WC:  $p<0.001$ ; BMI:  $p<0.001$ ). Hip circumference was higher for women compared to men in Cameroon (both sites,  $p < 0.001$ ) and lower in women compared to men in France ( $p<0.001$ ) (Table 1). Men had higher WHR in urban Cameroon and in France in comparison to women.

### *Interaction between gender and WC for obesity related abnormalities*

The association between WC and blood pressure, fasting blood glucose and total cholesterol did not vary according to gender, for each place of residence. The same increase in WC led to

a higher increase of HOMA-IR in men compared to women in rural Cameroon ( $p<0.01$ ), urban Cameroon ( $p<0.006$ ) and France ( $p<0.001$ ), and to a higher increase of fasting triglycerides in men compared to women in urban Cameroon ( $p<0.03$ ) and France ( $p<0.001$ ).

*Association of WC with obesity related abnormalities, and effects of urbanization and ethnicity*

In univariate analysis, all the obesity related abnormalities significantly increased with WC irrespective of gender and place of residence, except, in rural Cameroon, for fasting plasma glucose (both genders) and blood lipids (women) (Table 2). After adjustment for age, DBP and MAP (rural Cameroonian women), fasting plasma glucose (urban Cameroonian women), fasting total cholesterol (Cameroonian women and men) and fasting triglycerides (rural Cameroonian women) no longer varied significantly with WC (Figure 1).

In univariate analysis, for a 5 cm increase in WC, there was a higher increase in urban compared to rural Cameroonians for DBP (3 fold in women and 1.8 fold in men), HOMA-IR (2.2 fold in women), FPG (9 fold in men) and fasting triglycerides (6 fold in women and 3 fold in men) of urban compared to rural Cameroonians (Table 2). These trends persisted after adjusting for age (Figure 1).

In urban Cameroonians compared to the French, a 5 cm increase in WC was associated with a higher increase of SBP (significant only in men) and DBP but with a lower increase of HOMA-IR (1.3 fold in women), FPG (1.8 fold in men), fasting total cholesterol (1.6 fold in women and 1.3 fold in men) and fasting triglycerides (1.8 fold in women and 1.3 fold in men) of the French compared to urban Cameroonians (Table 2). After adjusting for age, fasting cholesterol did not significantly differ according to urbanization or ethnicity (Figure 1).

*Association of WHR and obesity related abnormalities, and effects of urbanization and ethnicity*

In rural Cameroon, only fasting triglycerides in men increased significantly with WHR. All the obesity related abnormalities increased significantly with WHR except HOMA-IR and fasting plasma glucose in urban women and fasting total cholesterol in urban Cameroonian women and men (Table 3). The same trends of increase in the obesity related abnormalities were found for a 0.10 point increase in WHR.

## **Discussion**

This is the first study addressing the comparison of correlates of WC between people living in Europe and in sub-Saharan Africa. There are three major findings in our study. First, for the same increase in WC, French individuals had higher increase in metabolic abnormalities compared to urban Cameroonians, and urban Cameroonians had higher increase in obesity related abnormalities compared to their rural counterparts. Second, a marked variation in the distribution of adiposity with gender, urbanization and ethnicity was observed after adjusting for age. Finally, WC correlated positively with obesity related abnormalities, regardless of urbanization, gender or ethnic background, indicating that increased abdominal girth is associated with increased likelihood of the presence of metabolic risk factors for Black Africans as well as Europeans.

Assays of plasma glucose, insulin and blood lipids used different methods in Cameroon and France. The values obtained for these metabolic characteristics were within the range of those expected. The different reagents used would have had an impact on plasma glucose, insulin and blood lipids across sites, and did not influence the type of the association between WC and these obesity related abnormalities. The main outcome in our analyses was the variations within populations according to WC. Since the assays were uniform in each population, this is not methodological drawback.

To measure the effect of ethnicity, we hypothesized that the impact of urbanization on obesity related abnormalities was the same in urban Cameroon and France. Urbanization is higher in France than in urban Cameroon, and this difference probably increased the effect of ethnicity when comparing subjects from these two settings. However, as shown between rural and urban Cameroon, urbanization had minor effects on the strength of the relationship between WC and obesity related abnormalities.

WC was larger in men than in women for Europeans, and the opposite was found in rural and urban Cameroonians. This intriguing sex-ethnic variation was also observed by other authors<sup>17, 26</sup> in Europeans and South Asians, and the reason for these differences merits further study. Different levels of physical activity, the nature and composition of diet as well as cultural variations in the perception of obesity are possible explanations. Cut-off points of WC recommended for abdominal obesity for Caucasians<sup>6, 27</sup> are higher for men than for women, reflecting the larger WC of men compared to women in these populations. Although the same cut-off points are recommended for Sub-Saharan Africans, WC of black African men is the same or lower than that of black African women, giving for native Africans, prevalences of abdominal obesity which do not reflect reality of CVD risk.<sup>18-20</sup>

As in other ethnic groups,<sup>17, 28, 29</sup> WC was positively correlated in Cameroon with almost all the obesity related abnormalities. WC could then be used in Sub-Saharan Africans to identify subjects at higher risk of cardiovascular diseases. The lack of association of WC with plasma glucose in the rural Cameroonians may reflect the time necessary for fat accumulation to saturate adipocytes, before spreading to liver, pancreas and muscle, with consequences on insulin production, sensitivity to insulin and fuel metabolism. In fact, HOMA-IR increased with WC. It is well known that insulin resistance, then increased fasting insulin in response to abnormal visceral fat accumulation are the precursors of impaired glucose tolerance.<sup>30</sup> Moreover, it has been demonstrated that high levels of physical activity, frequent in rural Cameroon<sup>20</sup> in comparison to urban Cameroon have protective metabolic effects, partly by increasing insulin sensitivity.<sup>1, 31</sup> All these mechanisms are known to counterbalance the elevation of fasting blood glucose.

We demonstrated a stronger association of WC with blood pressure in urban Cameroon in comparison to France, despite higher blood pressure levels in the French population. This greater predisposition of Black Africans to increase their blood pressure

when WC increases is in accordance with the higher prevalence of hypertension in black Americans compared to white Americans,<sup>32-34</sup> secondary to exposure to high energy diet and little physical activity. It is also a prelude to an explosion in the prevalence of hypertension in Cameroon if nothing is done to stop the obesity epidemic. However, it can also be just the reflection of a dose response relationship between WC and blood pressure, as WC was higher in urban Cameroonians compared to the French.

The difference observed between rural and urban Cameroonians, which are genetically similar populations, is due primarily to the environment. The environments of the two populations were different in terms of level of industrialization and its consequences for individual lifestyles. The environmental factors most influencing the relationship between adiposity and obesity related abnormalities are energy expenditure in the form of physical activity level, energy intake and dietary patterns. Not only did food resources differ between rural and urban populations in Cameroon,<sup>35</sup> but physical activity patterns differed enormously.<sup>20</sup> Energy intake and physical activity are both crucial determinants of body composition and most likely explain the shift in the relation between WC and obesity related abnormalities.

An increase in WC of the French had a larger effect on metabolic risk factors in comparison to Cameroonians. The higher age of the French population could be contributive to this finding. Urban Cameroonians may have had abdominal obesity for a shorter period compared to the French, explaining why despite being more obese they rather had lower metabolic parameters. The variation in risk factor levels between ethnic groups is partially driven by differences between ethnic groups in percent body fat at a given BMI.<sup>36</sup> Després et al found that<sup>15</sup> compared to black men, white men were characterized by increased visceral adipose tissue deposition, despite the fact that both groups had similar BMI and total body fat. Lovejoy et al. found that middle aged African American women had larger subcutaneous

abdominal fat depots, adjusted for total body fatness, but did not differ from white with regard to visceral adipose tissue.<sup>37</sup> Other studies have suggested that African American women have less visceral adipose tissue than age- and weight-matched white women.<sup>38-40</sup> Urban Cameroonian women and men had larger hip circumferences than their French counterparts. Accumulation of fat in parts of the body other than the visceral compartment can act as a buffer for the total amount of fat that can be stored, therefore reducing the adverse metabolic effects of excess body fat. Authors have found that a larger hip circumference was protective against CVD and diabetes.<sup>41-43</sup>

Marked differences in the distribution of abdominal obesity exist between genders, places of residence and ethnic groups. The use of the same cut-off points of WC for identification of abdominal obesity in Caucasians and black Africans is associated with large differences in levels of risk factors for CVD and diabetes, according to gender and place of residence. Existing action thresholds for the classification of abdominal obesity should be applied with caution in Black Africans. Improvement in diet and physical activity can slow the onset of CVD and diabetes. However, more precise estimates of risks are required before medical practitioners can determine when to suggest lifestyle changes to black Africans.

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## **FIGURES LEGENDS**

**Figure 1**—Age-adjusted mean arterial pressure (MAP) (A), fasting plasma glucose (B), HOMA-IR (C), and triglycerides (D) according to waist circumference, by place of residence and gender. R (rural), U (urban) and F (French) represent the increase in each parameter for a 5 cm increase in waist circumference.

The p for slope tests whether the slope differs from zero.