



## Cross-Sectional Study

### Prevalence and Determinants of Insulin Resistance in Asymptomatic Black Congolese with Essential Hypertension: A Cross-Sectional Study

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#### Abstract

**Background and aims:** Hypertensive patients with Insulin Resistance (IR) have an increased cardiovascular risk compared with those without IR. Thus, data on the prevalence and determinants of IR in essential hypertension are crucial to understanding the impact of this health problem and defining intervention or prevention strategies. The present study aimed to assess IR prevalence and identify its determinants in a consecutive hospital series of Black Congolese with essential hypertension.

**Methods:** A total of 105 asymptomatic, non diabetic participants with essential hypertension (56 men, 53.3%) aged  $57 \pm 11$  years were consecutively selected during outpatient consultations in Lomo Médical Clinic, Kinshasa, Democratic Republic of Congo. IR was defined as homeostatic model assessment-IR of  $\geq 2.5$ .

**Results:** IR prevalence was 48.5% (51/105). In multivariate analysis, adjusted for age, body weight, waist circumference, and BMI, the risk of IR was independently and significantly ( $p < 0.05$ ) associated

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**Citation:** Bernard KP, Aliocha NN, Muze M, Eleuthère KV, Jean-René MBK, et al. (2020) Prevalence and Determinants of Insulin Resistance in Asymptomatic Black Congolese with Essential Hypertension: A Cross-Sectional Study. J Cardiol Stud Res 6: 017.

**Received:** February 26, 2021; **Accepted:** March 10, 2021; **Published:** March 17, 2021

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with cigarette smoking (Odds Ratios [OR], 3.1; 95% Confidence Interval [CI], 1.2-8.5), hypertriglyceridemia (OR, 2.4; 95% CI, 1.1-5.3), hyperuricemia (OR, 2.7; 95% CI, 1.3-5.6), and uncontrolled hypertension (OR, 4.2; 95% CI, 2.1-7.4).

**Conclusion:** Almost half of the patients with essential hypertension appear to be insulin-resistant, and cardiovascular risk factors are more prevalent in this subset of patients. Smoking cessation, treating hypertriglyceridemia and hyperuricemia, and improving hypertension management could help prevent IR and the associated risks of morbidity and mortality in Black Congolese with essential hypertension.

**Keywords:** Black; Congolese; Determinants; Essential hypertension; Insulin resistance; Prevalence; Sub-Saharan African

#### Background

Essential hypertension is commonly associated with metabolic abnormalities, including Insulin Resistance (IR), the inability of a known quantity of exogenous or endogenous insulin to increase glucose uptake and utilization in an individual as much as it does in a normal population [1]. IR is a cardiovascular risk factor [2]. Indeed, IR assessed by Homeostatic Model Assessment (HOMA) has shown to be independently predictive of cardiovascular disease in several studies; one unit increase in IR is associated with a 5.4% increase in cardiovascular disease risk [3]. The link between IR and hypertension was confirmed by the European Group for the Study of IR, which demonstrated that Blood Pressure (BP) is directly correlated with IR and insulinemia, independently of age, gender, and obesity [4]. This correlation has serious consequences because IR and its manifestations have been shown to play a key role in the development of cardiovascular complications in patients with hypertension. Thus, insulin-resistant patients with hypertension would have an increased cardiovascular risk compared with non-insulin-resistant patients with hypertension and would require special medical attention [5-9]. Since almost all this information comes from studies conducted on Caucasian, American, and Asian populations, this study aims at determining the prevalence of IR and identifying its determinants in a Black Congolese population with essential hypertension. Indeed, data on the prevalence and determinants of IR in a population with hypertension is essential to understanding the importance of this health issue and defining intervention or prevention strategies.

#### Methods

Cross-sectional analysis was performed on data from 105 asymptomatic non diabetic participants with hypertension (56 men, 53.3%) aged  $57 \pm 11$  years. The participants were consecutively selected during outpatient consultations from January 5, 2012, to January 5, 2013, in Lomo Medical Clinic, a private hospital center in Limete, Kinshasa, Democratic Republic of Congo.

The inclusion criteria were age of 20 years and above; absence of previous cardiovascular history, including stroke, acute coronary

syndrome, and heart failure; and clinical or laboratory evidence of secondary hypertension and renal or hepatic disease. Participants in a gestational state were excluded from the study.

Participants were thoroughly assessed by a previously trained investigator for demographic data (age, sex), hypertension duration, and risk behavior (excess alcohol intake, cigarette smoking) using an ad hoc questionnaire. Anthropometric measurements (body weight in kg, height in cm, and waist circumference in cm) were taken of all participants using standard methods. Body Mass Index (BMI) was calculated as body weight (kg) divided by the square of body height (m<sup>2</sup>).

BP was noninvasively measured by home BP monitoring using an OMRON M6 BP monitor (OMRON Healthcare Co., Ltd., Kyoto, Japan) with a suitable cuff. The procedure was adequately explained to each participant.

Carbohydrate metabolism parameters (glycemia, insulin, glycated hemoglobin, HOMA-IR), lipid metabolism parameters (total cholesterol, high-density lipoprotein [HDL-C], low-density lipoprotein [LDL-C], triglycerides), and purine metabolism parameters (serum uric acid [SUA]) were assayed using standard methods. For all analyses, blood samples were collected between 7 a.m. and 9 a.m. from the cubital vein after an overnight fasting from 10 p.m. of the previous day. All analyses were conducted at the Lomo Médical Laboratory.

### Operational definitions

IR was defined as a HOMA-IR of  $\geq 2.5$  [10]. Uncontrolled hypertension was defined as an average home BP measurement greater than the treatment targets, i.e.  $> 130/80$  mmHg [11]. Cigarette smoking was defined as regular smoking for at least 30 days before the present study, regardless of the number of cigarettes [12].

Excessive alcohol consumption was defined as drinking  $> 2$  glasses of beer/day or the equivalent amount for at least one year. Hyperinsulinemia was defined as fasting insulin of  $>90$  mmol/L.

Abdominal obesity was defined as waist circumference of  $> 94$  cm for males and  $> 80$  cm for females [13]. Dyslipidemia was defined as HDL-C of  $<40$  mg/dL for males and  $<50$  mg/dL for females, an LDL-C of  $\geq 130$  mg/dL, total cholesterol level of  $\geq 185$  mg/dL, and/or triglyceride level of  $\geq 150$  mg/dL [14]. Hyperuricemia was defined as a uric acid of  $>7$  mg/dL [15].

### Statistical Analysis

Data were expressed as mean  $\pm$  standard deviation or relative frequency (%). Pearson's simple correlation coefficients were calculated to establish the relationship between two continuous variables. The independent determinants of IR were assessed using multiple linear regression.

Chi-square test and Student's t-test were used to compare the proportions and means of groups and subgroups, respectively.

Odds Ratios (ORs) and 95% Confidence Intervals (CI) were derived using logistic regression analysis to assess the relative contribution of each factor to the risk of a high HOMA-IR index. For the selection of variables in the logistic regression model, the minimum significance level to be included in the model was  $p < 0.05$ ,

which was considered the threshold of statistical significance.  $p < 0.01$  was considered the highly significant threshold, and  $p < 0.001$  was considered the very significant threshold.

### Ethical Considerations

This research was conducted in strict compliance with the recommendations of the Helsinki Declaration III. Approval to conduct the study was obtained from the National Health Ethics Committee (no. 219/CNES/BN/PMMF/2020). All respondents were debriefed on the results of the study.

### Results

Study participants ( $n = 105$ ) were all aged 35 years and over, with a mean age of  $50 \pm 6$  years (range, 35–60 years). Fifty-six (53.3%) were males and 49 (46.7%) were females. Men and women were distributed at a sex ratio of 1.14.

Table 1 illustrates similar values ( $p > 0.05$ ) of age, sex, hypertension duration, hypertension treatment, height, glycated hemoglobin, total cholesterol, and LDL-C in insulin-resistant group compared to non-insulin-resistant. Weight, WC, BMI, glycemia, insulinemia, and triglycerides were, on average, significantly higher ( $p < 0.05$ ) in the insulin-resistant group than in the non-insulin-resistant group. However, HDL-C was lower in the IR group.

| Parameters                | Whole group (n = 105) | IR+ (n = 51)    | IR- (n = 54)    | P      |
|---------------------------|-----------------------|-----------------|-----------------|--------|
| Age (years)               | 57 $\pm$ 11           | 57.1 $\pm$ 11.2 | 57.8 $\pm$ 13.4 | 0.750  |
| Males (%)                 | 56 (53.3)             | 32 (62.7)       | 24 (44.4)       | 0.342  |
| HTN duration (years)      | 10 $\pm$ 9.4          | 11 $\pm$ 6.7    | 10.8 $\pm$ 3.5  | 0.781  |
| Weight (kg)               | 87 $\pm$ 15           | 90.5 $\pm$ 14.8 | 71.1 $\pm$ 10.6 | 0.000  |
| Height (cm)               | 1.6 $\pm$ 0.1         | 1.6 $\pm$ 7.8   | 1.6 $\pm$ 6.8   | 0.989  |
| Waist circumference (cm)  | 99.3 $\pm$ 11.6       | 102.4 $\pm$ 9.6 | 85.0 $\pm$ 9.7  | 0.000  |
| BMI (kg/m <sup>2</sup> )  | 32.4 $\pm$ 6.1        | 33.6 $\pm$ 5.7  | 26.4 $\pm$ 4.4  | 0.000  |
| Glycemia                  | 100 $\pm$ 41          | 105 $\pm$ 10    | 95 $\pm$ 13     | 0.03   |
| Insulinemia ( $\mu$ U/mL) | 13.2                  | 17 $\pm$ 16     | 10 $\pm$ 5      | <0.001 |
| HOMA-IR                   | 8.7 $\pm$ 3.4         | 9.8 $\pm$ 2.7   | 2.1 $\pm$ 2.0   | 0.012  |
| Glycated hemoglobin (%)   | 5.0 $\pm$ 2           | 5.5 $\pm$ 1     | 5.1 $\pm$ 1     | 0.42   |
| Total cholesterol (mg/dL) | 190 $\pm$ 22          | 200 $\pm$ 20    | 195 $\pm$ 37    | 0.81   |
| HDL-C (mg/dL)             | 48.7 $\pm$ 12         | 40 $\pm$ 09     | 55 $\pm$ 10     | 0.012  |
| LDL-C (mg/dL)             | 123 $\pm$ 22          | 125 $\pm$ 28    | 122 $\pm$ 34    | 0.45   |
| Triglycerides (mg/dL)     | 170 $\pm$ 54          | 190 $\pm$ 81    | 118 $\pm$ 75    | <0.001 |
| SUA                       | 7.5 $\pm$ 5           | 9.2 $\pm$ 3     | 6 $\pm$ 5       | <0.001 |

**Table 1:** Demographic, clinical and biological characteristics of the study population.

IR: Insulin Resistance; HTN: Hypertension; BMI: body mass index; HOMA-IR: Homeostatic Model Assessment for Insulin Resistance; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density lipoprotein Cholesterol; SUA: Serum Uric Acid

The data presented in Table 2 indicate a statistically similar proportion of participants with heavy alcohol intake, overall obesity, high total cholesterol, and high LDL-C in the IR and non-IR groups. In contrast, the smoking rate, abdominal obesity, HDL-C, hypertriglyceridemia, and hyperuricemia were, on average, significantly higher in the IR groups.

Table 3 shows the IR prevalence of the study population and different subgroups of this population. At the threshold for defining

IR (HOMA-IR  $\geq 2.5$ ), the hospital IR prevalence rate was 48.5% (51/105). In patients with uncontrolled BP, the prevalence was 64.2% (45/70); in those with controlled BP, the prevalence was 26% (7/35). In obese hypertensive patients, the prevalence was 62.7% (42/67) vs. 39.5% (15/38) in non-obese hypertensive patients with hypertension who are nonobese.

| Parameters                     | IR+ (n = 51) | IR- (n = 54) | p      |
|--------------------------------|--------------|--------------|--------|
| Alcohol intake                 | 25.4 (13)    | 5.5 (3)      | 0.051  |
| Cigarette smoking              | 14 (7)       | 5.6 (3)      | 0.032  |
| WC > 94 cm (males)             | 43.1 (22)    | 22.2 (12)    | <0.001 |
| WC > 80 cm (females)           | 39.2 (20)    | 26 (14)      | <0.001 |
| BMI > 30 kg/m <sup>2</sup>     | 51 (26)      | 46.3 (25)    | 0.075  |
| TC > 185 mg/dL (%)             | 39.2 (20)    | 29.6 (16)    | 0.27   |
| HDL-C < 50 mg/dL (female)      | 19.6 (10)    | 7.4 (4)      | <0.001 |
| HDL-C < 40 mg/dL (male)        | 45 (23)      | 9.2 (5)      | <0.001 |
| LDL-C $\geq 130$ mg/dL         | 27.4 (14)    | 24.1 (13)    | 0.20   |
| Triglycerides $\geq 150$ mg/dL | 68.6 (35)    | 22.2 (12)    | <0.001 |
| SUA > 7 mg/dL                  | 64.7 (33)    | 29.6 (16)    | 0.012  |

**Table 2:** Cardiovascular risk factors according to the presence of IR.

IR: Insulin Resistance; WC: Waist Circumference; BMI: Body Mass Index; TC: Total Cholesterol; HDL-C: High-Density Lipoprotein Cholesterol; LDL-C: Low-Density Lipoprotein Cholesterol; SUA: Serum Uric Acid

| Subgroups                          | Prevalence % (n) |
|------------------------------------|------------------|
| Whole group                        | 48.5 (51/105)    |
| Participants with uncontrolled HTN | 64.2 (45/70)     |
| Participants with controlled HTN   | 26 (7/35)        |
| Obese participants                 | 62.7 (42/67)     |
| Nonobese participants              | 39.5 (15/38)     |

**Table 3:** Prevalence of IR in the study population and different subgroups of this population.

IR: Insulin Resistance; HTN: Hypertension

The risk factors for IR (Table 4) included age  $\geq 55$  years, uncontrolled BP, smoking, hypertriglyceridemia, total hypercholesterolemia, and hyperuricémie.

In multivariate analysis adjusted for age, body weight, waist circumference, and BMI, the risk of IR was independently and significantly ( $p < 0.05$ ) associated with cigarette smoking, hypertriglyceridemia, hyperuricemia, and uncontrolled hypertension (Table 5), as according to the following equation:

$$Y = -1.404 + 1.054 \text{ cigarette smoking} + 0.872 \text{ hypertriglyceridemia} + 0.983 \text{ hyperuricemia} + 0.852 \text{ uncontrolled hypertension.}$$

## Discussion

To our knowledge, this is the very first study to assess IR prevalence and determinants in a Congolese Black hypertensive in-hospital population. Cigarette smoking, hypertriglyceridemia, hyperuricemia, and uncontrolled hypertension appear to be independent determinants of IR. Additionally, a higher frequency of cardiovascular risk factors was noted among IR participants.

| Independent Variables  | OR (95% CI)<br>(% vs. %)<br>P           |
|--|---|
| Age<br><55 years vs. $\geq 55$ years                         | 2.1 (1.3-10)<br>84.7 vs. 15.3<br>0.03   |
| Uncontrolled HTN<br>Yes vs. No                               | 9.8 (4.9-10)<br>64.2 vs. 33.4<br>0.017  |
| Cigarette smoking<br>Yes vs. No                              | 3.1 (1.2-8.5)<br>14.0 vs. 2.0<br>0.03   |
| Triglycerides $\geq 150$ mg/dL<br>Yes vs. No                 | 2.7 (1.3-5.6)<br>68.6 vs. 22.2<br><0.01 |
| Total cholesterol (mg/dL)<br>$\geq 185$ mg/dL vs. <185 mg/dL | 9.9 (5-10.2)<br>39.2 vs. 29.0<br>0.008  |
| SUA > 7 mg/dL (%)<br>>6.5 mg/dL vs. $\leq 6.5$ mg/dL         | 2.2 (1.8-5.6)<br>64.7 vs. 29.6<br>0.04  |

**Table 4:** IR risk factors.

IR: Insulin Resistance; HTN: Hypertension; SUA: Serum Uric Acid

| Independent variables              | Nonstandardized coefficients |       |          | OR (95% CI)   | p       |
|------------------------------------|------------------------------|-------|----------|---------------|---------|
|                                    | B                            | SE    | $\chi^2$ |               |         |
| Cigarette smoking<br>Yes vs. No    | 1.054                        | 0.552 | 4.647    | 3.1 (1.2-8.5) | 0.049   |
| Hypertriglyceridemia<br>Yes vs. No | 0.872                        | 0.406 | 4.619    | 2.4 (1.1-5.3) | 0.032   |
| Hyperuricemia<br>Yes vs. No        | 0.983                        | 0.381 | 6.652    | 2.7 (1.3-5.6) | <0.0001 |
| Uncontrolled HTN<br>Yes vs. No     | 0.852                        | 0.381 | 8.293    | 4.2 (2.1-7.4) | <0.0001 |
| Constant                           | -1.404                       | 0.258 | 29.512   |               | <0.0001 |

**Table 5:** Independent determinants of IR in the study population.

IR: Insulin Resistance; OR: Odds Ratio; CI: Confidence Interval; HTN: Hypertension

Some studies have found a similar IR prevalence of almost 50% in essential hypertension [16-18]. However, Garcia-Puig et al. [19] obtained a prevalence of 9.3%, whereas Mohteshamzadeh et al. [20] obtained a prevalence of 20%. These results greatly differ from ours. Several explanations can justify this disparity, including the methodology used to characterize IR and, for studies that also used the HOMA-IR index, the definition thresholds used. For example, Garcia-Puig, et al. set the threshold arbitrarily at 3.8, whereas it was set at 3.0 in the study by Mohteshamzadeh, et al. [19,20]. Studies using direct diagnostic methods for IR, such as that by Lima, et al. [18], also concluded that nearly 50% of patients with essential hypertension were insulin-resistant, whether treated or not.

The HOMA-IR index has been the subject of numerous validations and has shown a satisfactory correlation ( $r = 0.72-0.82$ , depending on the studies) with the hyperinsulinemic-euglycemic clamp, the gold standard for measuring insulin sensitivity, without any notable

difference, depending on sex, age, weight, diabetic status, and elevated BP [21]. HOMA-IR has the advantage of ease of implementation. No standard HOMA-IR threshold has been established to define IR in the population of Sub-Saharan Black with hypertension. The threshold of 2.5 used in this study has been used in various studies conducted in African [22], African American [10], Euro-American [23], Caucasian [24], and Asian populations [25,26].

The present study identified cigarette smoking, hypertriglyceridemia, hyperuricemia, and hypertensive failure as independent determinants of IR in essential hypertension. Numerous studies have shown that smoking is associated with both insulin secretory deficiency and IR [27,28]. Insulin secretory deficiency is thought to be due to a direct deleterious effect of nicotine on the  $\beta$  cells of the islets of Langerhans. Indeed, nicotine has been found to influence insulin secretion by binding to nicotinic acetylcholine receptors located on the  $\beta$  cells of the islets of Langerhans and increase the apoptosis of these  $\beta$  cells [29-31]. According to some studies, smoking is associated with the hypertrophy of visceral adipose tissue, which is linked to IR [32]. Indeed, Canoy, et al. [33] demonstrated in a large British population study that the waist/hip ratio was higher in smokers compared with non smokers after adjusting for age, BMI, alcohol consumption, total energy intake, and physical activity level. The same study found that a higher waist/hip ratio was directly associated with the number of pack-years in current smokers and former smokers and conversely with the time since smoking cessation in former smokers. The effects of smoking on IR may therefore be mediated, at least in part, by visceral fatty tissue hypertrophy and subsequent systemic inflammation.

IR has been shown to be often accompanied by dyslipidemia as part of the metabolic syndrome. In fact, the current dominant paradigm is that IR leads to dyslipidemia. However, recent evidence from epidemiological, genetic, and interventional studies suggest that hypertriglyceridemia may also cause IR through mechanisms not yet understood [34].

The identification of hyperuricemia as a determinant of IR is in agreement with the study by Han, et al. who found that hyperuricemia may be a causative factor in the development of IR [35]. De Miranda et al. found a 91% increase in the chance of insulin resistance for every increase of 1 mg/dL in serum uric acid levels [36]. Another solid evidence of this causal relationship has been provided by Takir, et al. by demonstrating that the decrease in uric acid in hyper uricaemic is effective in improving insulin resistance [37].

No previous study has demonstrated a link between uncontrolled BP and IR. This result is in agreement with the study by Izzo et al. [38] who demonstrated in a prospective cohort of nondiabetic patients with hypertension that uncontrolled hypertension doubled the risk of developing type 2 diabetes mellitus regardless of age, BMI, BP, basal blood sugar, or fasting blood sugar.

The present study showed a higher frequency of smoking, abdominal obesity, low HDL-C, hypertriglyceridemia, and hyperuricemia in IR participants. This is in agreement with the many previous studies that have shown that IR patients with hypertension have an increased cardiovascular risk. As often described in the literature, the development of cardiovascular risk factors tends to aggregate to form IR syndrome or cardio metabolic syndrome [39].

The present study acknowledges the following methodological limitations:

1. The cross-sectional design of this study did not allow the establishment of causal links.
2. The single-center aspect of this study limits the generalization of the obtained results to the entire population with hypertension.
3. The alternative method of IR assessment used in the present study, although having been widely validated elsewhere for the assessment of IR in patients with hypertension, has relatively lower sensitivity compared with the standard reference method. This implies the possibility that the IR prevalence of IR obtained in the present study may be an underestimate.

To overcome these limitations, further studies are needed, and these studies should be longitudinal and community-based and, if possible, should define IR prevalence by the reference method. Notwithstanding these methodological limitations, the present study is the first to describe IR as a cardiometabolic risk factor in a population of Black Congolese with hypertension. Furthermore, the present study is the first to establish that the lack of BP management increases predisposition to IR.

## Conclusion

The present study showed that IR is present in almost half of the population of Black Congolese with hypertension. Cigarette smoking, hypertriglyceridemia, hyperuricemia, and uncontrolled hypertension appear to be independent determinants of IR. Furthermore, IR people with hypertension have a higher prevalence of cardiovascular risk factors, which suggests an increased risk of cardiovascular events.

## Acknowledgments

The authors are grateful to the medical and administrative staff of LomoMedical Clinic for accepting and facilitating the completion of this study.

## Contributorship

KPB, LMB, and MKJR: design and concept of study  
KPB, MM, and NNA: data acquisition  
KPB and MM: manuscript draft  
NNA, KPB, MM, KVE, LMB, and MKJR: data analysis and interpretation  
All authors have read and approved the final manuscript.

## Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## Ethical Approval

Approval to conduct the study was obtained from the National Health Ethics Committee (no. 219/CNES/BN/PMMF/2020). All respondents were debriefed on the results of the study.

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