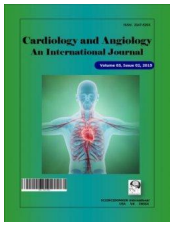

Cardiology and Angiology: An International Journal

7(3): 1-11, 2018; Article no.CA.41565
ISSN: 2347-520X, NLM ID: 101658392

Association of Metabolic Markers of Insulin Resistance with Blood Pressure in Prehypertensive Adults in Makurdi, Nigeria

Ayu Agbecha[1*], Rebecca M. Gali[2], Elija N. Yisa[3] and Chidozie E. Agu[3]

[1]Department of Chemical Pathology, Federal Medical Center Makurdi, Nigeria.
[2]Chemical Pathology Unit, Department of Medical Laboratory Science, University of Maiduguri, Nigeria.
[3]Chemical Pathology Unit, Department of Medical Laboratory Science, University of Calabar, Nigeria.

Authors' contributions

This work was carried out in collaboration between all authors. Author AA designed the study. Authors AA, RMG, ENY and CEA wrote the protocol of the study. Authors AA and RMG wrote the first draft of the manuscript. Authors AA, RMG, ENY and CEA managed the literature searches. Authors AA and RMG performed the statistical analysis. Authors AA, RMG and ENY managed the analyses of the study. All authors read and approved the final manuscript.

Article Informatioqn

DOI: 10.9734/CA/2018/41565
Editor(s):
(1) Thiago Andrade de Macedo, Hypertension Unit, Cardiology Division Heart Institute (InCor), Brazil.
Reviewers:
(1) Hassan A. Shora, Ismailia General Hospital, Egypt.
(2) Mra Aye, Melaka Manipal Medical College, Malaysia.
Complete Peer review History: http://www.sciencedomain.org/review-history/25893

Original Research Article

Received 7th March 2018
Accepted 11th May 2018
Published 16th August 2018

ABSTRACT

Background of Study: Previous studies observed insulin resistance in the hypertensive population. However, evidence-based studies of insulin resistance in prehypertension are scant.
Aim: Our study aimed at determining the presence of insulin resistance and its correlation with blood pressure in prehypertensive adults.
Materials and Methods: This was a case-control study involving randomly selected 70 healthy adults in Makurdi, Nigeria. Anthropometric parameters and metabolic markers of insulin resistance (fasting plasma glucose (FPG), homeostasis model assessment of insulin resistance [HOMA-IR], fasting serum insulin [FSI], triglycerides [TGs], triglyceride/high density lipoprotein cholesterol [HDL-C] ratio [TG/HDL-C]) in apparently healthy adults were measured. The metabolic markers of IR in 35

**Corresponding author: E-mail: agbechaayu@gmail.com;*

prehypertensives were compared with anthropometrically matched 35 normotensive controls using the student's *t*-test. Associations of blood pressure (systolic-SBP and diastolic-DBP) with metabolic markers of insulin resistance in prehypertensives and normotensives were determined using Pearson correlation analysis.

Results: A significantly elevated (P<0.05) SBP, DBP, FSI, and HOMA-IR was observed in prehypertensives compared to matched normotensive controls. A significant positive correlation (P<0.01) was observed between SBP and insulin (r=0.762), HOMA-IR (r=0.756), TGs (r=0.586), TG/HDL-C (r=0.499); DBP and insulin (r=0.659), HOMA-IR (r=0.634), TGs (r=0.469), TG/HDL-C (r=0.469) in prehypertensives. In normotensives, a significant positive correlation (P<0.05) was observed between DBP and TGs (r=0.371), TG/HDL-C (r=0.376); age (r=0.372), BMI (r=0.523), WC (r=0.338).

Conclusion: Our study shows that insulin resistance is associated with elevated blood pressure and could mediate the progression of normotension through prehypertension to hypertension.

Keywords: Prehypertension; insulin resistance; lipids; blood pressure.

1. INTRODUCTION

Insulin resistance is classically defined as decreased sensitivity or responsiveness of tissue cells to the metabolic actions of insulin [1]. Insulin resistance accompanied with compensatory hyperinsulinemia is a component and common pathway for other symptoms of the metabolic syndrome [1]. The Impaired sensitivity of cardiovascular tissues to insulin is linked with cardiovascular diseases and the development of hypertension [2].

Three different categories of blood pressure have been described by the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment (JNC 7) of high blood pressure [3]. These include; normotension when the systolic and diastolic blood pressure (BP) is <120 and <80 mm Hg respectively; prehypertension when systolic BP is 120 to 139 mm Hg or diastolic BP is 80 to 89 mm Hg; and hypertension systolic BP is ≥140, or diastolic BP is >90 mm Hg. Recently, America's JCN-8 proposed a new classification of high blood pressure [4]. This new guideline sub-divides the widely acceptable JNC-7 prehypertension into; raised blood pressure (as persons with systolic BP between 120-129 mmHg and diastolic BP less than 80 mmHg) and Stage 1- hypertension (systolic between 130-139 or diastolic between 80-89). Hypertension according to JCN-7 guideline is renamed stage 2 hypertension and the definition of normotension maintained. Data analysed from 30 958 US adults ≥20 years of age who participated in the National Health and Nutrition Examination Surveys between 1999 and 2012, put the prevalence of prehypertension as 28.2% [5]. This survey further showed that prehypertension frequently progressed to clinical hypertension over these years [5].

The euglycemic glucose clamp method is the standard gold method for the measurement of insulin resistance [6], but HOMA-IR is comparable. This method is difficult for use in large population studies, since it involves the intravenous infusion of insulin, frequent blood sampling over a three hour period, with continuous glucose infusion. The determination of plasma insulin levels and homeostasis model assessment of insulin resistance (HOMA-IR) are the widely used surrogate methods of evaluating insulin resistance [7]. Other methods adopted is the determination of plasma triglycerides (TGs) and triglycerides/high- density lipoprotein cholesterol (TG/HDL-C) ratio [8,9] with TG/HDL-C ratio proposed the most accurate among all the surrogate markers.

Elevated BP has been reported as the most prevalent component of the metabolic syndrome [10]. The presence of metabolic syndrome has been reported to increase the cardiovascular risk associated with high BP, which increases the deleterious vascular effects of hypertension [11]. There are reports of association of insulin resistance with hypertension [12]. However, few studies that reported insulin resistance in prehypertensives did not consider the confounding effects of lifestyle, age, and adiposity on elevated BP [13,14]. These non-homogenous samples led to the generalisation of results. We considered these confounding effects, in the selection of study participants to obtain results free from interferences. Our study aimed at determining insulin resistance and its association with blood pressure in prehypertensive individuals.

2. MATERIALS AND METHODS

2.1 Study Design

The case-control study compared the anthropometric and metabolic markers of insulin resistance in prehypertensives with normotensive controls.

2.2 Study Area and Population

A sample of male and female participants aged 18-55 years, was randomly drawn from patients attending general health checkup at the Federal Medical Centre Makurdi, from March 2016 to May 2016.

2.3 Sample Size

The sample size was determined using the formula for case-control studies that compare two group means [15]; $n=1+2C(s/d)^2$, At a significance level of 5%, and statistical power of 90%, the calculated sample size was 32.4, which was approximated to 35 for each group.

2.4 Selection Criteria

Individuals were eligible to participate in the study if they: (a) were adults and middle aged (18 to 55 years); (b) had no history of hypertension and were not using antihypertensive medications; (c) had no history of cardiovascular disease (coronary disease, stroke, peripheral vascular disease) and were not using lipid lowering drugs; (d) were free of any other major systemic illnesses (e.g. cancer, diabetes mellitus); (e) were nonsmokers; (f) were not pregnant; (g) were not overweight (≥25-29.9 kg/m²) or obese (≥30 kg/m²). All subjects were provided written informed consent, and the study was approved by the institutional ethical committee.

2.5 Data Collection

Participants on a 12 hour overnight fast provided information on their demographic characteristics, detailed medical history, dietary and lifestyle habits.

2.5.1 Blood pressure

All participants rested at least 30 min. Blood pressure measurements were taken using an aneroid manometric sphygmometer, three times with the right arm relaxed and well supported by a table, at an angle of 45-degrees from the trunk. Prehypertensives and normotensives were defined according to JNC 7 criteria [3].

2.5.2 Body mass index and waist circumference

Body weight to the nearest 0.1 kg and height to the nearest centimeter were measured and BMI was calculated as weight (kilograms)/height (meters squared). Waist circumference (WC) was measured horizontally at the level of the natural waist. Body mass index was categorized according to the international classification of world health organization [16]; underweight defined as persons with BMI ≤18.5 kg/m², normal weight as individuals with BMI ranging from 20-24.9 kg/m², those with BMI ≥25-29.9 kg/m² are overweight, and obese as individuals with BMI ≥30 kg/m².

2.5.3 Blood sample collection

Participant's blood samples were collected into plain and fluoride oxalate vacutainer tubes and centrifuged at 3000 rpm for 10 min within 1 h of blood collection. Blood in plain and fluoride oxalate vacutainers was respectively used for the determination of plasma lipids, insulin, and glucose. Fasting plasma glucose and lipids were determined immediately after separation; while serum extracted for insulin determination was stored at -20°C for laboratory evaluation.

2.6 Laboratory Methods

2.6.1 Determination of fasting plasma glucose and serum lipids

The Barham and Trinder glucose oxidase colorimetric end-point method was used in the determination of plasma glucose [17]. Total cholesterol, HDL‑C, and TGs were determined by the colorimetric end-point method. Low DL-C and VLDL‑C were estimated using the Friedewald equation [18].

2.6.2 Determination of serum insulin

The insulin enzyme-linked immunoabsorption assay (ELISA) method was used in determining serum insulin, based on the ELISA sandwich principle.

2.6.3 Homeostasis model of insulin resistance (HOMA-IR)

Insulin resistance was determined using a standardized Microsoft excel HOMA 2 calculator, based on Matthews et al.'s formula [19].

2.7 Statistical Analysis

The statistical package IBM Armonk, New York, United States SPSS version 21 was used in analyzing the data generated. Descriptive statistics were used in determining the mean and standard deviation of the parameters measured. The Student's *t*-test was used in comparing the mean of the parameters in prehypertensive and control groups. Pearson correlation analyses were done to test the association between parameters measured in prehypertensives and normotensives. Two-tailed $P < 0.05$ was considered statistically significant.

3. RESULTS

Table 1 shows systolic blood pressure (SBP), diastolic blood pressure (DBP), age, WC, BMI, fasting serum insulin (FSI), fasting plasma glucose (FPG), HOMA-IR, fasting total cholesterol, HDL-C, LDL-C, VLDL-C, and triglyceride in prehypertensives and normotensives. There was no significant ($P > 0.05$) difference between the mean age, WC, and BMI of prehypertensives and normotensives. However, a significantly elevated SBP ($P = 0.000$), DBP ($P=0.000$), FSI ($P=0.012$), and HOMA-IR ($P=0.016$) was observed in prehypertensives compared to anthropometrically matched normotensive controls. No significant ($P > 0.05$) difference in mean fasting plasma glucose and lipids was observed in prehypertensives compared to the matched normotensive controls.

A significant positive correlation was observed between SBP and insulin ($P=0.000$, r=0.762)[Fig. 1], DBP and insulin ($P=0.000$, r=0.659)[Fig. 2], SBP and HOMA-IR ($P=0.000$, r=0.756)[Fig. 3], DBP and HOMA-IR ($P=0.000$, r=0.634)[Fig. 4], SBP and TG/HDL-C ($P=0.002$, r=0.499)[Fig. 5], DBP and TG/HDL-C ($P=0.005$, r=0.469)[Fig. 6], in prehypertensives. Table 2 shows a significant positive correlation between SBP and TGs ($P=0.000$, r=0.586), DBP and TGs ($P=0.005$, r=0.469) in prehypertensive adults. A significant positive correlation was observed between DBP and TGs ($P=0.028$, r=0.371), age ($P=0.028$, r=0.372), BMI ($P=0.001$, r=0.523), WC ($P=0.047$, r=0.338), TG/HDL-C ($P=0.026$, r=0.376) [Table 3] in normotensive adults. However, no significant correlation ($P>0.05$) was observed between SBP and the metabolic parameters in the normotensive group.

Table 1. Blood pressure, anthropometric, Insulin, FPG, HOMA-IR in prehypertensive and normotensive adults

Parameters	PreHTN N=35	Control N=35	Calc. t-value	P-value
SBP mmHg	130.91±8.70	111.03±6.89	10.6	0.000*
DBP mmHg	83.17±5.86	70.40±3.87	10.8	0.000*
Age (years)	35.57±10.73	33.63±9.10	0.82	0.417
WC cm	69.17±10.04	68.20±5.96	0.57	0.568
BMI Kg/m²	24.72±3.39	24.40±3.51	0.40	0.694
Insulin pmol/l	70.81±34.58	50.50±30.74	2.60	0.012*
FPG mmol/l	4.31±0.59	4.24±0.51	0.52	0.603
HOMA-IR	1.25±0.61	0.91±0.54	2.46	0.016*
T.Chol. mmol/l	4.28±0.63	4.18±0.58	0.71	0.483
HDL-C mmol/l	1.61±0.37	1.59±0.37	0.98	0.848
LDL-C mmol/l U/L	2.21±0.70	2.14±0.70	0.45	0.658
VLDL-C mmol/l	0.49±0.22	0.45±0.13	1.10	0.274
TGs mmol/l	1.00±0.38	0.94±0.30	0.77	0.445

*mean ± standard deviation, *significant, SBP- systolic blood pressure, DBP- diastolic blood pressure, WC- waist circumference,*

BMI- body mass index, FPG- fasting plasma glucose, HOMA-IR- homeostatic model assessment of insulin resistance, HDL-C-high-density lipoprotein cholesterol, LDL-C- low-density lipoprotein cholesterol, VLDL-C- very low-density lipoprotein cholesterol, TGs- triglyceride

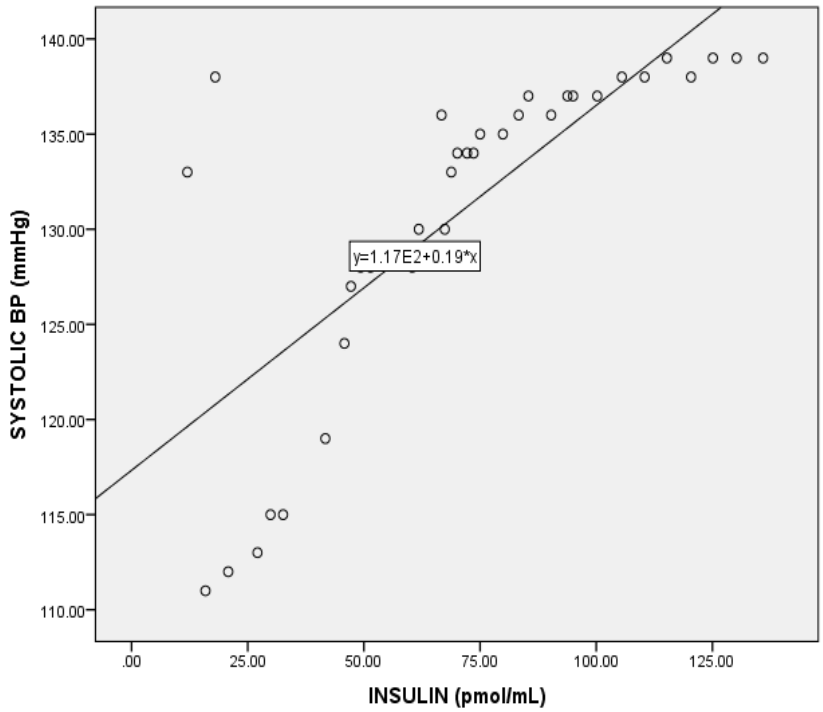

Fig. 1. Correlation of insulin with systolic blood pressure in prehypertensives
n=35, r=0.762, p=0.000, BP- blood pressure

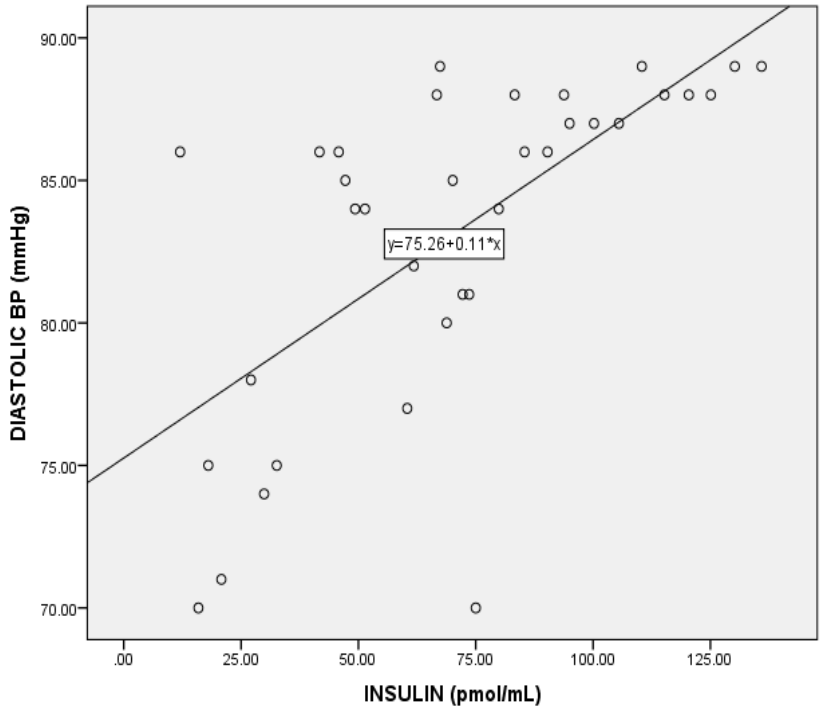

Fig. 2. Correlation of insulin with diastolic blood pressure in prehypertensives
n=35, r=0.659, p=0.000, BP- blood pressure

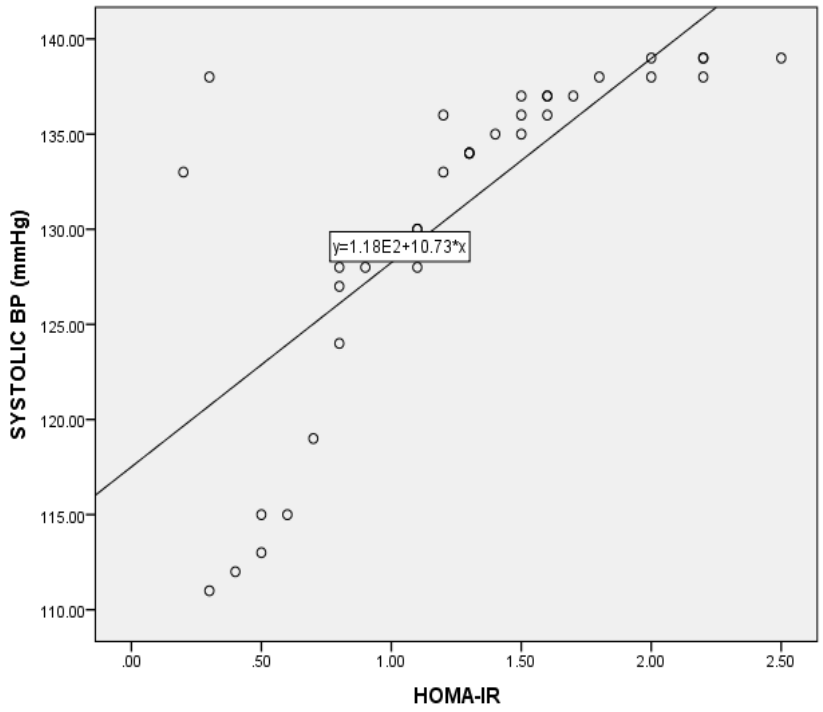

Fig. 3. Correlation of HOMA-IR with systolic blood pressure in prehypertensives
n=35, r=0.756, p=0.000, BP- blood pressure, HOMA-IR- homeostasis model assessment of insulin resistance

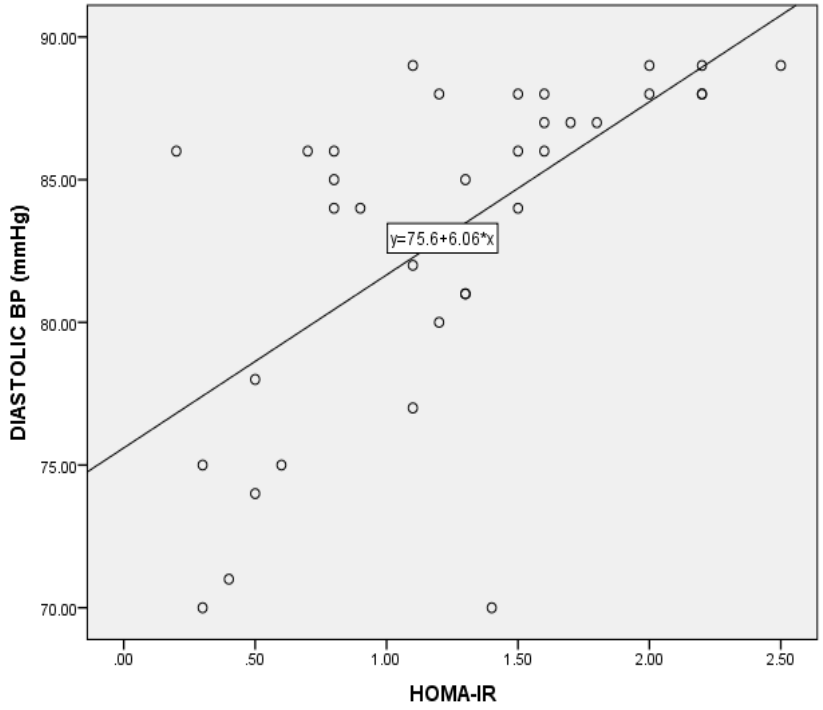

Fig. 4. Correlation of HOMA-IR with diastolic blood pressure in prehypertensives
n=35, r=0.634, p=0.000, BP- blood pressure, HOMA-IR- homeostasis model assessment of insulin resistance

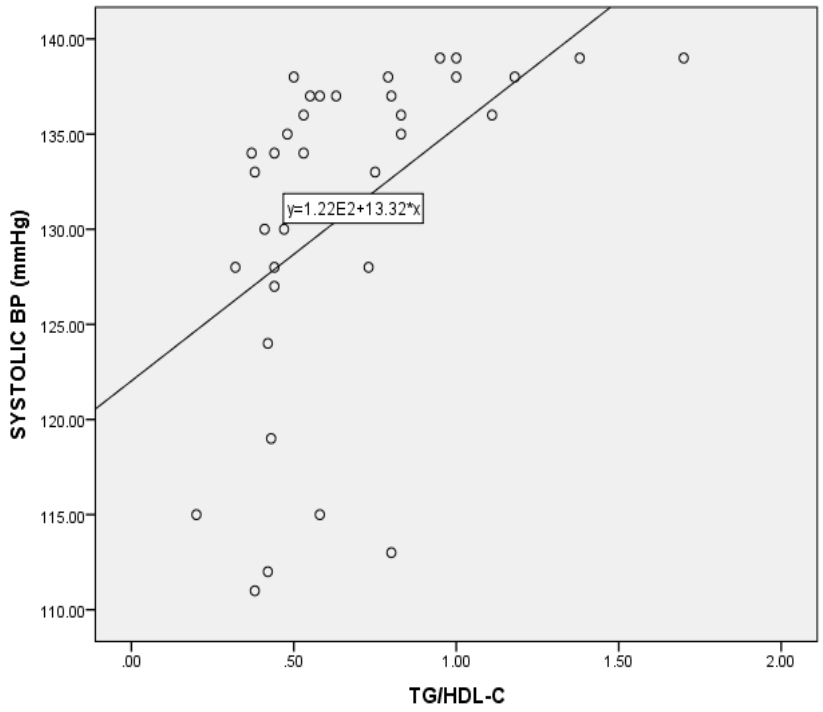

Fig. 5. Correlation of TG/HDL-C with systolic blood pressure in prehypertensives

n=35, r=0.499, p=0.000, BP- blood pressure, TG/HDL-C -triglycerides/high density lipoprotein cholesterol ratio

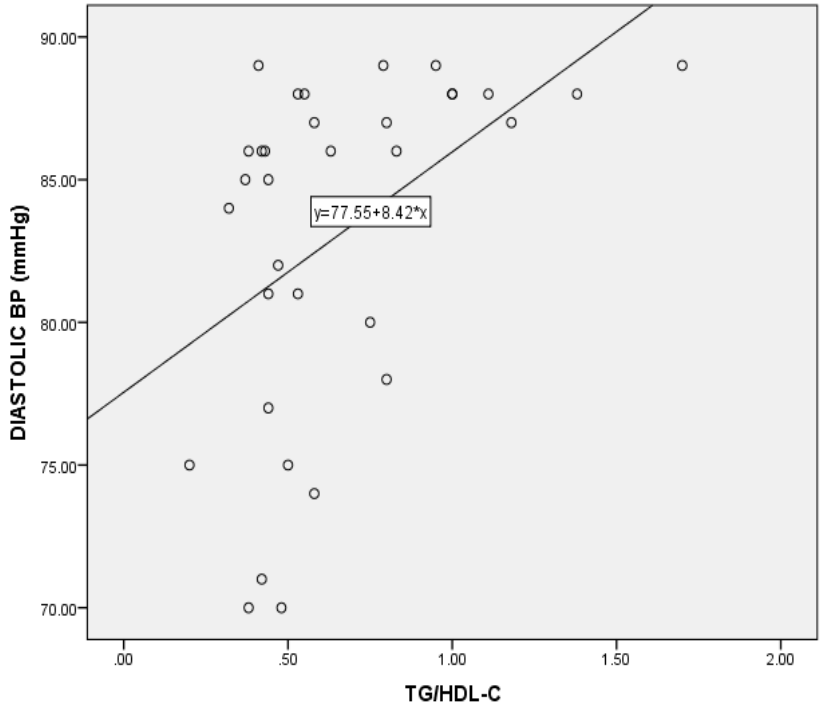

Fig. 6. Correlation of TG/HDL-C with diastolic blood pressure in prehypertensives

n=35, r=0.469, p=0.000, BP- blood pressure, TG/HDL-C -triglycerides/high density lipoprotein cholesterol ratio

Table 2. Pearson's correlation coefficients of blood pressure with some metabolic indices and age in prehypertensive adults

Parameters	SBP	DBP
TC	0.092	-0.127
HDL-C	-0.164	-0.281
LDL-C	0.037	-0.054
VLDL-C	0.482**	0.309
TGs	0.586**	0.469**
FPG	-0.126	-0.179
Age	-0.062	-0.075
WC	0.284	0.082
BMI	0.193	0.266

***Correlation is significant at the 0.01 level (2-tailed), SBP- systolic blood pressure, DBP- diastolic blood pressure, HOMA-IR- homeostatic model assessment of insulin resistance, HDL-C- high-density lipoprotein cholesterol. LDL-C- low-density lipoprotein cholesterol, VLDL-C- very low-density lipoprotein cholesterol, Triglycerides-TGs*

Table 3. Pearson's correlation coefficients of blood pressure level with metabolic indices and age in normotensive adults

Parameters	SBP	DBP
TC	-0.191	0.054
HDL-C	-0.047	-0.142
LDL-C	-0.154	0.052
VLDL-C	0.103	0.368*
TGs	0.046	0.371*
TG/HDL-C	0.050	0.376*
Insulin	0.178	0.149
HOMA-IR	0.188	0.163
FPG	0.072	0.134
Age	0.055	0.372*
WC	-0.136	0.338*
BMI	-0.013	0.523**

***Correlation is significant at the 0.01 level (2-tailed), *Correlation is significant at the 0.05 level (2-tailed). SBP- systolic blood pressure, DBP- diastolic blood pressure, HOMA-IR- homeostatic model assessment of insulin resistance, HDL-C- high- density lipoprotein cholesterol, LDL-C- low-density lipoprotein cholesterol, VLDL-C- very low density lipoprotein cholesterol, TGs- triglycerides,. TG/HDL-C -triglycerides/high density lipoprotein cholesterol ratio*

4. DISCUSSION

Insulin resistance (IR), defined as a reduced biological action of insulin, has emerged as a major pathophysiological factor in the development and progression of a number of cardio-metabolic disorders like type 2 diabetes mellitus, dyslipidemia, hypertension and cardiovascular diseases. We determined plasma TGs and TG/HDL-C ratio in addition to plasma insulin and HOMA-IR as indicators of insulin resistance, based on the reports of Baez-Duarte et al. and Salazar et al. [8,9]. An increase in blood pressure levels with age and BMI has been earlier described [14]. Our study population was recruited taking into account the confounding effect of age and adiposity. This allowed us to assess blood pressure level more likely related to insulin resistance and not on confounding effects. Since evidence-based studies regarding the risk factors of prehypertension are scant compared to hypertension, we sought to examine the presence of insulin resistance and its association with blood pressure in prehypertensive adults.

Our study observed elevated insulin level and HOMA-IR in prehypertensive adults compared to normotensive controls. We found a positive correlation between metabolic markers of insulin resistance (FSI, HOMA-IR, TG/HDL-C, TGs) with systolic and diastolic BP in prehypertensive adults. Substantial evidence suggests that hypertensive patients are insulin resistant compared with normotensive individuals [2,20, 21]. Similar reports of an association between blood pressure and insulin resistance in prehypertensives exist. Metabolic syndrome in active subjects in Spain (MESYAS) registry substudy reported that insulin resistance had an impact on prehypertension in 19,041 healthy active workers [14]. Among community-dwelling persons, Kawamoto et al. showed that SBP and DBP increased with HOMA-IR in prehypertensive subjects [22]. Hwu et al. without adjustment for confounding factors observed elevated fasting plasma insulin and HOMA-IR in prehypertensives compared to normotensives. After adjustment for confounding factors, no difference was observed between the two comparable groups. However, prehypertension was associated with IR, independent of age, gender, obesity and physical inactivity [13]. In other studies, TGs has been shown to be associated with prehypertension in young [23] and middle-aged subjects [24]. Cubeddu et al. argued that when the contribution of confounding variables such as older age, obesity and sedentary lifestyle was taken into account, the association between IR and BP would commonly disappear [25]. In our study, the subjects with prehypertension were associated with IR.

Hyperinsulinaemia accompanying insulin resistance in our study is a physiologic response mediated by the feedback stimulation of pancreatic beta cells, geared towards meeting the metabolic demands of the body [26]. The link between insulin resistance and blood pressure observed in our study could be due to the complex vascular actions of insulin that occur as either vascular protective or deleterious effects [27]. Insulin enhances vascular protective effects by stimulating nitric oxide (NO) -dependent mechanisms in the vascular endothelium, that subsequently induce vasorelaxation, inhibits vascular smooth muscle cell (VSMC) proliferation and induce anti-inflammation [28]. Vascular deleterious effects are mediated through the mitogen-activated protein kinase (MAPK) pathway with the subsequent induction of vasoconstriction, VSMC proliferation and proinflammatory activity [28]. In addition, insulin increases sodium reabsorption in the kidney and promotes sympathetic nerve activity [29]. Insulin can exert either inflammatory and anti-inflammatory effects depending on the metabolic state of the body [28,30]. In physiological condition, insulin stimulates endothelial NO production to exert a vasorelaxation and anti-inflammatory effect. Whereas, in the state of insulin resistance, the insulin-stimulated NO pathway is selectively impaired and the compensatory hyperinsulinemia may activate MAPK pathway, resulting in enhancement of vasoconstriction, proinflammation, increased sodium and water retention with resultant elevation of blood pressure [30,31].

The strength of our study is in the recruitment of study participants taking into account the confounding effects of elevated blood pressure. The present study was not without limitations. First, the sample size was small, and may not be representative of the study population. Second, studies are needed to verify the causal relationship between IR and elevation of BP. Third, direct measurements of IR were not applied to the study participants. However, the use of surrogate estimates to measure IR is considered satisfactory in clinical investigations like the present study [7-9]. Fourth, the study participants were not recruited by the JNC-8 BP classification.

5. CONCLUSION

We demonstrate that insulin resistance influences blood pressure. Our study reveals that insulin resistance has a pathophysiologic link with prehypertension. These findings are clinically relevant because preventing insulin resistance by adopting healthy lifestyles could reduce the progression from normotension to prehypertension and associated complications linked to hypertension.

CONSENT

The patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Ethical approval for this study was obtained from the ethics committee of Federal Medical Centre, Makurdi, Nigeria.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Gast KB, Tjeerdema N, Stijnen T, Smit JWA, Dekkers OM. Insulin resistance and risk of incident cardiovascular events in adults without diabetes: Meta-analysis. PLoS ONE. 2012;7(12):e52036.
2. Zhou MS, Wang A, Yu H. Link between insulin resistance and hypertension: What is the evidence from evolutionary biology? Diabetol Metab Syndr. 2014;6(1):12.
3. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: The JNC 7 report. JAMA. 2003; 289(19):2560-2572.
4. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, et al. Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: Executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. [e-pub ahead of print]. Hypertension; 2017.
5. Booth JN, Li J, Zhang L, Chen L, Muntner P, Egan B. Trends in prehypertension and hypertension risk factors in us adults.1999–2012. Hypertension. 2017; 70(2):275-284.

6. Singh B, Saxena A. Surrogate markers of insulin resistance: A review. WJD. 2010; 1(2):36-47.
7. Muniyappa R, Lee S, Chen H, Quon MJ. Current approaches for assessing insulin sensitivity and resistance *in vivo*: Advantages, limitations, and appropriate usage. Am J Physiol Endocrinol Metab. 2008;294(1):E15-26.
8. Baez-Duarte BG, Zamora-Gínez I, González-Duarte R, Torres-Rasgado E, Ruiz-Vivanco G, Pérez-Fuentes R. Triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) index as a reference criterion of risk for metabolic syndrome (Met.S) and low insulin sensitivity in apparently healthy subjects. Gac Med Mex. 2017;153:152-158.
9. Salazar MR, Carbajal HA, Espeche WG, Leiva Sisnieguez CE, March CE, Dulbecco CA, et al. Comparison of the abilities of the plasma triglyceride/high-density lipoprotein cholesterol ratio and the metabolic syndrome to identify insulin resistance. Diab Vasc Dis Res. 2013;10(4):346-352.
10. Metelskaya VA, Shkolnikova MA, Shalnova SA, Andreev EM, Deev AD, Jdanov DA, et al. Prevalence, components, and correlates of metabolic syndrome among elderly Muscovites. Arch Gerontol Geriatr. 2012;55(2):231–237.
11. Gui MH, Ling Y, Liu L, Jiang JJ, Li XY, Gao X. Effect of metabolic syndrome score, metabolic syndrome, and its individual components on the prevalence and severity of angiographic coronary artery disease. Chin Med J. 2017;130:669-677.
12. Nakamura M, Yamazaki O, Shirai A, Horita S, Satoh N, Suzuki M, et al. Preserved Na/HCO3 cotransporter sensitivity to insulin may promote hypertension in metabolic syndrome. Kidney Int. 2015; 87:535–542.
13. Hwu CM, Liou TL, Hsiao LC, Lin MW. Prehypertension is associated with insulin resistance. Q J Med. 2009;102:705–711.
14. Cordero A, Laclaustra M, Leon M, Grima A, Casasnovas JA, Luengo E, et al. Prehypertension is associated with insulin resistance state and not with an initial renal function impairment. Am J Hypertens. 2006;19:189-196.
15. Dell RB, Holleran S, Ramakrishnan R. sample size determination. ILAR J. 2002; 43(4):207-213.
16. WHO expert consultation appropriate body-mass index for asian populations and its implications for policy and intervention strategies. Lancet. 2004;363(9403):157–163.
17. Barham D, Trinder P. An improved color reagent for the determination of blood glucose by the oxidase system. Analyst. 1972;97(151):142-145.
18. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low‐density lipoprotein cholesterol in plasma, without the use of the preparative ultracentrifuge. Clin Chem. 1972;18(16): 499‐502.
19. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta‐cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985; 28(7):412‐419.
20. Sinha S, Akhter QS, Banik S, Islam MZ, Haque M. Correlation study of insulin resistance and essential hypertension among Bangladeshi male volunteers. Journal of Young Pharmacists. 2015; 7(3):200-205.
21. Mohan G, Kaur R, Nayyar GS, Singh P. To study the prevalence of insulin resistance in non-diabetes hypertensive subjects. Int J Adv Med. 2017;4(1):92-97.
22. Kawamoto R, Kohara K, Tabara Y, Abe M, Kusunoki T, Miki T. Insulin resistance and prevalence of prehypertension and hypertension among community-dwelling persons. J Atheroscler Thromb. 2010;17: 148-155.
23. Grotto I, Grossman E, Huerta M, Sharabi Y. Prevalence of prehypertension and associated cardiovascular risk profiles among young Israeli adults. Hypertension. 2006;48:254–259.
24. Kshirsagar AV, Carpenter M, Bang H, Wyatt SB, Colindres RE. Blood pressure usually considered normal is associated with an elevated risk of cardiovascular disease. Am J Med. 2006;119:133–141.
25. Cubeddu LX, Hoffmann IS. Insulin resistance and upper-normal glucose levels in hypertension: A review. J Hum Hypertens. 2002;16(Suppl 1): S52–55.
26. Soleimani M. Insulin resistance and hypertension: New insights. Kidney Int. 2015;87:497–499.
27. Schulman IH, Zhou MS. Vascular insulin resistance: A potential link between

cardiovascular and metabolic diseases. Curr Hypertens Rep. 2009;11:48-55.
28. Horita S, Seki G, Yamada H, Suzuki M, Koike K, Fujita T. Insulin resistance, obesity, hypertension, and renal sodium transport. Int J Hypertens. 2011; 2011:391762.
29. Muniyappa R, Montagnani M, Koh KK, Quon MJ. Cardiovascular actions of insulin. Endocr Rev. 2007;28(5):463-491.
30. Zhou MS, Schulman IH, Raij L: Vascular inflammation, insulin resistance, and endothelial dysfunction in salt-sensitive hypertension: The role of nuclear factor kappa B activation. J Hypertens. 2010; 28(3):527-535.
31. Oparil S, Zaman MA, Calhoun DA. Pathogenesis of hypertension. Ann Intern Med. 2003;139(9): 761-776.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/25893