



ORIGINAL ARTICLE

Insulin Resistance in Patients with Essential Hypertension Using Homeostatic Model Assessment

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ABSTRACT

**Introduction:** Insulin resistance has a strong relationship with the incidence of type II diabetes. It also has a direct relationship with other risk factors of diabetes, which together are known as metabolic syndrome. The aim of this study was to investigate the relationship between insulin resistance and hypertension. **Materials and Methods:** In this historical cohort study, 90 patients were divided into three different groups: those without hypertension, those with controlled hypertension, and those with uncontrolled hypertension. Systolic and diastolic blood pressure, body mass index, and laboratory test results such as cholesterol, triglycerides, low-density lipoprotein, high-density lipoprotein, fasting plasma glucose, and fasting plasma insulin were compared among the three groups. Data were analyzed with t-tests and the analysis of variance test, which were performed using statistical package for the social sciences version 20 software. **Results:** Age and sex were the same among the three groups; however, BMI, systolic blood pressure, and diastolic blood pressure in the uncontrolled-hypertension group were higher than in the controlled-hypertension and without-hypertension groups ( $P < 0.05$ ). Lipid profile ( $P < 0.05$ ), creatinine ( $P = 0.77$ ), and uric acid ( $P = 0.233$ ) were not significantly different among the groups, although fasting plasma insulin ( $P = 0.012$ ) and homeostatic model assessment of insulin resistance ( $P = 0.038$ ) were significantly higher in the uncontrolled-hypertension group than in the other groups. **Conclusion:** Homeostasis model assessment of insulin resistance in patients with uncontrolled hypertension was higher than in patients with controlled hypertension and those without hypertension. Therefore, homeostatic model assessment of insulin resistance can be used as a predictive clinical test for the early diagnosis of diabetes in patients with uncontrolled hypertension.

INTRODUCTION

Insulin resistance (IR) plays a pathophysiological role in type II diabetes. It is also directly related to obesity, hypertension, coronary artery diseases, dyslipidemia, and other disorders that are together known as metabolic syndrome (1, 2). Because of the rising worldwide incidence of obesity, the risks of type II diabetes and cardiovascular problems are increasing, so developing methods for evaluating and determining the nature of IR is crucial.

One of the most useful methods for evaluating IR is the homeostatic model assessment (HOMA) indicators, which quickly measure glucose and insulin (3). Glucose intolerance and disorders in fat profiles are related to insulin resistance, and because hypertension is one of the most important factors in cardiovascular diseases, there is no proven relation between them (4). Now, even IR is considered a prognostic factor for hypertension (5).

Therefore, the aim of this study was to evaluate IR in patients with hypertension.

MATERIALS AND METHODS

In this historical cohort study, the sample population consisted of 90 patients who were referred to the nonprofit and governmental hospitals in Yazd, Iran. They were divided into three groups those without hypertension, those with controlled hypertension, and those with uncontrolled hypertension by the easy access sampling method. Those who had a history of systemic disease, those who used alcohol, those who abused drugs, and those who were smokers were excluded from the study. Data were collected by clinicians. Blood pressure was measured twice and registered by one instrument. Then, fasting blood sugar was measured after 14 hours. After that, half of the blood samples were put in  $-20^{\circ}\text{C}$  and frozen after serum separation. Next, tests were performed on the other half of blood samples to measure uric acid, glucose, triglycerides, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Then, an IR test was performed in the hospital

on all samples. Cholesterol, triglycerides, and HDL-C were determined using enzymatic methods (Parsazmun, Karaj, Iran). LDL-C was calculated using the Friedewald formula (6) Insulin and C-peptide concentrations were determined by the radioimmunoassay technique (Immunotech, Prague, Czech Republic). Data were analyzed with statistical package for the social sciences (SPSS) version 20 software and with t-tests and the analysis of variance (ANOVA) test. HOMA-IR was calculated as follows: [Fasting Plasma Glucose (FPG) (mg/dl) × Fasting Plasma Insulin (FPI) (mU/L)]/405 (7).

## RESULTS

Patients were divided into three groups for assessment of laboratory test results and HOMA-IR. Patient age (mean ± standard deviation) in the without-hypertension group was 49.17 ± 3.65 years; patient age in the controlled-hypertension group was 50.35 ± 3.02 years; and patient age in the uncontrolled-hypertension group was 51.11 ± 2.95 years. The ANOVA statistical test showed no significant differences in age among the three groups ( $P>0.05$ ). In addition, by Fisher's exact test, no significant differences in sex were observed among the three groups ( $P>0.05$ ). Body mass index (BMI) in patients with uncontrolled hypertension was significantly higher than for patients in the other groups ( $P=0.048$ ). Systolic blood pressure in patients with

uncontrolled hypertension was 14.24 ± 2.01 mmHg, which was higher than for patients in the other groups ( $P=0.0$ ). Diastolic blood pressure in patients with uncontrolled hypertension was also significantly higher than for patients in the other groups ( $P=0.001$ ). Fasting glucose in patients with uncontrolled hypertension was 99.84 ± 1.52 mg/dL, whereas in patients with controlled hypertension and in patients without hypertension, the levels were 100.27 ± 1.43 mg/dL and 95.82 ± 1.59 mg/dL, respectively. The ANOVA test showed no significant differences among the groups ( $P=0.35$ ). Serum insulin in patients with uncontrolled hypertension was 3.48 ± 0.71 μU/mL, whereas in patients with controlled hypertension and in patients without hypertension, the levels were 3.68 ± 0.51 μU/mL and 3.83 ± 0.48 μU/mL, respectively. Serum insulin levels in patients with uncontrolled hypertension were not significantly different ( $P=0.112$ ) from patients with controlled hypertension and patients without hypertension. Cholesterol ( $P=0.13$ ), triglycerides ( $P=0.996$ ), LDL ( $P=0.62$ ), and HDL ( $P=0.051$ ) were significantly different among the three groups. Creatinine ( $P=0.77$ ) and uric acid ( $P=0.239$ ) were not significantly different among the three groups. HOMA was measured as a major parameter for assessing insulin resistance. HOMA in patients with uncontrolled hypertension was 1.35 ± 0.02, whereas these scores in patients with controlled hypertension and in patients without hypertension were 0.91 ± 0.007 and 0.92 ± 0.012, respectively.

**Table 1.** Demographic variable in three groups

Variables	Without hypertension (n=29)	Controlled hypertension (n=31)	Uncontrolled hypertension (n=33)	P-value
Age (years)	49.17±3.65	50.35±3.02	51.11±2.95	0.665*
Sex				
Men (percent)	10 (29)	12 (34)	13 (37)	0.835**
Women (percent)	13 (24)	21 (38)	21 (38)	
Body mass index (kg/m <sup>2</sup> )	25.21±2.56	28.4±2.69	29.41±1.89	0.048*
Systolic blood pressure (mmHg)	11.33±1.29	12.03±1.82	14.24±2.01	0.000*
Diastolic blood pressure (mmHg)	7.42±1.24	7.93±1.84	8.95±1.74	0.001*

\* Analysis of variance test; \*\* Fisher's exact test

**Table 2.** Laboratory findings in three groups

Variables	Without hypertension (n=29)	Controlled hypertension (n=31)	Uncontrolled hypertension (n=33)	P-value*
Serum insulin (μU/mL)	3.83±0.48	3.68±0.51	3.48±0.71	0.112
Glucose tolerance test (mg/dL)	125.79±4.21	128.68±4.95	127.26±4.54	0.103
Fasting glucose (mg/dL)	95.82±1.59	100.27±1.43	99.84±1.52	0.35
Cholesterol (mg/dL)	186.17±4.56	190.24±5.47	188.34±4.11	0.13
Triglycerides (mg/dL)	173.38±3.21	174.93±4.12	175.17±2.95	0.996
High-density lipoprotein (mg/dL)	41.3±0.68	47.06±0.94	45.78±0.75	0.051
Low-density lipoprotein (mg/dL)	121.31±2.64	125.8±2.94	123.9±2.01	0.62
Creatine (mg/dL)	0.89±0.04	0.93±0.05	0.92±0.08	0.77
Uric acid (mg/dL)	5.75±0.12	6.23±0.28	5.9±1.24	0.239
HOMA	0.92±0.012	0.91±0.007	1.35±0.02	0.038

(HOMA, homeostatic model assessment), \* analysis of variance test

## DISCUSSION

Insulin is known to activate endothelial nitric oxide synthase to regulate glucose metabolism (8). IR after reducing nitric oxide secretion is responsible for endothelial impairments and cardiovascular diseases, such as hypertension (9). In this study, we found that HOMA-IR was significantly correlated with uncontrolled hypertension and was an independent factor for predicting IR in patients with uncontrolled hypertension, confirming a hypothesis that was frequently presented in previous clinical studies (10, 11). Some of these previous studies confirmed our hypotheses (10-12), other studies did not (13, 14). The pathogenesis of the relation between hypertension and IR has not been clearly identified. In our study, patients were matched by age and sex, but patients with uncontrolled hypertension had significantly higher BMI. Some studies suggested that visceral fat accumulation and central obesity were related to hypertension and insulin resistance (15-17). In a clinical study, Sarafidis et al. reported the effect of some anti-hypertensive drugs on insulin resistance (18). In our study, patients with controlled hypertension had higher HOMA-IR scores than patients without hypertension. In other studies of patients with essential hypertension, plasma level of free fatty acid was identified as a risk factor for insulin resistance (19-21). In a recent clinical study, Guo et al. reported that high free fatty acid levels were related to the incidence of hypertension and insulin resistance, even if triglycerides, total count, HDL-C, and LDL-C were not significantly higher among different patient groups; this finding was the same as ours (22). It appears that many laboratory parameters can interface with IR and the pathogenesis of hypertension. Determining the most accurate variables requires more detailed studies with larger sample sizes. This can be considered a limitation of our study.

## CONCLUSION

In this study, we found that IR was significantly related to uncontrolled hypertension in the presence of matched fasting glucose in different groups. Based on these findings and those of similar studies, the HOMA-IR index can be a valuable clinical predictor for the incidence of diabetes mellitus in patients with uncontrolled hypertension. Furthermore, controlling hypertension can decrease HOMA-IR levels and reduce the incidence of diabetes mellitus.

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## AUTHOR CONTRIBUTIONS

All authors contributed equally in this study.

## CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

## ETHICAL STANDARDS

None

## REFERENCES

- Berzigotti A, Abraldes JG. Impact of obesity and insulin-resistance on cirrhosis and portal hypertension. *Gastroenterologia y hepatologia*. 2013;36(8):527-33.
- Deng W, Li C, Zhang Y, Zhao J, Yang M, Tian M, et al. Serum C1q/TNF-related protein-3 (CTRP3) levels are decreased in obesity and hypertension and are negatively correlated with parameters of insulin resistance. *Diabetology & metabolic syndrome*. 2015;7:33.
- Erice E, Llop E, Berzigotti A, Abraldes JG, Conget I, Seijo S, et al. Insulin resistance in patients with cirrhosis and portal hypertension. *American journal of physiology Gastrointestinal and liver physiology*. 2012;302(12):G1458-65.
- Genovesi S, Brambilla P, Giussani M, Galbiati S, Mastriani S, Pieruzzi F, et al. Insulin resistance, prehypertension, hypertension and blood pressure values in paediatric age. *Journal of hypertension*. 2012;30(2):327-35.
- Ghoreishian H, Tohidi M, Derakhshan A, Hajsheikholeslami F, Azizi F, Kazempour-Ardebili S, et al. Presence of hypertension modifies the impact of insulin resistance on incident cardiovascular disease in a Middle Eastern population: the Tehran Lipid and Glucose Study. *Diabetic medicine: a journal of the British Diabetic Association*. 2015;32(10):1311-8.
- Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*. 1972;18:499-502
- 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;28:412-9.
- Naderi N, Boobejame P, Bakhshandeh H, Amin A, Taghavi S, Maleki M. Insulin resistance in pulmonary arterial hypertension, is it a novel disease modifier? *Research in cardiovascular medicine*. 2014;3(3):e19710.
- Zhou MS, Wang A, Yu H. Link between insulin resistance and hypertension: What is the evidence from evolutionary biology? *Diabetology & metabolic syndrome*. 2014;6(1):12.
- Bonora E, Targher G, Alberiche M, Formentini G, Calcaterra F, Lombardi S, et al. Predictors of insulin sensitivity in Type 2 diabetes mellitus. *Diabetic Medicine*. 2002;19:535-42.
- Afsar B, Sezer S, Elsurur R, Ozdemir FN. Is HOMA index a predictor of nocturnal nondipping in hypertensives with newly diagnosed type 2 diabetes mellitus? *Blood Pressure Monitoring*. 2007;12:133-9.
- Watson KE, Peters Harmel AL, Matson G. Atherosclerosis in type 2 diabetes mellitus: The role of insulin resistance. *Journal of Cardiovascular Pharmacology and Therapeutics*. 2003;8:253-60.

13. Saad MF, Rewers M, Selby J, Howard G, Jinagouda S, Fahmi S, et al. Insulin resistance and hypertension: The Insulin Resistance Atherosclerosis study. *Hypertension*. 2004;43:1324–31.
14. Bonora E, Bonadonna RC, Del Prato S, Gulli G, Solini A, Matsuda M, et al. In vivo glucose metabolism in obese and type II diabetic subjects with or without hypertension. *Diabetes*. 1993;42:764–72.
15. Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, et al. Abdominal visceral and subcutaneous adipose tissue compartments: Association with metabolic risk factors in the Framingham Heart Study. *Circulation*. 2007;116:39–48.
16. Sironi AM, Gastaldelli A, Mari A, Ciociaro D, Positano V, Buzzigoli E, et al. Visceral fat in hypertension: Influence on insulin resistance and beta-cell function. *Hypertension*. 2004;44:127–33.
17. Anderson PJ, Critchley JA, Chan JC, Cockram CS, Lee ZS, Thomas GN, et al. Factor analysis of the metabolic syndrome: Obesity vs. insulin resistance as the central abnormality. *International journal of obesity and related metabolic disorders*. 2001;25:1782–8.
18. Sarafidis PA, McFarlane SI, Bakris GL. Antihypertensive agents, insulin sensitivity, and new-onset diabetes. *Current Diabetes Reports*. 2007;7:191–9.
19. Guo SX, Yang ZM, Zhang JY, Guo H, Zhang YH, Xu SZ, et al. Relationship of Free Fatty Acid and Insulin Resistance to Hypertension in Kazakh and Han Race of Xinjiang. *Chinese Journal of Hypertension*. 2010;18:459–64.
20. Boden G. Obesity, Insulin Resistance and Free Fatty Acids. *Current Opinion in Endocrinology, Diabetes and Obesity*. 2011;18:139–43.
21. Tabara Y, Takahashi Y, Kawaguchi T, Setoh K, Terao C, Yamada R, et al. Association of serum-free fatty acid level with reduced reflection pressure wave magnitude and central blood pressure: The Nagahama study. *Hypertension* 2014;64:1212–18.
22. Guo SX, Yan YZ, Mu LT, Niu Q, He J, Liu JM, et al. Association of Serum Free Fatty Acids with Hypertension and Insulin Resistance among Rural Uyghur Adults in Far Western China. *International journal of environmental research and public health*. 2015;12(6):6582-90.