To Study the Correlation between Insulin Resistance and Hypertension in Hypertensive Patients

Nishant Wadhera[1], Sidharth Mangla[2], Abhishek Gupta[3], Saurabh Singhal[4]

[1, 2, 3, 4] Department of Medicine, Chhatrapati Shivaji Subharti Hospital, Meerut, Uttar Pradesh, India.

ABSTRACT

BACKGROUND

Individuals developing type 2 diabetes generally go through phases of insulin resistance and pre-diabetes, though it may often remain un-noticed. This syndrome is due to decreased insulin secretion which even may be a part of a bigger collection of symptoms termed as metabolic syndrome. The study was conducted to correlate insulin resistance with hypertension and its correlations with various parameters such as Homeostatic Model Assessment of Insulin Resistance (HOMA–IR) test, lipid profile, and anthropometric measurements.

METHODS

This cross-sectional study was performed among 100 patients in the Department of Medicine at Chhatrapati Shivaji Subharti Hospital from December 2018 to March 2020. Data was collected by a preformed structured interviewer-administered questionnaire which was pretested and modified before the study commenced. Patients were interviewed for the demographic, socioeconomic status, medical history and previous treatment history. Anthropometric measurements such as height, weight, and waist circumference, were measured. BMI was recorded. Serum insulin and fasting glucose level in serum were measured as one of the diagnostic parameters for the confirmation of insulin resistance. HOMA-IR (Fasting Insulin (μU / mL) X Fasting Blood Glucose (mg / dL) / 405) was utilised to estimate insulin resistance.

RESULTS

Insulin resistance was present among 41 % and absent in 59 % of the hypertensive subjects. Mean HOMA-IR was 2.47 ± 0.67, 2.89 ± 0.53 and 3.51 ± 0.74 among subjects with Elevated / Hypertensive Stage I, Hypertensive Stage II and Hypertensive Emergency grades respectively ($p < 0.05$). Average fasting insulin was 5.93 ± 2.66, 7.61 ± 2.14 and 15.13 ± 4.91 among subjects with Elevated / Hypertensive Stage I, Hypertensive Stage II and Hypertensive Emergency grade respectively.

CONCLUSIONS

Hyperinsulinaemia and insulin resistance plays a fundamental role in pathophysiology of increased blood pressure. It is proposed that increase in BP is related to change in insulin action, sensitivity, and resistance. The study showed a significant increase of BMI and WC of essential hypertensive patients and more weight gain associated with severity of insulin resistance. Thus, the magnitude of weight gain and obesity is related with enhanced susceptibility to insulin resistance.

KEYWORDS

Hypertension, Insulin Resistance, HOMA-IR

Corresponding Author:
Dr. Sidharth Mangla,
Department of Medicine,
Chhatrapati Shivaji Subharti Hospital, Meerut, Uttar Pradesh, India.
E-mail: smangla70@gmail.com

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BACKGROUND

Insulin Resistance (IR) is a pathological situation resulting from failure of cells to normally respond to insulin. In order to control hyperglycaemia and detectable organ damage in the long run, the host body secretes insulin with entry of glucose into the blood stream following carbohydrate digestion (primarily) from the food consumed. Within regular circumstances, insulin retort prompts glucose consumed into cells of body, that is utilised for energy, and inhibiting the human body from consuming fat for energy, hence resulting in the blood glucose concentration to reduce, conforming within the normal limit even with larger carbohydrate consumption.[1,2]

With the body producing insulin due to insulin confrontation, the cells remain resilient to insulin and unable to utilise it efficiently. Pancreatic beta cells consequently raise insulin production, additionally contributing to a higher blood insulin concentration. This generally goes non-detected and leads of type 2 diabetes, obesity or latent auto immune diabetes of adults.[3] Though this type of chronic insulin resistance is malicious, in times of acute illness it is actually a fully evolved protective mechanism. An index of insulin resistance is known as subjective assessment of biological effect of endogenous or exogenous insulin in response to the ambient blood glucose level. IR is thought to be an independent risk factor in developing metabolic syndrome and diabetes. Predisposition to IR is multi-factorial, with strong genetic and environmental outcomes.[4]

Hypertension (HTN or HT), is a long-term medical situation wherein the blood pressure in the arteries is consistently increased. It generally don't produce symptoms. It is a great risk factor for coronary artery disease, stroke, heart failure, atrial fibrillation, peripheral vascular disease, loss of vision, chronic kidney disease and dementia.[5]

It is categorised into primary (essential) or secondary hypertension. Around 90 – 95 % times it is primary, which is defined as high blood pressure resulting from non-specific lifestyle and genetic variables. Lifestyle variables which enhance the risk add to excess salt in the diet, excess body weight, smoking tobacco, and alcohol consumption.[6] The rest 5 – 10 % of situation are classified as secondary high blood pressure, termed as high blood pressure because of an identifiable aetiology, like chronic kidney disease, kidney arteries thinning, an endocrine disorder, or the utilization of contraceptive pills.[6]

Individuals developing type 2 diabetes generally come across earlier stages of insulin resistance and pre-diabetes, though can remain undiagnosed most of the times. Insulin resistance is a syndrome (a set of signs and symptoms) arising from decreased insulin activity; it is even a component of a broader constellation of symptoms named as the metabolic syndrome.

The study was conducted to correlate insulin resistance with hypertension and its correlations with various parameters such as HOMA-IR test, lipid profile, and anthropometric measure.

METHODS

The current cross-sectional study was conducted in the Department of Medicine at Chhatrapati Shivaji Subharti Hospital from December 2018 to March 2020. The study group consisted of 100 patients, aged 18 years and above diagnosed as known case of hypertension and newly diagnosed hypertension. Cases were recruited into the study after obtaining written informed consent and permission from Institutional Ethical Committee.

Inclusion Criteria

Age > 18 yrs., known case of hypertension and newly diagnosed hypertension, euglycemic individuals (fasting glucose level < 110 mg / dl according to WHO).

Exclusion Criteria

Known case of diabetes mellitus, polycystic ovarian disease, tuberculosis, other systemic illness, liver disorders, renal disorders, congestive cardiac failure, patients on oral contraceptive pills, patients on statins and other therapies that are known to affect the study and pregnant women.

The data was collected by a preformed structured interviewer-administered questionnaire that was pretested with certain modifications done before employing into the study. The patients were interviewed that requests for the demographic, socioeconomic status, medical history and previous history of taking any medications and supplements. Anthropometric measurements such as height, weight, and waist circumference, BMI were measured.

Blood Pressure (BP): BP was recorded with a mercury sphygmomanometer in lying down position on the left arm. BP was categorized according to the American Heart Association (AHA) guidelines.

Insulin Measurement

HOMA-IR [Fasting Insulin (µU / mL) X Fasting Blood Glucose (Mg / dL) / 405]: was used to determine insulin resistance. HOMA-IR is a simple and consistent surrogate recording of insulin resistance. Benefit of the HOMA technique is that just a single venipuncture is needed because of its simplicity and easy to use. After getting insulin value, insulin resistance was calculated. Insulin resistance was measured by HOMA-IR formula. Fating insulin (microU/ml)* fasting glucose (nmol/l) / 22.5 or fasting insulin (µU / mL)* fasting glucose (mg / dL) / 405. After calculating insulin resistance, insulin resistance was classified into normal, moderate and severe insulin resistance (Table 1).[7]

Category	HOMA Score
Normal Insulin Resistance	< 3
Moderate Insulin Resistance	> 3 - 5
Severe Insulin Resistance	> 5

Table 1. Categorization of Insulin Resistance

Anthropometry Measurements

1. Weight was measured to the closest kilogram (Kg) with individuals standing on the weighing machine not wearing footwear and with less clothing. The same weighing machine was employed for every participant and the machine was validated before with a known set of weights for any possible error. Height was quantified with individual standing, barefoot, feet approximated, back and heels opposite the upright bar of height scale, head upright in Frankfort horizontal plane look straight ahead. BMI was recorded using the formula – [BMI = weight in kilogram / (height in meters)^2], as per W H O guidelines. i.e.

Underweight - < 18.5 Kg / m^2
Normal - 18.5 - 24.9 Kg / m^2
Pre-obese – 25 - 29.9 Kg / m^2
Obese – ≥ 30 Kg / m^2

2. Abdominal Circumference: It was measured in the standing position by putting a plastic tape horizontally midway between 12th rib and iliac crest on the mid-axillary line. The measurements were repeated twice by using the same device and mean value was recorded.

Specimen Collection and Analytic Procedures

Overall, 5 ml of venous blood was collected in a plain red-top venepuncture tube without additives. Blood was allowed to clot. Then, the specimen was centrifuged to separate the serum from the cells. If specimen could not be assayed in time for insulin assay, the serum was frozen and stored at – 30° C and measured within 30 days (as it is not stable at room temperature). Repeated freezing and thawing were avoided.

Serum total cholesterol, TAG, HDL-C, fasting blood glucose, blood urea nitrogen, and creatinine were analysed by Cobas c311 chemical analyser, Roche Diagnostics Deutschland GmbH, Mannheim, Germany. LDL-C was calculated by the formula devised by Friedewald and colleagues.

Statistical Analysis

Data was entered and tabulated in an excel sheet, under the guidance of statistician. The means and standard deviations of the measurements per group were used for statistical analysis (SPSS 24.00 for windows; SPSS inc., Chicago, USA). For each assessment point, data was statistically analyzed using one-way ANOVA test and the significance level was set at $p < 0.05$.

RESULTS

The study group consisted of 100 patients, aged 18 years and above diagnosed as known case of hypertension and newly diagnosed hypertension. Out of 100 subjects, 58 were males and 42 were females. Table 2 shows the age distribution among the study subjects. Maximum subjects belonged to > 60 years (30 %) of age group followed by 51 - 60 years (28 %). Minimum subjects were in the age group of 18 - 30 years (3 %) followed by 31 - 40 years (15 %). Body Mass Index (BMI) > 25 Kg / m^2 and < 25 Kg / m^2 was reported among 54 % and 46 % of the subjects respectively.

Age Group (in Years)	N	%
18 - 30	3	3
31 - 40	15	15
41 - 50	24	24
51 - 60	28	28
> 60	30	30
Body Mass Index		
> 25 Kg / m^2	54	54
< 25 Kg / m^2	46	46
Total	**100**	**100**

Table 2. Age Distribution and Body Mass Index in Hypertensive Group

Table 3 shows the incidence of insulin resistance in hypertensive group. Insulin resistance was present among 41 % and absent in 59 % of the hypertensive subjects. In this study, hypertensive emergency was reported among 25 % of the subjects while elevated / hypertensive Stage I and hypertensive Stage II was revealed in 41 % and 34 % of the subjects respective.

Hypertension Category	N	%
Elevated / Hypertensive Stage I	41	41
Hypertensive Stage II	34	34
Hypertensive Emergency	25	25
Insulin Resistance		
Absent	59	59
Present	41	41
Total	**100**	**100**

Table 3. Distribution of Subjects According to Hypertension Category and Insulin Resistance in Hypertensive Group

Table 4 shows the comparison of hypertension grades among patients according to HOMA-IR. Mean HOMA-IR was 2.47 ± 0.67, 2.89 ± 0.53 and 3.51 ± 0.74 among subjects with elevated / hypertensive stage I, hypertensive stage II and hypertensive emergency grade respectively. When hypertension categories were compared statistically according to mean HOMA-IR, it was found to be statistically significant as $p < 0.05$. Mean fasting insulin was 5.93 ± 2.66, 7.61 ± 2.14 and 15.13 ± 4.91 among subjects with elevated / hypertensive stage I, hypertensive stage II and hypertensive emergency grade respectively. When hypertension categories were compared statistically according to mean fasting insulin, it was found to be statistically significant as $p < 0.05$ as shown in Table 4.

Hypertension Category	Mean HOMA-IR	SD	Anova Test	P Value
Elevated / Hypertensive Stage I	2.47	0.67	7.83	0.008*
Hypertensive Stage II	2.89	0.53		
Hypertensive Emergency	3.51	0.74		
Total	**2.78**	**0.62**		
Hypertension Category	**Mean Fasting Insulin**	**SD**		
Elevated / Hypertensive Stage I	5.93	2.66	18.42	< 0.01*
Hypertensive Stage II	7.61	2.14		
Hypertensive Emergency	15.13	4.91		
Total	**9.68**	**3.78**		

Table 4. Comparing the Grades of Hypertension among Patients According to HOMA-IR and Fasting Insulin

*: statistically significant

Table 5 shows the comparison of HOMA-IR grades among patients according to mean BMI. Mean BMI was 24.73 ± 3.17, 29.81 ± 3.65 and 36.18 ± 4.22 among subjects with HOMA-IR < 1, 1 - 3 and 3 - 5 value respectively. When HOMA-IR categories were compared statistically according to mean BMI, it was found to be statistically significant as $p < 0.05$.

HOMA-IR	Mean BMI	SD	Anova Test	P Value
< 1	24.73	3.17		
1 - 3	29.81	3.65		
3 - 5	36.18	4.22	19.71	< 0.01*
Total	**30.96**	**3.76**		

Table 5. Comparing the Grades of HOMA-IR among Patients According to BMI

*: statistically significant

DISCUSSION

The occurrence of hypertension is increasing at a rapid rate globally and the effect is in particular felt in developing nations.[8] It is due to epidemiological trend found in developing nations resulting to alarmistic rise in non-communicable diseases, particularly diabetes and hypertension.[9] India's population has now bypassed the 1 billion count and it now stands as the greatest frequency of diabetic cases amongst any country across the globe. Hypertension follows in the next order.[10] Diabetes mellitus and Impaired Glucose Tolerance (IGT) are shown to rise the susceptibility of further cardiovascular morbidity and mortality.[11] Hence, in hypertensive cases early diagnosis and therapy of an impaired glucose metabolism could be particularly important to decrease cardiovascular disorder.[12] Though a greater quantity of studies evaluated the link between insulinaemia and increased blood pressure (BP), the findings are inconsistent with few reported strong and others weak, or none association. Fewer studies measured insulin resistance directly, greatly in lesser groups of subjects with still controversial findings. Hence, the present study was conducted to correlate insulin resistance with hypertension and its correlations with various parameters such as HOMA-IR test, lipid profile, and anthropometric measure.

In our study, out of 100 subjects, 58 were males and 42 were females. Zakir Hussain et al[13] in their study reported similar male preponderance among the study groups. Mohamed Alsenbsey et al[14] in their study showed similar findings too. The reason among men for the development of this condition are stress, alcohol intake, tobacco, and diet etc.

In our study, maximum subjects belonged to > 60 years (30 %) of age group while minimum subjects were in the age group of 18 - 30 years (3 %). No significant difference was found among hypertensive subjects according to mean age as $p > 0.05$ in the present study. These results were in accordance with study done by Zakir Hussain et al.[13]

Body mass index > 25 Kg / m^2 and < 25 Kg / m^2 was reported among 54 % and 46 % of the hypertensive subjects respectively. In a study by Zakir Hussain et al,[13] BMI > 25 Kg / m^2 was present in 27 (54 %) patients of hypertensive and 14 (28 %) patients of normotensive groups. Mohamed Alsenbsey et al[14] in their study revealed that there was a highly significant increase in BMI in hypertensive patients more than the control group ($p < 0.001$). These findings are in line with previously published data,[15] which reported that weight gain is associated with increased risk of hypertension, and even modest weight loss is associated with substantial reduction in BP in obese. However, other contrary findings reported that obesity is not often related to hypertension, as no significant increase of the BP level could be detected when compared with nonobese populations.[16]

In our study, insulin resistance was present among 41 % and absent in 59 % of the hypertensive subjects. Zakir Hussain et al[13] in their study revealed that 19 (38 %) of hypertensive patients and 7 (14 %) of normotensive patients had insulin resistance.

Increased insulin resistance results in elevated insulin levels that in turn alter the blood pressure by activating sympathetic system and by increasing sodium reabsorption. In our study, mean HOMA-IR was 2.47 ± 0.67, 2.89 ± 0.53 and 3.51 ± 0.74 among subjects with elevated / hypertensive stage I, hypertensive stage II and hypertensive emergency grade respectively with statistically significant difference. Zakir Hussain et al[13] in their study found that HOMA-IR was significantly higher in hypertensive patients 2.81 (± 0.6) than in normotensive patients (2.41 ± 0.07). Similar observations were made by Sinha et al.[17] Sinha S et al[17] study demonstrated that HOMA-IR was remarkably greater in hypertensive cohort than that of the control group, that was similar to our study. Recently, insulin resistance has taken momentum as its part in the pathogenesis of various metabolic disorders. The insulin resistance syndrome is a syndrome that includes multiple disorders such as hypertension, diabetes and hypercoagulability.[16]

Mean fasting insulin was 5.93 ± 2.66, 7.61 ± 2.14 and 15.13 ± 4.91 among subjects with elevated / hypertensive stage I, hypertensive stage II and hypertensive emergency grade respectively with statistically significant difference as $p < 0.05$ in our study. Zakir Hussain et al[13] in their study reported significantly higher fasting blood sugar (> 110 mg / dl) in hypertensive patient (50 %) than normotensive patients (24 %). Similar findings were noted in the study carried out by Garcia-Puig et al[18] (glucose metabolism in hypertension) and found an abnormal glucose metabolism 68.5 % of hypertensive cases. Mohamed Alsenbsey et al[14] in their study found significantly higher fasting insulin level ($p = 0.002$) in hypertensive patients 8.7 ± 5.7 than the control group 4.7 ± 2.9 was also reported in our study. These findings are in line with those who observed that fasting serum insulin levels were greatly higher in hypertensive cases compared with controls ($p < 0.01$). These findings correlate with Xun et al,[19] who concluded that hyperinsulinaemia in young adulthood was positively associated with incidence of hypertension later on in life for men and women, African American and whites, and those with normal weight and overweight. Some previous publications have stated that hypertensive patients were found to have significantly higher hyperinsulinaemia and IR

than normotensives (p = 0.02 and 0.04) and even that IR is considered as an independent risk factor for hypertension in Koreans.[20,21]

The limitation of present study is its cross-sectional design. Also, dietary assessment tools and questionnaires have not been inquired, as we found it could be subjective and instead, we used BMI and WC as objective measurements. In this frame, some characteristics of the effect of dietary habits in the studied group could have been missed. The strength of this preliminary study is that it investigates the role of hypertension in the pathogenesis of IR, so it gives perspectives for further analysis regarding its role and involvement in complications of related cardiovascular diseases.

CONCLUSIONS

Hyperinsulinaemia and insulin resistance may cause hypertension. It is proposed that increase in BP is related to change in insulin action, sensitivity, and resistance. The study showed a significant increase of BMI and WC of essential hypertensive patients and more weight gain associated with severity of insulin resistance. Thus, the magnitude of weight gain and obesity is correlated with enhanced risk of insulin resistance.

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REFERENCES

[1] Schulman IH, Zhou MS. Vascular insulin resistance: a potential link between cardiovascular and metabolic diseases. Curr Hypertens Rep 2009;11(1):48-55.
[2] Ginsberg HN. Insulin resistance and cardiovascular disease. J Clin Invest 2000;106(4):453-458.
[3] Ärnlöv J, Pencina MJ, Nam BH, et al. Relations of insulin sensitivity to longitudinal blood pressure tracking: variations with baseline age, body mass index and blood pressure. Circulation 2005;112(12):1719-1727.
[4] Ming-Sheng Z, Schulman IH. Link between Insulin resistance and hypertension: What have we learned from our ancestors? Autacoids 2012;1:e102.
[5] Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities – the role of insulin resistance and the sympatho adrenal system. N Engl J Med 1996;334(6):374-381.
[6] Cuffee Y, Ogedegbe C, Williams NJ, et al. Psychosocial risk factors for hypertension: an update of the literature. Curr Hypertens Rep 2014;16(10):483.
[7] Ferrannini E, Mari A. How to measure insulin sensitivity? J Hypertension 1998;16(7):895-906.
[8] Reddy KS. Hypertension control in developing countries: generic issues. J Hum Hypertens 1996;(10 Suppl 1):s33-s38.
[9] Stern MP, Knapp JA, Hazuda HP, et al. Genetic and environmental determinants of type II diabetes in Mexican Americans. Is there a descending limb to the modernization/ diabetes relationship? Diabetes Care 1991;14(7):649-654.
[10] King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025. Prevalence, numerical estimates and projections. Diabetes Care 1998;21(9):1414-31.
[11] Hanefeld M, Fischer S, Julius U, et al. Risk factors for myocardial infarction and death in newly detected NIDDM: the diabetes intervention study, 11 - years follow - up. Diabetologia 1996;39(12):1577-1583.
[12] Ford ES, Gile WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287(3):356-359.
[13] Hussain Z, Tripathi VD. A study to find out the relationship between insulin resistance and hypertension. Int J Adv Med 2017;4(5):1299-1303.
[14] Alsenbsey M, Asham B, Aly SS, et al. Role of insulin resistance in essential hypertensive patients in Qena Governorate, Egypt. Al-Azhar Assiut Medical Journal 2018;16(2):99-104.
[15] Kotsis V, Tabouli S, Papkatsika S, et al. Mechanisms of obesity-induced hypertension. Hypertens Res 2010;33(5):386-393.
[16] Oni OA, Odia JO, Iruegbukpe V. The effects of obesity on hypertension: does increase in body mass index equate persistent and poor control of hypertension in Nigeria? Int J Med Sci 2014;1(5):60-64.
[17] Sinha S, Akhter QS, Banik S, et al. Correlation study of insulin resistance and essential hypertension among Bangladeshi male volunteers. J Young Pharmacists 2015;7(3):200-205.
[18] Garcia-Puig J, Ruilope LM, Luque M, et al. AVANT Study Group Investigators. Glucose metabolism in patients with essential hypertension. Am J Med 2006;119(4):318-326.
[19] Xun P, Liu K, Cao W, et al. Fasting insulin level is positively associated with incidence of hypertension among American young adults: a 20- year follow up study. Diabetes Care 2012;35(7):1532-1537.
[20] Akande TO, Adeleye JO, Kadiri S. Insulin resistance in Nigerians with essential hypertension. Afr Health Sci 2013;13(3):655-660.
[21] Yoo TW, Sung KC, Shin HS, et al. Relationship between serum uric acid concentrations, insulin resistance, high sensitivity C-reactive protein as an independent risk factor for essential hypertension. Circ J 2005;69(8):928-933.