

Diagnostic Implications of TyG Index in Hypertensive Patients as a Predictive Marker for Future Risk of Cardiovascular Diseases

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Abstract

Aim: Researchers in this study looked at hypertensive individuals to see if there was a correlation between their apo-B/apo-A ratio and TyG index readings. Furthermore, the research aimed to assess the specificity and sensitivity of these two metrics in relation to their ability to predict hypertension within the study group.

Materials & Methods: The researchers at the Department of Biochemistry carried out this cross-sectional study. Researchers were able to enroll volunteers at the Medicine Outpatient Department (OPD) so long as they met the following criteria: One of the following conditions has to be met by the people: First, they had to be 45 or older; second, they had to have a systolic blood pressure (SBP) of 140 mmHg and a diastolic blood pressure (DBP) of 90 mmHg without medication to treat hypertension; or third, they couldn't take medication for their hypertension. After a diagnosis of essential hypertension, they began taking medication to lower their blood pressure.

Conclusion: The ApoB/ApoA1 ratio and TyG were the best predictive markers for multiple sclerosis (MS) because of their relatively comparable predictive values. As a result, the TyG index has the potential to function as a screening instrument for hypertensive inpatients who are insulin resistant.

Keywords: Hypertension, cardiovascular disease, stroke, chronic kidney disease, LDL, HDL.

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Introduction

Around 125 million disability-adjusted life years (DALYs) for men and 90 million DALYs for women are attributed to hypertension, according to estimates [1,2]. On a global scale, hypertension ranks as the leading risk factor for women and the number two risk factor for men. Thirty percent of Indians suffer from hypertension, with 34% residing in cities and 28% in rural regions, according to one estimate [3].

Among the most important risk factors that may be changed to lower the chance of getting cardiovascular disease (CVD), high blood pressure stands out. It is projected that the burden of hypertension in India would dramatically grow over the next few years [4,5]. This is due to the rapid changes in the environment and lifestyle that are the consequence of harmful working conditions and increasing social expectations for survival caused by the combination of these two factors.

The fact that the sickness process is asymptomatic is another factor that adds to the low awareness of the condition, which in turn leads to inadequate management of the disease. There have been a

number of adverse outcomes that have arisen as a consequence of this increase, including but not limited to a stroke, cardiovascular sickness, chronic renal disease, and harm to vital systems. Given this, it is very necessary to use extreme care while doing research on the course of this condition.

“The relevance of insulin resistance (IR) as a major pathological process that is intimately associated to a variety of disorders, including diabetes and obesity in the central region, has progressively come to light over the course of the last several years [6, 7]. There is a growing body of evidence suggesting that insulin resistance and hypertension are illnesses that are strongly related to one another [8].

Scientific evidence has shown that transporting molecules are present in all atherogenic lipoproteins, including LDL-C, VLDL-C, and IDL. This discovery was made earlier this year. An example that stands out among these molecules is the apolipoprotein B, often known as ApoB [9, 10]. When these molecules are investigated, it is possible that a more precise evaluation of

atherogenicity, a significant factor that is connected with hypertension, may be obtained. However, high-density lipoprotein cholesterol (HDL-C) contains the cholesterol molecule ApoA1, which is well-known for its important involvement in antiatherogenic activities [6,9].

Another indicator that has been proposed as a reliable and valid stand-in for insulin resistance (IR) is the triglyceride-glucose index, or TyG index [11]. To get the fasting triglycerides, divide the fasting glucose by the fasting triglycerides, and then multiply the result by 2. The fasting glucose level is calculated using this method. Although it is tightly associated with the hyperinsulinemia euglycemic clamp, the so-called "gold standard" for assessing insulin sensitivity, the processing is both costly and time-consuming, which limits its applicability [12].

Taking this into consideration, the present research was conducted with the purpose of determining the levels of TyG index and apo-B/apo-A ratio among hypertensive patients, as well as their connection to hypertension, and comparing the sensitivity and specificity of the prediction of hypertension among the population that was being studied."

Materials & Methods: Within the Department of Biochemistry, a cross-sectional investigation was carried out for the purpose of this research. When it came to the recruitment of study subjects, the following requirements were met, either inside the Medicine Outpatient Department (OPD) or outside of it: (1) They met one of the following criteria: they had to be 45 years of age or older; (2) In the absence of antihypertensive medication, a physician diagnosed patients with hypertension when their systolic blood pressure (SBP) was at least 140 mmHg and their diastolic blood pressure (DBP) was at least 90 mmHg. or (3) They were taking antihypertensive medication and had been diagnosed with essential hypertension. Volunteers who were in excellent health, both male and female, had normal blood lipid profiles, did not exhibit any symptoms or indications linked with hypertension, and did not have a family history of the condition were included in the control group. There was a total of one hundred ten people who participated in the research study; fifty-five of them had been diagnosed with hypertension, while the other fifty-five were healthy controls. Self-reported instances of diabetes, myocardial infarction, unstable angina pectoris, cerebrovascular disease that had occurred during the preceding six months, and uncontrolled thyroid dysfunction, coagulopathy, or malignancy were the criteria that were used to exclude participants from the study.

Clinical and anthropometric measurement: "The participant was measured while wearing loose-

fitting clothing and without shoes using a digital scale that was precise to within half a kilogram. The height measurements were taken using a calibrated stadiometer (Seca 217, Germany) to guarantee an accuracy of 0.1 cm. The waist circumference (WC) was measured to the nearest half centimeter using a nonelastic tape (Seca 201, Germany). Weight in kilograms divided by height in square meters (kg is the unit of measurement) is the formula for calculating the body mass index (BMI). The systolic and diastolic blood pressures were measured using a traditional mercury sphygmomanometer, and each measurement was taken twice. The measurements were all obtained from the same side (the right side) and averages were calculated after each measurement.

Biochemical Analysis: The laboratory procedures were all executed at the Keonjhar-based Central Laboratory of DD Medical College. The subjects were asked to fast for twelve hours before blood samples were taken from their veins. Blood samples were tested for plasma glucose, total cholesterol, HDL-C, low-density lipoprotein, Apo B, and Apo A1 cholesterol (LDL-C) using an automated analyzer made by Beckman Coulter after a ten to twelve hour fast. Beckman Coulter specialist kits were used to examine the results of these tests.

Statistical analysis: If the data was not parametric, the chi-square test or Fisher's exact test was used to establish a preliminary association between the categorical variables and the hypertension patients. To find out what kind of relationship there is between the TyG index and lipid characteristics, we used logistic regression to calculate the odds ratio (OR) and a confidence interval (CI) that covered 99 percent. A receiver operating characteristic (ROC) research was conducted to ascertain the diagnostic significance of the TyG index in individuals with a hypertension diagnosis."

Results

One hundred ten persons were a part of this particular study. According to the study's findings, the participants' ages ranged from an average of 39.41 to a standard deviation of 4.89 years.

Participants were 68 men (61.8% of the total) and 42 women (38% of the total). Table 1 shows comparisons between the control group and the intervention group on many measures.

Despite the fact that the patients had a mean age that was somewhat higher than the average age of the population (40.20 years as compared to 38.62 years), this difference did not satisfy the threshold for statistical significance (p.0.090).

Table 1: Comparison of baseline characteristics between case & control groups

Parameters	Case (N=55)	Control (N=55)	P value
Age			0.004
Mean (SD)	40.20 (5.18)	37.24 (5.37)	
Range	30.00 - 50.00	23.00 - 50.00	
Sex			0.050
Female	16 (29.1%)	26 (47.3%)	
Male	39 (70.9%)	29 (52.7%)	
Socio-economic status			<0.001
Average	17 (30.9%)	6 (10.9%)	
Good	30 (54.5%)	49 (89.1%)	
Low	8 (14.5%)	0 (0.0%)	
Life style			0.010
Hard work	9 (16.4%)	21 (38.2%)	
Sedentary	46 (83.6%)	34 (61.8%)	
Personality			0.15
A	21 (38.2%)	14 (25.5%)	
B	34 (61.8%)	41 (74.5%)	

There were 47.3% more females in the control group than there were in the other group, which comprised 29.1% of the total population. ($p = 0.21$) There was no obvious change in the socioeconomic condition of the individuals. However, there was a significant difference in the lifestyle choices that the patients made ($p = 0.010$), with a greater number of cases working long hours (38.2%) and a higher percentage of controls having sedentary lifestyles (61.8%).

This means that the patients' lifestyle choices were significantly different from one another. No statistically significant difference was found between the two groups with respect to personality type ($p = 0.15$).

This held true for those with Type A and Type B personalities equally.

Baseline Biochemical Parameters

Table 2: Levels of TyG Index and apoB/apoA ratio between hypertensive and non-hypertensive patients

Parameters	Case	Control	P-value
TyG Index	9.00 (0.36)	8.23 (0.31)	<0.001
apoB/apoA ratio	0.91 (0.11)	0.52 (0.16)	<0.001

In terms of the Tag Index and the proportion of apoB to apoA, the data makes it abundantly evident that there are significant disparities between the different cases and the controls.

With a p-value of less than 0.001, the TyG Index demonstrated a very significant difference between the cases (9.00 ± 0.36) and the controls (8.23 ± 0.31). This difference was found to be much larger

in the cases than in the controls. Moreover, it is notable that the ratio of apoB to apoA in cases (0.91 ± 0.11) was much bigger than in controls (0.52 ± 0.16), exhibiting a highly significant p-value of less than 0.001.

An examination of the relationship between the hypertension of the people who participated in the study and the TyG level.

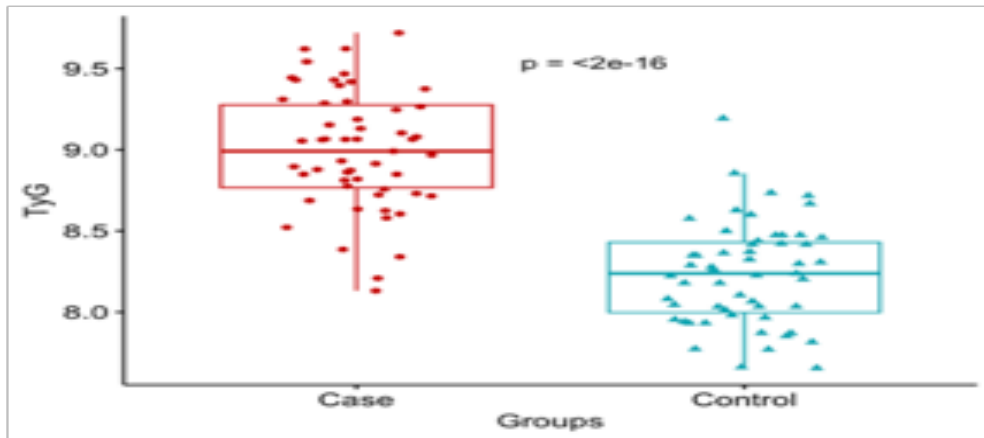


Figure 1: Correlation Graph

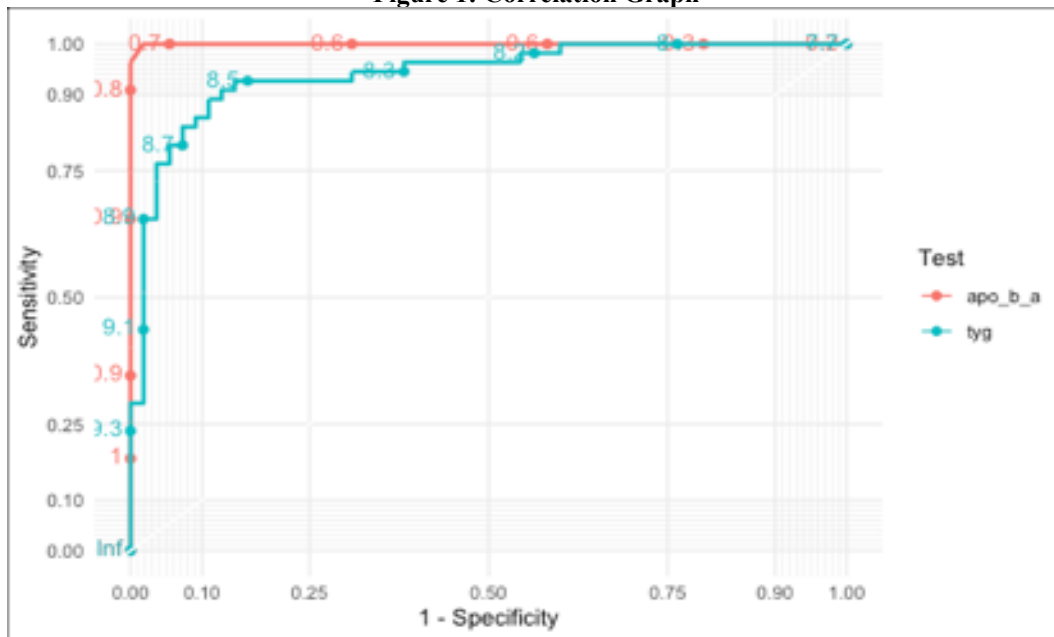


Figure 2: ROC curve for evaluation of diagnostic value for TyG index

“The receiver operating characteristic (ROC) curve, which was developed to evaluate the diagnostic accuracy of the two parameters, is shown in Figure 1. In addition, research was conducted to determine the sensitivity and specificity of the parameters. Compared to the apoB/apoA comparison, which produced a value of 0.940, the area under the curve (AUC) for the TyG Index was found to be 0.994. On the basis of the data, Table 3 presents a comparison of the sensitivity and specificity of the two tests.”

Table 3: Comparison of Sensitivity and Specificity between two tests

Parameters	Sensitivity	Specificity	Optimal Cut-off value
TyG Index	0.90	0.87	8.58
apoB/apoA ratio	1	0.98	0.74

According to Table 3, the TyG Index is able to reliably identify true-positive cases 90% of the time with a sensitivity of 0.90 and accurately identify true-negative cases 87% of the time with a specificity of 0.87. So, true-positive cases can be correctly identified 90% of the time using the TyG Index. Conversely, the apoB to apoA ratio was able to consistently identify all true positives due to its high sensitivity (1). Furthermore, it could accurately detect true negative cases 98% of the time because to its high specificity of 0.98. This ratio allowed for the exact identification of all true positive cases.

Table 4: Study of correlation between TyG index and lipid indices among hypertensive and non-hypertensive patients

	Chol	HDL	LDL	LDL/HDL	VLDL	Apo-A	Apo-B	Apo B/Apo-A
Chol								
HDL	0.44***							
LDL	0.94****	0.41**						
LDL/HDL	0.77****	-0.08	0.87****					
VLDL	0.32*	-0.16	0.00	0.03				
Apo-A	0.41**	0.07	0.39**	0.38**	0.15			
Apo-B	0.64****	0.53****	0.62****	0.38**	0.08	0.33*		
Apo-B/Apo-A	0.45***	0.51****	0.43**	0.19	0.01	-0.15	0.88*** *	
TyG Index	0.29*	-0.20	0.00	0.07	0.93****	0.08	0.04	0.00

The correlation coefficients that were obtained between the TyG Index and a very large number of other parameters that are connected with lipids are shown in the table that follows. Assessment of an individual's general health is accomplished via the use of the TyG Index, which is derived from the measurements of a person's fasting glucose and triglyceride levels. By calculating the correlation coefficient between the TyG Index and other variables, one is able to ascertain the type of the connections that exist between these variables as well as the extent to which they are connected to one another. In this specific case, the correlation between the TyG Index and Chol was determined to be 0.29, which indicates that there is a link between the two variables that is deemed to be fairly advantageous.

The TyG Index and Chol levels seem to have a low degree of association with one another, which is a conclusion that can be drawn from the information presented here. It was discovered that the TyG Index and HDL had a correlation of -0.20, which indicates that there is a connection between the two variables that is not in accordance with whatever one could anticipate. Given this information, it would indicate that HDL levels have a tendency to decline when the TyG Index rises, but at a slower pace than at other times. There is either no link at all or a very weak one, as shown by the fact that the correlation coefficients between the TyG Index and LDL, LDL/HDL, and VLDL were quite close to zero. Based on this, it seems that there may not be any connection at all.

However, it is vital to bear in mind that the TyG Index and VLDL had a substantially greater correlation coefficient (0.07), which shows that there is minimal positive link between the two variables. This is due to the fact that the correlation coefficient was significantly higher. The TyG Index and Apo-A were shown to have a correlation of 0.08, which indicates that there is a very weak positive link between the two. The TyG Index, as well as the Apo-B and Apo-B/Apo-A correlation coefficients, were quite close to zero, which indicated either that there was no link at all or that

there was a highly significant associations that were extremely weak. The correlation between the TyG Index and the several lipid-related metrics that are included in this table suggests that the connection between the two components is either very weak or very awful. This is the last point, but it is an important one. As a consequence of this, it seems that the TyG Index is not capable of having a significant influence or offering any kind of predictive value on the lipid variables that are being reviewed.

Discussion

According to the results of our most recent study, the ApoB/ApoA1 and TyG indices that were seen in hypertension patients were found to be substantially greater than those that were identified in the control group. This was the case because the control group had a lower level of hypertension. It is possible to directly assess the total amount of atherogenic particles that are circulating in the circulation by detecting the concentration of plasma apoB. Lipoprotein(a), very-low-density lipoprotein cholesterol, lipoprotein(a), and low-density lipoprotein (LDL) are all examples of particles that are classified under this group [13]. The Apo A1 ratio is a measure of the antiatherogenic capacity; larger values protect against cardiovascular risk, and a considerable body of research has demonstrated that the ApoB/ApoA1 ratio has a greater predictive power for cardiovascular disorders, obesity, and insulin resistance [14,15]. Apo A1 is a measure of the ability to prevent the development of atherosclerosis. One way to evaluate one's capacity to forestall the development of atherosclerosis is to use the Apo A1 test. It has been proven by a number of investigations that there is a substantial connection between hypertension and plasma apoB concentrations [16]. The results of these experiments were also seen in other research.

On the other hand, as far as the degree of causation that exists between plasma apoB levels and hypertension is concerned, it is not entirely simple. The proportion of visceral adipose depot was

shown to have a positive correlation with the levels of apoB, according to the findings of a research that was published in 2017. On the other hand, they exhibited an association that was opposite to that of insulin sensitivity.

According to the evidence presented here, diseases that are related with visceral obesity and insulin resistance are strongly associated with disturbances in the metabolism of apoB levels. It is possible to determine whether or not a person has insulin resistance or chronic cardiovascular disease by using the Apo B/A1 ratio, which has a strong predictive capacity. The findings of the research conducted by Ruhaak and colleagues [18] came to the conclusion that there is a correlation between being overweight and having diabetes. In addition, hypertension and dyslipidemia are also components of the metabolic syndrome, which is a condition that encompasses both of these characteristics. In most cases, hypertension and dyslipidemia are two conditions that are linked to one another. One of the most well-known types of pathogenicity is insulin resistance, which is also referred to as IR in some circles or circles.

The hypertension patients who participated in this study had a greater waist circumference, a higher FBS level, an increased TAG, and a lower HDL value when compared to the control group. These traits were all greater than those of the group that served as the control. All of these characteristics, which are symptoms of metabolic syndrome, are linked to atherosclerotic cardiovascular disease (ASCVD), which is something that may be avoided. There is a linkage between the two.

Some cross-sectional investigations [19] have shown that the presence of aberrant lipid levels has been shown to have a substantial connection to hypertension. These results were confirmed by the findings of this research. A large amount of dyslipidemia was found to be present in individuals who had been diagnosed with hypertension, according to the findings of this particular investigation. It is possible for hypertriglyceridemia to develop as a consequence of the presence of visceral fat, which in turn leads to an increase in the amount of free fatty acids that are present in the liver. Because of this, the liver's sensitivity to insulin is decreased, which ultimately results in an increase in the quantity of glucose that is generated by the liver [20]. There is a potential that the elevated levels of insulin, which lead to an increase in the number of LDL receptors, are associated to the higher levels of LDL that were seen in hypertensive individuals who participated in this research [21].

The TyG index is yet another one-of-a-kind marker that is achieved by the use of fundamental standard biochemical assays. All of this is done in

order to make up for the deficiencies that are present in the traditional infrared evaluation processes. Earlier research has shown that higher values of the TyG index, which is a new proxy for IR, may be of benefit in identifying the risk of HT across a variety of populations [22].

This has been established in earlier studies. A positive link between the TyG index and incident hyperglycemia was shown to exist after a follow-up period of 8.49 years. This association was found to exist independent of the individual's degree of obesity. According to the results of prior research, the TyG index demonstrated a high degree of sensitivity (96.5%) and a high level of specificity (85.0%) when it came to measuring insulin resistance (IR) in contrast to the hyperinsulinemia-euglycemic clamp test [23]. This was the case when comparing the two tests. We observed that the TyG index was considerably higher in hypertension patients when compared to the control group. This was proved by the outcomes of our study. Through the use of ROC curve analysis, we were able to ascertain the predictive value of the ApoB/ApoA1 and TyG index. As a result, we were able to employ the index in order to do forecasts. Both ratios were found to have diagnostic capacities that were comparable to one another, as indicated by the outcomes of this investigation (Table 3). At a threshold value of 0.940, the TyG index showed a sensitivity of 90% and a specificity of 87%. This was the case when applying the threshold value. In addition, sensitivity and specificity are discussed.

In contrast, when the cut-off value was established at 0.994, the Apo B/A1 index demonstrated a sensitivity of one hundred percent and a specificity of ninety-eight percent. This was the case when the cut-off value was set. As a result, the TyG index has the potential to be exploited as a sensitive screening test for insulin resistance in comparison to the ApoB/A1 test in hypertensive patients who are in situations where resources are limited to screen for insulin resistance in the tribal community. The reason for this is because the TyG index is also capable of identifying insulin resistance. An association between insulin resistance and both systolic and diastolic blood pressure has been shown by a number of studies [24]. As a consequence of this, a number of different kinds of adipose tissue, skeletal muscle, liver, and pancreas have a low degree of sensitivity to the action of insulin. When it comes to the mechanisms that are responsible for insulin resistance and how it affects blood pressure, we do not have a complete understanding of them.

Two disorders that have been related to a range of potential pathogenic links are high blood pressure and insulin resistance [25,26]. Both of these conditions have been associated to hyperglycemia.

Renal salt excretion, insufficient endothelium-dependent vasodilation, atherosclerosis, and inflammation are all examples of interactions that contribute to these conditions. Because of the toxic effects that insulin resistance has on the vasculature, it is possible for there to be an increase in blood pressure over a sustained period of time. It is of the highest significance to recognize this problem at an early stage in hypertensive patients as well as in the population that is at risk of developing hypertension. This is done in order to avoid the progression of the sickness.

The results of a meta-analysis that was conducted in 2012 and included sixty-five separate pieces of research [27] indicate that IR is an excellent predictor of cardiovascular disease. This was validated by HOMA-IR. 1. There are a number of non-insulin-based indications of insulin resistance that have been used in order to assess insulin action. Some of these indicators include ApoB/ApoA1, the ratio of total cholesterol to high-density lipoprotein cholesterol, the TyG index, and METSIR. Recently, these predictors that do not rely on insulin have been discovered as an alternative to the conventional hyperinsulinemia-euglycemic clamp method, which is both expensive and time-consuming [28].

Because the study was only conducted on the tribal group, it is not feasible to generalize the results to other groups. This is because the research was only conducted on the tribal group. Among the constraints, this is one of them. The HOMA-IR could not be carried out since there was an inadequate amount of infrastructure and facilities available. Despite the fact that this research did not establish a causal connection between the variables, it did find correlations between them. In conclusion, it is possible that the findings of our study were influenced by the fact that the sample size was rather small. This is something that should be taken into consideration. On the other hand, there has not been a single study that has been conducted up to this point that has included a comparison of the apoB/apoA1 ratio with the tag index with the intention of regularly screening for insulin resistance in a rural environment.

Conclusion

ApoB/ApoA1 ratio and TyG were the best prognostic factors for multiple sclerosis, with virtually comparable predictive values. In conclusion, these two measures were the best. As a result, the TyG index has the potential to function as a screening instrument for hypertensive inpatients that are insulin-resistant.

References

1. Forouzanfar MH, Liu P, Roth GA, Ng M, Biryukov S, Marczak L, Alexander L, Estep K,

- Abate KH, Akinyemiju TF, Ali R. Global burden of hypertension and systolic blood pressure of at least 110 to 115 mm Hg, 1990-2015. *Jama*. 2017 Jan 10; 317(2):165-82.
2. Liu J, Bu X, Wei L, Wang X, Lai L, Dong C, Ma A, Wang T. Global burden of cardiovascular diseases attributable to hypertension in young adults from 1990 to 2019. *Journal of Hypertension*. 2021 Dec 28; 39(12):2488-96.
3. Anchala R, Kannuri NK, Pant H, Khan H, Franco OH, Di Angelantonio E, Prabhakaran D. Hypertension in India: a systematic review and meta-analysis of hypertension prevalence, awareness, and control. *Journal of hypertension*. 2014 Jun; 32(6):1170.
4. Krittanawong C, Qadeer YK, Hayes RB, Wang Z, Virani S, Thurston GD, Lavie CJ. PM2. 5 and cardiovascular health risks. *Current problems in cardiology*. 2023 Jun 1; 48(6):101670.
5. Cox BD, Whicelow MJ, Prevost AT. The development of cardiovascular disease with anthropometric indices and hypertension in British adults. *International journal of obesity*. 1998 Oct; 22(10):966-73.
6. Fagerudd JA, Tarnow L, Jacobsen P, Stenman S, Nielsen FS, Pettersson-Fernholm KJ, Grönhagen-Riska C, Parving HH, Groop PH. Predisposition to essential hypertension and development of diabetic nephropathy in IDDM patients. *Diabetes*. 1998 Mar 1; 47(3):439-44.
7. Vladimirovna SV. Pathogenetic Relationships of Arterial Hypertension and Insulin Resistance. *IQRO*. 2023 Mar 16; 2(1):685-91.
8. Thaker V, Falkner B. Insulin Resistance and Other Mechanisms of Obesity Hypertension. *In Pediatric Hypertension 2023 Jan 10* (pp. 91-111). Cham: Springer International Publishing.
9. Ulloque-Badaracco JR, Al-kassab-Córdova A, Hernandez-Bustamante EA, Alarcon-Braga EA, Huayta-Cortez M, Carballo-Tello XL, Seminario-Amez RA, Herrera-Añazco P, Benites-Zapata VA. Association of apolipoproteins and lipoprotein (a) with metabolic syndrome: a systematic review and meta-analysis. *Lipids in Health and Disease*. 2023 Jul 7; 22(1):98.
10. Clarke R, Von Ende A, Schmidt LE, Yin X, Hill M, Hughes AD, Pechlaner R, Willeit J, Kiechl S, Watkins H, Theofilatos K. Apolipoprotein proteomics for residual lipid-related risk in coronary heart disease. *Circulation Research*. 2023 Feb 17; 132(4):452-64.
11. Simental-Mendía LE, Hernández-Ronquillo G, Gamboa-Gómez CI, Gómez-Díaz R, Rodríguez-Morán M, Guerrero-Romero F. The triglycerides and glucose index are associated with elevated blood pressure in apparently

- healthy children and adolescents. *European Journal of Pediatrics*. 2019 Jul 1; 178:1069-74.
12. Guerrero-Romero F, Rodríguez-Morán M. The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels: a randomized, double-anonymized, placebo-controlled clinical trial. *Journal of human hypertension*. 2009 Apr; 23(4):245-51.
 13. Morita SY. Metabolism and modification of apolipoprotein B-containing lipoproteins involved in dyslipidemia and atherosclerosis. *Biological and Pharmaceutical Bulletin*. 2016 Jan 1; 39(1):1-24.
 14. Jian ZH, Lung CC, Ko PC, Sun YH, Huang JY, Ho CC, Ho CY, Chiang YC, Chen CJ, Liaw YP. The association between the apolipoprotein A1/high-density lipoprotein-cholesterol and diabetes in Taiwan—a cross-sectional study. *BMC Endocrine Disorders*. 2013 Dec; 13:1-8.
 15. Nurtazina A, Kozhakhmetova D, Dautov D, Shakhanova A, Chattu VK. Apolipoprotein B/A1 ratio as a diagnostic alternative to triglycerides and HDL-Cholesterol for predicting metabolic syndrome among hypertensives in Kazakhstan. *Diagnostics*. 2020 Jul 23; 10(8):510.
 16. Borghi C, Rodriguez-Artalejo F, De Backer G, Dallongeville J, Medina J, Guallar E, Perk J, Banegas JR, Tubach F, Roy C, Halcox JP. The association between blood pressure and lipid levels in Europe: European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice. *Journal of hypertension*. 2016 Nov 1; 34(11):2155-63.
 17. Després JP, Lamarche B. Effects of diet and physical activity on adiposity and body fat distribution: implications for preventing cardiovascular disease. *Nutrition Research Reviews*. 1993 Jan; 6(1):137-59.
 18. Renee Ruhaak L, van der Laarse A, Cobbaert CM. Apolipoprotein profiling as a personalized approach to the diagnosis and treatment of dyslipidaemia. *Annals of clinical biochemistry*. 2019 May; 56(3):338-56.
 19. Ferrier KE, Muhlmann MH, Baguet JP, Cameron JD, Jennings GL, Dart AM, Kingwell BA. In isolated systolic hypertension, intensive cholesterol reduction lowers blood pressure and large artery stiffness. *Journal of the American College of Cardiology*. 2002 Mar 20; 39(6):1020-5.
 20. Matsuzawa Y, Shimomura I, Nakamura T, Keno Y, Kotani K, Tokunaga K. Pathophysiology and pathogenesis of visceral fat obesity. *Obesity research*. 1995 Sep; 3(S2):187s-94s.
 21. Misra A, Luthra K, Vikram NK. Dyslipidemia in Asian Indians: determinants and significance. *Japi*. 2004 Feb; 52:137-42.
 22. Sánchez-Íñigo L, Navarro-González D, Pastrana-Delgado J, Fernández-Montero A, Martínez JA. Association of triglycerides and new lipid markers with the incidence of hypertension in a Spanish cohort. *Journal of hypertension*. 2016 Jul 1; 34(7):1257-65.
 23. Fossum E, Høieggen A, Reims H, Moan A, Rostrup M, Eide I, Kjeldsen S. High screening blood pressure is related to sympathetic nervous system activity and insulin resistance in healthy young men—blood pressure. 2004 Jan 1; 13(2):89-94.
 24. Quesada O, Claggett B, Rodriguez F, Cai J, Moncrieff AE, Garcia K, Del Rios Rivera M, Hanna DB, Daviglius ML, Talavera GA, Bairey Merz CN. Associations of insulin resistance with systolic and diastolic blood pressure: a study from the HCHS/SOL. *Hypertension*. 2021 Sep; 78(3):716-25.
 25. Zhou MS, Schulman IH, Zeng Q. Link between therein—angiotensin system and insulin resistance: Implications for cardiovascular disease. *Vascular medicine*. 2012 Oct; 17(5):330-41.
 26. Fossum E, Høieggen A, Reims H, Moan A, Rostrup M, Eide I, Kjeldsen S. High screening blood pressure is related to sympathetic nervous system activity and insulin resistance in healthy young men—blood pressure. 2004 Jan 1; 13(2):89-94.
 27. Gast KB, Tjeerdema N, Stijnen T, Smit JW, Dekkers OM. Insulin resistance and risk of incident cardiovascular events in adults without diabetes: meta-analysis. *PloS one*. 2012 Dec 28; 7(12):e52036.
 28. Pacini G, Mari A. Methods for clinical assessment of insulin sensitivity and β -cell function. *Best Practice & Research Clinical Endocrinology & Metabolism*. 2003 Sep 1; 17(3):305-22.