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## SOCIAL AND BEHAVIORAL SCIENCES. Health Care Sciences



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B – Data collection;
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# Role of Lipid Profile, Apolipoproteins, and Their Ratio for Prediction of Cardiovascular Disease in Essential Hypertension



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Abs

	Abstract
Background and	Dyslipidemia is a risk factor for cardiovascular disease, and lipid metabolism
Aim of Study:	changes are linked to essential hypertension. The aim of the study: to investigate the
	significance of lipid parameters, apolipoproteins, and their ratio in predicting
	cardiovascular disease among individuals with essential hypertension.
Material and Methods:	250 patients with essential hypertension and 250 healthy control subjects were
	enrolled in this case-control study and their serum lipids and apolipoproteins were
	analyzed. Differences between cases and controls were examined using independent
	sample t-test and, a p-value $< 0.05$ was considered significant.
Results:	In the essential hypertensive group, fasting blood glucose (FBG), total cholesterol
	(TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), very low-
	density lipoprotein cholesterol (VLDL-C), apolipoprotein B100 (Apo B100) and Apo
	B100/Apo A1 ratio were increased significantly compared to control subjects.
	Essential hypertensive patients had significantly decreased levels of apolipoprotein
	Al (Apo Al) and high-density lipoprotein cholesterol (HDL-C) compared to
	controls. Moreover, age, body mass index (BMI), FBG, TC, TG, LDL-C, and VLDL-
	C, as well as the Apo B100/Apo A1 ratio, were significantly positively correlated
	with both systolic blood pressure (SBP) and diastolic blood pressure (DBP), but
	HDL-C and Apo A1 were significantly negatively correlated in essential
	hypertensive subjects. There was a significant positive correlation between apo
	B100 and SBP in people with essential hypertension. Apo B100 and DBP showed a
	positive association, however, it was not statistically significant.
<b>Conclusions:</b>	Essential hypertensive people with dyslipidemia and an elevated Apo B100/Apo A1
	ratio are at an increased risk for the development of cardiovascular disease.
Keywords:	essential hypertension, dyslipidemia, apolipoproteins, cardiovascular disease,
·	systolic blood pressure, diastolic blood pressure
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#### Introduction

The prevalence of hypertension has increased to the point where it is now a serious public health issue worldwide. It is the leading cause of chronic illness treated in primary care clinics and the most common type of non-communicable disease (Kossaify et al., 2014). In 1975, there were 590 million people (14.5%) with high blood pressure around the world. This number went up to 1.13 billion (15.3%) in 2015. The number of people with high blood pressure is expected to rise to 1.56 billion by 2025 (Forouzanfar et al., 2017). In India, the prevalence of hypertension among adults is generally over 30%, with 34% in urban areas and 28% in rural areas (Anchala et al., 2014).

Ninety percent of those who are diagnosed with hypertension have essential hypertension, which is defined as having high blood pressure for no obvious reason. Idiopathic persistent elevation of the systemic arterial pressure characterizes essential hypertension (Kossaify et al., 2013). In addition to dietary patterns, variables such as obesity, smoking, alcohol intake, and dyslipidemia are key contributors to the development of hypertension (Bhavani et al., 2003).

Dyslipidemia arises as a result of alteration in lipid metabolism and is considered a risk factor for atherosclerotic cardiovascular disease (Hussain et al., 2019). It is well-established that hypertension is linked to disturbances in lipid metabolism, which in turn lead to abnormalities in blood lipid and lipoprotein levels. The prognosis of hypertensive patients is also significantly hampered by the presence of hyperlipidemia, as has been well reported (Harvey et al., 1990). A tight relationship between dyslipidemia and hypertension has been suggested by several researchers (Nayak et al., 2016; Osuji et al., 2012). However, conventional lipid biomarkers do not provide sufficiently reliable measurements of dyslipidemia. Low-density lipoprotein cholesterol (LDL-C), very lowdensity lipoprotein cholesterol (VLDL-C), and intermediate-density lipoproteins (IDL) all contain transporting molecules like apolipoprotein B (Apo B), so determining these molecules allows for a more accurate estimation of atherogenicity than the traditional lipid parameters. Apolipoprotein A1 (Apo A1) is a key component of HDL-C, the antiatherogenic lipoprotein. Apo A1 is favored over high-density lipoprotein cholesterol in predicting cardiovascular diseases (HDL-C). The Apo B/Apo A1 ratio thus appears to be a more precise and comprehensive biomarker of lipid metabolism and cardiovascular disease prediction (Nurtazina et al., 2020).

Multiple studies have elucidated that lipid markers play role in essential hypertension (Bhavani et al., 2003; Osuji et al., 2012). However, the predictive value of apolipoproteins and their ratio (Apo B100/Apo A1 ratio) in cardiovascular disease risk assessment is still not well recognized. Because of the paucity of information on apolipoproteins in essential hypertension, we undertook this study to better understand the role of lipid parameters, apolipoproteins, and their ratio (Apo B100/Apo A1 ratio) for the prediction of cardiovascular disease in essential hypertension.

*The aim of the study*. To investigate the significance of lipid parameters, apolipoproteins, and their ratio in predicting cardiovascular disease among individuals with essential hypertension.

#### **Materials and Methods**

This case-control study was conducted in the Department of Biochemistry, Shyam Shah Medical College, Rewa, Madhya Pradesh, India over 12 months after receiving ethical clearance from Institutional Ethical Committee. A total of 500 subjects of either sex were selected for the present study. Of these, 250 were patients with essential hypertension and 250 were healthy control subjects. 250 patients of essential hypertension (of either sex) of the age group 35-75 years were selected from the OPD of Medicine ward of Shyam Shah Medical College and associated Hospital, Rewa, Madhya Pradesh, India. The JNC 7 (Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) criteria were used to determine which cases of essential hypertension should be included (Chobanian et al., 2003). 250 normal healthy subjects of the same age group with no symptoms and signs suggestive of hypertension and no family history of the hypertensive disease were selected from in and around the hospital as controls. Informed written consent was obtained from each participant once they had been fully explained about the study.

Patients with the following disease/condition were excluded from the present study: secondary hypertension, severe hepatic failure, renal failure, unstable cardiovascular condition, past incidences of cerebrovascular conditions, collagenous tissue disease, malignancy, thyroid disease, severe depression, dementia, and diabetes mellitus. Pregnant women were also excluded from the present study.

The standard apparatus was used to take measurements of both height and weight with the subjects dressed in minimal clothing and barefoot. Calibrated electronic weighing scales were used for the measurement of weight whereas height was measured to the nearest centimeter using a portable stadiometer. Body mass index (BMI) was calculated as weight in kilograms, divided by height in meters squared (kg/m<sup>2</sup>). The same person took all of the anthropometric measurements.

Following a resting period of 10 minutes, both the systolic and diastolic blood pressures were measured using a mercury sphygmomanometer following an accepted medical practice.

Under aseptic conditions, about 05 ml of fasting venous blood was drawn from both patients with essential hypertension and control participants, and the sample was distributed into two tubes based on the analysis to be done. Approximately 2 ml of blood was drawn into a fluoride bulb to determine fasting plasma glucose and the remaining 03 ml blood sample was dispensed into the plain tube for analysis of lipid parameters and apolipoproteins. After drawing blood, the samples were



centrifuged for 10 minutes at 3000 rpm to get serum/plasma. The routine biochemical parameters were analyzed by standard methods using a Biosystem BA-400 chemistry analyzer. Apo B100 and Apo A1 were measured by turbidimetric immunoassay, endpoint method. Low-density lipoprotein and very low-density lipoprotein cholesterol were calculated using Friedewald's equation (Friedewald et al., 1972).

#### Statistical analysis

The data were analyzed using Statistical Package for Social Science version 20 (IBM, SPSS Statistics 20, Armonk, NY, USA) and results were presented as mean±SD values. GraphPad Prism 5 was used to create the graph. Statistical differences between cases and controls were examined using the "student independent

#### Table 1

Baseline Characteristics of Studied Subjects

sample t-test". The chi-squared test ( $\chi^2$  test) was applied to the categorical information. To ascertain the correlation between important parameters, Pearson's correlation coefficient was determined. Significant was defined as the *p*-value is less than 0.05.

Results

Table 1 shows the baseline characteristics of the studied subjects. Patients with essential hypertension and those serving as controls were statistically indistinguishable from one another in terms of age and gender. Body mass index, SBP, and DBP were statistically significantly increased in essential hypertension cases compared to controls.

Variables	Controls	Cases
Age (years)	48.24±11.23	$48.70 \pm 11.82^{NS}$
Sex (M/F)	113/137	114/136 <sup>NS</sup>
BMI (Kg/m <sup>2</sup> )	21.89±1.00	27.60±1.68**
SBP (mmHg)	$115.32 \pm 3.95$	$155.35 \pm 7.40^{**}$
DBP (mmHg)	76.12±4.95	$96.03{\pm}5.57^{**}$

*Note.* <sup>NS</sup>Not significant (p>0.05); <sup>\*\*</sup>Significant at p<0.001; BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure.

Table 2 shows fasting blood glucose and lipid profiles in the studied subjects. In essential hypertension subjects, fasting blood glucose (FBG) and all the lipid parameters i.e. TC, TG, LDL, and VLDL except HDL were increased compared to control subjects and were statistically significant whereas HDL was statistically significantly reduced in essential hypertension subjects. Apolipoprotein B100 was increased in essential hypertension subjects whereas Apo A1 was reduced compared to normal healthy control subjects and these differences were statistically significant.

#### Table 2

Fasting Blood Sugar and Lipid Profile in Studied Subjects

Variables	Controls	Cases
FBG (mg/dl)	85.08±6.23	95.01±7.22**
TC (mg/dl)	$170.74 \pm 12.40$	220.57±11.48**
TG (mg/dl)	135.37±7.77	236.32±47.10**
HDL-C (mg/dl)	52.83±4.67	37.34±3.98**
LDL-C (mg/dl)	90.83±13.35	135.97±11.63**
VLDL-C (mg/dl)	27.07±1.55	47.26±9.42**
Apo A1(mg/dl)	$128.96 \pm 25.73$	87.83±4.14**
Apo B100 (mg/dl)	99.50±22.44	149.87±11.30**

*Note.* <sup>\*\*</sup>Significant at p < 0.001; FBG= Fasting blood glucose; TC=Total cholesterol; TG=Triglyceride; HDL-C=High density lipoprotein cholesterol; LDL-C=Low density lipoprotein cholesterol; VLDL-C=Very low density lipoprotein cholesterol.

Figure 1 shows the comparison of the Apo B100/Apo A1 ratio between essential hypertension subjects and controls. Essential hypertension patients had significantly increased levels of Apo B100/A1 ratio compared to control subjects.

Table 3 shows the correlation of studied parameters with systolic blood pressure and diastolic blood pressure in essential hypertension subjects.







#### Table 3

Correlation of Studied Parameters with Systolic Blood Pressure and Diastolic Blood Pressure in Essential Hypertension Subjects

Variables	With SBP		With DBP	
	<i>r</i> -value	<i>p</i> -value	<i>r</i> -value	<i>p</i> -value
Age	0.299	$0.000^{**}$	0.225	$0.000^{**}$
BMI	0.635	$0.000^{**}$	0.527	$0.000^{**}$
FBG	0.393	$0.000^{**}$	0.286	$0.000^{**}$
TC	0.540	$0.000^{**}$	0.388	$0.000^{**}$
TG	0.623	$0.000^{**}$	0.462	$0.000^{**}$
HDL	-0.449	$0.000^{**}$	-0.350	$0.000^{**}$
LDL	0.183	$0.004^{**}$	0.129	$0.042^{*}$
VLDL-C	0.623	$0.000^{**}$	0.462	$0.000^{**}$
Apo Al	-0.401	$0.000^{**}$	-0.301	$0.000^{**}$
Apo B100	0.148	$0.019^{*}$	0.111	0.080 <sup>NS</sup>
Apo B100/Apo A1	0.306	$0.000^{**}$	0.232	$0.000^{**}$

*Note.* <sup>NS</sup>Not significant (*p*>0.05); \*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed); BMI=Body mass index; SBP=Systolic blood pressure; DBP=Diastolic blood pressure; FBG= Fasting blood glucose; TC=Total cholesterol; TG=Triglyceride; HDL-C=High density lipoprotein cholesterol; LDL-C=Low density lipoprotein cholesterol; VLDL-C=Very low-density lipoprotein cholesterol.

In essential hypertension participants, age, BMI, FBG, lipid measures such as TC, TG, LDL, and VLDL, as well as the Apo B100/Apo A1 ratio, were significantly positively associated with both SBP and DBP, but HDL and Apo A1 were significantly negatively correlated. In persons with essential hypertension, there was a significant positive correlation between Apo B100 and SBP. Despite a favorable correlation between Apo B100 and DBP, it was not statistically significant.

#### Discussion

This case-control study took place in a hospital setting and included patients with essential hypertension. In the current study, an attempt was made to describe the abnormality of lipid parameters, apolipoproteins, and their ratio (Apo B/Apo A1 ratio) among patients with essential hypertension in a central Indian setting.

The present study found that both systolic and diastolic blood pressures were significantly higher in participants with essential hypertension compared to controls. This is in line with previous studies (Mahapatro et al., 2020; Nayak et al., 2016; Osuji et al., 2012; Pyadala et al., 2017; Sur et al., 2015). As blood pressure rises, so does the chance of cardiovascular events; the more hypertensive a person is, the greater the likelihood that he/she may suffer from cardiovascular disease. Since there was no statistically significant age difference between the people with essential hypertension and the controls, it can be concluded that the study participants were age-matched. In hypertensive participants, however, age was found to have a positive and statistically significant relationship with both systolic and diastolic blood pressures. Systolic blood pressure increases with age, which may be caused by an increase in artery stiffness brought on by atherosclerotic changes to the arterial wall. Numerous epidemiological studies have emphasized the link between arterial stiffness in hypertension patients and

other cardiovascular illnesses in older individuals as compared to younger people. There is an upward trend in the prevalence of hypertension and vascular stiffness as people age (AlGhatrif et al., 2013; Ferreira et al., 2012). Additionally, compared to controls, the hypertension participants in this study had statistically significantly higher BMI, which is consistent with studies done by Nayak et al. (2016); Osuji et al. (2012); Sur et al. (2015). Moreover, BMI was positively related to both SBP and DBP in essential hypertension subjects. This is due to the association between a greater BMI and a higher plasma volume and cardiac output. Therefore, obesity is a risk factor for hypertension. Losing weight has a significant influence on reducing cardiovascular morbidity and mortality in hypertensive people, including stroke, heart attack, and heart failure (Linderman et al., 2018).

In this study, essential hypertension participants had significantly higher fasting blood sugar levels than control subjects. This is following the study carried out by Nayak et al. (2016), who reported statistically significant increased levels of fasting blood sugar in both stage I and stage II hypertensive subjects. Furthermore, in our study, we found a significant and positive correlation of fasting blood sugar with both systolic and diastolic blood pressure in essential hypertension subjects. As the fasting blood glucose level increases as a result of metabolic disorders, obesity, and hyperglycemia with insulin resistance, the reninangiotensin system (RAS) may undergo alterations. This may have an effect on the patient's blood pressure (Jia et al., 2016; Zhou et al., 2015).

Alterations in lipid metabolism leading to abnormalities in blood lipid and lipoprotein levels have been related to hypertension. It has also been demonstrated that hyperlipidemia dramatically worsens the prognosis in hypertensive individuals (Harvey & Beevers, 1990). An abnormality in blood lipid and lipoprotein levels (also



known as dyslipidemia) is a major, controllable risk factor for cardiovascular disease (CVD) (Kannel et al., 1971). Abnormal serum lipid and lipoprotein levels have been identified as independent risk factors for essential hypertension, giving rise to the term "dyslipidemic hypertension" (Williams et al., 1988). In subjects with essential hypertension, we found that all of the lipid parameters (total cholesterol, triglycerides, low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol) were significantly higher than in controls, except for HDL, which was significantly lower. These results are consistent with the studies done by Mahapatro et al. (2020) and Nayak et al. (2016). Osuji et al. (2012) also found such a type of dyslipidemic pattern in hypertensive subjects compared to control subjects. In addition, we found a significant positive association of TC, TG, LDL-C, and VLDL-C with both systolic and diastolic blood pressures in essential hypertension subjects whereas HDL-C was significantly negatively associated with SBP and DBP in cases of essential hypertension. Hypertension and dyslipidemia are both well-known contributors to the development of cardiovascular disease (Carmena et al., 2004; Gotto, 2005). Endothelial dysfunction, which is exacerbated by dyslipidemia, is a major contributor to the etiology of several cardiovascular disease risk factors, including atherosclerosis, thrombosis, insulin resistance, and hypertension. Endothelial cells are known to be negatively affected by low-density lipoprotein (LDL) cholesterol and lipoproteins high in triglycerides, while high-density lipoprotein (HDL) cholesterol may have protective effects (O'Connell & Genest, 2001). Macrovascular problems like coronary heart disease (CHD) and stroke have been linked to elevated blood cholesterol levels (Albuche et al., 2000). Lewis suggested that blood TC in the range of 5.0-6.5mmol/L may be regarded as undesirable due to the increased risk of coronary heart disease when the cholesterol level reaches 5.0 mmol, as observed in various epidemiological studies (Lewis, 1986; McGill, 1968). Low HDL levels are associated with an increased risk of cardiovascular disease, albeit the reasons why are not well understood. According to experiments, HDL-C helps increase the outflow of cholesterol from foam cells in vascular atherosclerotic plaque depots to the liver, where it may be broken down and eliminated. HDL-C also possesses anti-inflammatory powerful and antioxidant characteristics, which lower the likelihood of developing atherosclerosis (Barter et al., 2004; Mackness et al., 2000). It has also been shown that the existence of additional atherogenic risk factors is linked to a low HDL-C level. According to Pavithran et al. (2007), modifications in lipid metabolism, including a drop in HDL-C, might result in endothelial damage and increased blood pressure, which may help to partially explain why it has such a high predictive value for coronary heart disease. It is well known that dyslipidemia and hypertension frequently coexist. This relationship has been attributed to underlying central obesity and the accompanying insulin resistance, which are crucial to the pathophysiology of both hypertension and dyslipidemia.

A 7-year follow-up study on Finnish males revealed that dyslipidemia, a component of the metabolic syndrome, foreshadowed the onset of hypertension (Laaksonen et al., 2008). Furthermore, Halperin et al. (2006) have shown that hypertension is brought on by dyslipidemia in people who appear to be in good health. According to Hausmann et al., people who have elevated TG levels along with low HDL-C have more widespread coronary atheromas than people who only have elevated LDL-C (Hausmann et al., 1996).

Numerous studies have demonstrated the significance of apolipoproteins- Apo A1 & Apo B100, the two main apolipoproteins for lipid transport in the processes of atherosclerosis and its consequences (Luc et al., 2002; Meisinger et al., 2005; Walldius et al., 2001; Yusuf et al., 2004). However, the association between apolipoprotein levels and the risk of hypertension has only been discovered in a few studies. Nayak et al. (2016) observed a non-significant fall in the value of serum Apo A1 in the hypertensive patients when compared to controls whereas a significant increasing trend was observed in the levels of Apo B100 from the control group to Stage I and Stage II hypertensive patients reflecting its contributing role as a cardiovascular risk marker. Consistent with these results, we found that people with essential hypertension had significantly higher levels of Apo B100 and lower levels of Apo A1 than controls. In addition, apo A1 was significantly inversely correlated with both SBP and DBP in essential hypertensive individuals, while Apo B 100 was positively correlated with both. In our study, the Apo B100/Apo A1 ratio was also increased significantly in essential hypertension subjects compared to controls and the ratio of Apo B100/Apo A1 was significantly and positively associated with both SBP and DBP, which is in accordance with Nayak et al. (2016). Similarly, Lee et al. (1986), found higher levels of Apo B100/Apo A1 ratio in hypertensive subjects compared to controls but was statistically insignificant. Even, the severity of atherosclerosis was found to have a strong correlation with serum Apo B in a normolipidemic subgroup, according to the findings of Haidari et al. (2001). After controlling for the impact of gender, age, smoking, and hypertension, Sabino et al. (2008), observed that both the Apo B level and the Apo B/A1 ratio independently linked with peripheral atherosclerosis and brain stroke. The ApoB/ApoA-I ratio is widely acknowledged as a more accurate predictor of cardiovascular risk than other conventional lipid markers (Montali et al., 2015). Therefore, essential hypertensive people with dyslipidemia and an elevated Apo B100/Apo A1 ratio are at an increased risk for the development of cardiovascular disease.

### Conclusions

The present study demonstrated that essential hypertension is characterized by dyslipidemia (increased total cholesterol, TG, LDL, and decreased HDL), alteration in apolipoproteins levels (increased Apo B100 and decreased Apo A1), and their ratio (increased Apo B100/Apo A1 ratio), suggesting that high blood pressure may be responsible for disturbances in lipoprotein



metabolism. Furthermore, the Apo B100/ Apo A1 ratio may be used as a complementary marker for the prediction of the risk of cardiovascular disease in essential hypertension subjects.

Prospects for further research include establishing a causal relationship between dyslipidemia and hypertension; identifying changes in the lipid profile caused by diet, physical activity, medications, or other influences; and determining the relationship of lipid parameters and apolipoproteins with other cardiovascular risk factors.

#### **Ethical Approval**

Institutional Ethical Committee approval was obtained from the institution (Reference No: IEC/MC/2020/459, dated 08/01/2021).

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