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Original Research Article

A Correlative Study of Serum Homocysteine with Serum Lipid Profile in Young Adult Hypertensive Patients in Indian Population

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ABSTRACT

Background: Hypertension and dyslipidemia are major risk factors for cardiovascular disease (CVD) and a leading cause of morbidity and mortality in both developed and developing countries. The prevalence of hypertension is projected to increase globally, especially in the developing countries. In recent years, rapid urbanization, unhealthy diet and lifestyle changes have led to an increased rate of CVD. Hyperhomocysteinemia (HHcy) has been regarded as a new risk factor related to hypertension. An elevated homocysteine level induces thrombogenicity, causes procoagulant state and promotes the proliferation of smooth muscle cells, which could lead to vascular constriction and stiffness. Our study was aimed to find out the status of serum homocysteine and serum lipid profile in hypertensive and normo- tensive subjects & correlation of serum homocysteine with serum lipid profile in hypertensive subjects. This study was limited and this topic needs to be further worked upon.

Materials and Methods: The present study was conducted on 100 patients with essential hypertension who attended the medical OPD of Jawahar Lal Nehru Medical College and Associated Group of Hospital, Ajmer. The results of patients were compared with 50 normotensive subjects. Anthropometric para- meters and biochemical estimation were performed after taking approval from Ethical Committee. The serum total cholesterol (TC), triglyceride (TG) and HDL cholesterol (HDL-C) were determined enzymatically, while LDL cholesterol (LDL-C) was calculated using the Friedewald formula & serum homocysteine was determined by ELISA technique.

Results: The mean serum level of homocysteine was elevated in hypertensive subjects as compared to normotensive subjects and was highly significant (P<0.0001). The mean values of serum TC, TG and LDL-C were significantly higher and statistically significant among the hypertensive patients compared to normotensive subjects & the mean HDL –C level was lower in the hypertensive subjects compared to normo-tensive subjects and was statistically significant. The present study has also shown the positive correlation between serum homocysteine and serum TC, TG and LDL-C & negative correlation between serum homocysteine and HDL-C in hypertensive subjects.

Conclusion: The observations of this study have revealed that there was significant alteration of serum homocysteine, cholesterol, triglyceride, HDL cholesterol and LDL cholesterol in hypertensive patients. Therefore, for routine monitoring of hypertensive patients to prevent the coronary heart disease (CHD) and other consequences, the reinforcement of these parameters may be recommended in daily clinical practice.

Keywords: Cardiovascular disease, Hyper homocysteinemia, Total Cholesterol, Triglyceride, HDL cholesterol, LDL cholesterol, Methylenetetrahydrofolate Reductase, Systolic Blood Pressure, Diastolic Blood Pressure.

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INTRODUCTION

Hypertension is defined as an average SBP ≥140 mmHg and DBP ≥90 mmHg without antihypertensive medication according to the seventh report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC-7)[1]. Hypertension and dyslipidemia are major risk factors for cardiovascular disease (CVD) and account for more than 80% of deaths and disability in low and middle-income countries[2,3]. The prevalence of hypertension is projected to increase globally, especially in the developing countries[3]. Several previous studies showed the relation between hyperlipidemia and hypertension[4,5]. An excessive daily intake of saturated fats, cholesterol, other sources of calories and subsequent disturbance of lipid profile leading to hypertriglyceridemia and hypercholesterolemia are associated with obesity and consequently, hypertension[6,7], increased peripheral resistance, cardiac output and salt congestion[6] are some of the responsible mechanisms which lead to hypertension. Epidemiological studies have established a strong association between hypertension and coronary artery disease[8]. Indians have been reported to have the highest incidence of CAD[9]. Hyperhomocysteinemia (HHcy) is a medical condition generally defined as serum homocysteine level ≥15 µmol/L. HHcy has been regarded as a new risk factor related to hypertension.[10-13]

Hyperhomocysteinemia in Indians

In contrast to the west, Indian studies examining the prevalence of hyperhomocysteinemia in the community have reported a much higher incidence of 52 to 84%[14-16]. The mean homocysteine levels are quiet high, varying from 19.5 to 23.2µmol/L[14-16]. HHcy can be

considered to be an important cardiovascular risk factor in Indians[17]. Homocysteine is an intermediate sulfur-containing amino acid in the metabolism of methionine. It is recycled either by transsulfration to cysteine or by remethylation to methionine and is mainly cleared through the kidneys[18,19]. Numerous nutritional deficiencies (folate, vitamins B_{12} and B_6 as cofactors of methionine metabolism), genetic variation (mutation of methylene tetrahydrofolate reductase enzyme), drugs (phenytoin, carbamazepine), or diseases (renal insufficiency) affect homocysteine metabolism and influence serum homocysteine levels[20]. A dietary deficiency of vitamins $B_{12,}$ folic acid, and B_6 is often present amongst Indians. The main source of vitamin B_{12} in the diet is non-vegetarian food viz. meat and eggs. Vegetarian food contains practically no vitamin B_{12}. As Indians are often vegetarian, it predisposes them to vitamin B_{12} deficiency. Vegetarians had a 4.4 times higher risk of low vitamin B12 than those who ate non-vegetarian food frequently and also a 3 times greater chance of hyperhomocysteinemia. Urban men were significantly more likely to have hyperhomocysteinemia than rural men[21]. Although majority of Indians are vegetarian, there is also a high incidence of folic acid deficiency reported[22]. Pyridoxine deficiency is also reported to be quite common amongst Indians[22,23]. A second important factor that predisposes Indians to hyperhomocysteinemia is a genetic defect in the enzymes that metabolize homocysteine, especially MTHFR. Studies have reported that upto one-third of Indians have a genetic defect which predisposes to decreased activity of MTHFR[24,25]. In a large epidemiological study (NHANES III) each 5µmol/L increase in plasma Homocysteine levels was associated with an increase in systolic (SBP) and diastolic blood pressure (DBP) of 0.7 and 0.5 mmHg, respectively, in men, and 1.2 and 0.7 mmHg, respectively, in women[26]. Our study was aimed to find out the status of serum lipid profile and homocysteine in hypertensive and normotensive subjects & correlation of serum homocysteine with serum lipid profile in hypertensive subjects. This study was limited and this topic needs to be further worked upon.

MATERIALS AND METHODS

The present study is a case control study, 100 subjects with Essential hypertension (group-2) and 50 age and sex matched healthy controls (group-1) both male and female between 30 -50 years of age were recruited from Jawahar Lal Nehru Medical College and Associated Group of Hospital, Ajmer. The present study is approved by Institutional Ethical Committee.

Exclusion criteria: Pregnant, lactating women and patients with diabetes, liver disease and patients on drugs which might influence the serum levels of lipid profile and Homocystiene were excluded from the study.

Height and weight were measured with the subject in light clothes without shoes, and BMI was calculated by using the formula:
[BMI = weight (Kgs) /height (metre)^2.

Blood pressure (BP) was measured by a physician. Patients who were found to have Systolic Blood Pressure (SBP) higher than 140 mmHg and/or Diastolic Blood Pressure (DBP) higher than 90 mmHg on three consecutive days were considered as hypertensive[27]. Serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels were classified on the basis of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III)[28]. Elevated TC was defined as having TC levels of (>200 mg/dL), Low HDL-C was defined as having HDL-C levels of (< 40 mg/dL) elevated LDL-C was defined as having LDL-C levels of (>130 mg/dL), Elevated TG was defined as having triglyceride levels of (>150 mg/dL). Blood samples were collected after an overnight fast (12-14hrs) under aseptic conditions from all the study participants. All samples were centrifuged and analyzed for serum lipid profile and serum Homocysteine. The Serum Total cholesterol, triglyceride and HDL cholesterol were determined enzymatically, while LDL cholesterol was calculated using the Friedewald formula & Serum Homocysteine was determined by ELISA technique.

Statistical analysis

All data were analysed by SPSS-13 version. P< 0.01 was considered as significant.

RESULTS

A total of 150 subjects were studied. The results are summarized in Tables and Figures. The Table 1, Fig 1 shows that the mean ± SD of weight and BMI were more in hypertensive patients than normotensive and the difference was significant (P<0.001) while the mean age was not significant (P>0.005). The Table 2, Fig 2 shows that the level of serum Homocysteine (18.97 ± 4.5 v/s 10.06 ± 2.9) in hypertensive patients compared to normotensive were highly significant (P<0.0001). The Table 2, Fig 2 also shows that the level of serum TC (223.13 ± 53.05 v/s 162.04 ± 34.01), serum TG (175.95 ± 75.26 v/s 120.02 ± 28.02), and serum LDL-C (148.06 ± 56.53 v/s 92.76 ± 16.5) in hypertensive patients compared to normotensive were significantly (P<0.001) raised while serum HDL-C (40.07 ± 6.5 v/s 50.06 ± 9.7) in hypertensive patients compared to normotensive was decreased significantly (P<0.001).

The serum Homocysteine showed positive correlation with TC (r=0.68) (Figure-3), TG (r = 0.65) (Fig 4), LDL-C (r=0.67) (Fig 6) and negative correlation with HDL-C (r=-0.66) (Fig 5) in hypertensive subjects.

Table 1: Anthropometric Parameters of Normotensive v/s Hypertensive Subjects

PARAMETERS	NORMOTENSIVE n = 50	HYPERTENSIVE n =100	P VALUE
Age (yrs)	39.84 ± 6.04	42.53 ± 5.49	> 0.005
Height (cm)	156.08 ± 7.19	150.18 ± 5.4	< 0.001
Weight (kg)	60.16 ± 10.19	67.72 ± 8.17	< 0.001
BMI (Kg/m^2)	21.75 ± 2.6	26.6 ± 2.9	< 0.001

Table 2: Biochemical Parameters of Normotensive v/s Hypertensive Subjects

BIOCHEMICAL PARAMETERS	NORMOTENSIVE n =50	HYPERTENSIVE n=100	P VALUE
Serum Homocysteine (µmol/l)	10.06 ± 2.9	18.97 ± 4.5	<0.0001
Total Cholesterol (mg/dl)	162.04 ± 34.01	223.13 ± 53.05	<0.001
Triglyceride (mg/dl)	120.02 ± 28.02	175.9 5± 75.26	<0.001
HDL-C (mg/dl)	50.06 ± 9.7	40.07 ± 6.5	<0.001
LDL-C (mg/dl)	92.76 ± 16.5	148.06 ± 56.53	<0.001

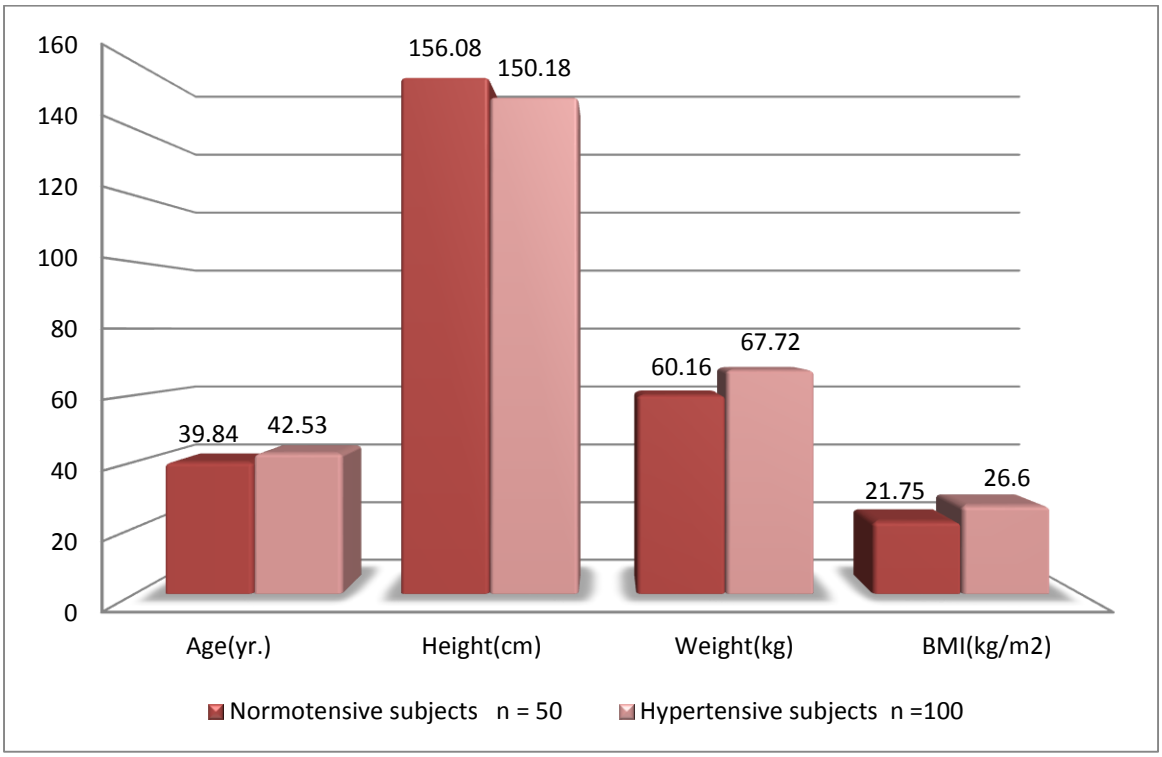

Fig 1: Comparision of Anthropometric Parameters of Normotensive v/s Hypertensive Subjects

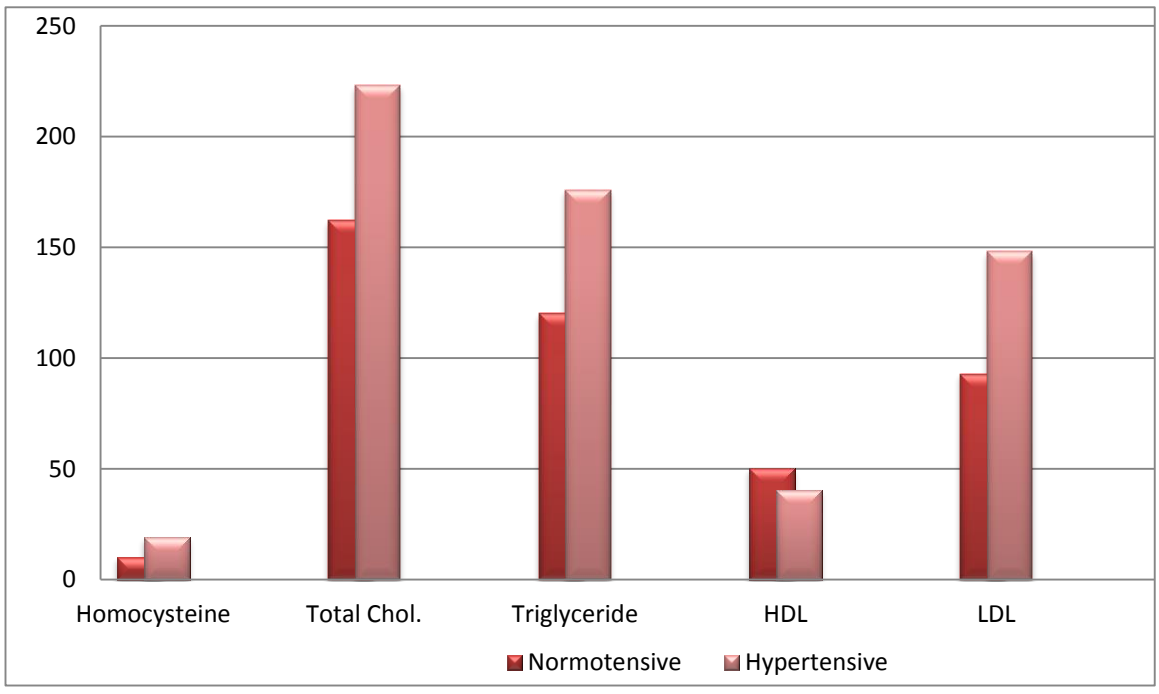

Fig 2: Comparision of Biochemical Parameters of Normotensive v/s Hypertensive Subjects

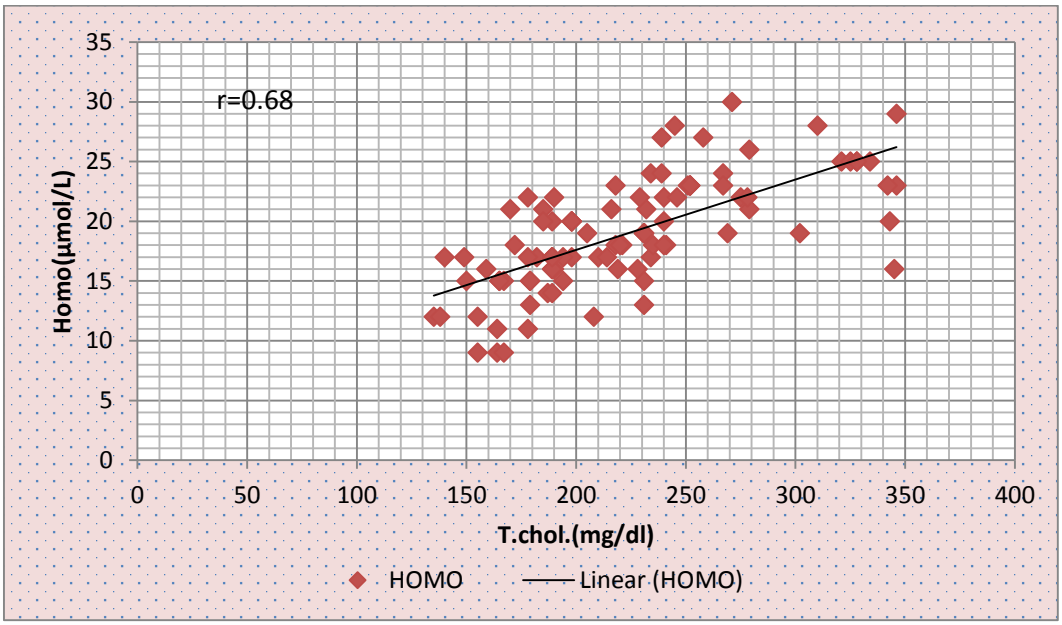

Fig 3: Correlation of Serum Homocysteine With Total Cholesterol in Hypertensive subjects (n=100).

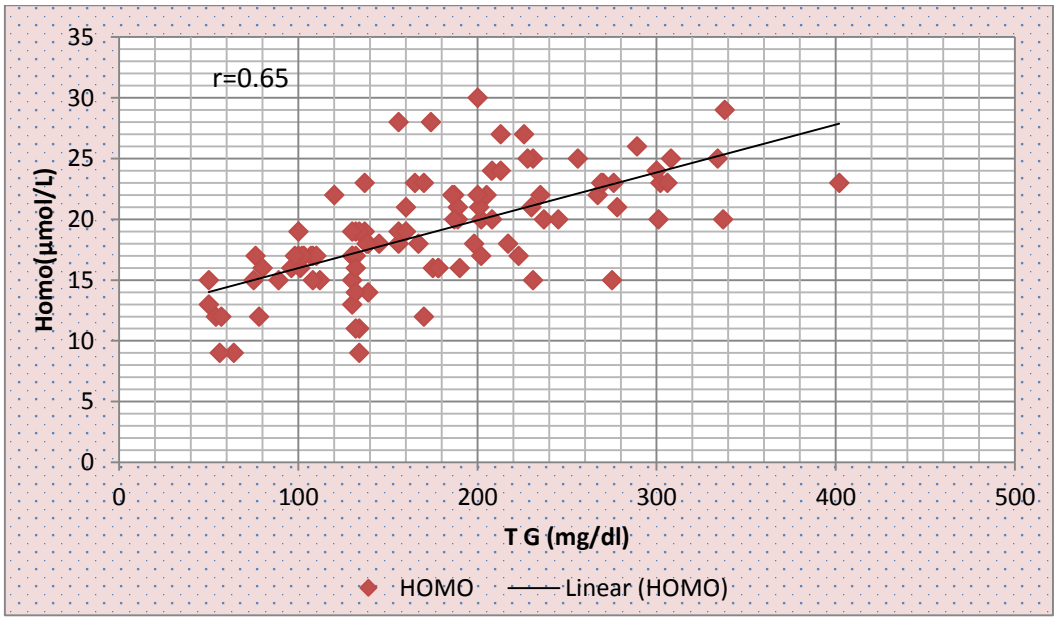

Fig 4: Correlation of Serum Homocysteine With Triglyceride in hypertensive subjects (n=100).

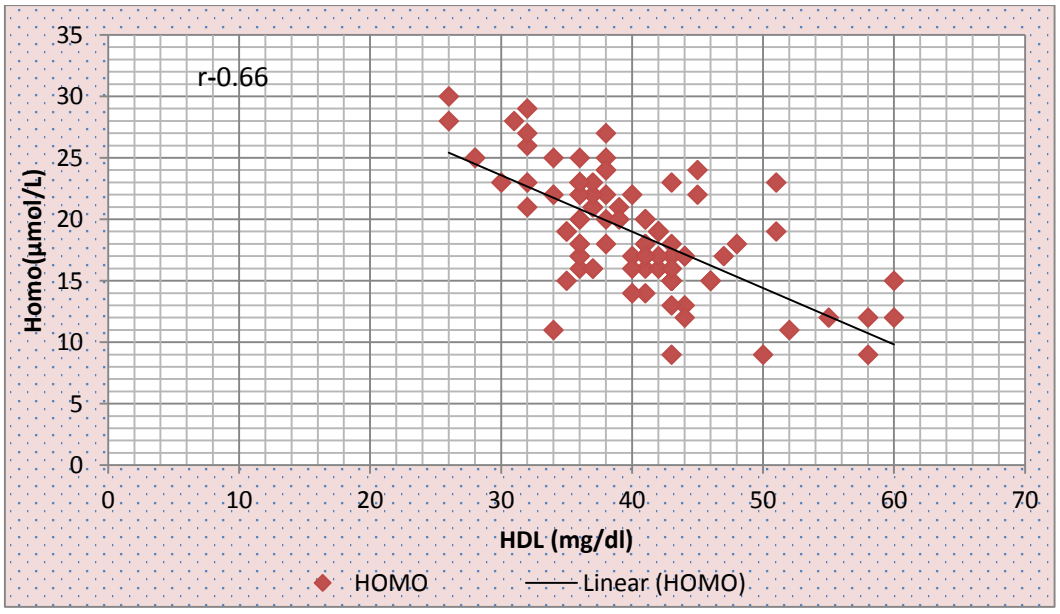

Fig 5: Correlation of Serum Homocysteine With HDL -Cholesterol in Hypertensive Subjects (n=100).

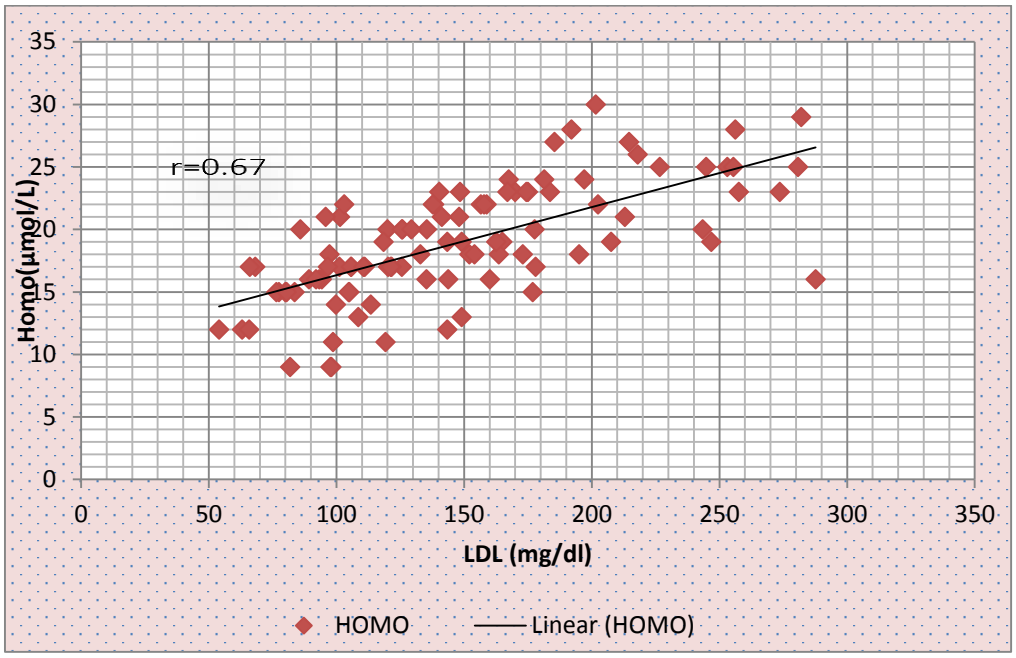

Fig 6: Correlation of Serum Homocysteine With LDL-Cholesterol in Hypertensive subjects (n=100).

DISCUSSION

Hypertension is recognized globally as a major risk factor for CVD, stroke, and renal diseases[29]. In the present study we have observed that the level of serum homocysteine was elevated in hypertensive subjects as compared to the normotensive subjects. Our finding are in agreement with Alina et al. (2008) found that the value of serum homocysteine (18.77±1.9µmol/l) in hypertensive subjects was highly significant than normotensive subjects[30]. It is also in concordance with the previous studies which also state that mean homocysteine levels are quiet high, varying from 19.5 to 23.2 µmol/L in hypertensive subjects[14-16].

Results of our study revealed that the mean values of serum TC TG and LDL-C were significantly higher and statistically significant among the hypertensive patients compared to normotensives. The mean HDL-C level was lower in the hypertensives compared to normotensives and was statistically significant.

It is in concordance with the previous studies which also state that mean values of serum TC , serum TG and serum LDL-C were significantly higher and statistically significant among the hypertensive patients compared to normotensive[31-34]. As the study had been carried out in Ajmer city (Rajasthan, India), where people usually eats oily and fried food. According to Pavithran et al. alteration in lipid metabolism including a decrease in HDL-C can result in endothelial damage and trigger an increase in blood pressure which may partially account for its strong predictive power for CHD[35].

The present study has also shown the positive correlation between serum homocysteine and total cholesterol, Triglyceride, LDL cholesterol & negative correlation between serum homocysteine and HDL cholesterol in hypertensive subjects. Hyperhomocysteinemia, through its oxidative effects could reduce vasodilators like nitric oxide as well as promote extracellular matrix accumulation and smooth muscle cell proliferation, leading to vascular constriction and stiffness[36,37]. The atherogenicity of homocysteine may involve several mechanisms including LDL-cholesterol oxidative modification, and HDL-cholesterol decrease[38].

CONCLUSION

The observations of this study have revealed that there was significant alteration of serum homocysteine, cholesterol, triglyceride, HDL cholesterol and LDL cholesterol in hypertensive patients. Therefore, for routine monitoring of hypertensive patients to prevent the coronary heart disease (CHD) and other consequences, the reinforcement of these parameters may be recommended in daily clinical practice.

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