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Assessment of Lipid Peroxide and Lipid Profiles in Patients with Essential Hypertension.

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ABSTRACT

In recent years, despite progress in prevention, detection and treatment of high blood pressure, hypertension yet remains an important public health challenge. The present study was undertaken to ascertain the role of lipid peroxide and different lipid profile parameters in essential hypertensive patients to find out the prevalence of abnormal lipid profile and overburden of oxidative stress in essential hypertensive patients. The study included 180 essential hypertensive patients i.e 90 pregeriatric subjects aged between 35-50 years and 90 geriatric subjects aged between 51-65 years which were further divided into three groups viz. mild (group-I), moderate (group-II) and severe (group-III) depending on their blood pressure, along with 30 pregeriatric and 30 geriatric normal healthy controls. It was observed that, essential hypertensive patients had significantly higher levels of serum lipid peroxide ($p<0.001$), serum total cholesterol (TC) ($p<0.001$), triglyceride (TG) ($p<0.001$), very low density lipoprotein cholesterol (VLDLc) ($p<0.001$) and low density lipoprotein cholesterol (LDLc) ($p<0.001$) as compared to normal healthy controls while serum levels of high density lipoprotein cholesterol (HDLc) was significantly lowered ($p<0.001$) in essential hypertensive patients as compared to normal healthy controls. These above findings suggested that, there is a greater risk of coronary artery disease with increased atherogenicity due to increased triacylglycerol, cholesterols, LDLc, VLDLc and decreased HDLc along with increased oxidative stress that could contribute towards the increasing risk of cardiovascular diseases in patients with essential hypertension.

Keywords: essential hypertension, lipid peroxide, lipid profile, oxidative stress.

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INTRODUCTION

Hypertension is one of the strong, major risk factor for cardiovascular diseases which is posing a health challenge by topping the list of killer diseases. It affects approximately 50 million people in the United State and about 1 billion individuals worldwide [1].

Presently in India, prevalence of hypertension is 59.9 and 69.9 per thousand males and females in urban areas and 35.5 and 35.9 per thousand males and females in rural population respectively. Out of all cases of hypertension, only 5-10 % have some definable cause and rest 90-95 % are essential and also called as primary or idiopathic type [2]. It has been appropriately called the silent killer because it is usually asymptomatic and undetected. Uncontrolled hypertension can cause damage to all organs of body[3]. Hypertension is correlated with the incidence of atherosclerosis. Previous clinical and epidemiological studies have defined plasma lipoprotein levels such as reduced HDLc, increased TC and LDLc as strong predictors of atherosclerosis and hypertension [2].

Dyslipidemia and hypertension are the commonest risk factors from coronary artery disease (CAD). Persons with combination of risk factors are particularly at high risk of CAD. Hypertensive subjects frequently have abnormalities in lipid and lipoprotein metabolism than normotensive subjects [3].

The lipid-lipoprotein studies in the past have generally emphasized the positive relationship of total cholesterol, LDLc, VLDLc and triglycerides to the risk of coronary diseases. Hypertension and dyslipidemia are two of the main risk factors for vascular diseases on atherosclerotic basis. However, higher plasma concentrations of lipoproteins could be an independent risk factor for atherosclerosis and could contribute towards increasing the incidence of cardiovascular disease in person with essential hypertension.

It is suggested that, increased oxidative stress and generation of free oxygen radicals can results in the modification of LDL to oxidized LDL that could lead to the formation of fat filled cells in atherosclerotic lesions [4, 5]. Hypertension appears to have a major influence on the development atherosclerotic disease. Lipid profile plays a central role in the atherosclerotic process accelerated by hypertension [1].

The lipids are exposed to the free radicals in cell membrane that causes the oxidation of lipids which is nothing but the process of lipid peroxidation. The products of lipid peroxidation are themselves reactive species and leads to extensive membrane, organelle and cellular damage. The free radical activity and the extent of tissue damage are related quantitatively to the amount of lipid peroxide level in the blood. Malondialdehyde (MDA) is one of the end products of lipid peroxidation, thus in the present study, extent of lipid peroxidation was measured by estimating MDA levels[3].

Hence, the present study was aimed to evaluate the possible involvement of free radicals and lipoproteins in patients with essential hypertension.

DESIGN AND METHODS

The present study was carried out in the Department of Biochemistry, Dr. V. M. Govt. Medical College, Solapur and Shree Chhatrapati Shivaji Maharaj General Hospital, Solapur (Maharashtra). The study comprised of 180 patients with essential hypertension and 60 healthy controls. The subjects were divided into 2 groups according to the age. Each group was further divided into 3 subgroups depending on the levels of blood pressure. The subjects were categorized and distributed in (**Table No. 1.)**

Table 1: Showing distribution of subjects

Age (years)	Controls	Blood Pressure (in mm of Hg)		
		(90-99/140-159) (Mild) Group-I	(100-109/160-179) (Moderate) Group-II	(≥ 110/ ≥180) (Severe) Group-III
Pregeriatric (35-50)	30	30	30	30
Geriatric (51-65)	30	30	30	30

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The hypertensive patients were selected in accordance with criteria from the guidelines of WHO/ISH (1999)[6]. The patients with the clinical history of diseases, which may lead to oxidative stress such as diabetes mellitus, cardiovascular diseases, renovascular diseases, stroke, atherosclerosis etc, having history of smoking, had received any antihypertensive therapy or supplementation of vitamins and/or minerals were excluded from the study. For the comparison purpose, normal non-hypertensive healthy persons were carefully selected and clinically diagnosed according to the age, sex, blood pressure, having no history of smoking, alcoholism, not taking any supplementation such as minerals, vitamins etc. and were taken as control group. The research project was approved and permitted by the ethical committee of institute.

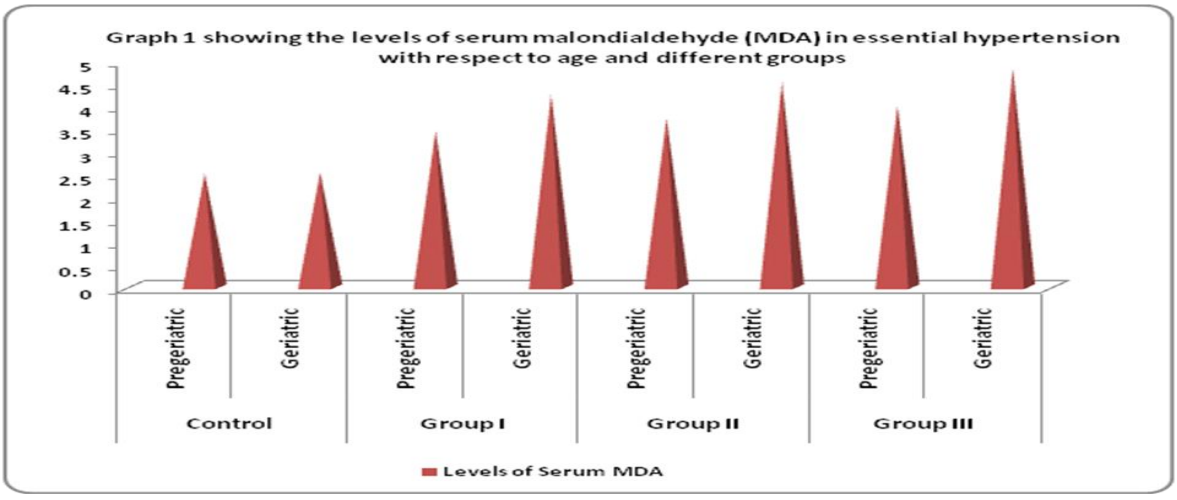
About 6-7 ml of venous blood was collected in sterile plain bulb and allowed to clot. The serum was separated by centrifugation at 3000 rpm for 10 minutes and used for different estimations. Serum lipid peroxide (Malondialdehyde) by Kei Satoh's method [7], serum total cholesterol, HDL cholesterol, serum triglycerides were estimated by enzymatic cholesterol oxidase-peroxidase (CHOD-POD) kit method [8]. VLDL cholesterol was calculated by calculation and LDL cholesterol was calculated by using Friedwald's formula.

The results were expressed in Mean ± S.D and statistical analysis was done by using student't'-test. Correlation coefficient was determined between lipid peroxide and different lipid profile parameters by using Pearson's correlation coefficient.

RESULTS

Serum lipid peroxide, total cholesterol, LDL cholesterol HDL cholesterol and triglyceride levels were shown in table 2. Hypertensive patients were observed significant differences in above parameters when compared with control groups with respect to age and blood pressure.

Significantly higher levels of serum lipid peroxide were observed in group I subjects when compared with controls ($p<0.001$). Similar observations were noted when group II subjects were compared with group I subjects ($p<0.001$) and group III were compared with group II subjects ($p<0.001$). (**Graph No. 1**). This suggests the gradual rise in lipid peroxide levels as there is increase in age and severity of hypertension (**Table No. 2**).



The present study was observed that, the hypertensive patients showed significant difference in lipid profile when compared to normal healthy controls.

Serum total cholesterol (TC), serum triglycerides (TG), serum very low density lipoprotein cholesterol (VLDLc) and serum low density lipoprotein cholesterol (LDLc) levels were significantly increased in group I patients when compared with controls ($p<0.001$). We also observed significantly higher levels of above parameters in group II subjects when compared with group I ($p<0.001$) and group III subjects when compared with group II subjects ($p<0.001$). Further, steep increase in above parameters were showed with the progression of age, while the levels of HDL cholesterol was significantly decreased in group I when compared with normal healthy controls ($p<0.001$). Similar findings were observed when group II subjects were compared

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with group I (p<0.001) and group III subjects were compared with group II (p<0.001). (**Graph No. 2**). We also observed that, the level of HDL cholesterol was decreased with increase in age (**Table No. 2**).

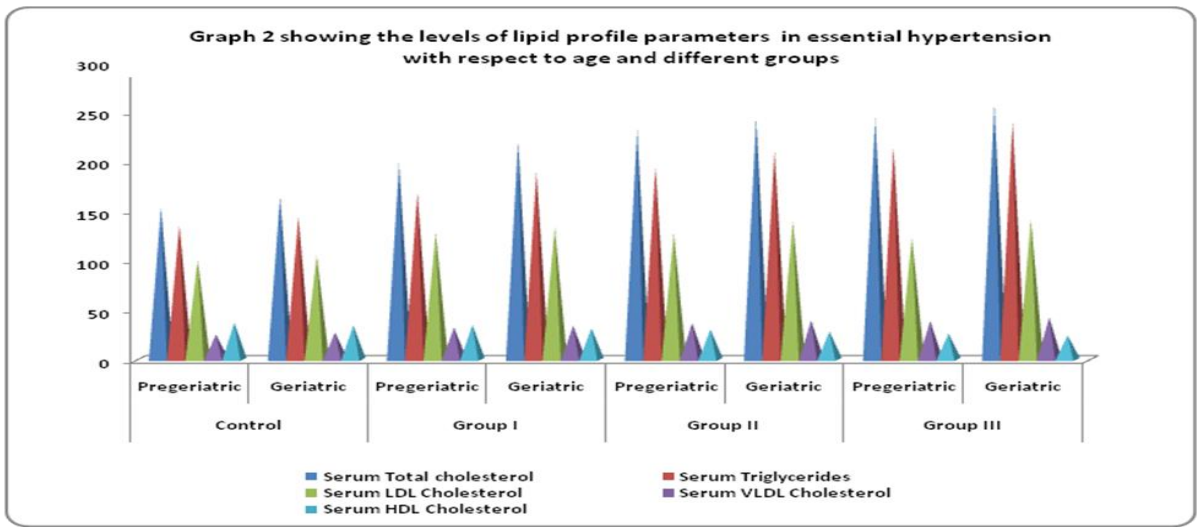

Table 2 showing the levels of lipid peroxide and lipid profile parameters in controls and hypertensive patients.

	Control		Group I		Group II		Group III	
Age / Parameters	Pregeriatric (n=30)	Geriatric (n=30)	Pregeriatric (n=30)	Geriatric (n=30)	Pregeriatric (n=30)	Geriatric (n=30)	Pregeriatric (n=30)	Geriatric (n=30)
LP	2.50±0.44	2.52±0.42	3.45±0.13*	4.25±0.09*	3.72±0.11*	4.52±0.12*	4.00±0.12*	4.82±0.09*
TC	153.39±4.55	164.30±4.50	197.83±3.33	220.01±2.34*	232.30±3.30*	244.10±3.39*	243.18±3.89*	257.93±3.26*
TG	135.68±9.34	143.68±9.41	168.30±16.61*	189.02±12.34*	193.70±16.29*	210.52±18.77*	213.81±12.67*	239.69±17.75*
LDLc	100.39±0.82	105.09±0.77	128.30±2.55*	133.10±2.28*	127.73±1.92*	139.90±2.07*	123.30±2.41	141.30±2.60*
VLDLc	25.12±2.65	27.32±2.35	32.30±1.79*	34.20±3.04*	36.71±0.92*	39.40±1.98*	38.92±2.41*	42.58±2.29*
HDLc	37.10±0.81	34.40±0.54	34.96±1.90*	31.70±1.95*	30.31±1.41*	28.30±1.77*	26.09±0.76*	24.30±1.17*
Statistical analysis			p<0.001	p<0.001	p<0.001	p<0.001	p<0.001	p<0.001
			As compared to controls		As compared to group-I		As compared to group-II	

Abbreviations: - LP-lipid peroxide, **TC**-total cholesterol, **TG**-triglycerides, **LDLc**-low density lipoprotein cholesterol, **VLDLc**-very low density lipoprotein cholesterol, **HDLc**- high density lipoprotein cholesterol.
Note: - *p<0.001-statistically highly significant

We found positive correlation of serum TC (r=0.97), serum TG (r=0.95), serum LDLc (r=0.96) and serum VLDLc (r=0.98) with lipid peroxide and negative correlation of serum HDLc (r=-0.98) with lipid peroxide.

DISCUSSION

Hypertension is one of the major public health issues, affecting approximately 25% of adult population in developed as well as in developing countries. The prevalence of high blood pressure increases dramatically with age, such that the lifetime risk of high blood pressure approaches 100% [2]. Some recent published data revealed that the free radical generation may increases risk of essential hypertension [3].

Generation of free radical causes oxidation of lipid membrane, which is termed as lipid peroxidation. The increased lipid peroxidation is indicated by increased MDA level that being intensively investigated because of its potential to cause injury and their pathogenic role in essential hypertension. The enhanced lipid peroxidation product may cause oxidative damage to vascular endothelium. Therefore it can be stated that, lipid peroxidation may contribute as one of the cause of essential hypertension [4, 5].

MDA is the most abundant among the reactive aldehydes derived from lipid peroxidation. These aldehydes have been implicated as the causative agents in cytotoxic processes and it is possible that aldehydes

released from the cell membrane may diffuse, interact and induce oxidative modifications in other cells and and in low density lipid molecules, thereby increasing the risk of cardiovascular damage[8-10].

These observations suggest that hypertensive patients are prone to oxidative damage. Our study reveals that oxidative stress is increases in patients with essential hypertension but its pathogenic and clinical relevance remain to be elucidated.

The study of serum lipid profile in essential hypertension has dealt with for a long time and by many workers. Hypertension is a common risk factor for cardiovascular diseases. Many Indian scientists have reported the coexistence of this risk factor. In the present study, hypertensive patients were compared with non-hypertensive healthy controls, which showed significantly different lipid profile.

Lipoprotein abnormality may blunt endothelium dependent vasorelaxation. The lipoproteins when reacts with endothelial cells then the oxidation of lipids takes place that leads to the formation of free radicals which may cause vasoregulatory impairment. The impairment in the lipoprotein metabolism may be associated with pathogenesis of essential hypertension[11, 12, 13].

M.J. Landray found that, the smaller LDL particles might be more atherogenic for a number of reasons: they have reduced affinity for LDL receptors, have increased binding for endothelial proteoglycans[12] and are better able to penetrate the arterial intima. In addition, these small LDL sub-fractions have reduced antioxidant defences and are therefore more readily oxidized by free radicals, leading to modification of the apolipoprotein-B of LDL and rapid uptake by macrophage scavenger receptors.

A.A. Tavasoli et al observed significantly higher total cholesterol and LDL cholesterol in hypertensive patients than in normal healthy controls. Our findings support Tavasoli AA, according to them, increased release of free fatty acid from adipose tissue, particularly from visceral fat into the portal veins, stimulates the production of triglyceride-rich lipoproteins in the liver with release of more and larger VLDL particles. This in turn has effects on other lipoprotein particles, resulting in reduced levels of HDL cholesterol [14].

Researchers from Bangladesh conducted a prospective study which was based in the Northern region of Bangladesh to investigate the lipid profile status in hypertensive patients as compared to healthy normotensive controls. Their study revealed similar findings of elevated serum total cholesterol, triglycerides and LDL cholesterol in the hypertensive subjects as compared to the controls, as observed in our study [13].

Few studies showed strong association of hypertension and dyslipidemia and suggests that, both may increase the patients' susceptibility to the development of coronary heart disease. A study conducted on Nigerian hypertensive patients found a significantly higher lipid profile which was similar to that found in our study[13 - 18]. Recently many authors have reported that, cholesterol and LDL have stimulatory effects on vascular smooth muscle cells, which are supposed to play an important role in the pathogenesis of essential hypertension.

Our findings of increased levels of total cholesterol in essential hypertensive subjects are similar to the findings of some other studies [19]. One more study which was carried out in Bangladesh to appraise the lipid profile in hypertensive subjects also observed similar findings as observed in our study [20]. A study done in Andhra Pradesh (India) on hypertensive persons have shown that the values of TC, TG, LDLc and VLDLc were higher in hypertensive persons than healthy controls. In their study also shown that HDLc was higher among healthy controls than hypertensive cases but the difference was not statistically significant [21].

In the present study, positive correlation was obtained between total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol with lipid peroxide and negative correlation of HDL cholesterol with lipid peroxide this suggests that, there is a greater risk of coronary artery disease with increased atherogenicity due to increased total cholesterol, triglycerides, LDL cholesterol, VLDL cholesterol and decreased HDL cholesterol.

In the final analysis, it appears that, essential hypertension is always associated with elevated serum total cholesterol concentration and other lipid abnormalities. Higher levels of these lipids may be contributed due to physical activity, stress, increased age; alcohol consumption and high consumption of dietary fats etc.

So timely assessment of lipid profile is must in all hypertensive cases to stop further aggravation and risks of coronary artery diseases.

The major concern of this observation was that, the subjects also had oxidative stress due to the abnormalities of lipids and their ratios. Therefore, the analysis of other risk factors which were associated with hypertension will be of immense importance in the eventual assessment of the risk status, as lipid abnormalities and oxidative stress result in the future risk of coronary artery disease.

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