CHAPTER – III : LIPID PROFILE AND KIDNEY FUNCTIONS IN
HYPERTENSION

(HYPERTENSION WITH AND WITHOUT COMPLICATIONS)

The present concept of pathogenesis of hypertension and atherosclerosis is based in response to injury hypothesis. This injury later may alter the functional characteristics of the endothelium leaving endothelial cell – cell nondisjunction and endothelial retraction exposing the underlying connective tissue and accumulation of foam cells such as macrophages, that form the first and ubiquitous lesion of atherosclerosis, the fatty streak.

The causes of cardiovascular diseases as a degenerative diseases are multiple. A lesion and subsequent obstruction of the blood vessels (plaque) is a major underlying condition referred as atherosclerosis. A plaque consists of cholesterol, lipids and cell deposited in the inside arteries. As the heart struggles to get by relief a diminished oxygen supply and typical chest pain or angina pectoris occurs.(48,49)

Systemic hypertension is an elevated arterial blood pressure, is a measure health problem, particularly in the developed and developing countries. Hypertension is associated with a increase risk for a variety of cardiovascular disorders and is a measure risk facor for atherosclerosis. A persitant and
sustained high blood pressure had damaging effect on the heart, brain, kidney, eyes etc. Hypertension is classified into two groups:

1) Primary or essential hypertension: in which the cause of increase blood pressure is unknown. It constitutes about 90-95% patients of hypertension.

2) Secondary hypertension: in which the increase blood pressure is caused by diseases of the kidneys, endocrine or some other organs. Secondary hypertension comprises about 5-10% of hypertensive cases. According to the clinical course both the hypertension may be benign or malignant.\(^{(2)}\)

Hypertensive heart diseases or hypertensive cardiomyopathy is the disease of the heart resulting from systemic hypertension of prolonged duration and manifesting by **left ventricular hypertrophy (LVH)**. As already pointed out, hypertension predisposes to atherosclerosis. Therefore, most patients of hypertensive heart disease have advanced **coronary atherosclerosis** and may develop progressive **IHD**. Amongst the causes of death in hypertensive patient, cardiac decomposition leading to **congestive cardiac failure (CCF)** or **coronary heart disease (CHD)** accounts for about one third of the patients, other causes of death are IHD etc.\(^{(2)}\)
Diabetes mellitus is a chronic clinical syndrome characterized by hyperglycemia due to deficiency or defective response to insulin. It is estimated that approximately 3% of population suffers from diabetes mellitus.\textsuperscript{(5)}

As a consequence of hyperglycemia of diabetes, every tissue and organ of the body undergoes biochemical and structural alterations which accounts for major complications in diabetes mellitus. Possibly these complications are related to the severity of hyperglycemia since control of blood glucose from clinical point of view is associated with minimizing the development of complications. The commonest complications (related to our study) is discussed.\textsuperscript{(5)}

1) Atherosclerosis

2) Diabetic nephropathy

This complications related in our study group.

**New aspects of conventional risk factors; blood lipid abnormalities, and coronary artery disease:**

The term **coronary atherosclerosis** indicates that a specific disease atherosclerosis, involves the coronary arteries, whereas the term atherosclerosis coronary heart disease signifies that the disease has progressed due to the point that impedes coronary
artery blood flow and produces varying degree of myocardial ischemia.

Newer aspects of conventional risk factors; blood lipids abnormalities and coronary artery disease is now on a role of oxidized LDL. There is strong evidence that such oxidation occurs, that is promoted by various factors, that increase the rate of formation of oxygen free radicals and that oxidized low density lipoprotein (LDL) is most noxious to the vascular intima than non-oxidized LDL form. Furthermore, oxidized LDL may provoke monocytes to produce cytokines such as tumor necrosis factor α, etc may participate in atherogenesis.\textsuperscript{(14,49)}

I] Role of lipid profile in hypertension :

i] Lipid Profile :

Krishaswamy V. and Radhakrishnan T. observed that in their studies, lower levels of plasma cholesterol below 150 mg/dl in patients with coronary artery disease.\textsuperscript{(50)}

Alwin et al, also observed the association of blood pressure with elevated lipid levels in cardiovascular disease risk factors. Recently, familial form of hypertension associated with dislipidemia (increase in cholesterol, triglyceride lower, HDL) has been proposed and estimated in account with essential hypertension. The decline magnitude of cholesterol – hypertension association noted after
control for baseline blood pressure also suggests that the relation may be due to at least in part, to underlying factors (eight genetic or environmental) that influence both blood pressure and serum cholesterols.\textsuperscript{(51)}

Corvette \textit{et al} describe that the catabolism of triglyceride rich lipoprotein is initiated by \textit{lipoprotein lipase}, which hydrolyses triglyceride moiety of chylomicrons and VLDL and releases fatty acid for a energy production in muscle and for storage in adipose tissue. In diabetic patient the activity of this enzyme is decrease lipolytic cascade is delayed for two reasons, there is a shortage of catalytic site on LDL and overproduction of triglyceride saturates that sites which are available, both these mechanism promotes hypertriglyceridemia.\textsuperscript{(52)}

The high levels of triglyceride rich lipoprotein and decrease levels of HDL are interwoven. Hypertriglyceridemia contributes to low HDL levels in two ways. Due to impaired lipolysis, fewer surface remnants are available to be incorporated into HDL particles. Second, the large amount of triglyceride rich lipoprotein and their prolonged resistance time in the circulation increase the exchange of esterified cholesterol from HDL to triglyceride rich lipoprotein and triglyceride to HDL particles. The resultant is enrichment of HDL particle core with triglyceride. The enriched HDL has a faster catabolic rate than normal HDL, which leads to
lower number of circulating HDL particles furthermore HDL particles are smaller owing to a high hepatic lipase activity. Additionally there is increase transfer of cholesteryl esters from LDL to VLDL and triglyceride from VLDL to LDL. The triglyceride enriched LDL loose their triglyceride by the action of hepatic lipase resulting in the formation of small and dense LDL.\(^{(52)}\)

Witzum and Steinberg observed that, there is a causative relationship between hypercholesterolemia and premature atherosclerosis. The importance of hypercholesterolemia as a causative factor CHD is called as “cholesterol controversy”. Intensive lipid lowering regimens have been shown that only is to slow the progression of atherosclerosis and reduce the risk of coronary events.\(^{(53)}\)

Selby et al, showed the serum cholesterol remained predictive of developing hypertension in this study, after controlling for baseline body mass index and the other standard risk factors. In the study plasma triglyceride level were found to be predictive of developing hypertension, but serum cholesterol apparently was not. But change in serum cholesterol was positively associated with change in systolic blood pressure, independent of change in weight.

**Hypertension is indisputably at the top of list of modifiable risk factors. Ischemic disease, heart failure and arrhythmias all pose significant risk for ischemic stroke.**\(^{(54)}\)
Hakim et al, observed that dislipidemia and hypertension is a common risk factors for coronary artery disease. In their studies they found the prevalence of dislipidemia in Asian hypertensive patients. The HDL-C were normal with high cholesterol levels. Males are more sufferer than females.\textsuperscript{(55)}

Finally it must be stressed that even though hypertension and cholesterol levels are correlated with low factor, they co-exist commonly and should ideally investigated for when one of them is initially abnormally detected. This will help not only to control these two factors for coronary artery disease, but also prevents the deterioration of lipid profile by certain antihypertensive agents.\textsuperscript{(55)}

Wannamethe S., Goya et al, Hyperlipidemia is commonly associated with hyperuricemia. There is a significant association between urate and serum triglyceride and cholesterol.\textsuperscript{(56)}

ii] Lipid Profile and Hypertension with Complications :

Corvette et al, mentioned that in the hypertriglycledemia, insulin resistance seems to be a common basis. The insulin resistant state impairs the normal suppression of fatty acid release from adipose tissue in the postparandeval state. Thus the flux of free fatty acid to the liver increase and overproduction of very low
density lipoprotein (VLDL) from these substances occur when hyperinsulinemia present.\textsuperscript{(52)}

Insulin is also involved in another defect of hepatic VLDL metabolism. Acute hyperinsulinemia such as that after a meal, suppresses the production of large buoyant VLDL particles. VLDL in the liver in non-diabetic people. These particles are analogous to the chylomicrons which should be released only in the fasting state when lipids from foods are not available, thus insulin function in non-diabetic people to maintain the balance between intestinally derived and liver derived triglyceride rich lipoproteins.

\textbf{In diabetic patient this regulation fails, inappropriate production of VLDL by liver occurs and the balance favours hypertriglyceridemia.}\textsuperscript{(52)}

Achari \textit{et al} observed abnormal lipid profile levels in non-diabetic patients of essential hypertensions. They reported similar levels. However, the levels of HDL-c reported were slightly higher as compared with this present study group.\textsuperscript{(57)}

They also observed that in non-diabetic patient with uncomplicated hypertension the mean cholesterol level is 191.7 mg\%. The assessment of hypertension with elevated serum uric acid and creatinine is significant.\textsuperscript{(57)}
Venolekar M.E. showed the incidence of coronary artery disease in both urban and rural India is on the rise. It has been suggested that rather than LDL-C hypertension, the other factors like DM, hypertriglyceridemia, low HDL-C, high Lp(a) and insulin resistance, and truncal obesity might play a dominant role in the pathogenesis of coronary artery disease.\(^\text{58}\)

Frohlich E.D. \textit{et al} showed that abnormal uric acid concentration are encountered regularly in varied pathophysiological problems such as hypertension, coronary artery disease, obesity, hyperlipidemia, DM, polycythemia and toxemia of pregnancy. Of course several of these problems are otherwise linked: coronary artery disease (CAD).\(^\text{59}\)

Salonen J.J. and Salonen R. (1988), reported that the direct association in lipid peroxidation and progression of atherosclerosis in humans is lacking, even though there are epidemiological studies and animal experiments have provided evidence supporting the role of lipid peroxidation. Thus in the studies, the association of lipid peroxidation products with the progression of early carotid atherosclerosis in hypercholesterolemic men.\(^\text{60}\)

Mehta \textit{et al} described and discuss the traditional risk factors for coronary artery disease.\(^\text{61}\)
James I. Cleeman in the third panel of National Cholesterol Education Programme (NCEP) (2001), updated clinical guidelines for cholesterol testing and management. It report updates the existing recommendations for clinical management of hypercholesterolemia.\(^{(62)}\)

Wannamethee \textit{et al}, described that middle aged new regular drinkers experienced lower risks of major coronary heart disease events than stable occasional drinkers or non-drinkers, but had increased risk of non-cardiovascular mortality and total mortality. These findings provide little smile and support for encouraging older men who do not drink or who drink only occasionally to take up regular drinking, whether or not they have coronary artery disease.\(^{(63)}\)

\textbf{II] Role of Kidney Function in Hypertension :}

This topic deals with the kidney function tests in patients with hypertension.

\textbf{ij] Hyperuricemia in Hypertension :}

New Land H. has concluded that, hyperuricemia is significantly associated with hypertension and renal disease. It was also suggested that, recommended additional studies to address the possibility that chronic hyperuricemia may contribute to alterations in renal structure and functions.\(^{(66)}\)
Takkunen et al, suggested that hyperuricemia is a good predictor of cardiovascular mortality based on results of multivariate analysis. Hyperuricemia observed in untreated hypertension, may reflect decrease renal blood flow and early hypertensive nephrosclerosis.\(^{(67)}\)

**Thus according to National Health and Nutrition Survey (NHANES) uric acid is an independent risk factor for hypertension associated morbidity and mortality. The association of abnormal uric acid metabolism and a multimetabolic syndrome conferring heightened cardiovascular risks holds important implications for the role of purine metabolism in human vascular biology.**

Brand et al, reported consistently higher serum uric acid levels in antihypertensive treated patients in both the sexes. Serum uric acid levels were correlated with systolic and diastolic blood pressure. The uric acid relationship with acute myocardial infarction and in hypertension was equally strong, even correcting for antihypertensive treatment. In hypertensive patients hyperuricemia was due to antihypertensive therapy. The coronary drug research project group was found that fatal acute myocardial infarction (AMI) was more common in hyperuricemic patients, but the predictive power of serum uric acid was reduced when data were adjusted for diuretic use.\(^{(68)}\)
The uric acid relationship with myocardial infarction was equally strong in both the sexes, thus uric acid predicted for the subsequent development of coronary heart disease, in general, and myocardial infarction, but not for angina pectoris. However due to multivariable analysis, uric acid did not add independently to the prediction of coronary heart disease.

In hypertension, the association of uric acid remains unclear because hyperuricemia may occur secondary concomitant renal diseases similarly as age increase, the uric acid levels also increases.

Selby et al described the various factors responsible for essential hypertensin. Uric acid is loosely linked to development of hypertension and may be markers of susceptibility or intermediate steps in pathways leading to hypertension.[54]

The assessment of hypertension with elevated serum uric acid and creatinine is significant. However serum creatinine, uric acid and lipid profile did not prove to be the independent predictors of hypertension.

The uric acid - hypertension association also did not appear to be due to an effect of attained blood pressure level on uric acid metabolism at baseline. Rather uric acid is either itself casually
related to development of hypertension or perhaps more likely associated with a casual factor.\(^{54}\)

Hakim A.S. \textit{et al} observed that dislipidemia and hypertension are common risk factors for CAD. The commonest abnormalities is high cholesterol with normal triglycerides (55%), normal HDL-C (93%), and total cholesterol/HDL ratio is more than 4.5 in 15% of patients. This knowledge and prevalence of disease aids a physician to plan better management protocols.\(^{55}\)

Wannamethe \textit{et al}, observed several epidemiological and clinical studies have reported a significant association between hyperuricemia and hypertension.\(^{56}\)

Raised triglyceride is often accompanied by a rise in cholesterol and in our study the relation between raised urate and raised cholesterol appears to be largely mediated through triglyceride. The hyperuricemia is associated with clustering risk factors but it has been suggested that serum uric acid, together with increase small dense lipoprotein cholesterol particles, may be a part of insulin resistance syndrome which in turn leads to CHD. It is therefore possible that the association between urate and CHD is largely mediated by triglyceride metabolism.\(^{56}\)

Ward H.J. showed raised uric acid concentration is commonly encountered in essential hypertension. The
hyperuricemia may observed in untreated patients may reflect decrease in renal blood flow and early hypertensive nephrosclerosis. However, antihypertensive drug regimens, especially those including diuretics, do confound the link between uric acid and risk of hypertension associated morbidity and mortality. In this study, the cardioprotective benefits of diuretics was muted for each successive rise in serum uric acid quartile and the reasoned that uric acid may be in part response for the short fall between cardioprotection expected and that observed in (clinical protection of trial) studies.\(^{(69)}\)

It is well established that serum uric acid increase arterial blood pressure and is associated with reduction in renal blood flow. High uric acid concentration may increase sodium reabsorption at nephron sites proximal to the distal tubule and it has been proposed that metabolic perturbations (e.g. hyperinsulinemia) may mediate some of these effects in hypertension. The observation is that insulin exerts a direct effect on increase renal sodium reabsorption has led to the proposal of a unifying hypothesis that links hyperuricemia, low urinary uric acid excretion and decrease glucose utilization. Hyperuricemia may represent the culmination of a multimetabolic syndrome in which insulin mediated renal hemodynamic abnormalities leads to hypertensive renal damage.

**Thus for now hyperuricemia in hypertension may be an early**
indicator of hypertensive cardiorenal disease, which is commonly associated with multimetabolic syndrome.\textsuperscript{(69)}

The uric acid and other purine play a protective role in vascular endothelium as scavengers of reactive oxygen species. Purine oxidation and uric acid production are associated with LDL oxidation and can led to further lipid peroxidation in vascular tissues. Adenosine is another purine that inhibits oxygen radical production of human white blood cells by a Ca\textsuperscript{++} dependent mechanism. An antioxidant role for uric acid also seems plausible, since blood concentration of purine such an adenosine, hypoxanthine and uric acid usually rises after coronary occlusion.\textsuperscript{(69)}

Alderman \textit{et al} found hyperuricemia is associated with increase mortality in the elderly and is an independent predictor for both fatal and non-fatal in patients with diabetes.\textsuperscript{(70)}

Commerson J.S. and Maroo (1998), showed hyperuricemia may lead to increase platelet aggregation and uric acid crystals can also activate platelets \textit{in vitro}. This has lead to hypothesis that hyperuricemia may place patient with underlying coronary artery disease at increase risk of coronary thrombosis and enhances thrombotic tendency.\textsuperscript{(71)}
Witzum J.L. and Steinberg C. showed the serum creatinine, uric acid and lipid profile did not prove to be independent predictors of hypertension. Serum creatinine - uric acid level association for hypertension is not detected in this study. Inclusion of creatinine in a predictor model did not alter the uric acid – hypertension association. Uric acid level also has strong genetic determinants and it is possible that an increase level of uric acid is a marker for genetic susceptibility to developing hypertension. This genetic trait could, for example influence renal functions altering with renal urate excretion and rennin angiotensin homeostasis or renal handling of sodium.\(^{(53)}\)

Johnson R.J. found hyperuricemia is caused by decrease renal excretion. In this study we suggest that hyperuricemia may be mediated by intrarenal ischemia with lactate generation and inhibition of secretion of urate by the renal exchange transport system.\(^{(72)}\)

Annethe Dobson et al observed that as human beings do not have enzyme uricase that breakdown the uric acid to water-soluble form that easily excreted. Instead uric acid is filtered and reabsorbed by various processes. Only small amount are excreted and the balance can easily be disturbed by disorders that increase production or interference with clearance.\(^{(73)}\)
Cappucio F.P. found elevated uric acid levels in-group of patients as a part of a National Survey Programme and the prevalence of cardiovascular risk factors along with other traditional risk factors. They found that sodium ion is a major determinant of the fractional excretion of lithium, which in turn may be related to the elevation in uric acid levels.\(^{74}\)

It is speculated that risk factor hyperuricemia in cardiovascular disease itself, reflects the impact of ageing on renal blood flow and its exacerbation by coexistent reduction in renal blood flow produce by atherosclerosis and nephrosclerosis and is present to varying degrees with hypertension.

**ii] Role of Kidney Function in Hypertension (General)**

*Selby et al*, describe the risk factors for hypertension. Previous analysis have confirmed hypothesis that baseline weight subsequent weight gain, alcohol consumption, parental history of hypertension.\(^{54}\)

*Grotta J.C.* often concern us more with treating the disease than the preventing it. Yet the old axian about the ounce of prevention equally a pound of cure strongly applies to stroke.\(^{75}\)

**iii] Role of Kidney Function in Hypertension (with Complications)**
Muzakova V. and Vojtisek P. (2005), observed in their study of low levels of serum antioxidant vitamin C, bilirubin, and ceruloplasmin to coronary artery disease factors. They found the decrease in antioxidant levels according to the severity of coronary artery disease. All the modifiable risk factors have to be suitably modified in order to maintain reasonably high levels of these antioxidants, as the risk factors are inversely related to the serum antioxidant levels.\(^{(76)}\)

Hence they suggest that all the conventional risk factors need to be modified more aggressively in Indians as a modest increase in them may predispose to coronary artery disease.

Johnson R.J. et al found that some of the oxidation products of cholesterol are directly cytotoxic and have been implicated in atherogenesis.\(^{(72)}\)

Association of blood pressure with elevated lipid levels have been noted in studies clustering of cardiovascular diseases risk factors. Recently familial form of hypertension associated with dislipidemia has been proposed and estimated in account with essential hypertension.\(^{(72)}\)
Experimental Design: Study Group

This study comprises of two study groups namely:

I) Hypertension

II) Hypertension with complications. This further subdivided as:
   a) Hypertension with diabetes mellitus
   b) Hypertension with congestive cardiac failure

Fifty patients with essential hypertension and forty patients with coronary artery disease (CAD) and eighty healthy, age matched controls composed of our study population. All of them were informed about this study and consent was provided. The age group of patient was from 30 to 60 years onwards.

In hypertensive patients (both essential hypertension, hypertension without complication) fifty (men and women, mean age group was 38.0±12.1). This group consisted of patients who have been diagnosed as essential hypertension for the first time or patient who have not normotensive although they have been using antihypertensive drugs for several months. The duration of hypertension was from 10 months – 10 years. All patients had outpatient casual measurements of blood pressure > 140/90 mmHg on the 3 separate occasions.

(For graphical presentation the kidney function parameters are expressed in percentage).
The criteria for inclusion were:

1. Left ventricular hypertrophy proved by electrocardiographic measurements (septal thickness and posterior wall thickness > 11 mm).
2. No e/o heart failure, myocardial infarction, angina pectoris or of complicating congenital or valvular heart diseases.
3. No concomitant therapy.

Patients with coronary heart disease (CHD) group consists of patients with mean age (53.8 ± 8.6) and who have been clinically diagnosed and with laboratory (ECG, Echocardiography). All of them had a typical angina (retrosternal chest pain on exercise, decreasing the pain in 10 minutes on rest, disappearing the pain by sublingual nitrite in 5 minutes) and a significant ST segment depression in the precordial or inferior leads on their ECG during exercise or at rest. All of them have a normal ejection fraction and IVS/PW ratio eco-cardiographically. None of the patients had a history of prior myocardial infarction or previous cardiac surgery. There was no important concomitant disease.

Eighty normal subjects (48 males, 32 females) with mean age (39.2 ± 10.5) with no history of cardiac or coronary disease, with a normal ECG and physical examination were served as controls.

Venous blood samples was collected after an overnight fast of 12 hours and the serum was used for the estimation of total
cholesterol (TC), triglycerides (TG) and high density lipoprotein (HDL-C), blood urea, creatinine and uric acid. The fasting and postprandial blood glucose levels were also recorded. LDL-C and VLDL-C were calculated using the Friedwald’s formula.

**Methodology** :

The serum uric acid levels represented both as a kidney function tests and as secondary antioxidant group. This property is described in Chapter VI.

The details of methods of estimations of various parameters in this chapter are given in Chapter – II (Material and methods).

**Statistical Analysis** :

Mean and S.D. values were calculated for all measured parameters. A student ‘t’ test is used to identify differences in each parameter between patients and controls.
Results and Discussion:

This chapter describes the results of lipid profile and kidney functions in patients suffering from hypertension and hypertension with complications.

The results from Table No. 1 and Figure No. 1 describe the lipid profile test group study. It is evident that more than 60% of hypertensive patients from all the three groups i.e. essential hypertension, hypertension with DM, and hypertension with CCF had abnormal lipid profile levels. The most common pattern of the lipid abnormality observed was significantly raised levels of serum cholesterol in all groups of hypertension compared to control group. Similarly, in all the hypertensive patients the serum triglyceride levels were also found to be increased as compared to the control group. The low levels of HDL-C were observed in hypertensive patients. Similar rise in (abnormal pattern of lipid profile) total cholesterol and triglycerides and significantly decreased in HDL-C level in the serum were reported by Cross Marry et al\(^{65}\) in which the risk factor were classified categorically leading towards the progression of atherosclerosis and cardiovascular diseases.

The serum triglyceride levels were found to be elevated significantly in hypertension with diabetes mellitus (DM) compared with other two-group study.\(^{65}\)
Table – I

Lipid profile in hypertension

(Hypertension with and without complications)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control group</th>
<th>In hypertension with and without complications</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Serum lipid profile</td>
<td>Hypertension</td>
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<tr>
<td></td>
<td>Serum total cholesterol (mg/dl)</td>
<td>177.33±20.80</td>
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<tr>
<td></td>
<td>Serum Triglycerides (mg/dl)</td>
<td>116.87±36.16</td>
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<tr>
<td></td>
<td>Serum HDL cholesterol (mg/dl)</td>
<td>53.28±9.39</td>
</tr>
<tr>
<td></td>
<td>Serum LDL cholesterol</td>
<td>100.69±2.02</td>
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<tr>
<td></td>
<td>Serum VLDL cholesterol</td>
<td>23.37±7.2</td>
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</tbody>
</table>

Values are mean ± SD,

(a) \(p<0.001\),

(b) \(p<0.01\)

(c) \(p<0.05\)
The decrease levels of HDL-C were also reported earlier.\textsuperscript{[53, 57]} The traditional risk factors of the above all group studies, included hypertension with DM, have a good growing evidence towards leading cardiovascular disease and its morbidity and mortality.

Present study observed abnormal lipid profile levels in non-diabetic patients of hypertension. However the, HDL-C levels were slightly higher as compare with present study group. Similar observations were reported by Achari \textit{et al.}\textsuperscript{[57]}

The elevated levels of serum cholesterols, which are the chief precursors for the essential hypertension, leading to congestive cardiac failure. Johnson R.J. observed the similar findings of the abnormal lipid profile levels, which is predictive in the development of essential hypertension and coronary heart disease and also reported the abnormal patterns of lipid profile in all types hypertensive disorders.\textsuperscript{[72]}

Daniel Stainberg \textit{et al} reported the abnormal pattern of lipid profile and the concepts of lipoproteins and the atherogenesis, which correlates with our present study group. They also described that the abnormal lipid levels are the processing components of atherogenesis.\textsuperscript{[64]}

The \textbf{LDL-C levels}, which are associated with the atherogenesis, \textit{were elevated in various groups of the present study}. The LDL-C levels were highly elevated in the hypertension
with diabetes mellitus and marginally raised in hypertension with CCF as compared with the control group with levels (Table 1 and Figure 1). These findings are well correlated with the earlier reports also indicated a similar pattern. (54,64,65,72,75) It has been suggested that this precursor is a causative factor in leading towards atherogenesis and atherosclerosis. Similarly, high levels of VLDL-C were registered in all the study groups compared with control levels of 23.37±7.23 mgs%. (Table 1 and Figure 1)

Thus the association of blood pressure with elevated lipid profile levels have been noted in the present study.

In the present study, the hypertensives below 40 years of age had an high cholesterol levels and lower HDL-C as compared to control. Also triglycerides levels in hypertensives showed a steadily declining trend with increase in age and there was a steadily increase in cholesterol levels with a severity of hypertension. In 60% of our cases, the most striking abnormality of all age group was abnormal total cholesterol/HDL-C ratio, which is more than 4.5%. (Table 1 and Figure 1)

In case of hypertension with diabetes mellitus, the uric acid itself is the most predictive factor. Increase in serum uric acid increases arterial blood pressure and thus associated with reduction in renal blood flow. High uric acid concentration increases sodium reabsorption at nephron site proximal to distal
tubules and it has been proposed that the metabolic perturbations (e.g. hyperinsulinemia) may mediate some of these effects in hypertension. **Insulin** exerts a direct effect on increased renal sodium reabsorption and this leads to the links with **hyperuricemia**, low urinary uric acid excretion and decrease glucose utilization. Thus hyperuricemia in hypertension may be an early indicator of hypertensive cardio-renal diseases, which is associated multimetabolic syndrome.

Our findings suggested that hyperuricemia may be predictive for both fatal and nonfatal in patients with diabetes. *(Table 2 and Figure 2)*

The association between diabetes mellitus and hypertriglyceredemia, pointing out that the VLDL particles, produce in the liver to release excess energy, is the adipocyte triglycerice with VLDL remnant particles, enriched in cholesterol either recycling to the liver or utilized for LDL formation. These adipocytes releases free fatty acids, increase hepatic VLDL production, and leading to hypertriglyceridemia. In addition the enzyme lipoprotein lipase (LPL) is regulated by insulin. With insulin resistance or insulin deficient state decrease in LDL activity and further increase triglyceride levels. There is also an inverse relationship between triglyceride and HDL-C.
Table No. II and Figure 2 describe the study of kidney function tests in hypertension. It has been observed from various studies that the rise in blood pressure levels both systolic and diastolic causes the insufficiency of blood supply which may leads to less cardiac output and thus the less renal circulation insufficiency leads abnormal functions of kidneys were its excretion process and products such as urea, creatinine, uric acid etc are found to be hampered and diminished. This leads to increase and abnormal levels of the kidney function test values.

Brand F.N. also reported high levels of serum uric acid which were consistently higher in subjects with both the sexes and also reported that elevated uric acid subsequently predicts the development of CHD and AMI. (68)

Blood urea and serum creatinine levels raised considerably as compared with the control group in the earlier / at the time of detection of hypertension. Hypertension may leads to primary renal diseases. (Table 2 and Figure 2)

The elevated values of blood urea found in cases with essential hypertension, hypertension with CCF and with diabetes mellitus. The significant abnormality in diabetes mellitus with hypertension and kidney functions observed and is also correlated the prognostic values of the disease. Also, the correlating factor i.e.
serum creatinine levels were also found to be raised in all the present study 0.71±0.05 mgs%.

The elevated serum uric acid levels in various types of hypertensive disorders have been reported. In present study, the incidence of hyperuricemia is more prominently found in cases of DM with hypertension and with hypertension with CCF. In the hypertension without any complications the uric acid levels also significantly raised, indicating that uric acid may be considered as a predictive factor for the development of myocardial diseases. These findings were also correlated with previous studies. (54,72)

When serum uric acid levels increased along with that of serum creatinine, the highest uric acid level could reflect an early decline in renal function and further it can be correlated with increased serum cholesterol levels (hypercholesterolemia). Thus serum creatinine, uric acid and lipid profile may prove to be the predictors of the hypertension.

Wannanethee et al (56) also reported elevated levels of serum uric acid in all the types of hypertensive disorders, which is in highly correlation with the present study group. The hyperuricemia observed in the present study may be responsible in the formation of serum urates (uric acid crystals) and thus may increases the risk factors for various heartdisorders. The presence
Table – II

Kidney functions in hypertension

(Hypertension with and without complications)

<table>
<thead>
<tr>
<th>Parameters</th>
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<th>In hypertension with and without complications</th>
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<td>Hypertension</td>
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<td></td>
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<td>Hypertension with DM</td>
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<td>Hypertension with CCF</td>
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<tr>
<td>Kidney functions :</td>
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<tr>
<td>6) Blood urea (mg/dl)</td>
<td>19.21±2.5</td>
<td>31.40±1.70&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
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<td>39.66±0.22&lt;sup&gt;a&lt;/sup&gt;</td>
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<td></td>
<td></td>
<td>53.36±4.42&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>7) Serum creatinine (mg/dl)</td>
<td>0.71±1.15</td>
<td>0.90±0.07&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
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<td>1.23±0.32&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
<td></td>
<td>1.75±0.28&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>8) Serum uric acid (mg/dl)</td>
<td>3.20±0.32</td>
<td>5.03±0.32&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td></td>
<td></td>
<td>6.20±1.73&lt;sup&gt;c&lt;/sup&gt;</td>
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<tr>
<td></td>
<td></td>
<td>6.4±0.15&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values are mean±SD,

(a) p<0.001,

(b) p<0.01

(c) p<0.05
of pre-existing myocardial infarction and the widespread underlying of atherosclerosis, as well as the clustering of risk factors were found due to elevation of uric acid levels. Williams and Beard et al.\textsuperscript{70} also reported hyperuricemia in various hypertensive diseases, which were in correlation with the present study.\textsuperscript{56}

In hypertension, the hyperuricemia might be due to antihypertensive therapy. The concept of hyperuricemia as a risk factor for cardiovascular diseases has recently supported by the finding that uric acid stabilizes platelet aggregation and enhances thrombotic tendency.

Our present study data suggests that uric acid levels are significantly related to the incidence of coronary heart disease in general to myocardial infarction in particular, in both the sexes independent of antihypertensive treatment. The probability should be ruled out that hyperuricemia does not occur due to secondary renal diseases and with the age factors because as the age increases, uric acid also increases.

Blood urea and serum creatinine levels raised considerably as compared with the control group in the earlier / at the time of detection of hypertension. Hypertension may leads to primary renal diseases. \textit{(Table 2 and Figure 2)}

It must be pointed out that even though the hypertension and serum cholesterol and triglyceride levels are correlated with a
low values, they coexist commonly and should ideally be investigated for, when one of them is initially detected as abnormal. This not only helps to control the two major risk factors of lipid profile and kidney functions of hypertension, may progress and lead to coronary artery disease, but also prevents the deterioration of the lipid profile by certain antihypertensive drugs. As compared to lipid profile, the kidney functions are less altered in hypertensive patients. This might be due to antihypertensive therapeutic effect, which is helping to increase the peripheral vascular resistance and mediate vascular complications. Further the nitrous oxide (NO) radical by the endothelium has been found to play a vital role in maintenance of vascular tone. This endothelium-relaxing factor might have reduced in the above diseases or to exaggerated production of vasoconstrictor substances of endothelial origin.

The kidney functions parameters increase gradually in hypertension and hypertension with complications may suggest their role in the further progression of oxidative stress.

It is indicated that the assessment of level of oxidative stress may help us in identifying the subject at a risk of diseases. Thus it can be delay the onset or retard the progression of the disease with therapeutic measures. Also the assessment of these parameters
may prove valuable as a prognostic tool to evaluate the efficacy of presently available therapeutic measures.

The increase in the oxidative stress affects the lipid profile and kidney function tests. The study related to this affect and the scavenging role of antioxidant is presented in next Chapter - IV