Chapter – IV

Serum ACE Levels, Lipid Profile and Other Parameters in Newly Detected Complicated Hypertensives (Organ Damage – II Test Group Study)
Chapter - IV

Serum ACE Levels, Lipid Profile and Other Parameters in Newly Detected Various Complicated Hypertensives (Organ Damage – II Test Group Study)

Introduction

The adverse effects of untreated hypertension increases the risk of vascular damage, involving both small (resistance) arteries and arterioles and large (conduct) arteries. These lesions lead to cardiac, renal, retina and cerebrovascular morbidity and mortality. The incidence of these different lesions is also dependent upon the level of other risk factors (such as plasma cholesterol, diabetes etc.) in the community.

Although the extent of organ damage often correlates with the levels of blood pressure, it is not always the case. In addition the rate of progression of organ damage varies from one individual to another depending on many influences, most of which are incompletely understood. Blood pressure and organ impairment should be evaluated separately, since markedly high pressure may be observed without organ damage also. Conversely, organ damage may be present with only moderate elevation of blood pressure.\(^1,9\)

In over 95% of patients with hypertension, no specific cause can be identified. These patients are diagnosed as having primary hypertension. But the small minority of patients i.e about 5% with age group of < 45 years in whom a specific cause related with organ damage is identified and diagnosed.

Precise staging of hypertension by extent of various organ damage will depend on diagnostic tests and other procedures. Some of them are costly or uncomfortable for the patients.\(^1,9,10\)
But to rule out the specific organ damage some of the biochemical investigation have diagnostic importance for e.g. in acute renal failure, estimation of blood urea followed by serum creatinine shows significant abnormal levels. Same is the condition with acute myocardial infarction, where CPK-MB is found to be the outmost diagnostic test during the onset of severe chest pain. and the funduscopic examination of the retina shows the extent of damage caused to retina due to raised and untreated blood pressure.\textsuperscript{152,153}

The present study was made in the following three groups:

1. Acute Renal Failure (ARF)
2. Acute Myocardial Infarction (AMI) and
3. Hypertensive Retinopathy

In carrying out this hypertensive study group, indoor patients (IPD) were examined and selected. The study was carried out in the newly detected subjects, who were untreated, first time admitted for hypertensive treatment and were of complicated with organ damage (initially). The study group was considered as a ‘complicated group’ because there was complications due to increase in blood pressure (SBP/DBP) levels related with kidney, heart and retina i.e. there was acute renal failure (ARF), acute myocardial infarction (AMI) and retinopathy respectively. In the first two classified group study, to rule out acute renal failure, blood urea and serum creatinine levels were estimated and serum creatinine kinase MB (isoenzyme CK-MB) was estimated in acute myocardial infarction (for cross check). This diagnostic test series are considered to give and had given positive results. For the study in retinopathy group, the hypertensive subjects were selected from OPD on fundus examination. However, the elimination of retinopathy was observed within 3-4 weeks of duration, depending on the severity of the retinopathy. This test group (complicated group) study deals with the irrespective of antihypertensive treatment.
The present study was carried in the hypertensive subjects with acute renal failure, acute myocardial infarction and retinopathy. The details of patients selection are elaborated in the respective group study.

1. **Acute Renal Failure (ARF) Group Study**

**Introduction**

The kidney is an important target of hypertension-induced organ damage. Severe and malignant (accelerated) hypertension often leads to renal insufficiency with a few years, mostly as a consequence of fibroid necrosis of small renal arteries. In less severe focus of hypertension, renal damage caused by arteriosclerosis is rather mild and develops more slowly. The development of renal damage in hypertension is commonly heralded by proténeurias. The current definition of proténeurias is a urinary protein excretion of greater than 300 mgs a day. The term micro-albuminuria has been coined during the past decade to define an abnormally elevated urinary albumin excretion (30 - 300 mgs/day) in the absence of clinical proteinuria as measured by standard laboratory methods.1,154

Proteinuria has been found to be an independent risk factor for mortality from all causes and cardiovascular disease. Reduction of proteinuria can be achieved by effective blood pressure reduction. Although antihypertensive patients with accelerated renal deterioration, more recent trials of treatment of patients with mild and moderate hypertension have demonstrated little benefit for renal functions despite the well known reduction in the incidence of stroke. This may be because in mild hypertension, renal disease progresses too slowly to be significantly appreciated during the relatively short duration of a controlled trial.102,103
None the less, hypertension remains a leading cause of renal disease accounting for 15-20% of all cases of renal failure in the USA and for 33% in the black Americans.

In addition to being a cause, renal disease may also be a result of hypertensive damage to renal vessels. Longstanding untreated hypertension may lead to proteinuria and progressive renal failure. Renal artery stenosis often causes refractory hypertension and should be considered in patient with severe hypertension that is difficult to control or has develop rapidly.

Renal arteriography provides the most detailed information about the renal vessels and can permit perentaneous balloon dilatation of renal artery stenosis.\textsuperscript{155,156}

Lowenthal D.T. \textit{et al.} (1985) reported that impaired renal function resulted in elevated serum and plasma concentrations of Enalapril maleats and decreased excretion rates and minor recovery of Enalapril maleate to Enalapril in their study on effect of renal function on Enalapril kinetics.\textsuperscript{25}

The protracted blood pressure reduction in the patients with CRF (Group-I & II) is possibly related to the elevated plasma Enalaprilate at concentration. Plasma ACE levels are suppressed by Enalapril. Hypothetically, had Enalaprilate at levels been measured at 72 to 96 hours and found to be zero. The blood pressure reduction may have been related to ACE inhibition, tissue binding of drug to vascular smooth muscle, kinin-kininogen accumulation or other factors. Therefore for blood pressure control, lower dose or less frequent dosing of Enalapril maleats may be indicated for patients with renal insufficiency than for those with normal renal function.
Yvonne Fogarty et al. (1989) measured SACE by the method of Neels et al. using the substrate 3-(2-furylacyloyl)-L-phenylalanyl-Glyc Glycine adopted to a Rotochem II parallel fast centrifugal analyser. All specimens from each subject were analysed in duplicate in a single batch to minimise analytical variation. The potential usefulness of measurements of serum ACE activity was examined using data on the analytical and biological variation in 15 ostensibly healthy subjects. Their estimations had shown mean levels of SACE in healthy were 13.5 to 35.0 U/L. the reference interval range was 12-52 U/L.

Saulo Klahr (1989) describe kidney has a dual role in hypertension. It may cause it and it may suffer the untoward effects of an elevation in blood pressure. Primary or essential hypertension has been attributed in part to alterations in renal sodium excretion.

Secondary hypertension is most commonly attributable to renal disease. Systemic hypertension, whether primary or secondary, may cause renal disease or may accelerate the loss of function in kidneys with established parenchymal disease. Several morphologic changes, collectively termed nephrosclerosis, have been described in the kidneys of patients with primary or essential hypertension.

Further, in his study stated that, deterioration of renal function, defined as an increase in serum creatinine concentration with ≤ 1.5 mg% was observed in 10 of the 61 patients. From his observations, he further suggested that age could have contributed to the loss of renal function in patients with adequate control of blood pressure even in normotensive persons, the glomerular filtration rate declines at the rate of 1 ml per year after the age of 35 years.

Mikus G. et al. (1991) reported the antihypertensive effect of nitrendipine, a dihydropyridine calcium channel blocker. The study
was made in twelve patients with impaired renal function with moderate to severe hypertension. Significant reduction of blood pressure was observed after four weeks of treatment.

Garcia-Cosmes P. et al. (1992) studied and reported that in the treatment of high blood pressure, organ protection is the main goal. Consequently, this protective capacity should be one of the main characteristics of any drug used in the treatment of hypertension. They also suggested that the renal protective agent should protect the kidney from intrinsic renal vasoconstriction and exogenous agents, and should also protect, or at least delay, the decline in renal function in the presence of renal insufficiency, by mechanisms other than increasing glomerular filtration pressure. Further their had reported that the calcium antagonist verapamil is very effective in renal protection.

Luis M. Ruilope et al. (1992) studied and reported whether antihypertensive effect of verapamil calcium antagonist is influenced by dietary sodium intake in patients in the early stages of chronic renal failure. They had also conducted a study in which a low sodium intake (4 gm daily) was compared with a high intake (11 gm daily) in hypertensive patients treated with sustained release verapamil. The study was made in fourteen subjects diagnosed as having essential hypertension. Before start with the antihypertensive study the washout period was of four weeks. Verapamil 240 mg/day for 14 days treatment was started. The recorded blood pressure before treatment was SBP 168.5 ± 19.6 mm Hg and DBP 99.9 ± 8.8 mm Hg serum creatinine levels were 1.23 mg/dl to 1.76 mg/dl.

Sennesael J. et al. (1992) observed the effect of ACE inhibitor Perindopril in twenty three hypertensive patients with stable chronic renal failure. The dose size was 2 or 4 mg once a day according to the
degree of renal failure. Serum ACE activity was measured by a method derived from that described by Cushman and Cheung (1983) using hippuryl-L-histidyl-L-leucine (HHL) as the substrate.

Allan D. Struthers (1992) had delivered a lecture to the British Pharmacological Society in London. In his lecture he said that primary renal diseases such as glomerulonephritis in hypertension, has long been known. If the kidney in transplanted from a spontaneously hypertensive rat to a normotensive rat, then the hypertension follows the kidney. This suggests that the kidney is of major aetiological importance in the development of essential hypertension. It has also recently been shown that one of the earliest abnormalities to be found in the first degree relatives of hypertensive patients is a decrease in renal blood flow.

The next general medical condition where renal function is abnormal is chronic heart failure where renal sodium and fluid retention is usually the first clinical sign of the disease. DM is another medical disease where renal dysfunction is prominent.

This is a curious finding since angiotensin II and aldosterone are adjacent components of the RAAS cascade. The clinical relevance of this is that as a patients goes from early heart failure to late heart failure, one feature is that their kidneys retain more salt and water. If ACE inhibitor are given during early heart failure. This might prevent not only the antinatriuretic effect of angiotensin II but also the antinatriuretic effect of noradrenaline.

Angiotensin II is known to be a renal vasoconstrictor while prostaglandin (PG) are renal vasodilators. Much animal data suggests that PGs act in a counter regulatory manner against angiotensin II’s vasoconstrictors effect especially against its effect on the renal afferent arterial.
Luis M. Ruilope et al. (1993) reported the existence of relationship between the kidney and blood pressure. The renal origin of arterial hypertension has been demonstrated in different animal models resembling human hypertension, with data from humans seeming to confirm this hypothesis.

Further, in their review described that the renal vasculature also suffers from the consequences of arterial hypertension and renal insufficiency can develop as a result of elevated blood pressure levels. Antihypertensive therapy can prevent the development of renal damage secondary to hypertension.

Schohn D.C. et al. (1993) studied the calcium antagonists such as verapamil among the antihypertensive agents categorised as first line treatments for essential hypertension. They have also shown efficacy in secondary forms of hypertension, including hypertension associated with chronic renal failure, irrespective of the degree of renal impairment.

Systemic and renal haemodynamic parameter and renal function were analysed in fifteen hypertensive patients with mild to severe chronic renal failure after a two week placebo period and after four weeks of administration of verapamil sustained release (SR) 240 mg per day. After four weeks of treatment with verapamil SR, blood pressure was normalised in all patients. Arterial pressure decreased as a result of the decrease in systemic vascular resistance. While cardiac output and heart rate remained unchanged. Their had also measured blood urea, creatinine, electrolytes, etc.

Mancia G. et al. (1993) reviewed in their article about the relationship between hypertension and the kidney. It was suggested and it has been confirmed by many authors that prolonged hypertension damages the kidney. End-stage renal failure occurs more frequently in
elderly hypertensive patients as well as in young and middle-aged subject. In this connection they had further reported that it has not yet been established whether antihypertensive treatment will have a beneficial effect on hypertension-related kidney failure, because intervention trials have generally been of insufficient duration to observe enough patients through the onset of end-stage renal disease. Therefore it has not been possible to meaningfully investigate any difference between untreated and treated hypertensive patients in the onset of end-stage renal disease.

N.D.C. Sturrock and A.D. Struthers (1993) describe non-steroidal anti-inflammatory drugs (NSAIDS) and ACE inhibitors both are finding important place in the treatment of renal failure with variable.\textsuperscript{17}

Schneider R. \textit{et al.} (1994) and Alberto Zanchetti (on behalf of the Italian Nifedipine GITS study group had studied the effect of Nifedipine GITS (Gastro-Intestinal Therapeutic System) in hypertensive subjects with chronic renal impairment and raised blood pressure respectively.\textsuperscript{165} They had found that once daily administration of 30 mg Nifedipine is very beneficial in the reduction and regulation of 24 hours blood pressure levels.

WHO (1996) Renal mechanism have often been implicated in the pathogenesis of hypertension either through an altered pressure natriuresis leading to sodium retention through an altered release of pressure factors (such as renin) or of depressor factors (such as prostaglandin and medullipin).\textsuperscript{1}

Leese G.P. \textit{et al.} (1996) studied and had reported similar findings.\textsuperscript{166} They had suggested that CE inhibitors have additional renoprotective action with lowering blood pressure levels compared with other antihypertensive drugs.
Patients Selection (Before Treatment)

In carrying out this study group, 50 hypertensive patients with acute renal failure who were newly detected, untreated and were first time admitted in the hospital for acute hypertensive treatment were examined and selected for study. Out of which 9 (18%) were female and 41 (82%) were male. The age group was 46.26 ± 5.97 years as a mean with mean body weight 69.24 ± 4.02 kgs.

Postrenal Failure (After Treatment)

After 7 days of ‘run in period’ antihypertensive treatment i.e. at the time of discharge (recovery), same study protocol was followed in the same selected patients and same procedure was adapted for recording blood pressure, body weight and blood sample collection. Then the study for this particular group was concluded.

On physical examination, blood pressure recorded after treatment was SBP 122.96 ± 6.94 mm Hg and DBP 86.40 ± 4.06 mm Hg as a mean. The body weight noted as 69.24 ± 4.02 kgs.

The results of the recorded blood pressure levels i.e. the physical examination and biochemical investigations of the ARF group has been summarised in Table 4.1 and 4.2 (test group before treatment) and Table 4.3 and 4.4 (test group after treatment i.e. the intervention study group).
Table 4.1

Physical Examination of Newly Detected Hypertensive, Untreated and were Complicated Subjects Hypertensive with Acute Renal Failure (ARF) Group Before Treatment v/s Control Group

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Subjects</th>
<th>Age in years</th>
<th>Body wt. in kgs.</th>
<th>SBP as mm Hg</th>
<th>DBP as mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control Group n = 50</td>
<td>39.88 ± 5.37</td>
<td>66.06 ± 5.86</td>
<td>117.60 ± 7.57</td>
<td>77.00 ± 4.21</td>
</tr>
<tr>
<td>2.</td>
<td>Test Group n = 50</td>
<td>46.26 ± 5.97</td>
<td>69.24 ± 4.02</td>
<td>185.16 ± 13.26</td>
<td>111.46 ± 5.85</td>
</tr>
</tbody>
</table>

*All values are mean with ± standard deviation.*

Table 4.2

The Biochemical Parameters in Newly Detected Hypertensive, Untreated Complicated Subjects.

Acute Renal Failure Group - Before Treatment

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Parameters</th>
<th>Group</th>
<th>Mean S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Random Pl. Glu (mg/dl)</td>
<td>C</td>
<td>73.52 ± 07.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>84.70 ± 08.96*</td>
</tr>
<tr>
<td>2.</td>
<td>Blood Urea (mg/dl)</td>
<td>C</td>
<td>18.71 ± 02.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>78.94 ± 24.16*</td>
</tr>
<tr>
<td>3.</td>
<td>Sr. Creatinine (mg/dl)</td>
<td>C</td>
<td>0.71 ± 00.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>2.73 ± 00.78*</td>
</tr>
<tr>
<td>4.</td>
<td>Sr. Sodium (meq/L)</td>
<td>C</td>
<td>141.98 ± 01.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>145.08 ± 04.51*</td>
</tr>
<tr>
<td>5.</td>
<td>Sr. Potassium (meq/L)</td>
<td>C</td>
<td>4.43 ± 00.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>5.71 ± 00.45*</td>
</tr>
<tr>
<td>6.</td>
<td>SACE (U/L)</td>
<td>C</td>
<td>22.52 ± 03.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>71.04 ± 04.00*</td>
</tr>
<tr>
<td>7.</td>
<td>Sr. Total Chol. (mg/dl)</td>
<td>C</td>
<td>180.46 ± 13.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>203.88 ± 17.61*</td>
</tr>
<tr>
<td>8.</td>
<td>Sr. Trigly (mg/dl)</td>
<td>C</td>
<td>99.72 ± 19.66</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>178.64 ± 27.11*</td>
</tr>
<tr>
<td>9.</td>
<td>Sr. HDL-C (mg/dl)</td>
<td>C</td>
<td>39.82 ± 03.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>33.18 ± 03.71*</td>
</tr>
<tr>
<td>10.</td>
<td>Sr. LDL-C (mg/dl)</td>
<td>C</td>
<td>120.70 ± 13.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>134.98 ± 17.97*</td>
</tr>
<tr>
<td>11.</td>
<td>Sr. VLDL-C (mg/dl)</td>
<td>C</td>
<td>19.94 ± 03.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>35.72 ± 05.56*</td>
</tr>
</tbody>
</table>

*All values are mean with ± standard deviation.*

C = Control; T = Test; * P < 0.05
### Table 4.3
Physical Examination of Acute Renal Failure Group After Treatment. Before Treatment Group was treated as Control (baseline) (Intervention Study)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Subjects</th>
<th>Age in years</th>
<th>Body wt. in kgs.</th>
<th>SBP as mm Hg</th>
<th>DBP as mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control Group n = 50</td>
<td>46.26 ± 5.97</td>
<td>69.24 ± 4.02</td>
<td>185.16 ± 13.26</td>
<td>111.46 ± 5.85</td>
</tr>
<tr>
<td>2.</td>
<td>Test Group n = 50</td>
<td>46.33 ± 5.97</td>
<td>69.24 ± 4.02</td>
<td>122.96 ± 6.94</td>
<td>86.40 ± 4.06</td>
</tr>
<tr>
<td>3.</td>
<td>Mean Difference</td>
<td>7 days</td>
<td>--</td>
<td>+62.22</td>
<td>+25.06</td>
</tr>
</tbody>
</table>

*All values are mean with ± standard deviation.*

### Table 4.4
The Biochemical Parameters in Acute Renal Failure Group After Treatment. Before Treatment Group was treated as Control (baseline) (Intervention Study)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameters</th>
<th>Group</th>
<th>Mean</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Random Pl. Glu (mg/dl)</td>
<td>C</td>
<td>84.70 ± 08.96</td>
<td>-3.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>87.82 ± 04.43*</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Blood Urea (mg/dl)</td>
<td>C</td>
<td>78.94 ± 24.16</td>
<td>+55.72</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>23.22 ± 02.99*</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Sr. Creatinine (mg/dl)</td>
<td>C</td>
<td>2.73 ± 00.78</td>
<td>+1.89</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>0.84 ± 00.12*</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Sr. Sodium (meq/L)</td>
<td>C</td>
<td>145.08 ± 04.51</td>
<td>+3.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>141.72 ± 01.89*</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Sr. Potassium (meq/L)</td>
<td>C</td>
<td>5.71 ± 00.45</td>
<td>+1.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>4.38 ± 00.23*</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>SACE (U/L)</td>
<td>C</td>
<td>71.04 ± 04.00</td>
<td>+40.92</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>30.12 ± 03.31*</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Sr. Total Chol. (mg/dl)</td>
<td>C</td>
<td>203.88 ± 17.61</td>
<td>+11.68</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>192.20 ± 13.87*</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Sr. Trigly (mg/dl)</td>
<td>C</td>
<td>178.64 ± 27.11</td>
<td>+13.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>164.88 ± 26.03*</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Sr. HDL-C (mg/dl)</td>
<td>C</td>
<td>33.18 ± 03.71</td>
<td>-8.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>41.82 ± 03.53*</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Sr. LDL-C (mg/dl)</td>
<td>C</td>
<td>134.98 ± 19.97</td>
<td>+18.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>116.90 ± 13.95*</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Sr. VLDL-C (mg/dl)</td>
<td>C</td>
<td>35.72 ± 05.56</td>
<td>+2.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>33.48 ± 05.02*</td>
<td></td>
</tr>
</tbody>
</table>

*All values are mean with ± standard deviation.*

C = Control; T = Test; *P < 0.05
Results and Discussion

It has been widely documented that there is a relationship between the kidney and arterial hypertension. In the hypertensive process, the kidney appears to be both culprit and victim: an abnormality in renal function has been proposed as the initiating factor in most forms of hypertension. Renal vessels are damaged by persistently elevated blood pressure levels, which leads to the development of renal insufficiency. The decline in renal function takes place when blood pressure is increased. Thus, antihypertensive treatment can prevent the development of renal damage in severe hypertensive.

In this context, the present group study was conducted by selecting acute renal failure subjects from indoor patient department (IPD) who were newly detected, untreated and first time admitted for hypertensive treatment. On admission recording of blood pressure levels and blood sample was drawn for biochemical investigations which was made sooner when the patient was admitted and after seven days of admission and at the time of discharge (recovery) same protocol was followed. The comparison of the results of (before treatment) was made with the 50 control (normotensive) subjects. ‘Intervention’ study i.e. after treatment results were compared with before treatment test group treated as baseline values. The test group study was made in same selected and number of subjects.

Table 4.1 shows the mean values and standard deviation of the blood pressure levels before treatment. The blood pressure levels recorded in 50 ARF hypertensive subjects before treatment was compared with control group. The rise in blood pressure levels were highly significant (p < 0.05).
Table 4.3 shows the results of the 'intervention' study. The antihypertensive treatment was for seven days. After antihypertensive treatment study was made, about +62.22 mm Hg of SBP and +25.06 mm Hg of DBP fall in blood pressure levels has been noted as a mean difference. The fall in blood pressure levels compare with baseline were highly significant. Kidney has a dual role in hypertension reported by Saulo Klaar.\textsuperscript{156} They further suggested that kidney may cause it and it may suffer the untoward effects of an elevation of blood pressure. Tremendous reduction in blood pressure levels was demonstrated by Mikus et al.\textsuperscript{157} after antihypertensive treatment in severe hypertensive patients with kidney failure. Also Luis M. Ruilope et al.\textsuperscript{162} demonstrated increase in blood pressure levels in ARF before treatment. Similar increase in the levels of blood pressure was demonstrated by Schohn D.C. et al.\textsuperscript{163} in mild to severe chronic renal failure patients at the time of before treatment. Considerable fall in blood pressure levels were observed after antihypertensive treatment. For ARF group figure 4.1 & 4.2 shows the comparison of SBP levels before and after treatment while figure 4.3 & 4.4 shows the comparison of DBP levels before and after antihypertensive treatments.

Table 4.2 (before treatment) and Table 4.4 (after treatment) i.e. intervention study shows the mean values and standard deviation of biochemical investigations. The results of before treatment were considered as baseline for intervention study.

The fasting plasma glucose levels showed significant rise compared with control. The levels were found to be increased moderately in intervention study compared with baseline. The moderate difference in the mean rise of levels was –3.12 mg/dl. It has been demonstrated by Mancia et al.\textsuperscript{71} that patient with elevated blood pressure, insulin sensitivity is reduced. Thus there is moderate increase
in plasma glucose in such type of hypertensive subjects. Figure 4.5 & 4.6 shows the comparison of fasting plasma glucose level of ARF group before and after antihypertensive treatment.

Blood urea were found to be raised tremendously compared with control group. The increase in levels was highly significant, but the levels were tremendously lowered in intervention study compared with baseline. The decrease in the levels was highly significant. The mean difference in the decrease of levels was +55.72 mg/dl. Similarly, serum creatinine levels were also found to be raised compared with control. The increase in the levels was highly significant (p < 0.05). But the levels were decreased in intervention study with mean levels 0.84 ± 0.12 mg/dl compared with baseline. The decrease in the values were significant. The mean difference in the decrease of values was + 1.89 mg/dl. Similar rise and fall in blood urea and serum creatinine levels were demonstrated by Saulo Klahr. Several morphologic changes, collectively termed nephrosclerosis have been described in the kidneys of patients with primary or essential hypertension. As the kidneys are that chief excretory organ of the non-protein nitrogenous constituents, damage to kidneys, leads to the loss of kidney (renal) function. Hence due to deterioration of renal function, there is increase in blood urea and serum creatinine levels. But the levels were lowered by the kidneys due to increase in glomerular filtration rate. This is achieved when blood pressure levels are in good control. Similar reduction in blood urea and serum creatinine levels were reported by Schöhn D.C. et al. Renal plasma and blood flows were markedly and significantly increased after antihypertensive treatment. Figure 4.7 & 4.8 (blood urea) and figure 4.9 & 4.10 (serum creatinine) shows the comparison of respective levels in ARF group before and after antihypertensive treatment.
Serum sodium levels were raised moderately compared with control group. The increase in the levels was highly significant ($p < 0.05$). But the levels were found decreased in ‘intervention study’ compared with baseline. The decrease in the levels was significant ($p < 0.05$). The Mean difference in the fall of sodium levels was +3.36 meq/L. while serum potassium levels were significantly increased compared with control group. The rise in the levels were highly significant. But the values were returned to normal in intervention study with mean 4.38 ± 0.23 meq/L compared with baseline. The decrease in the levels were significant. The mean difference in the decrease of serum potassium levels was +1.33 meq/L. Many theories had been explained in the reduced capacity of the kidney to excrete sodium. Thus elevation of sodium levels are increased but after antihypertensive treatment the levels are decreased and normaled due to the normal renal functions. Hyperkalemia or increase in the potassium level suggest that muscle of the greater part of the blood potassium is in the cells, part of the retained sodium shifts into cells, thus displacing some amount of potassium. Hyperkalemia may often cause fatal complications. Similar coresembling hyperkalemia in ARF was reported by Harve et al.\textsuperscript{30} Luis M. Ruilope et al.\textsuperscript{159} demonstrated that abnormality in renal failure is the primary defect in hypertensive subjects for excretion and regulation of sodium ion.

Biff F. Palmer reported that hyperkalemia develops in those hypertensive subjects with impaired renal function in whom a defect in the excretion of renal potassium exists.\textsuperscript{226} Figure 4.11 & 4.12 (serum sodium) and figure 4.13 & 4.14 (serum potassium) shows the comparison of respective levels in ARF group before and after antihypertensive treatment.
About three folds increase in the SACE levels was noted compared with control group. The increase in the levels was highly significant. But the level were lowered in intervention study compared with baseline. The decrease in the levels was highly significant. The decrease in the mean difference levels of SACE was by +40.92 U/L. Similar correlating fall in SACE levels was demonstrated by J. Sennesael et al.\textsuperscript{160} A steady state of ACE inhibition was achieved within 3 days with a maximal inhibition of about 90%. Figure 4.13 & 4.14 shows the comparison of respective levels of SACE in ARF group before and after antihypertensive treatment.

Serum lipid profile showed elevation in total cholesterol compared with control group. The rise in the levels was highly significant (p < 0.05). But the levels were reduced in the intervention study compared with baseline. The decrease in total cholesterol levels was significant. The decrease in the mean difference was +11.68 mg/dl. Also tryglycerides levels were found to be raised compared with control group. The rise in the levels was highly significant (p < 0.05). The levels were found to be lowered in intervention study compared with baseline. The decrease in the levels were significant (p < 0.05). The mean difference in the decrease of values was +13.76 mg/dl.

HDL-C showed decrease in the levels compared with control group. The decrease in the levels was highly significant (p < 0.05). But there was significant improvement in the levels in intervention study compared with baseline. The mean difference in the increase of HDL-C levels was −8.64 mg/dl.

The significant rise in LDL-C and VLDL-C was also registered compared with control group respectively. But the levels were lowered in intervention study respectively compared with baseline. The decrease in the levels was statistically significant (p < 0.05). The mean
difference in decrease of LDL-C and VLDL-C levels were +18.08 mg/dl. and +2.24 mg/dl respectively. Hyperlipidemia is the most common abnormality seen with azotemia and frequently occurs in the predialysis state when renal function is reduced. The major way in which renal failure affects plasma triglycerides metabolism is by reducing lipoprotein lipase activity (LPL). It may be due to the excessive presence of excretory substances in plasma, that inhibit the synthesis or release of the enzyme (LPL).

Similar corresembling and changes in levels of lipid profiles values were observed by Eastham and Tietz in renal failures. Increase in cholesterol and triglycerides and decrease in HDL-C levels were reported. Similarly Begdade J.P. *et al.*, Bhagwat R. *et al.* and Shashikala *et al.* demonstrated abnormal pattern of lipid profile in the various stages of renal failure. They reported increase in cholesterol and triglyceride levels while decrease in HDL-C levels were observed in mild to moderate renal failure. Figure 4.17, 4.19, 4.21, 4.23 & 4.25 (before treatment) and figure 4.18, 4.20, 4.22, 4.24 & 4.26 (after treatment) shows the comparison of respective level of lipid profile parameters in ARF group.

The main aim of this study was to examine the influence of renal insufficiency on the disposition of antihypertensive treatments and its active metabolites and on SACE inhibition. From the results, in one week treatment, significant fall in SACE and blood pressure levels were achieved. However the findings suggest that acute renal failure prolongs the duration of plasma ACE inhibition in patients with renal insufficiency suggesting that dose (antihypertensive treatment) adjustment in necessary in patients with severe renal failure.

It is generally accepted that treatment of arterial hypertension protects the kidney from the renal vascular injury that would otherwise
results from sustained elevated blood pressure especially in severe hypertension. Several studies have described a progressive deterioration in renal function in hypertension patients.19,160

2) Acute Myocardial Infarction (AMI) Group Study

Introduction

Coronary constriction, proliferation of smooth muscle cells and arrhythmia are involved in the pathophysiology of coronary heart disease and its complications such as myocardial infarction and sudden death. All these effects are favoured by high angiotensin II levels. Angiotensin II is the main effector molecule of the renin angiotensin system. The generation of angiotensin II depends on ACE, it is quite conceivable that population with enhanced expression of ACE would have higher incidence of coronary events than other.167

The immediate objectives are relief of pain and initiation of treatment to reduce mortality. Subsequent management is concerned with treatment of complications, dysrhythmias, heart failure and emboli and then secondary prevention of further myocardial infarction. The reduction in mortality is due mainly to prevention of cardiac rupture, which appears interestingly to remain the only complication of MI.10,167

Determination of serum CK-MB activity, plays a main role in the differential diagnosis of myocardial infarction. In atleast 10% of the patients, the ECG findings do not necessarily permit a clear diagnosis to be made. Approximately 20% of myocardial infarcts are silent, occurring particularly in the elderly, diabetes and hypertensive patients. Determination of CK-MB along with other enzyme such as SGOT, LDH, etc. play a major role in the differential diagnosis and monitoring of myocardial infarction. Determination of these cardiomarker enzymes permits a highly sensitive diagnosis of transmural myocardial infarction.
In such patient the diagnosis of AMI can be confirmed by the clinical symptoms and change in the ECG in addition to the enzyme assays.

Thus, the CK-MB values are seen to be elevated only 5-6 hours after the onset of chest pain has begun. Hence an early cardiac marker of AMI shall be greatly welcome. The measurement to serum enzymes as a reflection of damage to myocardial muscle cells still play an important role in the diagnosis of AMI.\textsuperscript{153,167}

Grumbach L. et al. (1954) reported that, potassium plays a central role in the maintenance of cellular polarisation and is critical for the transmission of electrical impulses through the myocardium.\textsuperscript{168} Alterations in the normal balance between intracellular and extracellular potassium concentrations can lead to serious arrhythmia. The adverse association between hypokalemia and arrhythmia in animal models appears to become significant in the pressure of AMI.

Nordrehang J.E. and Vonder Lippe G. (1983) reported that in patients with AMI, low serum potassium levels obtained on hospital admission are associated with the development of ventricular tachycardia or fibrillation.\textsuperscript{169}

Johanson B.V.V. and Dziamski (1984) reported significant elevations of extracellular potassium generally thought to be above 7.0 meq/L reduces the resting potential across the cell membrane and lead to an inability to conduct an electrical change.\textsuperscript{170}

Milder elevations of potassium levels have infrequently been found to be associated with development of arrhythmia.

Amery A. et al. (1986) reported the principle results of the clinical trial conducted by the European Working Party on high blood pressure in the elderly (EWPNE) were published in 1985.\textsuperscript{171} They demonstrated statistically significant reduction in cardiovascular
mortality in the actively treated patients compared with the placebo group. Cardiovascular mortality increased with advancing age and also with increasing SBP at presentation but not with increasing DBP. This could be related to the observation that, for the total study population the blood pressure at randomisation was related to age, the SBP increasing with age and the DBP being lower with advancing age.

R.H.M. Peters et al. (1987) described the adaptation of the method of Kasahara and Ashihara for the fully automatic determination of ACE with the Cobas Fara centrifugal analyser in blood donors serum samples.43 Further, they stated that many methods for determining ACE activity have been published, most of them based on the enzymatic cleavage of a tripeptide substrate, with subsequent quantification of one of the cleavage products by spectrophotometric, fluorometric, radiometric or ‘high-performance’ liquid chromatographic methods. But it was observed that most of these methods are time consuming and not suitable for automation. It was also reported that storage of serum ample at 4°C for one week or at −20°C for several months did not influence the ACE activity. This was also similarly reported by many other authors.

John G.F. Cleland et al. (1987) reported in their study on total body electrolytes composition in patient with heart failure.172 A comparison with normal subjects and untreated hypertensive. The study was made in 40 patients referred to the cardiac department. 20 subjects were without evidence of cardiac or other disease and 20 subjects with untreated essential hypertension.

Blood pressure in these hypertensive subjects was > 170/105 mm Hg. Serum electrolytes, sodium level were significantly higher in those patient with hypertension while potassium levels were decreased. Blood urea and serum creatinine levels were higher in heart failure. Blood urea and serum creatinine levels were raise in both the conditions but more
raised values in heart failure patients. While potassium depletion was
greater in heart failure. Plasma concentration of active renin,
angiotensin II and aldosterone were considerably higher in subject with
heart failure. Final conclusion was that activation of the renin-
angiotensin-aldosteron system (RAAS) was however, related to
hyperkalemia and potassium depletion.

John D. Brunzell and Melissa A. Austin (1989) studied and
reported plasma TG levels and coronary disease in 4156 men and 3419
women in age group of more than 30 years.\textsuperscript{173} In this study, preliminary
analysis of these prospective data has shown TG levels to be a strong
predictor of the risk of death from coronary heart disease, particularly
among men with lower levels of LDL-C.

Mebazaa A. \textit{et al}. (1989) reported that the circulating Renin-
Angiotensin System (RAS) has been described as an endocrine system
consisting of three components each of which is localised in three
different tissues:\textsuperscript{174} angiotensinogen synthesised by the liver; renin
secreted by the kidney; and Converting Enzyme (CE) by the endothelial
cells and, in particularly, in the endothelium of pulmonary blood vessels.
Renin cleaves angiotensinogen which is converted into an inactive
peptide, angiotensin I (Ang I). Under the influence of CE, Ang I is
converted into an active peptide angiotensin II (Ang II). The RAS
includes a final element Ang II receptors, which are widespread and
especially numerous in the vascular endothelium.

Arthur J. Moss and Jesala Benhorin (1990) studied and reported
the current knowledge about the diagnosis and treatment of patients with
first myocardial infarction.\textsuperscript{175} The study was made in the subjects who
were first time suffered from acute myocardial infarction. The study was
also useful for others who suffered with myocardial infarction more than
one time.
Haralambos Gauras (1991) reported an increase in systemic vascular resistance in the cardinal hemodynamic characteristic of congestive cardiac failure.\textsuperscript{176} All three major peressor system the renin-angiotensin system, the sympathetic nervous system, and action of vasopressin (AVP) contribute to the maintenance of high peripheral resistance (i.e. after load) to various extents.

François Cambien \textit{et al.} (1992) reported that factors involved in the pathogenesis of atherosclerosis, thrombosis and vasoconstriction, contribute to the development of coronary heart disease.\textsuperscript{177} In a study comparing patients after myocardial infarction (M.I) with controls, they had explored a possible association between CHD and a variation found in the gene encoding ACE.

This enzyme plays a key role in the production of angiotensin II and in the catabolism of bradykinin, two peptides involved in the modulation of vascular tone and in the proliferation of smooth muscle cells. High levels of circulating ACE were noted more significantly in M.I (n = 610) than in controls (n = 733).

ACE-exists predominantly as an ectoenzyme of vascular endothelial cells and plays a key part in the renin-angiotensin and kallikrein-kinin systems by activating angiotensin I into angiotensin II and in activating bradykinin. These two peptide harmones have opposite effects on vascular tone and on smooth muscle cell proliferation and as neointimal proliferation and vasospasm may be involved in the pathogenesis of coronary heart disease, the most likely mechanism by which the ACE polymorphism affects the risk of myocardial infarction is by modulating the level of these peptides in the coronary arteries. This hypothesis is compatible with earlier results and with a study of hypertensive patients with high renin.
Profiles, a condition likely to be associated with increase in angiotensin II, who were found to be at higher risk of coronary heart disease than those with low renin profiles.

Jorgen Fischer Hansen (1992) studied and reported that calcium antagonists play important role in the prevention of secondary acute myocardial infarction.\textsuperscript{178} The study was made with three calcium antagonists viz. Nifedipine, ditiazem and verapamil. All have comparable effect in the prevention of secondary AMI. But, verapamil was found to be more beneficial. Thus, in patients without heart failure during the acute event, verapamil may be used as the first choice of drug was the final conclusion.

Massie B.M. (1992) presented the discussion of documented and possible cardioprotective effects of ACE inhibitors, examines the variety of sites along the pathway to end stage heart disease at which they might intervene.\textsuperscript{179} The ability of ACE inhibitor to prevent the progression of congested heart failure (CHF) and reduce mortality is documented and a summary of data demonstrating benefits of their use in post-myocardial infarction patients with low ejection fraction is presented.

Felix Burkart (1992) critically reviewed the recent multicentre studies evaluating the therapeutic value of calcium antagonists in reducing the incidence of cardiovascular complications after myocardial infarction (secondary prevention) and in retarding the development of atherosclerosis in coronary artery disease (tertiary protection).\textsuperscript{180} Further in their review, they had suggested that the prognosis of patient after acute myocardial infarction can be improved not only by interventional ensures such as aortocoronary bypass surgery or precutaneous transluminal catheter angioplasty, but also by various drugs.
Weber M.A. (1993) reported that reduction of blood pressure is the only therapeutic goal of antihypertensive treatment may no longer be appropriate.\textsuperscript{181} High blood pressure is associated with an increased risk of cardiovascular events, but clinical trials of antihypertensive therapy have shown an inconsistent reduction in major cardiovascular end points. Importantly, the incidence of coronary artery disease has been reduced to only a small extent, suggesting that factors beyond high blood pressure are important in the genesis of atherosclerotic disease in hypertensive patients. Therefore, it is evident that patients with hypertension have an exaggerated vulnerability to the consequences of lipid abnormalities.

Schoenberger J.A. (1993) reported that coronary heart disease (CHD) is the major cause of death in the United States.\textsuperscript{182} Major modifiable risk factors for CHD are hypertension, hypercholesterolemia and cigarette smoking, with concomitant risk factors, especially left ventricular hypertrophy, that act synergistically to significantly increase overall risk. Antihypertensive therapy, while reducing the incidence of stroke, has not consistently reduced the incidence of CHD. This may be a result, in part, of adverse effects on the metabolic profile, especially on blood lipids by diuretics and certain β-blockers. He has also suggested that guidelines of the ‘Joint National Committee on Detection, Evaluation and Treatment of high blood pressure should also be followed since they improve the lipid profile as well as reduce blood pressure.

Mancia G. \textit{et al.} (1993) briefly reviewed the recent evidences concerning the relationship between hypertension and alteration in glucose and lipid metabolism and renal and cardiac damage.\textsuperscript{164} Moreover, it is now clear that high blood pressure is frequently associated with insulin resistance and dyslipidaemias. This suggests a
possible pathogenic link between hypertension and deranged metabolism.

Alex Roca Cusachs (1993) presented in his article about the lowering of blood pressure levels.\textsuperscript{183} It was suggested that, there is a general consensus that high blood pressure must be lowered gradually. Indeed, this approach was recommended by the World Health Organisation in 1978. A reduction in blood pressure beyond the limits of the autoregulatory curve may comprise perfusion of vital organs resulting organ ischaemia. However, a reduction in high blood pressure offers protection against cerebral events, and some protection against coronary heart disease. Autoregulation maintain local blood flowing response to changes in blood pressure. This explaines why a reduction in blood pressure that is too rapid or too intense can produce signs and/or symptoms of organ damage.

Wyld P.J. \textit{et al.} (1994) suggested that ACE inhibitors have been used successfully to treat hypertension and congestive heart failure for many years.\textsuperscript{20} The ACE inhibitor currently marketed are dipeptide or as amino acid derivatives that differ mainly in the chemical nature of the zinc binding ligand. They used idrapril as an ACE inhibitor and plasma sample were analysed for ACE activity. Plasma ACE activity was maximally inhibited (94 - 96\%) at all dose levels and remained more than 80\% depressed from 2 to atleast 6 hours after dosage.

Pfeffer M.A. (1995) reported the use of ACE inhibitors in patients with myocardial infarction has improved survival and reduced the rates of major non-fatal cardiovascular events, especially when these agents are used from the long term treatment in high risk patients such as those with signs of heart failure, evidence of left ventricular systolic dysfunction both.\textsuperscript{185} Similar, opinions were reported by many authors.
Consequently, the international guidelines recommended ACE inhibitors as first-line therapy for such patients.

Fortunately progress in this field had been swift and most of the information required to make a rational therapeutic practice is available. Just a decade ago it was hypothesized that ACE inhibitors might attenuate ventricular modelling after myocardial infarction. In this regard many studies have come forward. Bertram Pitt (2004) also had similarly reported.\textsuperscript{186}

Steven Reed \textit{et al.} (1995) studied to test the hypothesis whether basal renin angiotensin aldosterone system (RAAS) activity impairs the acute natriuretic response to furosemide in patients with mild or moderate congestive heart failure (CHF).\textsuperscript{187} As part of the compensatory, homeostatic adjustments that accompany the failing left ventricle, retention of salt and water by the kidney substantially contributes to the pathophysiology of CHF. While increase in plasma volume can improve cardiac performance via the Frank Starling mechanism, intravascular volume expansion can also lead to incapacitating pulmonary congestion and peripheral oedema. Consequently maintenance of optimal plasma volume is an essential therapeutic goal in the treatment of CHF. Although ACE inhibitors are useful in the treatment of heart failure because they can improve functional capacity and decrease the mortality rate, prior studies have shown that they alone are insufficient to manage the excess total body volume overload that often accompanies the failing heart. Thus loop diuretics, the most efficacious class of natriuretic drugs, remain essential agents in the management of this condition.

Ettore Ambrosioni \textit{et al.} (1995) studied ACE inhibitors in acute anterior myocardial infarction and reported that long-term treatment with an ACE inhibitor may improve outcome by attenuating acute myocardial infarction.\textsuperscript{188} Their had investigated whether the ACE inhibitor
zofenopril, administered for six weeks after myocardial infarction, could improve both short-term and long-term outcome. This drug was started within 24 hours after the onset of acute arterial myocardial infarction and continued for six weeks. At this time they had assessed the incidence of death or severe congestive heart failure. The patients were re-examined after one year to assess survival.

Newby D.E. et al. (1995) studied a case report of Enalapril overdose complicated by profound hypotension and anuria. A 46 years old woman was found collapsed at home having drunk 5 pints of strong larger and taken 14 to 20, 10 mg tablets of Enalapril over an 18 hours period for chest pain.

Three months previously she sustained a subendocardial myocardial infarction with pulmonary oedema, but good left ventricular function (ejection fraction of 54%) and was commenced on an ACE inhibitor (maintenance medication included diltiazem, bumetanide and isosorbide mononitrate).

Gary E. McVeigh et al. (1995) studied and reported that antihypertensive therapy has been used for almost 40 years to reduce blood pressure and to prevent morbidity and mortality related to the hypertensive state. Cardiovascular events are related to the initial elevation of blood pressure were the benefits of treatment are well established.

Leonetti and Cuspidi (1995) reviewed choosing the right ACE inhibitors for the treatment of hypertension because the family of ACE inhibitors is already very numerous. Inspite of this abundance of agents belonging to the same family raises a question: how to choose one or another ACE inhibitor for the treatment of arterial hypertension, cardiac failure or patients with myocardial infarction. They had
suggested that arterial hypertension was the first clinical indication for the use of ACE inhibition and therefore there is a great experience with these agents in the clinical condition. Many review have been published on Captopril, Enalapril and lisinopril, the first available ACE inhibitors in the market.

The aims of antihypertensive treatment is to lower the elevated blood pressure as a means to reduce or prevent the cardiovascular complications of hypertensive patients. Thus in this review they had tried to find out if there are pharmacokinetic or pharmocodynamic differences among the ACE inhibitors more frequently employed in the field of hypertension that are indicative of a greater or more appropriate antihypertensive efficacy or more suitable for patients as found in of age, organ damage, metabolic alteration or concomitant disease.

Kloke H.J. et al. (1996) studied and reported the effect of pharmacokinetic and pharmacodynamic properties of the angiotensin converting enzyme (ACE) inhibitor cilazapril in thirty hypertensive patients with various degrees of renal function. As the ACE inhibitor is hydrolysed in the liver and chiefly excreted by the normal kidneys. They had observed in patients with renal insufficiency, that chronic once daily treatment with cilazapril in effective in patients with renal impaired.

Megarry S.G. et al. (1997) reported that large randomised clinical trails of ACE inhibitors shown improved survivals after acute myocardial infarction (AMI). They had proposed that the benefit of ACE inhibitor therapy is largely confined, post-AMI, to those with evidence of left ventricular, dysfunction clinically or on investigation, and suggest the continuing importance of treatment distant from the acute event. They also argued, that the beneficial effects are, atleast in part, related to reduction in the direct toxic effects of angiotensin II and
catecholamines or cardiomyocytes resulting from the long term excess stimulation of the renin-angiotensin and sympathetic systems in these patients.

Gerd Heusch *et al.* (1997) reported myocardial ischaemia, where severe and sustained for more than 40 minutes, results in invisible damage i.e. myocardial infarction.\textsuperscript{193} However, with early reperfusion, damage in reversible. Complete recovery of contractile function requires some time, despite fully or almost fully restored blood flow. This phenomenon has been termed myocardial stunning. This findings were also confirmed by other authors about the experimental evidence showing that ACE inhibitors (Captopril, Enalapril and ramipril) limit the development of infarct size, reduce the incidence of ischaemic and reperfusion arrhythmia, and enhance the recovery of contractile function of stunned myocardium. It was also confirmed that cardioprotective effect of ACE inhibitors are mediated by an attenuated degradation of bradykinin.

Ashavaid T.F. *et al.* (2000) described that coronary constriction, proliferation of smooth muscle cells and arrhythmia are involved in the pathophysiology of coronary heart disease and its complications such as myocardial infarction and sudden death.\textsuperscript{167} All these effects are favoured by high angiotensin II levels. Angiotensin II is the main effective molecule of the renin angiotensin system. Consequently each component of this system represents a potential candidate in the aetiology of cardiovascular disease.

Further they had stated that because the generation of angiotensin II depends on ACE it is quite conceivable that population with enhanced expression of ACE would have higher incidence of coronary events than other subpopulations. ACE, a carboxypeptidase, exists predominantly as an ectoenzyme of vascular endothelial cells and
is also a component of the kallirein kinin systems where it inactivates bradykinin a potent vasodilator.

John G.F. Cleland et al. (2000) in their study had suggested that heart failure is common, serious and treatable, so great efforts should be made to manage it correctly.\(^{194}\) Only once a diagnosis of heart failure has been established and underlying left ventricular systolic dysfunction confirmed is treatment with a combination of angiotensin converting enzyme inhibitor or β-blockers are generally appropriate. They had also suggested that most cases of heart failure are diagnosed during a hospital admission - 56% according to surveillance studies in UK general practice and 82% according to epidemiological data. Prevention is often acute and secondary to myocardial infarction or to arterial fibrillation.

Bhatnagar D. et al. (2001) had studied lipid profile levels in acute myocardial infarction.\(^{195}\) They had observed hypercholesterolaemia and also normal lipid profile may lead to myocardial infarction. Specially in hypertensive subjects. Therefore, screening of hypercholesterolaemia in hypertensive subjects may prevent from AMI and the consequences of presenting with vascular symptoms.

Monkman D. (2001) our findings are in accordance with those of other studies.\(^{196}\) Doctors overestimate their patients knowledge about cholesterol as a risk factor for coronary heart disease. The individuals who are at highest risk, thus it has become accepted policy to test cholesterol concentration only when additional risk factors are present e.g. smoking, age factor and blood pressure are concerned. The patients should modify their risk factors and prescribe more efficiently. The ratio of total cholesterol to HDL-C allows the risk of coronary heart disease to be calculated for individuals who are being considered for primary prevention. Most patients who are admitted to hospital with a
myocardial infarction have their lipid concentration checked within 24 hours of the onset of symptoms. If these measurements are abnormal than treatment with a Statin is started.

Sonnenblick E.H. (2001) studied the effect of ACE inhibitors perindopril once daily in congestive heart failure patients. Its use is associated with a low risk of first-dose hypertension and no unwanted effects on blood pressure in normotensive patients. It also improves arterial compliance in hypertensive patients.

Hitesh Shah and N. Haridas (2003) studied and reported the diagnosis of acute myocardial infarction. AMI has traditionally been based on the characteristics clinical history, electrocardiographic abnormalities and increase serum concentrations of cardiac marker enzymes. As the differential diagnostics value of chest pain is limited and the ECG changes have various degrees of sensitivity and specificity, the measurements of serum enzymes as a reflection of damage to myocardial muscle cells still play an important role in the diagnosis of AMI. Measurement of Creatine Kinase (CK), aspartate aminotransferase etc are well established methods for this. They had also reported that considerable effort has been made in recent years to improve the specificity and sensitivity of methods for diagnosing AMI.

Nigam P.K. et al. (2004) studied the levels of serum lipid profile in patients with AMI, during acute phase (day 1,2,3), predischARGE and after three months. The study was made in 29 patients aged between 40 - 70 years admitted to ICCU. The diagnosis of MI was made by clinical, ECG and serum cardiac enzymes examination. Fasting samples were taken as soon as possible after admission (day 1 and average 14 hours after chest pain). They had observed decrease in HDL-C levels and had suggested that, the optimum time for estimation of serum lipids in patients with MI appears to be within 24 hours of acute episode.
Sanjay O.P. (2004) studied potassium levels in AMI. He reported that although potassium is critical for normal electrophysiology, the association between pre-operative serum potassium level and peri-operative adverse events such as arrhythmias in cardiac surgery have not been examined in detail. Hyperkalemia (serum potassium levels < 3.5 meq/L) was found in AMI.

**Patients Selection (Before Treatment)**

In carrying out this study group, 50 hypertensive patients with acute myocardial infarction who were newly detected, untreated and were first time admitted in the hospital for the treatment were examined and selected for study. Out of which 9 (18%) were female and 41 (82%) were male. The age group was 47.52 ± 4.66 years with body weight 70.06 ± 4.97 kgs as a mean. The recorded blood pressure was SBP 157.48 ± 16.92 mm Hg and DBP 103.68 ± 9.54 mm Hg as a mean.

**Postmyocardial Infarction (After Treatment)**

After 7 days of i.e. ‘run in period’ antihypertensive treatment i.e. at the time of discharge (after recovery) same study protocol was followed in the same selected patients and same procedure was adapted for recording blood pressure, body weight and blood sample collection. Then the study for this particular group was concluded.

On physical examination, blood pressure recorded after treatment was SBP 123.96 ± 5.39 mm Hg and DBP 84.96 ± 3.96 mm Hg as a mean. The body weight noted as 70.06 ± 4.97 kgs as a mean.

The results of the recorded blood pressure levels i.e. the physical examination and biochemical investigation of the AMI group study has been shown in Table 4.5 and 4.6 (test group ‘before treatment’) and Table 4.7 and 4.8 (test group ‘after treatment’ i.e. the intervention study group).
Table 4.5
Physical Examination of Newly Detected Hypertensive, Untreated and were Complicated Subjects of Acute Myocardial Infarction. Before Treatment v/s Control Group

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Subjects</th>
<th>Age in years</th>
<th>Body wt. in kgs.</th>
<th>SBP as mm Hg</th>
<th>DBP as mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control Group n = 50</td>
<td>39.88 ± 5.37</td>
<td>66.06 ± 5.86</td>
<td>117.60 ± 7.57</td>
<td>77.00 ± 4.21</td>
</tr>
<tr>
<td>2.</td>
<td>Test Group n = 50</td>
<td>47.52 ± 4.66</td>
<td>70.06 ± 4.97</td>
<td>157.48 ± 16.92</td>
<td>103.68 ± 9.54</td>
</tr>
</tbody>
</table>

All values are mean with ± standard deviation.

Table 4.6
The Biochemical Parameters in Newly Detected and Untreated complicated subjects of Acute Myocardial Infarction Group - Before Treatment

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Parameters</th>
<th>Group</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Random Pl. Glu (mg/dl)</td>
<td>C</td>
<td>73.52 ± 07.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>96.50 ± 09.54*</td>
</tr>
<tr>
<td>2.</td>
<td>Blood Urea (mg/dl)</td>
<td>C</td>
<td>18.71 ± 02.60</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>26.73 ± 07.49*</td>
</tr>
<tr>
<td>3.</td>
<td>Sr. Creatinine (mg/dl)</td>
<td>C</td>
<td>0.71 ± 00.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>1.12 ± 00.32*</td>
</tr>
<tr>
<td>4.</td>
<td>Sr. Sodium (meq/L)</td>
<td>C</td>
<td>141.98 ± 01.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>145.90 ± 04.04*</td>
</tr>
<tr>
<td>5.</td>
<td>Sr. Potassium (meq/L)</td>
<td>C</td>
<td>4.43 ± 00.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>3.66 ± 00.46*</td>
</tr>
<tr>
<td>6.</td>
<td>SACE (U/L)</td>
<td>C</td>
<td>22.52 ± 03.20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>50.14 ± 11.30*</td>
</tr>
<tr>
<td>7.</td>
<td>Sr. Total Chol. (mg/dl)</td>
<td>C</td>
<td>180.46 ± 13.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>225.46 ± 24.50*</td>
</tr>
<tr>
<td>8.</td>
<td>Sr. Trigly (mg/dl)</td>
<td>C</td>
<td>99.72 ± 19.66</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>214.08 ± 73.49*</td>
</tr>
<tr>
<td>9.</td>
<td>Sr. HDL-C (mg/dl)</td>
<td>C</td>
<td>39.82 ± 03.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>32.74 ± 03.98*</td>
</tr>
<tr>
<td>10.</td>
<td>Sr. LDL-C (mg/dl)</td>
<td>C</td>
<td>120.70 ± 13.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>149.43 ± 21.75*</td>
</tr>
<tr>
<td>11.</td>
<td>Sr. VLDL-C (mg/dl)</td>
<td>C</td>
<td>19.94 ± 03.93</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>43.30 ± 13.71*</td>
</tr>
</tbody>
</table>

All values are mean with ± standard deviation.
C = Control; T = Test; * P < 0.05
### Table 4.7
Physical Examination of Acute Myocardial Infarction Group (After Treatment).
Before Treatment Group was Treated as Control (baseline) (Intervention Study)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Subjects</th>
<th>Age in years</th>
<th>Body wt. in kgs.</th>
<th>SBP as mm Hg</th>
<th>DBP as mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control Group n = 50</td>
<td>47.46 ± 4.66</td>
<td>70.06 ± 4.97</td>
<td>157.48 ± 16.92</td>
<td>103.68 ± 9.54</td>
</tr>
<tr>
<td>2.</td>
<td>Test Group n = 50</td>
<td>47.46 ± 4.66</td>
<td>70.06 ± 4.97</td>
<td>123.96 ± 5.39</td>
<td>84.96 ± 3.96</td>
</tr>
<tr>
<td>3.</td>
<td>Mean Difference</td>
<td>+7 days</td>
<td>--</td>
<td>+33.52</td>
<td>+18.72</td>
</tr>
</tbody>
</table>

All values are mean with ± standard deviation.

### Table 4.8
The Biochemical Parameters in Post Acute Myocardial Infarction Group Subjects After Treatment. Before Treatment Group was treated as Control (baseline) (Intervention Study)

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Parameters</th>
<th>Group</th>
<th>Mean</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Random Pl. Glu (mg/dl)</td>
<td>C</td>
<td>96.50 ± 09.54</td>
<td>+6.10</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>90.40 ± 06.29*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Blood Urea (mg/dl)</td>
<td>C</td>
<td>26.73 ± 07.49</td>
<td>+9.30</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>19.80 ± 02.32*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Sr. Creatinine (mg/dl)</td>
<td>C</td>
<td>1.12 ± 00.32</td>
<td>+0.32</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>0.80 ± 00.11*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Sr. Sodium (meq/L)</td>
<td>C</td>
<td>145.90 ± 04.04</td>
<td>+3.20</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>142.70 ± 01.34*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Sr. Potassium (meq/L)</td>
<td>C</td>
<td>3.66 ± 00.46</td>
<td>-0.82</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>4.48 ± 00.14*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>SACE (U/L)</td>
<td>C</td>
<td>50.14 ± 11.30</td>
<td>+22.13</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>28.01 ± 02.37*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Sr. Total Chol. (mg/dl)</td>
<td>C</td>
<td>225.46 ± 24.50</td>
<td>+21.04</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>225.42 ± 12.97*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Sr. Trigly (mg/dl)</td>
<td>C</td>
<td>214.08 ± 73.49</td>
<td>+16.38</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>197.70 ± 60.98**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Sr. HDL-C (mg/dl)</td>
<td>C</td>
<td>32.74 ± 03.98</td>
<td>-9.66</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>42.40 ± 02.99*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Sr. LDL-C (mg/dl)</td>
<td>C</td>
<td>149.43 ± 21.75</td>
<td>+26.95</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>122.48 ± 16.05*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Sr. VLDL-C (mg/dl)</td>
<td>C</td>
<td>43.30 ± 13.71</td>
<td>+3.76</td>
</tr>
<tr>
<td></td>
<td>T</td>
<td>39.54 ± 12.19**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All values are mean with ± standard deviation.

C = Control; T = Test; * P < 0.05; ** P > 0.05
Results and Discussion

Cardiovascular mortality increased with advancing age and also with increasing SBP after treatment presentation but not with increasing DBP. Angiotensin converting enzyme inhibitors are effective in reducing the risk of heart failure, myocardial infarction and death from cardiovascular cases in patients with left ventricular systolic dysfunction of heart failure.\textsuperscript{199}

In this context, the present group study was conducted by selecting 50 acute myocardial infarction (AMI) subjects from indoor patient department (IPD) who were newly detected, untreated and first time admitted for hypertensive treatment.

Recording of blood pressure levels and estimation of various biochemical parameters from the blood sample was made sooner when the patient was admitted and after seven days of admission at the time of discharge (recovery). The comparison of the results (before treatment) was made with 50 control (normotensive) subjects. ‘Intervention’ study i.e. after treatment results were compared with before treatment test group treated as baseline values.

The test group study was made in same selected and number of subjects.

Table 4.5 shows the mean values and standard deviation of the blood pressure levels before treatment. The blood pressure levels recorded in 50 hypertensive subjects before treatment was significantly raised compared with control group. The rise in blood pressure levels were highly significant (\(p < 0.05\)).

Table 4.7 shows the results of the ‘intervention study’. The antihypertensive treatment was given for seven days. After treatment and at the time of discharge (recovery) the intervention study was
made. About +33.52 mm Hg of SBP and +18.72 mm Hg of DBP fall in blood pressure levels has been noted as a mean difference. The fall in blood pressure levels compared with baseline were highly significant with $p < 0.05$.

John G.F. Cleland et al. stated that in AMI patients there is high plasma renin which correspondingly increases the plasma concentration of angiotensin II and aldosterone.

Similar increase in blood pressure levels were demonstrated by Amery A. et al. Significant decrease in blood pressure specially SBP was noted after treatment. The CONSENSUS trial study also reported decrease in blood pressure levels after one week of antihypertensive treatment. Similar increase in blood pressure levels were observed by John G.F. Cleland et al. in 20 patients heart failure. For AMI group figure 4.1 & 4.2 shows the comparison of SBP levels before and after treatment while figure 4.3 & 4.4 shows the comparison of DBP levels before and after antihypertensive treatments.

Table 4.6 (before treatment) and Table 4.8 (after treatment i.e. intervention study) shows the mean values and standard deviation of biochemical investigations. The results of before treatment were considered as baseline for intervention study.

The fasting plasma glucose levels showed significant rise compared with control. The levels were found to be increased in 'intervention study' compare with baseline. The rise in the levels were statistically significant ($p < 0.05$). The difference in the mean raised levels was +6.10 mg/dl. Thomas Pollare et al. demonstrated that hypokalemia affects the release of insulin from the pancreas and rise in glucose level were observed but after antihypertensive treatment, the levels were moderately decreased. Figure 4.5 and 4.6. shows the
comparison of fasting plasma glucose levels in AMI group before and after antihypertensive treatment.

Blood urea levels was found to be raised significantly compared with control group. The increase in the levels were significant. But in the intervention study, the values were highly significant. The decrease in the mean difference was +9.30 mg/dl. Serum creatinine levels was found increased significantly compared with control group. But in the intervention study, the values were lowered with mean 0.80 ± 0.11 mg/dl compared with baseline. The decrease in the levels were statistically significant with p < 0.05. The mean difference in decrease of levels was +0.32 mg/dl. Similar increase in serum creatinine levels were reported by CONSENSUS trial study. They had suggested that increase in serum creatinine levels as a consequence reduced renal perfusion is common caused by angiotensin II. Subodh Verma et al. reported serum creatinine level about > 2 mg/dl in AMI. Correlating increase in serum creatinine levels with 2.5 mg/dl was reported by Ettore Ambrosioni et al. on admission. Similarly, John G.F. Cleland et al. demonstrated increase in blood urea and serum creatinine levels in 20 patients with heart failure and AMI. Figure 4.7 & 4.8 (blood urea) and figure 4.9 & 4.10 (serum creatinine) shows the comparison of respective levels in AMI group before and after antihypertensive treatment.

Serum sodium levels were increased compared with control group. The increase in the levels were highly significant (p < 0.05). but the levels were found decreased significantly in intervention study compared with baseline. The mean difference in the fall of the sodium levels was +3.20 meq/L while serum potassium levels were lowered significantly compared with control group. But the values were found significantly elevated in the intervention study compared with
baseline. The mean difference in the rise of serum potassium levels was 
-0.82 meq/L. The CONSENSUS trial study similarly reported increase 
in sodium and severe decrease in potassium levels (hypokalemia) at the 
time of admission and before treatment. But levels of sodium were 
normaled and potassium levels were significantly increased in one week 
of antihypertensive treatment. Hypokalemia was reported by 
Nordrehang et al. and Johansan et al. Similar coresembling 
increase in levels of serum sodium and decrease in potassium levels was 
reported by John G.F. Cleland et al. and Sanjay et al. in AMI. 
Hypokalemia in this condition was also demonstrated by Fang J. He 
et al. and also improved potassium levels has been reported after 
treatment. Figure 4.11 & 4.12 (serum sodium) and figure 4.13 & 4.14 
(serum potassium) shows the comparison of respective levels in AMI 
group before and after antihypertensive treatment.

Increase in more than two folds rise of SACE levels was noted 
compared with control group. The increase the level was highly 
significant. The levels were significantly lowered in intervention study 
compared with baseline. The fall in the mean difference of SACE levels 
was +22.13 U/L. The increase in SACE levels before treatment may be 
due to renin-angiotensin-aldosterone system which activated excessively. 
Also primary aldosteronism is produced due to hypokalemia may also 
be responsible. O’Neil et al. demonstrated similar correlating levels of 
SACE before treatment but the levels were reduced after antihypertensive 
treatment. Figure 4.15 and 4.16 shows the comparison of SACE levels 
in AMI group before and after antihypertensive treatment.

Serum lipid profile showed significant elevation in total 
cholesterol compared with control group. The levels were significantly 
found lowered in intervention study compared with baseline. The 
mean difference in the fall of total cholesterol levels was +21.04 mg/dl.
Also serum triglyceride levels were tremendously increased which was highly significant compared with control group. But in intervention study, the levels were decreased significantly compared with baseline values. The mean difference in the decrease of serum triglyceride levels was +16.38 mg/dl.

HDL-C levels magnificently lowered compared with control group which was highly significant. But in intervention study, levels were improved which were highly significant compared with baseline. The mean difference in the increase of HDL-c levels was −9.6 mg/dl.

The rise in LDL-C and VLDL-C was significantly registered compared with control group. The increase in the levels was statistically significant (p < 0.05). But the levels were significantly lowered in intervention study compared with baseline values. The mean difference in the fall of LDL-C was +26.95 mg/dl and VLDL-C was +3.76 mg/dl. Subodh Verma et al.\textsuperscript{139} also reported similar resembling levels of increased LDL-C in AMI. Nigam P.K. et al.\textsuperscript{153} had demonstrated abnormal lipid profile levels in AMI. They had abnormal great variation in all the components of lipid profile specially on 3\textsuperscript{rd} day of treatment. John D. Brunjell et al.\textsuperscript{173} had reported correlating levels of lipid profile. Increase in TGs and decrease in HDL-C levels were reported. Arthur J. Moss et al.\textsuperscript{175} demonstrated that as per the guidelines for lipid lowering have been published by the expert panel of the National Cholesterol Education Programme and this systematic approach to treatment is directly relevant for patient surviving their first myocardial infarction. Cholesterol level above 250 mg/dl are associated with an increased cardiovascular risk. Decrease in HDL-C and increase LDL-C levels are after treatment at higher risk. Abnormal lipid profile levels had been observed by Bertram et al.\textsuperscript{186} and Monkman D.,\textsuperscript{196} on admission of AMI subjects. Figure 4.17, 4.19, 4.21, 4.23 & 4.25 (before
treatment) and figure 4.18, 4.20, 4.22, 4.24 & 4.26 (after treatment) shows the comparison of respective level of lipid profile parameters in AMI group.

After treatment in AMI, the available data suggest that some moderate reduction in lipid profile levels in patient who had high lipid levels before treatment. In AMI, use of ACE inhibitors are very beneficial as the bradykinin (non reactive peptides) may be responsible for lowering blood pressure even though if the SBP and DBP are in normal range. The use of ACE inhibitors are beneficial for AMI treatment.

Blockade of the renin-angiotensin system has been shown to prolong survival and reduce adverse outcomes in patients with systolic heart failure or left ventricular dystrophy. Indeed, ACE inhibitors have become a corner stone in this patients.

3) Hypertensive Retinopathy Group Study

Introduction

Pathological lesions affecting the retina in hypertensive patients is called as hypertensive retinopathy.

Examination of the eye grounds has been a traditional way of evaluating organ damage in hypertensive patients. The signs of damage of retina shows abnormalities on fundoscopic examination. The optic fundi reveal a graduation of changes lined to the severity of hypertension and hence provide an indication of the arteriolar damage.

Untreated hypertensive retinopathy may lead into the malignant phase of hypertension were there is a full development of papilloedema and demands an urgent treatment. ‘Cotton Wool’ exudates are associated with retinal ischaemia or infarction and fade in a few weeks.
'Hard' exudates are small white dense deposits of lipid which may present for years.\textsuperscript{1,200}

Prashant K. Rohatgi et al. (1981) studied and estimated the SACE activity by determining in duplicate using a radiochemical assay based on quantification of tritiated (\textsuperscript{3}H) hippuric acid released from p-(\textsuperscript{3}H) hippuryl-glycyl-glycine as described previously in methods.\textsuperscript{39}

Ten microlitres of serum were routinely used in a total reaction mixture of 100 ml and hydrolysis was carried out at 37°C for 60 minutes at pH 8.0. Enzyme activity was computed in munits/ml (mU/ml). 1 u equals the hydrolysis of 1 μmol of substrate per minute at 37°C.

Thomas G. Pickering (1991) reported that, retinopathy may be particularly pronounced in patients with renovascular hypertension, perhaps because of its more brief and stormy course.\textsuperscript{201} In one series of patients with DBP > 125 mm Hg and haemorrhages or exudation in the fungus were observed, renovascular hypertension was diagnosed in patients with grade-III & IV hypertension retinopathy.

WHO (1996) Untreated hypertension increased the risk of vascular damage involving both small arteries and arterioles and large arteries. These lesions lead to coronary heart disease, congestive heart failure, stroke and renal dysfunction.\textsuperscript{1}

Concurrence of other risk factors, such as smoking, raised serum cholesterol and diabetic will augment and accelerate organ damage and may also influence the type of lesion incurred (retina).

Lars-Olof Hattenbach et al. (1998) examined 60 subjects having hypertension out of which five subjects were affected with hypertensive retinopathy.\textsuperscript{202} The presence of retinopathy was defined as generalised or localised arteriolas narrowing, arteriovenous crossing abnormalities, the presence of retinal haemorrhages and/or hard exudates, cotton wool
spots, venous beading, disk oedema and retinal new vessels. Mild fundus changes with narrowing of arteriolar. Systolic blood pressure ranged from 170 to 250 mm Hg and DBP ranged from 100 to 150 mm Hg.

Gp Capt. Ganjoo R.K. (VSM) and Avm (Mrs. Bandopadhyay (AVSM, VSM) (2002) studied white coat hypertension (WCH), a high blood pressure recorded in the clinic with abnormal ambulatory blood pressure monitoring (ABPM) using automated devices. The study was made in 55 a symptomatic aircrew (37 professional pilots and 18 military aviators) who were not on any antihypertensive medications with blood pressure levels SBP/DBP > or = 140/90 mm Hg were noted at the time of periodic medical evaluation for fitness for flying.

P.N. Nagpal et al. (2002) reported that hypertension is a major risk factor for retinopathy. The area of retina supplied by the occluded microvasculature get insufficient nutrition and oxygen due to which partial ischaemia occurs and creates the strain on the remaining healthy tissues and reduces the quality of functioning of retina.

Mark W.J. Strachan and John A. McKnight (2005) reported a short case history of a women with 34 years of age suffered badly from hypertensive retinopathy. She was untreated and newly detected hypertensive patient. On clinical check up her SBP levels were 240 mm Hg and DBP levels were 150 mm Hg Her funduscopic examination showed widespread haemorrhages in the left eye with soft and hard exudates and surveling of the optic disc. Blood urea and serum creatinine levels were increased.

Grosso A. et al. (2005) studied and reported that hypertension is associated with cardiovascular risk and systemic target organ damage. Retinopathy is considered as one of the indicators of target organ
damage. This review elaborates the recent studies on hypertensive retinopathy and their implications for clinical care. Early recognition of hypertensive retinopathy signs remains an important step in the risk stratification of hypertensive patients.

David L. Easty and John M. Sparrow reported clinical findings of hypertension may not occur until at least 5 to 10 years after the onset of hypertension. May patients with mild to moderate systemic hypertension may have no visual complaints. Some of the early clinical retinal findings may be diffuse narrowing of the retinal vessels with an increase in the arteriole reflex. There may also be thickening of the small arteriole and arteriolar walls. Patient who develop severe hypertension may have more marked arterioles constriction and focal evidence of vascular damage to the vessel wall. Associated findings may be closure of the retinal arterioles with focal areas of whitening of the retina called cotton-wool patches, which represents focal ischaemic changes. There is also evidence of an increased permeability and remottling of the retinal capillaries, sometimes with microaneurysmic formation. Retinal haemorrhages, which may be flame-shaped, may occur around the optic disc and along the major retinal vessels. Dot and blot haemorrhages may also occur and are located in the deeper layers of the retina. Hard exudates are frequently present and may have a star-shaped configuration. Cotton-wool spots are usually located superficial to the retinal vessels and may be peripapillary.

Patients Selection (Before Treatment)

In carrying out this study group, 50 hypertensive patients with retinopathy who were newly detected, untreated and were first time taking antihypertensive treatment were examined and selected for study. Out of which 7 (14%) were female and 43 (86%) were male. The age
group was 49.16 ± 3.11 years with body weight 73.32 ± 5.25 kgs as a mean. The recorded blood pressure was SBP 157.48 ± 16.92 mm Hg and DBP 103.68 ± 9.54 mm Hg as a mean. Table 4.9 shows the contents of physical examination of the hypertensive subjects with retinopathy before treatment and Table 4.10 shows the results of the biochemical analysis of the various parameters before treatment.

Hypertensive Retinopathy (After Treatment)

After 7 days i.e. 'run in period' of antihypertensive treatment same study protocol was followed in the same selected patients and same procedure was adapted for recording blood pressure, body weight and blood sample collection. Then the study for this particular group was concluded.

On physical examination, blood pressure recorded after treatment was SBP 117.82 ± 2.33 mm Hg and DBP 82.16 ± 2.31 mm Hg as a mean. The body weight noted as 73.32 ± 5.25 kgs. Table 4.11 shows the physical examination of hypertensive retinopathy subjects after treatment and Table 4.12 shows the results of the various biochemical parameters after treatment (intervention study).
Table 4.9
Physical Examination of Newly Detected Hypertensive, Untreated and were Complicated Subjects of Retinopathy. Before Treatment v/s Control Group

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Subjects</th>
<th>Age in years</th>
<th>Body wt. in kgs.</th>
<th>SBP as mm Hg</th>
<th>DBP as mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control Group</td>
<td>39.88 ± 5.37</td>
<td>66.06 ± 5.86</td>
<td>117.60 ± 7.57</td>
<td>77.00 ± 4.21</td>
</tr>
<tr>
<td></td>
<td>n = 50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Test Group</td>
<td>49.16 ± 3.11</td>
<td>73.32 ± 5.25</td>
<td>170.72 ± 7.74</td>
<td>105.40 ± 5.94</td>
</tr>
<tr>
<td></td>
<td>n = 50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All values are mean with ± standard deviation.*

Table 4.10
The Biochemical Parameters in Newly Detected and Untreated Hypertensive complicated Subjects of Retinopathy Group Before Treatment

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameters</th>
<th>Group</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Random Pl. Glu (mg/dl)</td>
<td>C</td>
<td>73.52 ± 0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>97.02 ± 0.43*</td>
</tr>
<tr>
<td>2.</td>
<td>Blood Urea (mg/dl)</td>
<td>C</td>
<td>18.71 ± 0.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>24.81 ± 0.66*</td>
</tr>
<tr>
<td>3.</td>
<td>Sr. Creatinine (mg/dl)</td>
<td>C</td>
<td>0.71 ± 0.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>1.13 ± 0.13*</td>
</tr>
<tr>
<td>4.</td>
<td>Sr. Sodium (meq/L)</td>
<td>C</td>
<td>141.98 ± 0.80</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>146.16 ± 2.05*</td>
</tr>
<tr>
<td>5.</td>
<td>Sr. Potassium (meq/L)</td>
<td>C</td>
<td>4.43 ± 0.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>3.24 ± 0.26*</td>
</tr>
<tr>
<td>6.</td>
<td>SACE (U/L)</td>
<td>C</td>
<td>22.52 ± 0.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>64.14 ± 0.74*</td>
</tr>
<tr>
<td>7.</td>
<td>Sr. Total Chol. (mg/dl)</td>
<td>C</td>
<td>180.46 ± 13.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>195.72 ± 0.36*</td>
</tr>
<tr>
<td>8.</td>
<td>Sr. Trigly (mg/dl)</td>
<td>C</td>
<td>99.72 ± 19.66</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>166.28 ± 11.26*</td>
</tr>
<tr>
<td>9.</td>
<td>Sr. HDL-C (mg/dl)</td>
<td>C</td>
<td>39.82 ± 0.32</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>30.36 ± 0.19*</td>
</tr>
<tr>
<td>10.</td>
<td>Sr. LDL-C (mg/dl)</td>
<td>C</td>
<td>120.70 ± 13.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>132.11 ± 0.69*</td>
</tr>
<tr>
<td>11.</td>
<td>Sr. VLDL-C (mg/dl)</td>
<td>C</td>
<td>19.94 ± 0.39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>33.25 ± 0.25*</td>
</tr>
</tbody>
</table>

*All values are mean with ± standard deviation.*
C = Control; T = Test; * P < 0.05
Table 4.11
Physical Examination of Retinopathy Group (After Treatment)
Before Treatment Group was Treated as Control (baseline) (Intervention Study)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>No. of Subjects</th>
<th>Age in years</th>
<th>Body wt. in kgs.</th>
<th>SBP as mm Hg</th>
<th>DBP as mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control Group n = 50</td>
<td>49.16 ± 3.11</td>
<td>73.32 ± 5.25</td>
<td>170.72 ± 7.74</td>
<td>105.40 ± 5.94</td>
</tr>
<tr>
<td>2.</td>
<td>Test Group n = 50</td>
<td>49.23 ± 3.11</td>
<td>73.32 ± 5.25</td>
<td>117.88 ± 2.33</td>
<td>82.16 ± 2.31</td>
</tr>
<tr>
<td>3.</td>
<td>Mean Difference</td>
<td>7 days</td>
<td>--</td>
<td>+52.84</td>
<td>+23.24</td>
</tr>
</tbody>
</table>

All values are mean with ± standard deviation.

Table 4.12
The Biochemical Parameters in Retinopathy Group Subjects After Treatment. Before Treatment Group was treated as Control (baseline) (Intervention Study)

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Parameters</th>
<th>Group</th>
<th>Mean</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Random Pl. Glu (mg/dl)</td>
<td>C</td>
<td>97.02 ± 06.43</td>
<td>+4.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>92.16 ± 05.68*</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Blood Urea (mg/dl)</td>
<td>C</td>
<td>24.81 ± 03.66</td>
<td>+6.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>18.76 ± 02.52*</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Sr. Creatinine (mg/dl)</td>
<td>C</td>
<td>01.13 ± 00.13</td>
<td>+0.33</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>00.80 ± 00.08*</td>
<td></td>
</tr>
<tr>
<td>4.</td>
<td>Sr. Sodium (meq/L)</td>
<td>C</td>
<td>146.16 ± 02.05</td>
<td>+3.26</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>142.90 ± 01.46*</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Sr. Potassium (meq/L)</td>
<td>C</td>
<td>03.24 ± 00.26</td>
<td>-1.39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>04.63 ± 00.12*</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>SACE (U/L)</td>
<td>C</td>
<td>64.14 ± 08.74</td>
<td>+30.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>29.02 ± 02.36*</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Sr. Total Chol. (mg/dl)</td>
<td>C</td>
<td>195.72 ± 09.36</td>
<td>+8.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>187.60 ± 08.27*</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Sr. Trigly (mg/dl)</td>
<td>C</td>
<td>166.28 ± 11.26</td>
<td>+7.30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>158.98 ± 10.23*</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Sr. HDL-C (mg/dl)</td>
<td>C</td>
<td>30.36 ± 01.94</td>
<td>-8.84</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>39.20 ± 01.64*</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>Sr. LDL-C (mg/dl)</td>
<td>C</td>
<td>132.11 ± 09.69</td>
<td>+1.55</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>116.61 ± 08.04*</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>Sr. VLDL-C (mg/dl)</td>
<td>C</td>
<td>33.25 ± 02.25</td>
<td>+1.46</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
<td>31.79 ± 02.04*</td>
<td></td>
</tr>
</tbody>
</table>

All values are mean with ± standard deviation ±.
C = Control; T = Test; * P < 0.05; ** P > 0.05
Results and Discussion

In this context, the present group study was conducted by selecting 50 hypertensive subjects from OPD who were newly detected, untreated and first time affected with hypertensive retinopathy. Funduscopic examination of retina was done which was one of the selection criteria of this group. Recording of blood pressure levels and estimation of various biochemical parameters from the blood sample was made. Study was made before and after antihypertensive treatment. The comparison of results (before treatment) was made with 50 control (normotensive) subjects. ‘Intervention’ study i.e. after treatment results were compared with ‘before treatment’ test group (treated s baseline values). The test group study was made in same selected and number of subjects.

Table 4.9 shows the mean values and standard deviation of the blood pressure levels before treatment. The SBP levels were found to be raised significantly compared with control group. The rise in blood pressure levels were highly significant (p < 0.05).

Table 4.12 shows the results of the ‘intervention’. The antihypertensive treatment was given for seven days. After antihypertensive treatment the intervention study was made. About +52.84 mm Hg of SBP and +23.24 mm Hg of DBP fall in blood pressure levels has been noted as a mean difference. The fall in blood pressure levels compared with baseline were highly significant (p < 0.05). Similar correlating increase in blood pressure levels was demonstrated by Lars-Olof Hattenbach et al.202 and Mark W.J. Starchan et al.205 Reported high blood pressure levels with SBP 240 mm Hg and DBP 150 mm Hg. Funduscopic examination revealed hypertensive retinopathy. But after antihypertensive treatment, the blood pressure levels were lowered to normal and the retina showed progressive
improvement. For hypertensive retinopathy group figure 4.1 & 4.2 shows the comparison of SBP levels before and after treatment while figure 4.3 & 4.4 shows the comparison of DBP levels before and after antihypertensive treatments.

Table 4.10 (before treatment) and Table 4.12 (after treatment i.e. intervention study) shows the mean levels and standard deviation of various biochemical parameters. The results of before treatment were considered a baseline for intervention study.

The fasting plasma glucose levels shows significant rise compared with control group. The levels were found moderately reduced in intervention study compared with baseline. The decrease in the levels were significant (p < 0.05). The mean difference in reduction was +4.86 mg/dl.

Similar correlating fall in plasma glucose level was reported by Lacourciere et al. (1991).23 Improvements in the increasing potassium levels increase the levels of insulin from the pancreas were moderate decrease in glucose levels. Figure 4.5 & 4.6 shows the comparison of fasting plasma glucose levels in retinopathy group before and after antihypertensive treatment.

Blood urea levels were significantly raised compared with control group. But the levels was tremendously lowered in intervention study compared with baseline. The decrease in the levels were statistically significant (p < 0.05). The mean difference in the decrease of blood urea levels was +6.05 mg/dl. Similarly serum creatinine levels were found to be elevated compared with control group. The increase in the levels was highly significant (p < 0.05). But the levels were decreased in intervention study compared with baseline. The decrease in the elves were statistically significant (p < 0.05). The mean difference
in the decrease of levels was +0.33 mg/dl. Similar corresponsive levels of increased blood urea and serum creatinine levels were observed by Mark W.J. et al.\textsuperscript{205} in severe hypertensive retinopathy subject. Renal function was highly impaired with blood urea levels 31.0 mg/dl and serum creatinine levels 3.4 mm/dl. But after antihypertensive treatment both the levels were significantly lowered to normal. Also Kazda S.\textsuperscript{131} has reported that increase in blood urea and serum creatinine are always found in hypertensive subjects. But the levels are lowered after antihypertensive treatment. Figure 4.7 & 4.8 (blood urea) and figure 4.9 & 4.10 (serum creatinine) shows the comparison of respective levels in retinopathy group before and after antihypertensive treatment.

Serum sodium levels were highly increased compared with control group. The increase in the levels was highly significant. But the levels were found decreased in the intervention study compared with baseline. The decrease in the levels was statistically significant ($p < 0.05$). The mean difference in the decrease of serum sodium levels was by +3.26 meq/L while serum potassium levels were significantly reduced compared with control group. The decrease in the levels was highly significant. But the levels were found moderately increased in the intervention study compared with baseline. The increase in the levels was statistically significant ($p < 0.05$). The mean difference in the increase of serum potassium levels was $-1.39$ meq/L. Similar resembling increase in sodium levels were reported by Jerome W. Cohn\textsuperscript{232} reported decrease in potassium levels. But the levels showed improvements after antihypertensive treatment. Also, Murphy et al.\textsuperscript{230}, Harvey et al.\textsuperscript{30} and Liberti et al.\textsuperscript{74} also demonstrated similar levels of electrolytes in severe hypertensive subjects before and after antihypertensive treatment. Figure 4.11 & 4.12 (serum sodium) and figure 4.13 & 4.14 (serum potassium) shows the comparison of
respective levels in retinopathy group before and after antihypertensive treatment.

About three folds rise in the SACE levels was found compared with control. The increase in the levels was highly significant. But there was tremendous fall in levels in intervention study compared with baseline. The decrease in the levels was highly significant (p < 0.05). The mean different in the decrease of SACE levels was +35.12 U/L. O’Neil et al.\textsuperscript{105} reported similar correlating levels of SACE before start with antihypertensive the treatment but the levels were reduced to 50% after antihypertensive treatment. Estimation of SACE activity was made spectrophotometrical. Figure 4.15 & 4.16 shows the comparison of respective levels of SACE in retinopathy group before and after antihypertensive treatment.

Serum lipid profile showed significant elevation in total cholesterol compared with control group. But moderate fall in the levels were noted in intervention study compared with baseline. The decrease in the levels was highly significantly (p < 0.05). The mean difference in the decrease of total cholesterol levels as +8.12 mg/dl.

Also serum triglycerides levels were also found to be raised considerably compared with control group. The rise in the levels was statistically significant (p < 0.05). But the levels were moderately decreased in intervention study compared with baseline. The reduction in the levels was significant. The mean difference in the decrease of serum triglyceride was +7.30 mg/dl.

HDL-C showed decrease in the levels compared with control group. The decrease in the levels was highly significant. But the levels were found increased in intervention study which were nearly equal compared with baseline. The increase in the levels was statistically
significant (p < 0.05). The mean difference in the increase of HDL-C levels was -8.84 mg/dl.

Significant rise in LDL-C and VLDL-C was registered compared with control group.

The increase in the levels were statistically significant (p < 0.05). But the levels lowered significantly in intervention study compared with baseline. The mean difference in decrease of LDL-C and VLDL-C levels were +15.5 mg/dl and +1.46 mg/dl respectively.

Similar correlating abnormal pattern of lipid profile in severe hypertensive patients was demonstrated by many other authors. Thomas Librettie et al., Pollare et al. and Maria Catalano et al. reported improvements in the lipid profile pattern after antihypertensive treatment. Figure 4.17, 4.19, 4.21, 4.23 & 4.25 (before treatment) and figure 4.18, 4.20, 4.22, 4.24 & 4.26 (after treatment) shows the comparison of respective level of lipid profile parameters in retinopathy group.
Figure 4.1
Comparison of Organ Damage with Control Group

Levels of Systolic Blood Pressure - Before Treatment

Figure 4.2
Comparison of Intervention with Control

Levels of Systolic Blood Pressure - After Treatment
Figure 4.3
Comparison of Organ Damage with Control Group

Levels of Diastolic Blood Pressure - Before Treatment

Figure 4.4
Comparison of Intervention with Control

Levels of Diastolic Blood Pressure - After Treatment
Figure 4.5
Comparison of Organ Damage with Control Group

Levels of Fasting Plasma Glucose - Before Treatment

Fasting Plasma Glucose Levels (mg/dl)

Control | ARF | AMI | Retinopathy
---|---|---|---
73.52 | 84.70 | 96.70 | 87.02

Study Groups

Figure 4.6
Comparison of Intervention with Control

Levels of Fasting Plasma Glucose - After Treatment

Fasting Plasma Glucose Levels (mg/dl)

Control | ARF | AMI | Retinopathy
---|---|---|---
73.52 | 87.82 | 90.4 | 92.16

Study Groups
Figure 4.7
Comparison of Organ Damage with Control Group

Levels of Blood Urea - Before Treatment

Blood Urea Levels (mg/dl)

Control    ARF    AMI    Retinopathy

Figure 4.8
Comparison of Intervention with Control

Levels of Blood Urea - After Treatment

Blood Urea Levels (mg/dl)

Control    ARF    AMI    Retinopathy
Figure 4.9
Comparison of Organ Damage with Control Group

Levels of Serum Creatinine - Before Treatment

Serum Creatinine Levels (mg/dl)

Control | ARF | AMI | Retinopathy
---------|-----|-----|---------
0.71     | 2.73| 1.12| 1.13    

Study Groups

Figure 4.10
Comparison of Intervention with Control

Levels of Serum Creatinine - After Treatment

Serum Creatinine Levels (mg/dl)

Control | ARF | AMI | Retinopathy
---------|-----|-----|---------
0.71     | 0.84| 0.8 | 0.8     

Study Groups
Figure 4.11
Comparison of Organ Damage with Control Group

Levels of Serum Sodium - Before Treatment

Figure 4.12
Comparison of Intervention with Control

Levels of Serum Sodium - After Treatment
Figure 4.13
Comparison of Organ Damage with Control Group

Levels of Serum Potassium - Before Treatment

Figure 4.14
Comparison of Intervention with Control

Levels of Serum Potassium - After Treatment
Figure 4.15
Comparison of Organ Damage with Control Group

Levels of SACE - Before Treatment

Figure 4.16
Comparison of Intervention with Control

Levels of SACE - After Treatment
Figure 4.17
Comparison of Drug Effect with Control Group

Levels of Serum Cholesterol - Before Treatment

Serum Cholesterol Levels (mg/dl)

Study Groups

Control  ARF  AMI  Retinopathy

Figure 4.18
Comparison of Intervention with Control

Levels of Serum Cholesterol - After Treatment

Serum Cholesterol Levels (mg/dl)

Study Groups

Control  ARF  AMI  Retinopathy
Figure 4.19
Comparison of Organ Damage with Control Group

Levels of Serum Triglycerides - Before Treatment

Figure 4.20
Comparison of Intervention with Control

Levels of Serum Triglycerides - After Treatment
Figure 4.21
Comparison of Organ Damage with Control Group
Levels of Serum HDL-c - Before Treatment

Figure 4.22
Comparison of Intervention with Control
Levels of Serum HDL-c - After Treatment
Figure 4.23
Comparison of Organ Damage with Control Group

Levels of Serum LDL-c - Before Treatment

Figure 4.24
Comparison of Intervention with Control

Levels of Serum LDL-c - After Treatment
Figure 4.25
Comparison of Organ Damage with Control Group

Levels of Serum VLDL-c - Before Treatment

Figure 4.26
Comparison of Intervention with Control

Levels of Serum VLDL-c - After Treatment