

SERUM LIPID PROFILE AND ELECTROLYTES IN ESSENTIAL HYPERTENSION

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ABSTRACT

To compare the levels of lipid profile parameters and serum electrolytes (Na^+ and K^+) in normotensive individuals and in patients with essential hypertension with or without complications. And also to evaluate any association between these parameters and blood pressure. A Case control study carried out in the Department of Biochemistry in collaboration with the Department of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, during the period August 2011 to July 2013. Altogether 120 individuals were taken for the study (i.e. 40 normal healthy individuals as control, 40 hypertensives without complication and 40 hypertensives with complication). A study on the lipid profile shows that serum triglyceride (TG), total Cholesterol, low density lipoprotein(LDL), and very low density lipoprotein (VLDL) were found to be raised above the respective reference ranges and serum high density lipoprotein (HDL) was found to be below the reference range in the hypertensive cases. There was a positive correlation between TC and blood pressure and also between LDL and blood pressure but a negative correlation was found between HDL and blood pressure. The levels of serum sodium (Na^+) and potassium (K^+) conc among the hypertensive group was found to be within the reference range . however a positive association was found between serum (Na^+) and blood pressure, but a negative and weak association was observed between serum K^+ and blood pressure. Elevated LDL may be responsible for progression of essential hypertension as well as etogenesis of atherosclerosis and its subsequent complications. The negative correlation of HDL with increased blood pressure suggest a protective role in atherogenesis and also Na^+ plays an important role in the etogenesis of essential hypertension but it cannot be used as a biomarker of hypertension , for few days own homeostatic mechanism tries to maintain serum Na^+ level within a narrow range.

INTRODUCTION

Hypertension is a chronic condition of concern due to its role in the causation of coronary heart disease, stroke and other vascular complications. It is the commonest cardiovascular disorder, posing a major public health challenge to population in socio – economic and

epidemiological transition. It is one of the major risk factors for cardiovascular mortality which accounts for 20-50 per cent of all deaths [1].

“Essential hypertension” is high blood pressure for which there is no defined aetiology. Essential hypertension comprises more than 90% of hypertension. In 2000, it was estimated that 25% of the world’s total population were hypertensive and predicted that this would rise to 29 % by 2025 [2]. The pathogenesis of essential hypertension is a complex interplay between (1) genetic

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predisposition (2) lifestyle and environmental influence and (3) disturbances in vascular structure and neuro-humoral mechanisms. The specific role of rennin-angiotensin-aldosterone system in the development of essential hypertension remains unclear but therapeutic agents that inhibit this system have proved to be very effective.

It is an established fact that hypertension and hyperlipidemias are important risk factors in causing coronary heart disease and cerebrovascular accidents [3, 4]. Increased blood pressure both diastolic and systolic imposes an accelerated risk of atherogenesis. This risk is steadily increased with severity of hypertension and with association of other risk factors which include smoking, diabetes, male gender and advanced age.

Epidemiological research has shown that dietary sodium is an important contributor to the pathogenesis of hypertension [5]. While higher blood pressure values are being currently observed in population with higher salt intake [6], treatment strategies based on lowering salt ingestion have demonstrated their effectiveness in lowering blood pressure [7]. A proportion of individuals 5-16%, classified as salt dependent would benefit from salt restriction [8]. In essential hypertension, the mean concentration of Na⁺, Cl⁻, K⁺, Hb, triglycerides were increased and that of HDL cholesterol was decreased, the average intraindividual variation did not significantly differ between the two groups [9].

A high potassium diet has been claimed to give protection in subjects on high sodium diet, but in most population studies no such association has been found. A positive correlation has also been found between sodium/potassium molar ratio and blood pressure by some studies but denied by others [10]. Decrease in urinary Na/K molar ratio was strong predictor of lowering blood pressure, so decreased Na intake and increased potassium intake or both together may be effective in prevention or even treatment of hypertension [11].

The Manipur population is mainly non-vegetarians who ingest more saturated fats and cholesterol and some are habitual cigarette smokers thereby exposing to nicotine inhalation which makes them vulnerable to develop hypertension and its complications. Moreover our population have the habit of consumption of extra salts along with fried fish or meats and sometimes with fruits. It was therefore planned to undertake the serum lipid profile and electrolytes (Na⁺, K⁺) in known hypertensives and hypertensives associated with other risk factors in order to evaluate and to predict the premature atherosclerotic changes.

The present study has been an attempt to contribute to the understanding of the etiology of hypertension and hence to evaluate the role of serum electrolytes (sodium and potassium) and various fractions of circulating lipoproteins (serum lipid profile) in the genesis of associated complications of the essential hypertension.

AIMS AND OBJECTS

To estimate serum lipid profile and Serum electrolytes [Sodium (Na⁺) and Potassium (K⁺)] in patients with Essential Hypertension with or without complications. And also to compare the results with that of normal healthy individuals.

MATERIALS AND METHODS

A Case control study carried out in the Department of Biochemistry in collaboration with the Department of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur from August 2011 to July 2013. The study population consisted of hypertensive patients coming from different areas of Manipur and attending Medicine OPD or admitted in the Medicine Wards of RIMS, Imphal, Manipur. Approval of the Ethics Committee of RIMS was taken. Altogether 120 individuals were taken for the study (i.e. 40 normal healthy individuals as controls, 40 hypertensives without complication and 40 hypertensives with complication).

Patients with normal blood pressure, secondary hypertension, febrile illness, primary renal disease, secondary renal diseases (not caused by essential hypertension), hepatic failure, and thyroid disorders were excluded from the study.

Specimens (5ml) of venous blood were collected in sterile vials from hypertensives as well as control groups after overnight fasting, centrifuged at 700 x g for 10 minutes and the sera thus separated were used for estimation of lipid profile and electrolytes (sodium and potassium). Detail history regarding the duration of disease, age of onset of disease, associated symptoms of complications have been taken and recorded.

Blood pressure was measured according to the routine clinical practice with the sphygmomanometer, with the patient lying at ease. Based on the criteria used by National Health and Nutritional Survey for 1976-1980, the patients have been diagnosed as having hypertension when his/her blood pressure is $\geq 140/90$ mmHg. The right arm was selected for each individual for recording blood pressure. The arm was placed in a roughly horizontal position at the level of the heart and cuff applied to the upper arm with the lower border not less than 2.5 cm from the cubital fossa. Systolic and diastolic blood pressures were recorded according to the appearance of Korotkov sounds.

Serum lipid profile estimation were done by Enzymatic Colorimetric Test with lipid clearing factor (LCF) by using kits marketed by Human Gesellschaft fur Biochemica and Diagnostica mbH. Estimation of total cholesterol was carried out by the enzymatic method of Allain CC *et al* [12] and serum triglyceride by the method adopted by Bucole G and Harold D [13]. Enzymatic determination of high density lipoprotein fraction was done by method of Steele BW *et al* [14]. LDL and VLDL cholesterol were calculated indirectly using the formula of



Friedwald T *et al* [15]. Estimation of serum sodium and potassium was done by flame photometry [16].

RESULTS AND OBSERVATIONS

Figure 1 shows age wise distribution of Control, hypertension without complications (HTN) and hypertension with complication (HTNcml). It shows the maximum cases of hypertension (HTN) without complications fall in the age group of 40-49years (35%), followed by age groups of 50-59years (30%) and 30-39years (20%) and maximum cases of hypertension with complication (HTNcml) fall in the age group of 70-79years (30%), followed by age groups of 50-59years (25%) and 60-69years (20%).

Figure -2 show the sex wise distribution of control and in hypertensives with and without complications. It is evident in both that the percentages of males in controls and hypertensives are 55% and 52.5% respectively and that of females are 45% and 47.5% respectively which are statistically not significant. But the sex distribution in case of hypertensives with complications is 70% (male) and 30% (female) which is statistically significant ($p < 0.001$).

Table -I shows values (expressed in mean \pm SD) of blood pressure (systolic and diastolic) in control and in hypertensive without and with complications. In this figure it is evident that, the mean \pm SD of systolic blood pressure in hypertensive group is 151.16 ± 7.5 mmHg and that of control group is 115.25 ± 5.0 mmHg, the difference is statistically significant ($p < 0.001$); and the mean \pm SD of diastolic blood pressure in hypertensive group is 95.87 ± 6.3 mmHg and that of control group is 75.37 ± 4.8 mmHg whose difference is also statistically significant. In the same figure it is also evident that the mean \pm SD of systolic blood pressure in hypertensive with complication is 161.17 ± 17.18 mmHg and diastolic blood pressure is 100.0 ± 7.6 mmHg, and when compared with the respective values in the control group, the differences are statistically significant ($p < 0.001$ each).

Table - II shows the summary of biochemical data in control, hypertension with and without complications. All the values are expressed in mean \pm SD.

Regarding the lipid parameters: the mean value of serum triglyceride (TG) in hypertensive (HTN) group is 220.95 ± 90.71 mg/dl and 164.0 ± 56.8 mg/dl in the control group, the difference being statistically significant ($p < 0.01$) whereas the mean value of TG in hypertensive with complication is 184.18 ± 42.47 mg/dl which is statistically not significant when compared with that of healthy control individuals; the mean values of serum total cholesterol (TC) in control and HTN are 148.2 ± 32.5 mg/dl and 205.5 ± 62.47 mg/dl respectively ($p < 0.001$) and the mean value of TC in HTN with complication is 240 ± 39.98 mg/dl which is statistically highly significant ($p < 0.001$); the mean values of serum VLDL (very low density lipoprotein) in control and HTN are 32.97 ± 11.31 mg/dl and 44.1 ± 18.57 mg/dl respectively ($p < 0.01$); the mean values of serum LDL (low density lipoprotein) in control and HTN are 73.5 ± 29.8 mg/dl and 126.12 ± 57.28 mg/dl respectively ($p < 0.001$) and that in HTN with complication is 158.45 ± 42.72 mg/dl ($p < 0.001$); the mean values of serum HDL (high density lipoprotein) in control and HTN are 42.7 ± 7.7 mg/dl and 34.22 ± 7.89 mg/dl respectively ($p < 0.001$) and that in HTN with complication is 34.12 ± 6.99 mg/dl ($p < 0.001$).

Regarding the serum electrolytes: the mean values of serum sodium (Na) in control and HTN groups are 139.3 ± 2.7 meq/L and 140.07 ± 2.4 meq/L respectively indicating no statistically significant difference, but serum Na in HTN with complication is raised with a statistically significant mean value of 142.42 ± 3.84 meq/L when compared with that of the control group ($p < 0.001$); and lastly the mean values of serum potassium in control and HTN groups show a difference of statistical significance with 4.15 ± 0.45 meq/L and 4.46 ± 0.53 meq/L respectively ($p < 0.01$).

Table 3 shows correlation between serum TC, LDL and sodium (S. Na) and blood pressure. In this table it is evident that there is a positive correlation between serum TC, LDL, serum sodium (S. Na) with SBP and DBP ($p < 0.001$). It is also seen from table IV that serum TG, VLDL level and serum K⁺ was positively correlated with both SBP and DBP and HDL has negative correlation with SBP and DBP but statistically not significant ($p > 0.05$).

Table 1. Blood pressure(Systolic and Diastolic) in Control, HTN and HTN with complication (expressed in mean \pm SD)

Parameters	Control Mean \pm SD	HTN without complication Mean \pm SD	P-value	HTN with Complication Mean \pm SD	P-value
Systolic BP (mmHg)	115.25 ± 5.0	151.16 ± 7.5	< 0.001	161.17 ± 17.18	< 0.001
Diastolic BP (mmHg)	75.37 ± 4.8	95.87 ± 6.3	< 0.001	100.0 ± 7.6	< 0.001

Table 2. Summary of Biochemical data in Control, HTN and HTN with complication (values expressed in means \pm SD)

Parameter	Control (n = 40)	HTN without complication (n = 40)	HTN with complication (n = 40)
	Mean \pm SD	Mean \pm SD	Mean \pm SD
Serum TG (mg/dl)	164 ± 56.8	220.95 ± 90.71 ^{a***}	184.18 ± 42.47
Serum TC(mg/dl)	148.2 ± 32.5	205.5 ± 62.47 ^{a***}	240.0 ± 39.98 ^{b***}
Serum VLDL(mg/dl)	32.97 ± 11.31	44.1 ± 18.57 ^{a***}	36.9 ± 8.74
Serum LDL(mg/dl)	73.5 ± 29.8	126.12 ± 57.28 ^{a***}	158.45 ± 42.72 ^{b***}



Serum HDL(mg/dl)	42.7± 7.7	34.22 ± 7.89 ^{a***}	34.12 ± 6.99 ^{b***}
Serum Na(meq/L)	139.3± 2.7	140.07 ± 2.4	142.42 ± 3.84 ^{b***}
Serum K(meq/L)	4.46 ± 0.45	4.27 ± 0.53	4.15 ± 0.47 ^{b**}

a → comparison between control and hypertension (HTN) without complication. b → comparison between control and hypertension (HTN) with complication. p* → <0.05, p** → <0.01, p*** → <0.001

Table 3. Correlation between total cholesterol (TC), LDL, serum sodium and blood pressure (SBP and DBP)

Parameter	SBP	DBP
TC	0.543**	0.491**
Serum LDL	0.482**	0.482**
Serum sodium (S.Na)	0.333**	0.305**

**correlation is significant at the 0.01 level

Table 4. Correlation between triglyceride (TG), HDL, VLDL and serum Potassium and blood pressure (SBP and DBP)

Parameter	SBP	DBP
TG	0.03(p>0.05)	0.06(p>0.05)
Serum HDL	-0.158(p=0.161)	-0.164(p=0.146)
Serum VLDL	0.039(p>0.05)	0.039(p>0.05)
Serum potassium (S.K)	0.20(p>0.863)	0.054(p=0.637)

Fig 1. Age wise distribution of Control, Hypertension (HTN) without complications and HTN with complication

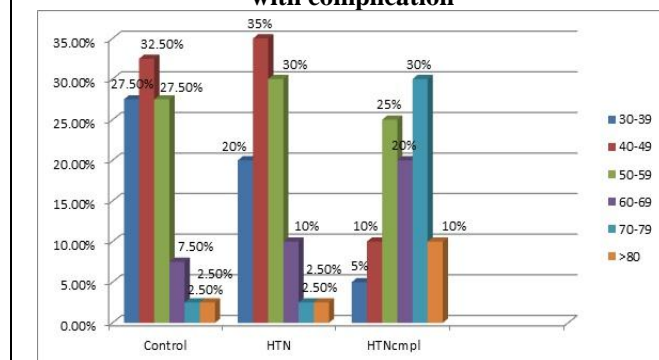
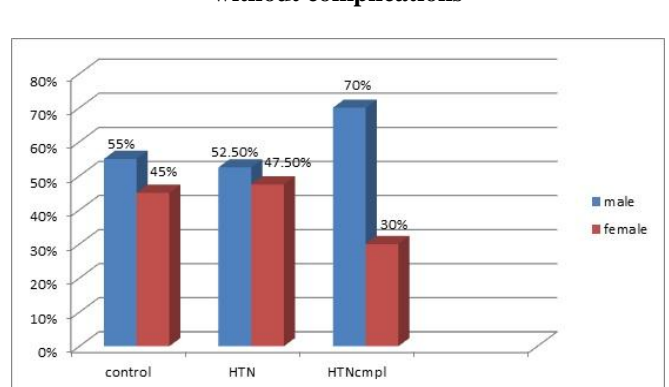


Fig 2. Sex wise distribution of Control and HTN with and without complications



DISCUSSION

Hypertension is a disorder, which is known to man since ancient times. Tremendous advancement has been made in our understanding of the pathophysiology of essential hypertension in recent years. Hence prevention of hypertension is a high priority goal of health policy and health care systems. For effective prevention of hypertension and its subsequent complication, it is important to know about the various etiological factors as well as the various mechanisms underlying the development of various complications. Increasing evidence is accumulating that dietary sodium, saturated fats and cholesterol play important role in the etiology of hypertension and their estimation can help in finding out pre disposing factors, knowing about the prognosis and devising strategy for prevention.

This study showed that majority of hypertension occurs after the age of 40 years. The incidence of complications with increasing age group may be due to the fact that complications develop in long standing hypertensive status with irregular or inappropriate

treatment regimens or the consequent metabolic derangements particularly lipid and electrolytes. The lower incidence of hypertension in females as seen in this study may be due to protective actions of oestrogen in the development of atherosclerosis and also males have other associated risk behaviours like smoking and alcohol consumption which predisposes them to early advanced atherosclerosis.

Serum Lipid Profile and Hypertension

It has been observed that, dyslipidemia, in combination with hypertension and platelet dysfunction is gaining ground in the acceleration of progress of atherosclerosis and contributes significantly to higher cardiovascular morbidity and mortality in hypertensive group. Elevated fasting triglyceride was found to have a strong correlation to the degree of end organ involvement in hypertension.

In the present study, it was seen that the serum TG levels (mean ± SD) in both the study groups are found to be elevated when compared to that in the normal healthy



control group ($164 \pm 56.8\text{mg/dl}$), which is statistically significant in case of HTN ($P < 0.01$). The present observation is in agreement with findings of previous studies that reported a consistent association between fasting triglyceride level and hypertension along with its associated complications [17, 18]. Triglyceride may influence risk of coronary artery disease by its correlation with increase plasminogen activator inhibitor levels [19]. The elevated fasting triglyceride (TG) level observed in the present study can be explained in the light of the findings of Kolovou GD *et al.*, [20] who reported that the plasma TG concentrations increased significantly after fat loading in hypertensive group compared to normal controls and it was concluded that patients with hypertension have an exaggerated response and delayed clearance of plasma TG concentration after fat loading.

The fasting serum level of total cholesterol (TC) of hypertensive cases with complication and without complications was significantly elevated when compared with that of the control group ($p < 0.001$). table-II. The increase in the level of total cholesterol in the hypertensives may be contributed by the elevated level of of serum LDL and VLDL level and this finding is in agreement with the findings of Chokowska EW. In the table – II, the fasting serum VLDL in control is $32.97 \pm 11.31\text{mg/dl}$ and that of HTN is $44.1 \pm 18.57\text{mg/dl}$, which is significantly higher than that in control ($p < 0.01$) and that of HTN with complication is $36.9 \pm 8.74\text{mg/dl}$, which is slightly elevated than that in the control but not statistically significant ($p > 0.05$).

The serum LDL in HTN with and without complications, which is significantly elevated when compared with that in the control group ($p < 0.001$). This observation of significantly elevated serum (LDL) level and strong positive correlation with blood pressure, made in this study is in agreement with the findings of other previous workers that elevated low density lipoprotein (LDL) cholesterol concentration has been firmly established as a modifiable risk factor for cardiovascular diseases [20,21]. It is also in agreement with the findings of Stampfer MI *et al* [22] and Campos G *et al* [23] that LDL locus was significantly greater in hypertensive group along with triglyceride concentration.

In this study, the fasting serum HDL in the hypertensive patients were significantly lowered compared to te controls. fasting serum HDL showed a weak but negative association with the blood pressure which is not statistically significant. This is in agreement with the findings of Dinng YA *et al.*, [24] the occurrence of cerebro-vascular accident might closely be related to reduced serum HDL cholesterol and phospholipid levels.

Serum Electrolytes (Sodium And Potassium) In Essential Hypertension

Dietary sodium is the major cause of the rise in blood pressure with age, for an increase salt intake induces a small rise in plasma sodium, which in turn is responsible

for the tendency to an increased extracellular volume rendering to a rise in the blood pressure [25]. Some workers have suggested that the role of sodium in hypertension is more complex than simply elevating arterial pressure, it can also increase left ventricular mass in essential and experimental hypertension may be due to altered hemodynamics [26].

In the present study, it was observed that the mean value serum sodium (Na^+) in control group is 139.3 ± 2.7 meq/L, and those of HTN with and without complications were 140.07 ± 2.4 meq/L and 142.42 ± 3.83 meq/L respectively. It is evident from this observation that, mean (\pm SD) values of serum sodium in all the three study groups fall within the normal reference range of our laboratory (136- 146 meq/L). This observation is in agreement with the previous observation that serum sodium (Na^+) level is maintained within a very narrow range [27]. The mean values of the control and HTN without complication group does not show a statistically significant difference, but the difference in the mean values of the control and HTN with complication group is statistically significant ($p < 0.001$). This observation is in agreement with the previous observation that there is a modest increase in sodium concentration in older people [28] as is evident in fig.1 and table-1 that the maximum of the HTN with complication group occur in the older age group(70-79 years) whereas the maximum of the control group is in age group of (40-49 years).

Again when linear regression analysis was performed, there was a positive correlation between serum sodium and both the blood pressure levels: SBP ($r = 0.333$, $p < 0.001$) and DBP ($r = 0.305$, $p < 0.001$). This observation is in agreement with the observations made by many of the previous workers who even suggested that higher serum sodium levels may be a marker of high BP [29, 25]. Many scientific evidence support this possibility. First, acute intervention studies in individuals with hypertension suggest that a reduction in dietary salt intake results in a fall in serum sodium ($\sim 3\text{mmol/L}$) paralleled by a fall in systolic BP ($\sim 17\text{mmHg}$) [27]. Second, salt loading in normotensive people results in a modest rise in serum sodium ($\sim 3\text{mmol/L}$) accompanied by a rise in pulse pressure [29]. Third, chronic interventions reducing dietary salt in patients with hypertension results in more modest falls in serum sodium ($\sim 0.5\text{mmol/L}$), but such a reduction is accompanied by modest sustained reductions in systolic BP ($\sim 8\text{mmHg}$). Last, in some cross-sectional studies serum sodium has been associated positively with systolic BP (especially in those with hypertension) [28]. Although other investigations that have evaluated larger samples have reported a lack of association, or noted an inverse relation to diastolic BP [30]. Wardener and colleague [25] postulated that changes in serum sodium may drive extracellular volume responses, which can alter blood pressure. They also proposed that small changes in the plasma sodium may directly affect the hypothalamus, the



local rennin – angiotensin system the heart and vasculature all of which play a role in changing blood pressure.

In the table – II, , we can also observe that the mean levels of serum (K +) in both these hypertensive groups are lowered than that of the control group, but only in the HTN with complication the difference in the mean level is statistically significant ($p < 0.01$). It was also observed that the mean values of serum potassium (K+) in all the study groups fall within the normal reference value of our laboratory (3.5 -5.0meq/L). This observation is also in agreement with the previous observation that serum potassium level is also tightly regulated along with serum (plasma) sodium by the renal mechanism of renin-angiotensin-aldosterone axis and maintained in a narrow range [27].

CONCLUSIONS

From this present study, it can be concluded that elevated serum LDL is mainly responsible for the progression of essential hypertension as well as in the etiology of atherosclerosis and its subsequent complications commonly associated with essential hypertension. The elevated level of serum total cholesterol (TC) observed in this study may be mainly contributed by the LDL fraction as both the parameters are found to be elevated and positively correlated with essential hypertension. The negative correlation between HDL and

elevated blood pressure along with its associated complication, observed in the present study suggests a protective role in atherogenesis. It is also concluded that, from among the serum electrolytes serum sodium plays an important role in the etiology of essential hypertension as is evident from its significant positive correlation with blood pressure, but it (serum sodium level) cannot be used as a biomarker of hypertension, for body's own homeostatic mechanism tries to maintain serum sodium level within a narrow range via renin-angiotensin aldosterone axis. Serum potassium also showed a weak negative association with the blood pressure level but the mean concentrations in all the study groups were within the reference range, the same mechanism as in the case of serum sodium being operated.

Therefore, a changed attitude towards lifestyle including a moderate restriction in dietary consumption of saturated fat and common salt (sodium chloride), can be recommended after the third decade of life, for the primary prevention of essential hypertension and its subsequent associated complications

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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