

**ASSOCIATION OF SODIUM AND POTASSIUM
CONCENTRATIONS WITH CARDIOVASCULAR DISEASES
AND HYPERTENSION**

THESIS

By

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(S-2010-30-17)**

Submitted to



**CHAUDHARY SARWAN KUMAR
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PALAMPUR - 176 062 (H.P.) INDIA**

in

Partial fulfilment of the requirements for the degree

of

**MASTER OF SCIENCE IN BASIC SCIENCES
(DEPARTMENT OF BIOLOGY AND ENVIRONMENTAL SCIENCES)
(BIOLOGY)**

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*Since my birth to adulthood, you
were there with me...*

*To bolster in all highs n lows of
my life, you were there with me...,*

*Dear PAPA & MUMMY, I
really owe all my success to you and
thank you for shaping my future
fabulously.*

*Dedicated to the Most
Cherished Persons of my life.....*

*Nanu, Nani and My
Parents*

Dr. Navneet K. Gupta
Professor and Head

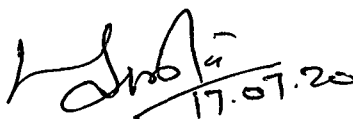
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CERTIFICATE – I

This is to certify that the thesis entitled “**Association of Sodium and Potassium Concentrations with Cardiovascular Diseases and Hypertension**” submitted in partial fulfilment of the requirements for the award of the degree of **Master of Science (Basic Sciences)** in the discipline of **Biology** of CSK Himachal Pradesh Krishi Vishvavidyalaya, Palampur is a bonafide research work carried out by Ms. **Priyanka Sharma S-2010-30-17** daughter of Shri Kalyan Chand and Smt Urvashi Sharma under my supervision and that no part of this thesis has been submitted for any other degree or diploma.

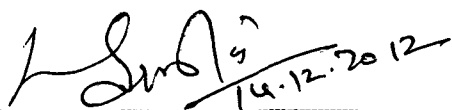
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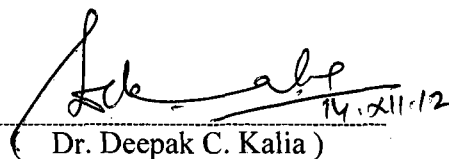

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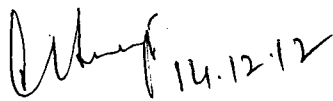
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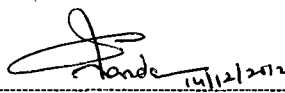
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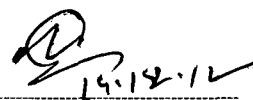
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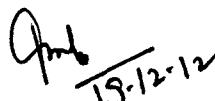
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Place: Palampur

Dated: 17 July, 2012

Priyanka Sharma
(Priyanka Sharma)

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LIST OF ABBREVIATIONS USED

mEq/ L	Milli equivalent per litre
HT	Hypertension
CVD	Cardiovascular Disease
HC	Healthy Controls
mm	Millimeter
Hg	Mercury
mmol	Millimole
gm	Gram
Kg	Kilogram
DBP	Diastolic Blood Pressure
SBP	Systolic Blood Pressure
BMI	Body Mass Index
SD	Standard Deviation
i.e.	Idest (that is)
<i>et al.</i>	et alii (and others)
rpm	Rotations per minute

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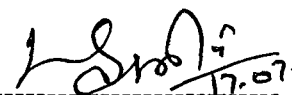
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ABSTRACT

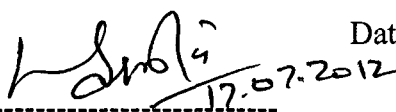
High serum sodium level and low serum potassium level occur in hypertension and cardiovascular diseases. The purpose of this study was to evaluate the reliability and accuracy of serum sodium and potassium estimation in patients with hypertension and cardiovascular diseases. This study was conducted on total of 150 subjects to analyse serum sodium and potassium concentration and to find out relationship of serum sodium and potassium, sodium-potassium ratio, age and sex with blood pressure in hypertensives, patients with cardiovascular diseases and healthy controls. The first group comprised of 50 healthy controls(28 males and 22 females), the second group (risk group) had 100 patients grouped into two subgroups; 50 patients with hypertension(32 males and 18 females) and 50 patients with cardiovascular diseases (26 males and 24 females). Serum sodium and potassium concentrations were measured by Atomic absorption spectrophotometer/flame photometric method. Serum sodium concentrations were significantly higher whereas serum potassium concentrations were significantly lower in patients with hypertension and heart disease as compared to control group and have a ($p < 0.05$). Significant variation was observed in serum sodium and potassium concentrations with age and sex. Serum sodium was found to be significantly higher in males as compared to females whereas serum potassium was found to be significantly lower in males as compared to females. There was statistically increased sodium – potassium ratio ($p < 0.05$) in hypertension and heart disease patients. Hypertension is the most important preventable risk factor for premature death worldwide. Serum electrolytes (sodium and potassium) assessment in blood serum can be used for monitoring patients suffering from hypertension and at increased risk of cardiovascular diseases.



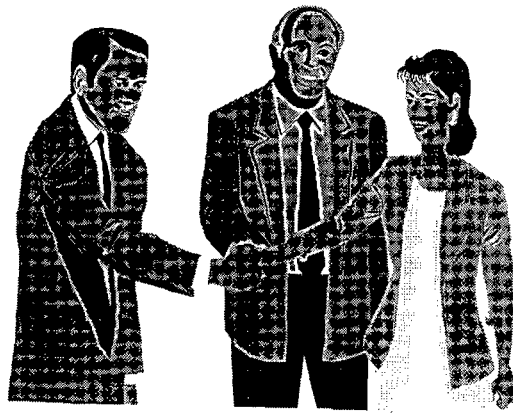
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INTRODUCTION

1. INTRODUCTION

Hypertension affects approximately 25 per cent of the adult population worldwide, and its prevalence is predicted to increase by 60 per cent by 2025, when a total of 1.56 billion people may be affected. Nearly one in every seven people in India suffers from hypertension. 49 per cent population of Himachal Pradesh is under hypertension. Hypertension (HTN) or high blood pressure, sometimes arterial hypertension, is a chronic medical condition in which the blood pressure in the arteries is elevated. Normal blood pressure is below 120/80mm of Hg. Blood pressure between 120/80 and 139/89mm of Hg is called prehypertension and blood pressure of 140/90mm of Hg and above is considered Hypertension. Hypertension is mainly classified as either primary (essential) hypertension or secondary hypertension. In the majority of cases over 90 percent-no specific cause for the elevated blood pressure can be identified. This type of hypertension is categorized as primary hypertension. Some researchers believe that this type of high blood pressure may be due to hormonal factors relating to the handling of salt by the kidneys and/or to the elaboration of certain substances that cause constriction of blood vessels. In up to 10 per cent of patients, high blood pressure may be a consequence of another disorder, or a side effect of medication. This type of hypertension is referred to as secondary hypertension.

Hypertension is also linked to cardiovascular diseases like coronary heart disease, stroke. It is an important cardiovascular risk factor. The pathogenesis of hypertension in humans is not fully understood. This disease is a multifactorial combination of genetic and environmental factors. Certain environmental factors such as high salt, low potassium diet and chronic stress play important role in causing hypertension. Diet and nutrition have been extensively investigated as risk factors for major cardiovascular diseases. The mineral elements play a central role in the normal regulation of blood pressure (Smith *et al.* 1988). The elements, especially sodium and potassium, also regulate the fluid balance of the body and, hence, influence the cardiac output.

Sodium is primarily found bound to the anion chloride. It has long been considered as the pivotal environmental factor in the disorder. It is an essential mineral

required for the regulation of extracellular fluid volume and plasma. Sodium chloride, also known as salt, is made up of 40 per cent sodium and 60 per cent chloride. In the food supply, small amounts are found naturally in some foods but the primary source of sodium is processed foods. Sodium is added to foods during processing to enhance flavor, control the growth of bacteria and act as a preservative. It is also a carrier for iodine.

Sodium is considered as the dominant environmental factor in the pathogenesis of primary hypertension and its associated cardiovascular risk. Primary hypertension and age related increases in blood pressure are virtually absent in populations in which individual consumption of sodium chloride is less than 50 mmol per day; these conditions are observed mainly in populations in which people consume more than 100 mmol of sodium chloride per day. Evidence has also accumulated to show that high consumption of sodium is one of the factors maintaining raised blood pressure and reducing the efficacy of antihypertensive drugs. In normotensive volunteers the variation of the daily sodium intake between 10 to 800 mmol has little influence on the blood pressure. The blood pressure of most normotensive individuals rises only if the daily sodium intake is higher than 800 mmol. The blood pressure increased, however, in hypertensives when the intake of salt was increased from 10 mmol to 410 mmol per day.

Beside sodium, potassium is also an important factor that regulates hypertension. It is the most abundant intracellular cation and is essential for the life of the organism. Required amount of Potassium is 4.7 gm/day. Potassium is obtained through the diet, and common potassium rich foods include meats, beans, fruit and potatoes. In experimental animals, an increase in the intake of potassium protects them against induced hypertension. A high intake of potassium may also protect humans against the development of hypertension reported by Maxwell and Madias (1987). Several studies also suggest that the sodium/potassium ratio in the diet is a more important determinant of blood pressure than the amount of sodium consumed alone (Karppanen, 1989). In a proportion of hypertensive patients not on antihypertensive drugs, potassium supplements have lowered blood pressure, by as much as 5 to 10 mm Hg.

The present study **“Association of Sodium and Potassium Concentrations with Cardiovascular Diseases and Hypertension”** was undertaken with the following objectives:

- To determine serum sodium and potassium concentration in normal and hypertensive patients.
- To correlate variations in the concentrations of sodium and potassium with hypertension and cardiovascular diseases.



REVIEW
OF
LITERATURE

2. REVIEW OF LITERATURE

The mineral elements sodium and potassium have a central role in regulating blood pressure, influencing both the peripheral resistance and cardiac output. A moderate restriction of sodium intake or an increase in potassium intake exerts remarkable antihypertensive effects (Karppanen 1991). A marked reduction of sodium intake is effective in treating even severe hypertension.

Some of the work done in abroad and India on different aspects of “Association of Sodium and Potassium Concentrations with Cardiovascular Diseases and Hypertension” has been reviewed under the following:

2.1 Hypertension

2.2 Role of minerals in hypertension and cardiovascular diseases

2.3 Sodium and blood pressure

2.4 Potassium and blood pressure

2.5 Sodium and Potassium - link with cardiovascular diseases.

2.6 Combined Reviews

2.1 Hypertension

People develop hypertension or high blood pressure for several reasons. It may be in the genes or due to a kidney disorder as well as stress related factors. The most common cause however is due to dietary intakes that results from excessive salt in our body. Excessive salt intake will result to an imbalance between sodium and potassium that causes hypertension in our body. High blood pressure or hypertension means high pressure (tension) in the arteries. The development of hypertension involves several interrelated regulatory systems. Although causes of most cases of hypertension are unknown. Family history can provide an indication of risk but other influences such as diet, drugs and stress are also involved (Brenda, 1992). The Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure has classified hypertension according to the degree of BP elevation. Stage 1 patients have a systolic BP

of 140 to 159 mm Hg. Stage 2 individuals have a systolic BP of 160 to 170 mm Hg or a diastolic BP of 100 to 109 mm Hg, whereas stage 3 includes a systolic BP pressure ≥ 180 mm Hg or a diastolic BP ≥ 110 mm Hg. Stage 3 hypertension has also been called severe hypertension or accelerated hypertension.

Researchers agree that moderate and severe hypertension is best controlled if detected early. And critical to timely discovery and control of hypertension is access to health care. Researchers are also in agreement that social variables are linked to hypertension. Their consensus that:

- An inverse relationship exists between socioeconomic status and hypertension. The higher the class, the lower the prevalence of morbidity and mortality.
- A significantly higher prevalence of hypertension has been noted in urban dwellers than rural populations.
- Hypertension mortality differs between races, with both male and female nonwhites showing a greater mortality rate in every age group than whites in the same category (Salcido 1979).

A greater understanding of the risk factors that account for the increase in hypertension could potentially contribute to its future prevention by addressing its root causes. Public health efforts to reduce the prevalence of hypertension have rightly focused on non-pharmacological approaches that lower blood pressure. The World Health Organization (WHO) report states that a 2 per cent reduction in diastolic blood pressure could prevent 3,00,000 deaths from cardiovascular diseases (CVD) by 2020. Current guidelines recommend lifestyle modifications, including salt reduction, as one of the most effective approaches to prevent hypertension and indeed as first line treatment for mild hypertension. In young to middle-aged subjects, hypertension and cardiovascular disease are more common in men than in women. Cardiovascular risk then increases with age in both sexes. However, this increase is sharper in women, so that in old age women have similar rates of cardiovascular disease, and even higher prevalence of hypertension than men (Wenger, 1995).

Hypertension is one of the most prevalent and powerful contributors to cardiovascular diseases, the leading cause of death in the United States. There is, on

average, a 20mm Hg systolic and 10mm Hg diastolic increment increase in blood pressure from age 30 to 65 years. Hypertension contributes to all of the major atherosclerotic cardiovascular disease, outcomes increasing risk, on an average, 2-3 folds (William and Kannel, 1996).

High blood pressure or hypertension usually has no noticeable symptoms. The most important causes of hypertension are stress and a faulty style of living. People who are usually tense suffer from high blood pressure, especially when under stress. If the stress continues for a long period, the pressure may become permanently raised. A normal blood pressure reading is 120/80 or less and the value over 140/90 indicates a person suffering from blood pressure. High blood pressure can place a high level of stress on the internal organs. If this is left unchecked, high blood pressure can cause stroke and heart and kidney failure. The adoption of certain lifestyle modifications has been shown to be effective in lowering blood pressure and should be recommended for all patients with hypertension. These modifications include weight control, exercise, dietary sodium restriction and potassium enhancement, moderation of alcohol intake, and adoption of the Dietary Approaches to Stop Hypertension (DASH) eating plan, which emphasizes a high intake of fruits, vegetables, complex carbohydrates and low fat dairy products and restriction of saturated fats. The reductions in systolic blood pressure that are achieved with these approaches have averaged 5 to 10 mm Hg for a weight decrease of 10 kg, 8 to 14 mm Hg for the DASH eating plan, 2 to 8 mm Hg for dietary sodium reduction, 4 to 9 mm Hg for increased physical activity and 2 to 4 mm Hg for moderation of alcohol consumption. (Appel *et al.*,1997).

Pfeffer (2007) found that lowering blood pressure (BP) in patients with hypertension is probably one of the most important population-based preventive measures for heart failure. In caring for patients with hypertension, the sphygmomanometer remains the key tool for titrating antihypertensive therapy to achieve and ensure adequate BP lowering. Although hypertension is a promiscuous risk factor, importantly involved in the pathogenesis of most major cardiovascular morbidities such as stroke, myocardial infarction and rupture as well as the development of the syndrome of congestive heart failure, elevated BP is the major population- attributable risk factor for heart failure.

Blood pressure remains uncontrolled most often because of elevated systolic blood pressure. Patient characteristics associated with resistant hypertension include older age, African American race, obesity and the presence of chronic kidney disease, diabetes, or left ventricular hypertrophy (Calhoun *et al.*, 2008).

Elevated blood pressure is the second leading modifiable cause of death, accounting for an estimated 3,95,000 preventable deaths in the United States in 2005 (Danaei *et al.*, 2009).

There is a strong relationship between hypertension and developing heart failure, and numerous studies have demonstrated reduced incidence of heart failure with antihypertensive therapy (Hunt *et al.*, 2009).

Arterial hypertension is a common and preventable cardiovascular risk factor, leading to about 1.7 million deaths/ year worldwide. There are two types of hypertension: Primary or essential hypertension (97-98 per cent) which has no clear underlying cause but appears to be the result of an interplay of complex genetic and environmental factors and Secondary hypertension (2-3 per cent) which is caused by a specific underlying mechanism usually involving kidneys or endocrine system. Several pathophysiological mechanisms contribute to the development of primary hypertension. The factors include: Genetics, high salt intake, low physical activity, obesity, insulin resistance, Renin-angiotensin system, sympathetic nervous system and intrauterine nutrition and low birth weight. The causes of secondary hypertension are unusual but are important because the causes may be curable. These are endocrine causes (Cushing's syndrome, Conn's syndrome, acromegaly, hyperparathyroidism), Renal causes (Glomerulonephritis, diabetic nephropathy polycystic kidney disease and renal artery stenosis) and other causes like pregnancy associated hypertension, alcohol, acute stress etc (Llyas, 2009).

2.2 Role of minerals in hypertension and cardiovascular diseases

Minerals are the nutrients required by the body in small amounts such as iron, calcium, and potassium. There are 2 categories of minerals – Macro minerals which are found in body tissue in relatively high amounts and are measured in milligrams, include calcium, phosphorus, potassium, magnesium, sodium etc and Trace elements which are found in body tissue in very minute quantities and are measured in micrograms. Sodium

and Potassium are intracellular electrolytes, a general term for the minerals necessary to give the body the proper fluid balance, especially those used in the heartbeat. Karppanen (1991) worked on mineral elements sodium, potassium, calcium and magnesium and found that without sodium chloride (common salt) and other sodium compounds being added to the diet arterial hypertension would be virtually non-existence. He found that a fall in sodium consumption and increase in potassium and magnesium consumption are useful in preventing and treating arterial hypertension.

The sodium-potassium balance influences blood pressure levels. Altering this balance can be achieved by decreasing sodium intake or increasing potassium intake. Many of the intervention diets such as the DASH (Dietary Approaches to Stop Hypertension) diet have lower sodium content and higher potassium content. Increased intakes of potassium, as well as other minerals such as calcium and magnesium, have also been shown to decrease blood pressure irrespective of sodium levels (Hooper *et al.*, 2002).

Meervaala *et al.* (2005) reviewed the role of dietary sodium, potassium, calcium, and magnesium in the pathogenesis, prevention, and treatment of elevated blood pressure (hypertension) and concluded that the present average sodium (salt) intake of approximately 3000-4500 mg per day in various industrialized populations is remarkably higher than the recommended intake and even exceeds the level of 2500 mg, which has been recently given as the maximum level of daily intake that is likely to pose no risk of adverse effects on blood pressure. The present average potassium, calcium and magnesium intakes are remarkably lower than the recommended intake levels. Decreased intake of sodium alone, and increased intakes of potassium, calcium and magnesium each alone decrease elevated blood pressure. The most pronounced effects are brought about by a combination of several of the dietary factors. The most recent US recommendations emphasize decrease in sodium, and increase in potassium, calcium, and magnesium intakes, which are characteristic of the so called DASH (Dietary Approaches to Skip Hypertension) diets. Such changes bring the levels towards the levels that are encountered in the Natural Diet, and have an excellent blood pressure lowering effect. For the prevention and basic treatment of elevated blood pressure (arterial hypertension), various methods to decrease the intake of sodium and to increase the intakes of

potassium, calcium, and magnesium should be comprehensively applied in the communities.

Androque and Madias (2007) examined the interdependency of sodium and potassium minerals influence on blood pressure and concluded that the interaction of sodium and potassium is the dominant environmental factor in the pathogenesis of primary hypertension and its associated cardiovascular risk.

2.3 Sodium and hypertension

Most of the sodium one consumes is in the form of salt, and the vast majority of consumed sodium is in processed and restaurant foods. Too much sodium is bad for health. It can increase blood pressure and risk for a heart attack and stroke. It is a matter of controversy that limiting salt in the diet would lower high blood pressure and help prevent heart disease. Scientists, researchers and doctors staunchly divided with strong opinion on both sides.

The current high salt intake is a modern development. The development of agriculture and farming has lead to a steady increase in salt consumption over the last few millennia. The arrival of modern food processing and high salt “fast” food in the last few decades has ensured that daily intake of salt is now many times that needed to maintain the normal physiological function of sodium. Indeed, in industrialized society the typical consumption of salt (NaCl) often exceeds 12g/day. Although expert groups such as the British Hypertension Society (BHS) suggest that it should not exceed 6g/day, and public health benefits in terms of CVD can be expected if this was reduced further to 3g/day (Law *et al.*, 1991).

Excess sodium intake induces hypertension by increasing fluid volume and preload, thereby increasing cardiac output. Sodium excess may increase blood pressure in multiple other ways as well; affects vascular reactivity and renal function. Diets in non-primitive societies contain many times the daily adult sodium requirements, an amount that is beyond the threshold level needed to induce hypertension (Barba *et al.*, 1996).

Dietary habits of Asian Indians indicate that the salt intake in them may be higher than some other populations. Excess salt intake occurs due to intake of pickles, papads, salty snacks, and chutneys which are popular household dietary choices, in addition to

increasing consumption of salted potato chips by children. Salt consumption was found as a significant predictor of hypertension even in a rural community in north India. Increased mean arterial pressure was seen to correlate with increased sodium consumption, in both urban as well as rural tribals, and hypertensives from both the groups showed higher urinary sodium excretion (Goel and Kaur, 1996).

Morris *et al.* (1999) observations demonstrated that in most normotensive black men but not white men, salt sensitivity occurs when dietary potassium is even marginally deficient but is dose dependently suppressed when dietary potassium is increased within its normal range. Such suppression might prevent or delay the occurrence of hypertension, particularly in the many blacks, in whom dietary potassium is deficient.

Vollmer *et al.* (2001) conducted a study and highlighted that the potential for decreased sodium intake, coupled with the DASH diet, to reduce blood pressure in diverse subgroups, including nonhypertensive and older persons. Given the overwhelming evidence that increased blood pressure increases the risk for cardiovascular morbidity throughout a wide range of hypertensive and non-hypertensive blood pressures, the DASH diet plus decreased sodium intake should be broadly recommended for prevention and treatment of hypertension.

Variation in dietary sodium intake over the usual range plays a minor role in blood pressure regulation in the general population, and appears not to be a determinant of cardiovascular disease outcomes. However, a variety of genetic and environmental factors have been identified that modulate the effects of dietary sodium on cardiovascular disease events and survival, as well as blood pressure. These include diet quality, age, body mass and race/ethnicity. Emphasis on improving diet quality, as in the DASH eating plan, and on weight control with a combination of increased physical activity and reduced caloric intake, as recommended by recent guidelines for the prevention and management of hypertension, will likely reduce the salt sensitivity of blood pressure and the risk of cardiovascular disease in many important population groups (Franco and Oparil, 2006).

Salt intake can make a substantial contribution to hypertension and that contribution is more likely if the patient is old rather than young, obese rather than lean, black rather than white, has diabetes mellitus with hypertension, or evidence of renal injury (Hollenberg 2006).

Modifying salt intake to lower blood pressure is an important strategy to help lower an individual's blood pressure on or off antihypertensive therapy. This therapy may itself make use of diuretics, especially thiazide diuretics, to promote salt wasting. (Glover *et al.* 2011).

2.4 Potassium and Hypertension

Several nutritional factors, such as sodium, calcium, magnesium, and fat, as well as potassium, have been linked to the pathogenesis and treatment of high blood pressure. Potassium is the essential mineral the body needs for fluid balance, mainly an intracellular electrolyte; it contributes to heartbeat, proper kidney function, and muscle and nerve activity, such as sending oxygen to the brain. Previous reports suggest that potassium balance may be related to blood pressure in two different ways. Potassium deficiency may be etiologically linked to the development of high blood pressure, and potassium supplementation may lower blood pressure in persons with established hypertension. Furthermore, movement from an area of high potassium intake to an area of low potassium intake is associated with increase in blood pressure. These associations generally are attributed to differences in sodium intake. In general, persons who consume large quantities of potassium have lower blood pressure than persons with similar sodium intake but lower potassium consumption. In the United States, where hypertension in blacks is more common and is associated with more severe target organ damage than in whites, at least one large population survey shows that blacks ingest both less sodium and less potassium than whites (Frisancho *et al.*, 1984).

An increase in dietary potassium, coupled with a decrease in sodium intake, is an important dietary choice to help reduce the risk of high blood pressure. Potassium ion depletion and/or low dietary potassium ion play a pivotal role in BP regulation in patients with essential hypertension as well as in normotensive individuals. An even more striking correlation between dietary potassium and hypertension is observed when the Na^+/K^+ ratio is employed as a more comprehensive indicator of dietary preferences, with higher values quite obviously favoring a greater prevalence of hypertension. These epidemiological data, together with a number of other observations, strongly suggest that K^+ homeostasis is critically linked to Na^+ effects as related to BP (Krishna, 1993).

Coruzzi *et al.* (2001) studied the role of dietary potassium in hypertension and found that dietary potassium restriction increases systolic blood pressure in patients with

mild essential hypertension. Potassium depletion plays a critical role in the pathogenesis of essential hypertension. They confirmed that potassium depletion may exacerbate essential hypertension by modifying natriuretic ability and calcium excretion in hypertensive subjects evaluated for degree of salt sensitivity. They suggested that not only sodium restriction, but also potassium and calcium supplementation, could be particularly advisable in salt-sensitive hypertensive patients.

He *et al.* (2008) observed a strong inverse association between potassium intake and blood pressure, with substantial evidence showing that potassium exerts an anti-pressor (blood pressure lowering) effect. A high potassium diet has clearly been shown to reduce the risk of stroke.

2.5 Sodium and Potassium- link with cardiovascular diseases

Body cells contain fluids composed of several minerals, which includes sodium, potassium, calcium, magnesium, and chloride. A proper balance between the sodium and potassium minerals contained in every cell is needed for these cells to function properly.

Some of the important cell functions attributed to sodium and potassium balance are:

- The production of acid and digestive enzymes used to break down food to provide energy for the body.
- To enable the nerves to react in terms of impulse reactions to external factors such as heat, cold, or pain felt by the body.
- To enable the heart or cardiovascular system to function properly.

Whelton *et al.* (1996) concluded, from a meta-analysis of randomized controlled trials, that potassium supplements reduced mean blood pressures (systolic/diastolic) by 1.8/1.0 mmHg in normotensive subjects and 4.4/2.5 mm Hg in hypertensive subjects. An increase in dietary intake of potassium, from approximately 60–80 mmol/day was shown to be inversely and significantly related to the incidence of stroke in women.

Any deficiency in sodium or potassium does not result to life threatening issues, but any serious distortion or disproportion with the amount of potassium or sodium, creates complications often resulting to heart attacks. The researchers found a direct

relationship between salt consumption and systolic blood pressure, but not between salt consumption and diastolic blood pressure. It could be that higher diastolic blood pressure, meaning the blood vessels don't get a chance to recover from high blood pressure between heart beats, is a more important factor in heart disease. Modifying lifestyles in populations can have a major protective effect against high blood pressure and cardiovascular diseases. Lowering blood pressure decreases deaths from stroke, coronary events and heart failure. Observational and experimental data support an independent, positive relationship between sodium intake and blood pressure, most clearly in hypertensive populations. Potassium intake, on the other hand, has been inversely related to blood pressure. Since hypertension is a strong predictor of cardiovascular disease (CVD), especially stroke, inadequate intake of sodium and potassium is likely to be associated with increased cardiovascular morbidity and mortality. Only recently, population based studies on dietary salt intake in relation to CVD and non cardiovascular events have received priority (Perry 2000).

2.6 Combined Reviews

Levine *et al.* (1961) conducted a study to define more accurately the associations between serum sodium, serum potassium, and blood pressure level by standardizing to the greatest degree possible all methods and measurements, and by assessing the importance of such variables as age, sex, and body build. An additional purpose of their study was to evaluate further the relationship of stated salt intake to blood pressure level and serum electrolyte concentrations. Fifty normotensive and 43 hypertensive patients were studied. No significant associations were found between the height of the blood pressure, the serum sodium or potassium level, and the stated salt intake.

Simpson *et al.* (1978) found that mean 24 hour sodium excretion at all ages was significantly higher in males as compared to females.

From 1979 through 1984, a randomized epidemiological survey in Belgium assessed the dietary intake of sodium, potassium, calcium, and magnesium using 24-hour food records checked by trained dietitians. Dietary cation intake levels were correlated with blood pressure both in the total group (4167 men and 3891 women) and in the group not taking antihypertensive medication (3814 men and 3329 women). Serum sodium, potassium, calcium, and phosphorus were also measured. Multiple regression analysis

adjusting for age, body mass index, heart rate, alcohol intake, and total caloric intake revealed a significant positive correlation between sodium intake and blood pressure in the group not treated for hypertension except for diastolic blood pressure in women. A significant negative correlation was found between dietary calcium intake and diastolic blood pressure in men and between dietary magnesium intake and systolic blood pressure in women. No independent effect of dietary potassium intake on blood pressure could be established. Significant but weak correlations were found between the dietary intake of sodium, potassium and calcium and their serum values. The study confirms the hypothesis that at the population level dietary cations are related to the regulation of blood pressure (Kesteloot and Joosens 1988).

Khaw and Barrett-Connor (1988) examined the relationship between blood pressure and dietary sodium and potassium intake estimated from 24 hr diet recall in a population of 584 men and 718 women 30 to 79 years old in Southern California. In men, but not women, age adjusted systolic and diastolic blood pressure correlated significantly with dietary sodium intake. In both men and women, age adjusted diastolic blood pressure significantly inversely correlated with dietary potassium intake. Age-adjusted systolic and diastolic blood pressure correlated significantly with the dietary sodium / potassium ratio in each sex; correlations were better for the ratio than for either sodium or potassium alone.

Cross sectional observations of the effect of age were made from studies in 230 hypertensive and 430 normotensive subjects. Sodium sensitivity of blood pressure increased significantly with increasing age in the entire population. The relation was more striking in hypertensive subjects in whom a progressive increase in salt sensitivity with decades was seen than in the normotensive group in whom salt sensitivity was not observed until the sixth decade. Salt sensitive subjects had a significantly greater increase in systolic and diastolic pressure over time than those who were salt resistant (Weinberger and Fineberg 1991).

Singh *et al.* (1998) conducted cross sectional surveys in women in six to twenty urban streets in different cities from five different corners of India. Evaluation was by a physician and dietitian, an administered questionnaire, a physical examination and using a sphygmomanometer. Multivariate logistic regression analysis on pooled data from the

five cities, after adjustment for age, showed that age, body mass index and obesity were strongly associated with hypertension. A sedentary lifestyle and salt intake were weakly associated and alcohol intake was not a factor with these women.

Hajjar *et al.* (2001) studied the association of major dietary factors with blood pressure and with age related changes in blood pressure in a representative sample of the US population. Data were obtained on all individuals 20 years or older (n=17030) surveyed in the Third National Health and Nutrition Examination Survey (NHANES III) including demographic data, dietary intake (sodium, potassium, calcium, magnesium, protein, alcohol and total energy), based on 24 hr recall and blood pressure. They found that systolic blood pressure was positively associated with higher sodium, alcohol, and protein intakes and negatively associated with potassium intake. Diastolic blood pressure was negatively associated with potassium and alcohol intakes and pulse pressure was positively associated with sodium, protein and alcohol intakes.

Gupta (2004) studied the trends in hypertension epidemiology in India and reported steadily increasing hypertension prevalence from 5 per cent in 1960's to 12-15 per cent in 1990's and found that prevalence is lower in rural Indian population and higher among urban adults.

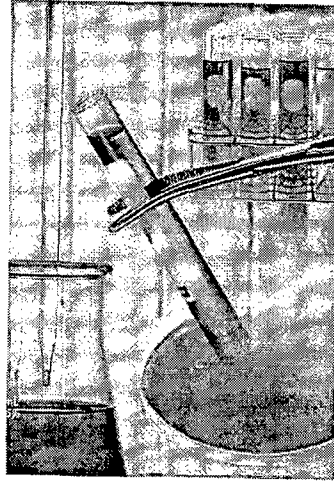
One hundred thirty five hypertensive patients and equal number of age and sex matched healthy controls were taken up for studying the relationship of 24 hour urinary sodium and potassium excretion, sodium- potassium molar ratio and body mass index (BMI) with blood pressure in normotensive and hypertensive population in Kashmir. There was statistically significant elevated 24 hr urinary sodium excretion ($p < .001$), increased $\text{Na}^+ - \text{K}^+$ molar ratio, significantly higher BMI in hypertensive population as compared to controls whereas there was a lower 24 hr urinary excretion of potassium ($p > .20$) in patients with hypertension. Thus sodium and potassium excretion, $\text{Na}^+ - \text{K}^+$ molar ratio and body mass index has direct bearing in perpetuation or causation of hypertension in Kashmir which may be related to intake of salt tea (Jan *et al.* 2006)

Radhika *et al.* (2007) conducted a study to determine the mean dietary salt intake in urban south India and its association with hypertension. Phase 1 recruited 26,001 individual aged ≥ 20 years, of whom every tenth subject was invited to participate in phase 3 for detailed dietary studies. Participants with self reported history of

hypertension, diabetes or heart disease were excluded from the study and they concluded that intake of dietary salt in urban south India is higher than currently recommended and increasing salt intake is associated with increased risk for hypertension even after adjusting for potential cofounders.

A pooled meta analysis of 33 randomized controlled trials on the effects of potassium chloride supplementation (average of 75 mmol/day) on BP in hypertensive and normotensive patients demonstrated a significant reduction in average BP of 3.1/2.0 mm Hg with potassium. The BP lowering effects of potassium tended to be greater in hypertensive patients (4.4/2.5 mm Hg) than in normotensive patients (1.8/1.0 mm Hg). Therefore, maintenance of adequate dietary potassium intake show promise in the prevention and treatment of hypertension and should be thought of as part of the armamentarium of lifestyle changes (Kapoor and Kapoor 2009).

Yang *et al.* (2011) conducted a study and concluded that people consuming too much salt and too little potassium in their diet have had a significantly raised risk of death from cardiovascular disease compared with those who had the lowest ratio of sodium to potassium. The study with an average of 14.8 years of follow up, collecting data on 12,267 people, found an association between high blood pressure and high levels of salt consumption and low levels of potassium intake.



MATERIALS AND METHODS

3. MATERIALS AND METHODS

The present investigation entitled “**Association of Sodium and Potassium Concentrations with Cardiovascular Diseases and Hypertension**” was carried out in the Department of Biology and Environmental Sciences, CSK Himachal Pradesh Krishi Vishvavidyalaya, Palampur in collaboration with the Department of Veterinary Physiology, College of Veterinary and Animal Sciences, CSKHPKV, Palampur, during the year 2011-2012. The detail of material used and methods employed in the present investigation are described as follows:

3.1 Selection of Hypertension and Cardiovascular disease patients:

The data related to patients with hypertension and cardiovascular diseases were collected from hospitals and clinics in the Palampur region. Fifty patients each of hypertension and heart diseases of both sexes aged between 21 and 65 years were selected for the study. The diagnosis of essential hypertension was based on at least two separate blood pressure readings within a minimum of two week intervals and laboratory examinations. Blood pressure was measured by mercury sphygmomanometer. All subjects were referred from the same geographic area and two sets were established: Group 1 included determination of sodium and potassium in healthy controls and patients with hypertension. Group 2 included the determination of sodium and potassium in healthy control group and patients with cardiovascular diseases.

Exclusion criteria

The following exclusion criteria were employed in the study:

- All cases of hypertension secondary to other diseases were excluded from the study.
- Patients with history of alcoholism, cigarette smoking, drug abuse or any form of mental disorder.
- Patients with angina pectoris.

- Female patients- neither pregnant nor lactating mothers nor on any oral contraceptives at the time of the study.
- All obese patients (BMI of patients not $>27 \text{ kg/m}^2$)
- Patients with diabetes mellitus
- Patients with evidence of renal disease.

Selection of healthy subgroups (Controls)

Fifty apparently healthy subjects of both sexes, aged between 18 and 52 years were selected with their blood pressure in the normal range. They were all non- smokers and non- alcoholics and were mainly students, office workers and traders. They were not taking any medication during the period of the study. The control group was selected as much as possible to match the hypertensive group in age, sex and BMI.

Collection of Blood

About 5- 10 ml venous blood was obtained from the subjects using disposable needle and syringes and about 3 ml of blood dispensed into heparinized tubes containing lithium heparin was frozen as heparinized whole blood sample; the remaining blood sample was dispensed into plain tubes/vials containing EDTA.

Serum extraction

After collection of the blood, the blood was allowed to clot by leaving it undisturbed at room temperature for 15 to 30 minutes.(Both sodium and potassium remain stable in serum for several hours at $25\text{-}35^\circ \text{C}$ and for 3 months at -20°C .) The clot was then removed by centrifuging it at 1000-2000 rpm for 10 minutes in a refrigerated centrifuge. The resultant supernatant was designated serum. Serum was immediately transferred into a clean polypropylene tube using a Pasteur pipette. The samples were maintained and stored at -20°C till analysis.

3.3 Chemicals and instruments

The chemicals and reagents used in this study were either of Analytical Grade (AR) or of highest purity. The glass wares were thoroughly washed with liquid detergent, cleaned and rinsed with distilled water and dried in hot air oven. The instruments used in experimental work are:

- Systronics Flame photometer 129
- Atomic Absorption Spectrophotometer PERKIN ELMER AANALYST 400
- Deep freezer
- Centrifuge Remi21
- B.O.D Incubator
- Electronic weighing machine ANAMED
- Polypropylene Test tubes
- Test tubes holder

3.3.1 Estimation of Sodium and Potassium concentrations in serum samples

The sodium and potassium in serum samples were measured by Atomic Absorption Spectrophotometer PERKIN ELMER AANALYST 400 and Systronics flame photometer 129. Since the values obtained for sodium and potassium showed no difference when analyzed in either of the two instruments, some of the samples were analyzed by Systronics flame photometer 129 only.

Reagents:

1. Sodium stock standard solution (200mEq/litre) (stock standard -1)

1.169 g of sodium chloride was weighed accurately, dissolved in about 75 ml of glass distilled water and diluted to 100 ml with glass distilled water in a volumetric flask. Stored in a pyrex glass bottle at 25-35°C (stable for one year).

2. Potassium stock standard solution (10 mEq/ Litre) (stock standard solution-2)

0.0746 g of potassium chloride (KCl) was accurately weighed, dissolved in about 75 ml of glass distilled water and diluted to 100 ml with glass distilled water in a volumetric flask. Stored in a Pyrex glass bottle at 25-35° C (solution stable for one year).

3. Sodium –Potassium mixed working standards:

This solution has a good similarity for Na^+ and K^+ with regards to their amounts generally found in serum and compensates the interference of one element with the other. It was prepared as given below by pipetting of stock solutions of Na^+ and K^+ into 500 ml volumetric flasks and the final volume made with deionized double distilled water. These working standards were quite stable.

SOLUTION NO.	SODIUM STOCK SOLUTION (ml)	POTASSIUM STOCK SOLUTION (ml)	Na ⁺ CONC. (mEq/L)	K ⁺ CONC. (mEq/L)
1.	0.850	0.8	1.7	0.08
2.	0.50	0.1	1.0	0.01
3.	0.65	0.40	1.3	0.04

Sample dilution:

Each serum sample was diluted with distilled water by mixing 0.05ml sample with 4.95 ml distilled water.

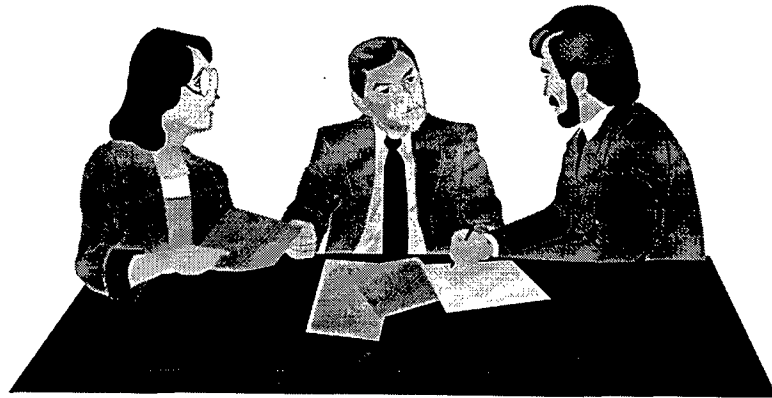
Procedure:

1. Labelled the test tubes Blank, Standard and Sample. Add 5 ml distilled water to blank.
2. Arranged two rows of 15 ml test tubes and appropriately number the tubes in the first and second row according to the sample number of serum sample to be analysed. Include one tube in each row for a reagent blank.
3. Aspirated deionized water for at least 2 minutes to clean out and stabilize the unit.
4. Pulverized the prepared standard solutions (i.e. with known concentration) one after the other into the flame and read the intensity of electrical signal.
5. The diluted serum samples were fed one by one into the instrument through the suction tube and noted down the reading.

ELEMENT	EMISSION WAVELENGTH (nm)	FLAME COLOUR
SODIUM (Na)	589	YELLOW
POTASSIUM (K)	766	VIOLET

Analytical techniques:

Different analytical techniques of statistics like mean, standard deviations, standard error, and test of significance were used to analyze and interpret the results. All p values < 0.05 was considered statistically significant.



RESULTS AND DISCUSSION

4. RESULTS AND DISCUSSION

The experimental result emanating from the present study entitled “**Association of Sodium and Potassium concentrations with Cardiovascular Diseases and Hypertension**” have been presented in this chapter and also attempts have been made to discuss the findings of the experiments in the light of available scientific literature and work done earlier by other investigators. The result and discussion has been given under the following heads and subheads:

- 4.1 Serum Sodium Concentration in Hypertension, Cardiovascular disease (CVD) Patients and Healthy Controls and Statistical Analysis with Student t-test.**
- 4.2 Serum Potassium Concentration in Hypertension, Cardiovascular disease Patients and Healthy Controls and Statistical Analysis with Student t-test.**
- 4.3 Minerals Status in HT, CVD and HC Groups on the Basis of Age and Sex**
 - 4.3.1 Serum Sodium in Hypertension Patients and Normotensives**
 - 4.3.2 Serum Potassium in Hypertension Patients and Normotensives**
 - 4.3.3 Serum Sodium in Cardiovascular Disease Patients and Healthy Controls**
 - 4.3.4 Serum Potassium in Cardiovascular Disease Patients and Healthy Controls**
- 4.4 Sodium-Potassium Ratio in Hypertension Patients, Cardiovascular Patients and Healthy Controls**

During the study, 100 patients were identified. Of these, 50 had hypertension and 50 had heart diseases. 50 healthy subjects were used as controls. The first sets of investigations were conducted for serum sodium and potassium concentration in 50 healthy control subjects who had neither a previous history of hypertension nor did their current blood pressure status reveal hypertension and 50 known cases of hypertension patients. Of these control subjects, 28 were males and 22 were females and hypertension patients comprised of 32 males and 18 females. The second sets of investigations were conducted in 50 healthy control subjects who had neither a previous history of cardiovascular disease nor did their current heart status reveal cardiovascular disease risk

and 50 known cases of cardiovascular disease patients. Of these control subjects, 28 were males and 22 were females and cardiovascular disease patients comprised of 26 males and 24 females. All cases of hypertension secondary to other diseases were excluded from the study and patients with history of alcoholism, cigarette smoking, drug abuse or any form of mental disorder were also excluded. Serum sodium and potassium concentration varied with gender and age, therefore, results from different ages of males and females were grouped separately.

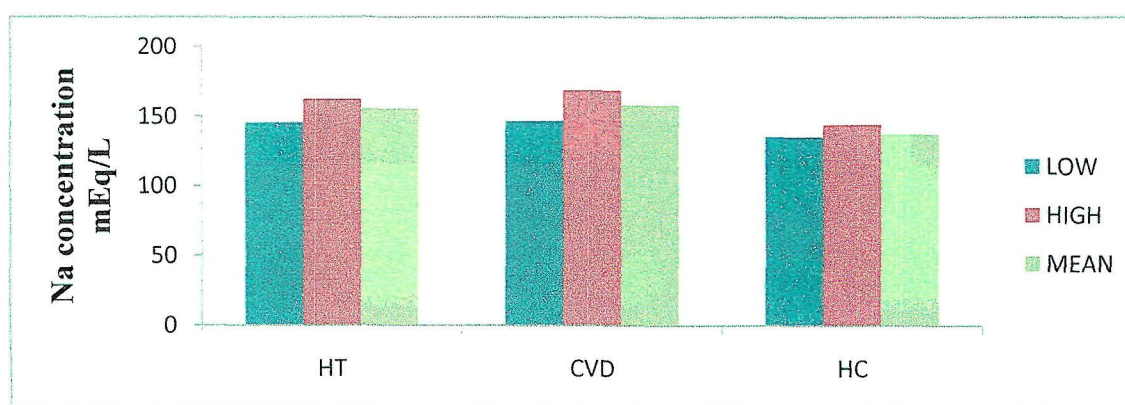
4.1 Serum Sodium Concentration in Hypertension, Cardiovascular Disease Patients and Healthy Controls and Statistical Analysis with Student t-test.

Mean Serum sodium concentration was significantly higher in cardiovascular disease patients than hypertension patients. Both hypertension and cardiovascular disease patients had higher mean serum sodium concentration than healthy controls as shown in Table 4.1.

TABLE 4.1: Mean Levels of Serum Sodium (mEq/L) in HT, CVD and HC

	HT (n=50)	CVD (n=50)	HC (n=50)
Range	145.6- 162.5	146.7-168.9	135.4- 144.2
Mean	155.6 ±0.943	157.7±1.086	137.2±0.462
SD	6.67	7.68	3.27
p <0.05	Significant		

HT=Hypertensive Patients, CVD= Cardiovascular Disease Patients, HC= Healthy Controls



HT= Hypertensives, CVD= Cardiovascular disease patients, HC= Healthy Controls

Fig 4.1: Serum Sodium in HT, CVD and HC

The present study showed that, the serum sodium concentration of the three study groups differ with each other as shown in fig 4. 1. Mean serum sodium concentration of patients with hypertension (155.6 ± 0.943) and cardiovascular diseases (157.7 ± 1.086) had a significant difference ($p < 0.05$) as compared to healthy controls (137.2 ± 0.462), indicating that serum sodium has a positive significant association with hypertension and cardiovascular diseases. Serum sodium found to be increased in hypertensives and its level was too high in cardiovascular disease and an increased salt intake results in sodium retention and hence increased blood volume (Haddy 1985). The present study indicated that high sodium intake is strongly and independently associated with an increased risk of hypertension and cardiovascular disease. The results of the present study are in conformity with the earlier findings of Lever *et al.* (1981), INTERSALT (1988) and Umesawa *et al.* (2008).

4.2 Serum Potassium Concentration in Hypertension, Cardiovascular Disease Patients and Healthy Controls and Statistical Analysis with Student t-test.

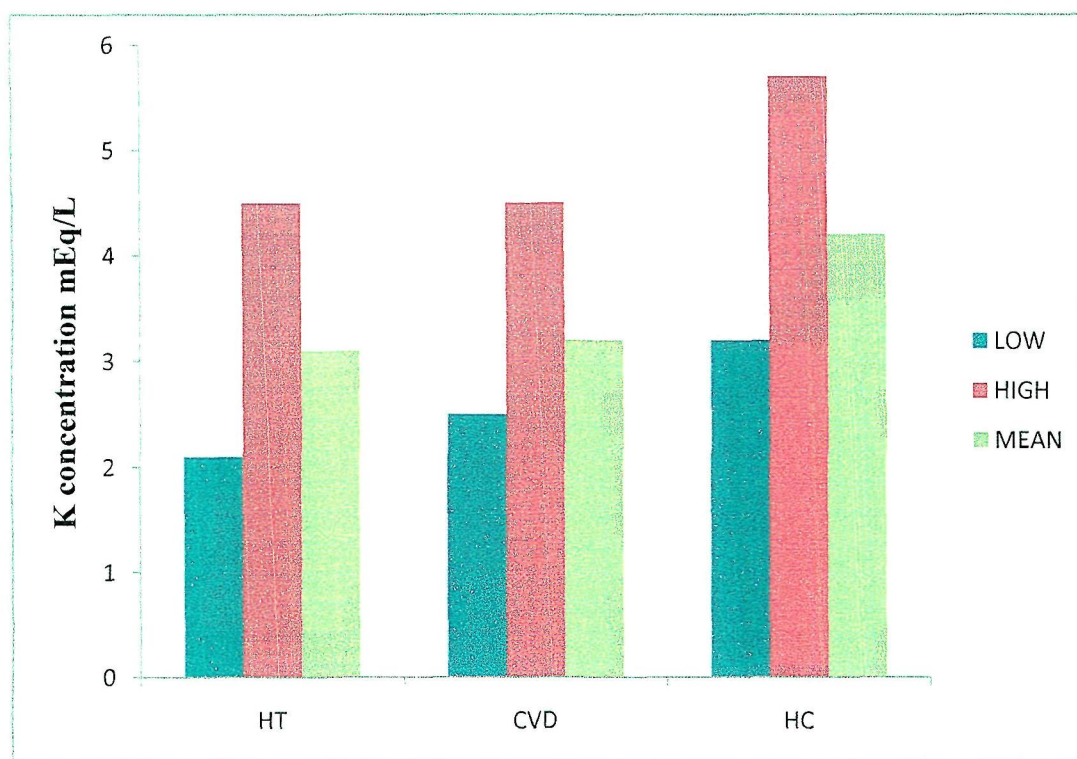
Mean Serum potassium concentration was significantly lower in cardiovascular disease and hypertension patients as shown in Table 4.2.

TABLE 4.2: Mean Levels of Serum Potassium (mEq/L) in HT, CVD and HC

	HT (n=50)	CVD (n=50)	HC (n=50)
Range	2.1- 4.5	2.5- 4.5	3.2- 5.7
Mean	3.1 ± 0.09	3.2 ± 0.08	4.2 ± 0.09
SD	0.65	0.58	0.61
p <0.05	Significant		

HT=Hypertensive Patients, CVD= Cardiovascular Disease Patients, HC= Healthy Controls

The present study showed that, the serum potassium concentration of the three study groups differ with each other as shown in fig 4. 2. Mean serum potassium of patients with hypertension (3.1 ± 0.09) and cardiovascular disease (3.2 ± 0.08) has a significant difference ($p < 0.05$) as compared to healthy controls (4.2 ± 0.09).



HT= Hypertensives, CVD= Cardiovascular disease patients, HC= Healthy Controls

Fig 4.2 Serum Potassium in HT, CVD and HC

This indicated that potassium has an inverse relationship with hypertension and cardiovascular diseases and low level of potassium is linked with an increase risk of hypertension and cardiovascular diseases. The present study also supported the evidence that potassium intake is a critical determinant of blood pressure and K^+ is critical to the maintenance of CV health (Sica *et al.*2002).An inverse correlation has also been found between potassium Intake and the prevalence of hypertension supporting that potassium depletion elevates blood pressure in normotensive subjects and hypertensive subjects ingesting normal amounts of sodium (Krishna 1990).

4.3 Minerals Status in HT, CVD and HC Groups on the Basis of Age and Sex

4.3.1 Serum Sodium in Hypertension Patients and Normotensives

Fig. 4.3.1 shows variation in serum sodium concentration in hypertensives and healthy controls with age and sex.

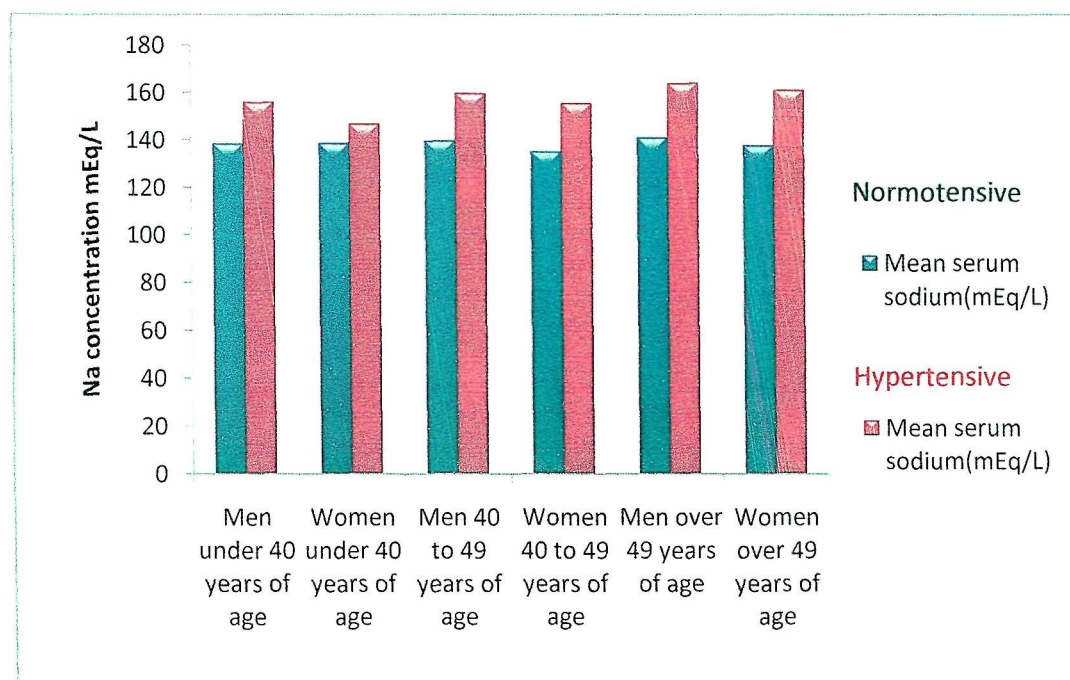


Fig.4.3.1 Variation in Serum Sodium Concentration with Age and Sex in Hypertensives and Normotensives

Fig. 4.3.1 shows variation in serum sodium concentration in hypertensives and healthy controls with age and sex. The average serum sodium concentration in control group was $137.2 \pm 0.462 \text{ mEq/L}$. In control group the value of average serum sodium concentration in males and female under 40 years of age was $138.6 \pm 0.466 \text{ mEq/L}$ ($n=19$) and $138.8 \pm 0.401 \text{ mEq/L}$ ($n=9$), respectively. The value of average serum sodium concentration in males and female between 40 to 49 years of age was $139.8 \pm 0.586 \text{ mEq/L}$ ($n=4$) and $135.2 \pm 0.576 \text{ mEq/L}$ ($n=7$), respectively. In males and females over 49 years of age the value of average serum sodium concentration was $141.2 \pm 0.635 \text{ mEq/L}$ ($n=5$) and $137.8 \pm 0.342 \text{ mEq/L}$ ($n=6$), respectively. The average serum sodium concentration in hypertensive group was 155.6 ± 0.943 . In hypertensive group the value of average serum sodium concentration in males and female under 40 years of age was $156.1 \pm 0.901 \text{ mEq/L}$ ($n=9$) and $146.8 \pm 0.551 \text{ mEq/L}$ ($n=4$), respectively. The value of average serum sodium concentration in males and female between 40 to 49 years of age was $159.8 \pm 0.731 \text{ mEq/L}$ ($n=10$) and $155.7 \pm 1.209 \text{ mEq/L}$ ($n=6$), respectively. In males and females over 49 years of age the value of average serum sodium concentration was $164.1 \pm 1.023 \text{ mEq/L}$ ($n=13$) and $161.2 \pm 0.594 \text{ mEq/L}$ ($n=8$), respectively. These variables differ significantly ($p < 0.005$) in males versus female subjects and also with age

(APPENDIX I) .The concentration of serum sodium found to be significantly higher ($p<0.05$) in males as compared to females in hypertensive group. Thus, present study indicated that hypertension is more prevalent in men as compared to women. A few studies also supported that this disorder is more prevalent in men (Lakka *et al.*1999) and (Alderman *et al.*1999). Also, men start to develop hypertension a decade earlier than women (Sullivan 2012). Sodium sensitivity of blood pressure increased significantly with increasing age (Weinberger and Fineberg 1991). The results showed that age is a known risk factor for high blood pressure and it may be due to:

- Age- related changes in hormone profiles
- A tendency for older people to over salt their food because of decreased taste bud sensitivity (Weber 2007)

4.3.2 Serum Potassium in Hypertension Patients and Normotensives

The present study showed that, serum sodium concentration of normotensives and hypertensives differ with each other as shown in fig.4.3.2.The average serum potassium concentration in control group was 4.2 ± 0.09 mEq/L. In control group the value of average serum potassium concentration in males and female under 40 years of age was 3.8 ± 0.089 mEq/L ($n=19$) and 4.8 ± 0.101 mEq/L ($n=9$), respectively. The value of average serum potassium concentration in males and female between 40 to 49 years of age was 4.2 ± 0.062 mEq/L ($n=4$) and 3.9 ± 0.093 mEq/L ($n=7$), respectively. In males and females over 49 years of age the value of average serum potassium concentration was 4.5 ± 0.054 mEq/L ($n=5$) and 4.1 ± 0.063 mEq/L ($n= 6$), respectively. The average serum potassium concentration in hypertensive group was 3.1 ± 0.09 mEq/L. In hypertensive group the value of average serum potassium concentration in males and female under 40 years of age was 3.2 ± 0.096 mEq/L ($n=9$) and 3.3 ± 0.097 mEq/L ($n=4$), respectively. Mean serum potassium concentration was higher in females as compared to males of the same age group. The value of average serum potassium concentration in males and female between 40 to 49 years of age was 2.8 ± 0.075 mEq/L ($n=10$) and 3.1 ± 0.088 mEq/L ($n=6$), respectively. Mean serum potassium concentration varied significantly in males and females ($p <0.05$). Mean serum potassium concentrations of females were found to be higher than males (APPENDIX II). In males and females over 49 years of age the value of average serum potassium concentration was 3.1 ± 0.091 mEq/L ($n=13$) and 3.6 ± 0.097 mEq/L ($n= 8$), respectively.

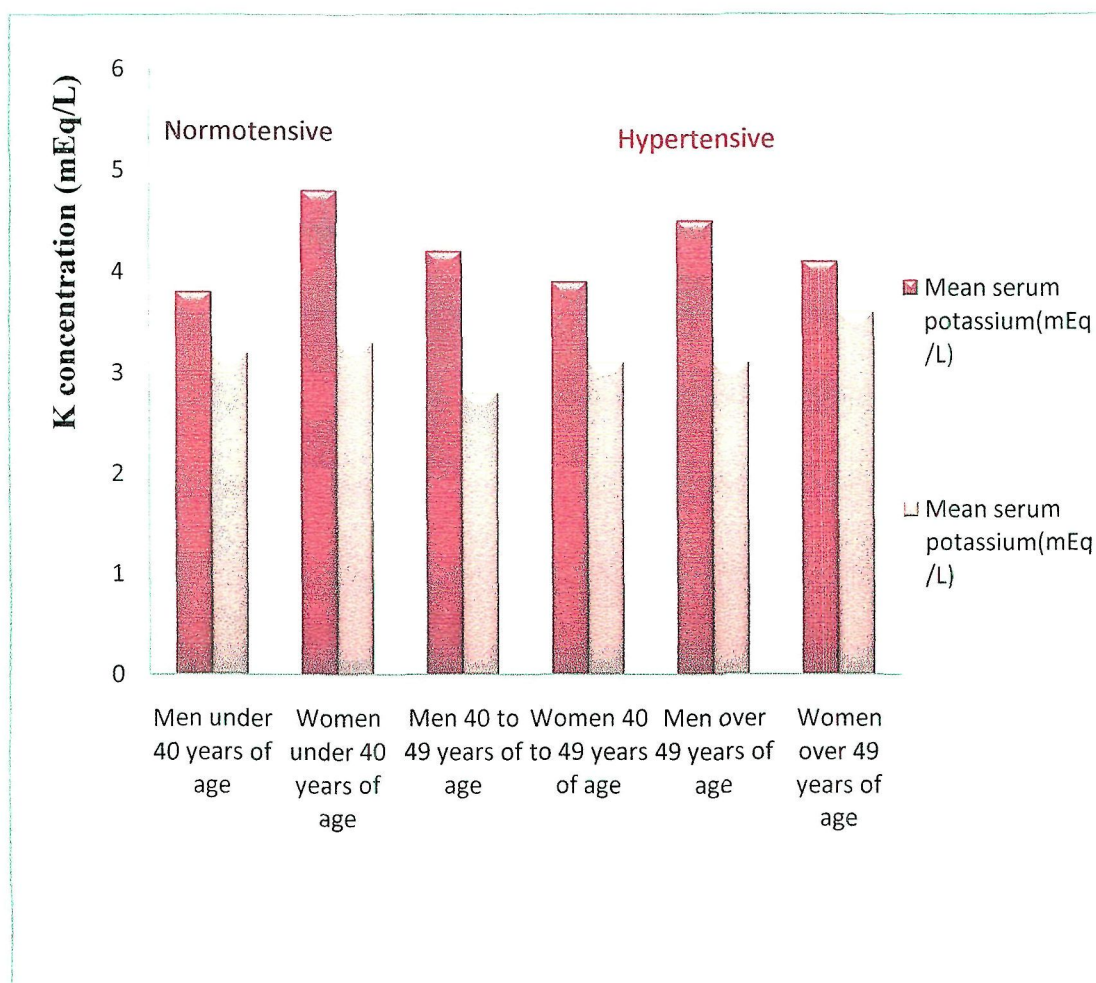
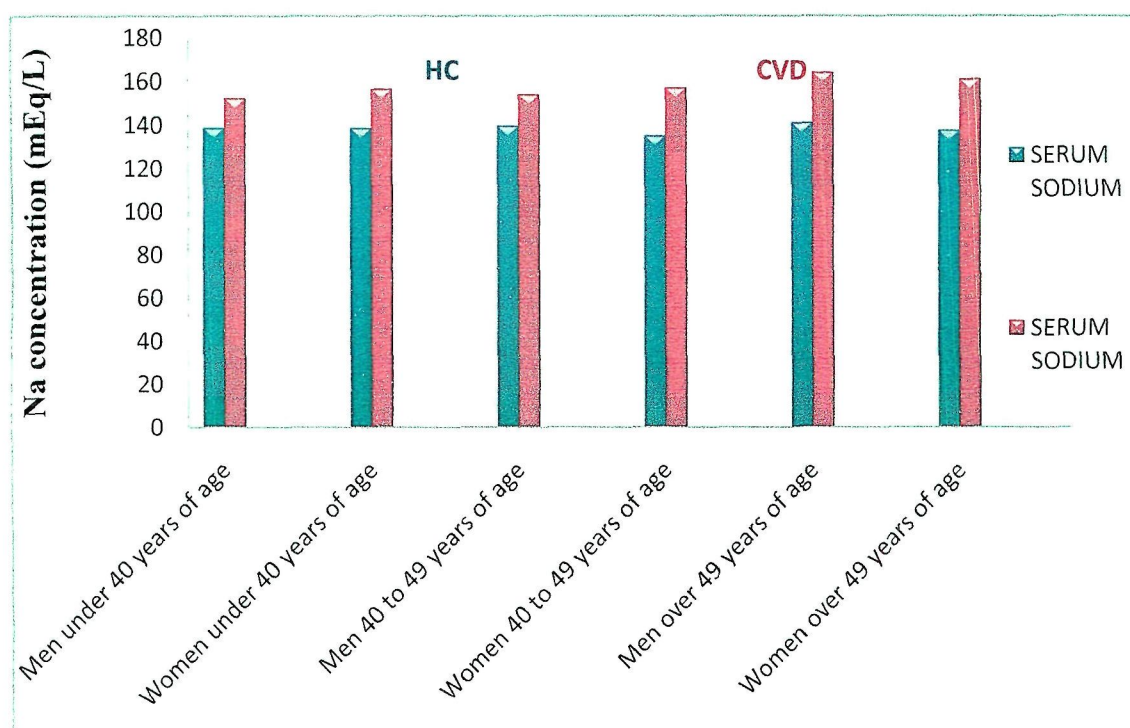


Fig.4.3.2 Variation in Serum Potassium Concentration with Age and Sex in Hypertensives and Normotensives

In the present study mean serum potassium was found to be higher in females as compared to males indicating that females are less prevalent to hypertension as compared to males. The results of the present study are in conformity with the earlier findings of Calhoun and Oparil (1997) and August and Oparil (1999). The incidence of hypertension and its cardiovascular consequences are inversely related to the amount of dietary potassium consumed (Meneely *et al.* 1976; Page *et al.* 1981; Kesteloot 1984).

4.3.3 Serum Sodium in Healthy Controls and Cardiovascular Disease Patients

Serum sodium concentration in healthy controls and patients with cardiovascular diseases, respectively, in males and females is presented in fig. 4.3.3



HC= Healthy Controls, CVD= Cardiovascular Disease Patients

Fig.4.3.3 Variation in Serum Sodium Concentration with Age and Sex in HC and CVD

The average serum sodium concentration in control group was 137.2 ± 0.462 mEq/L. In control group the value of average serum sodium concentration in males and female under 40 years of age was 138.6 ± 0.466 mEq/L (n=19) and 138.8 ± 0.401 mEq/L (n=9), respectively. The value of average serum sodium concentration in males and female between 40 to 49 years of age was 139.8 ± 0.586 mEq/L (n=4) and 135.2 ± 0.576 mEq/L (n=7), respectively. In males and females over 49 years of age the value of average serum sodium concentration was 141.2 ± 0.635 mEq/L (n=5) and 137.8 ± 0.342 mEq/L (n= 6), respectively. The average serum sodium concentration in cardiovascular disease group was 157.7 ± 1.086 mEq/L. In this group the value of average serum sodium concentration in males and female under 40 years of age was 152.3 ± 0.540 mEq/L (n=9) and 156.5 ± 0.698 mEq/L (n=10), respectively. The value of average serum sodium concentration in males and female between 40 to 49 years of age was 154.2 ± 1.07 mEq/L (n=7) and 157.2 ± 1.58 mEq/L (n=8), respectively. In males and females over 49 years of age the value of average serum sodium concentration was 164.3 ± 0.927 mEq/L (n=10) and 161.2 ± 1.07 mEq/L (n= 6), respectively. These variables differ significantly

($p < 0.05$) in males versus female subjects. However, no significant variation ($p > 0.05$) has been observed in serum sodium concentration of heart disease males and females under 40 years age group but significant difference ($p < 0.05$) was observed in risk groups males and females of age group 40-49 years (APPENDIX III). Mean serum sodium concentrations of females were found to be higher than males. Patients of over 40 years age group do not show significant variation. Although mean serum sodium was higher in males as compared to females but there is no significant variation between the two ($p > 0.05$).

Franco and Oparil (2006) have also reported significant association between serum sodium and risk of cardiovascular disease. Clinical disturbances of the circulating sodium concentration are both a cause and a consequence of cerebrovascular disease (Wannamethee *et al.*, 1994). Serum sodium level is considered to be one of the important contributing factors in the pathogenesis of hypertension and cardiovascular diseases (Vollmer *et al.*, 2001).

4.3.4 Serum Potassium Concentration in Cardiovascular Disease Patients and Healthy Controls

Serum potassium concentration in healthy controls and patients with cardiovascular diseases, respectively, in males and females is presented in fig. 4.3.4

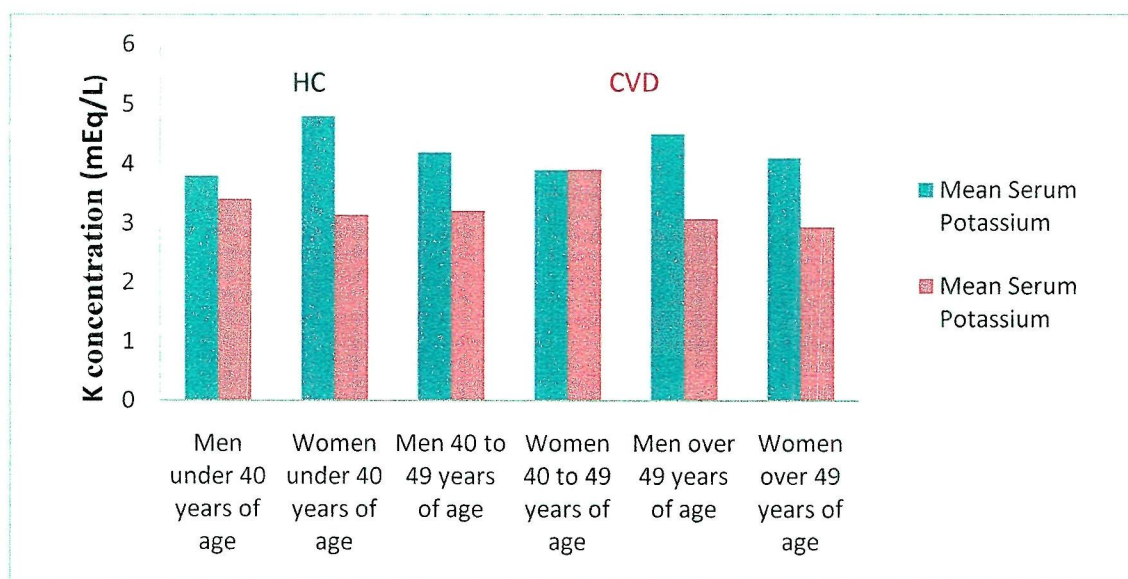


Fig.4.3.4 Variation in Serum Potassium concentration with age and sex in Healthy Controls (HC) and cardiovascular disease patients (CVD)

The average serum potassium concentration in control group was 4.2 ± 0.09 mEq/L. In control group the value of average serum potassium concentration in males and female under 40 years of age was 3.8 ± 0.089 mEq/L (n=19) and 4.8 ± 0.101 mEq/L (n=9), respectively. The value of average serum potassium concentration in males and female between 40 to 49 years of age was 4.2 ± 0.062 mEq/L (n=4) and 3.9 ± 0.093 mEq/L (n=7), respectively. In males and females over 49 years of age the value of average serum potassium concentration was 4.5 ± 0.054 mEq/L (n=5) and 4.1 ± 0.063 mEq/L (n= 6), respectively. The average serum potassium concentration in cardiovascular disease group was 3.2 ± 0.08 mEq/L. In cardiovascular disease group the value of average serum potassium concentration in males and female under 40 years of age was 3.41 ± 0.10 mEq/L (n=9) and 3.14 ± 0.059 mEq/L (n=10), respectively. The value of average serum potassium concentration in males and female between 40 to 49 years of age was 3.21 ± 0.06 mEq/L (n=7) and 3.91 ± 0.11 mEq/L (n=8), respectively. In males and females over 49 years of age the value of average serum sodium concentration was 3.07 ± 0.058 mEq/L (n=10) and 2.93 ± 0.084 mEq/L (n= 6), respectively.

There was significant variation ($p < 0.05$) in serum potassium concentration of male and female patients under 40 years age group. Mean serum potassium concentration were higher in males (3.41 ± 0.10 mEq/L) as compared to females (3.14 ± 0.059 mEq/L) of the same age group. No Significant difference ($p > 0.05$) was observed in risk groups males and females of age group 40-49 years (APPENDIX IV). Patients over 40 years age group showed significant variation ($p < 0.05$). Mean serum potassium was higher in males (3.07 ± 0.058 mEq/L) as compared to females (2.93 ± 0.084 mEq/L). The results showed significant variation of serum potassium concentration in cardiovascular disease patients with age and sex. The results also indicated that age is a known risk factor for Hypertension and Cardiovascular diseases and it may be due to:

- Changes that happen in the walls of arteries and other blood vessels
- Decreased efficiency of heart (Weber, 2007)

Several observational studies have reported an inverse association between dietary potassium intake and risk of cardiovascular disease (He *et al.* 2008 and Coruzzi *et al.* 2001). Low serum potassium levels may identify individuals at increased risk for cardiovascular events because of insufficient dietary potassium intake (Sasaki *et*

al.,1995). The results of the present study are in conformity with the earlier findings of Mendelsohn and Karas (1999); Meervaala *et al.* (2005); Hunt *et al.* (2009). In young to middle-aged subjects, hypertension and cardiovascular disease are more common in men than in women. Cardiovascular risk increases with age in both sexes. However; this increase is sharper in women, so that in old age women have similar rates of cardiovascular diseases (Wenger, 1995).

4.4 SODIUM- POTASSIUM RATIO:

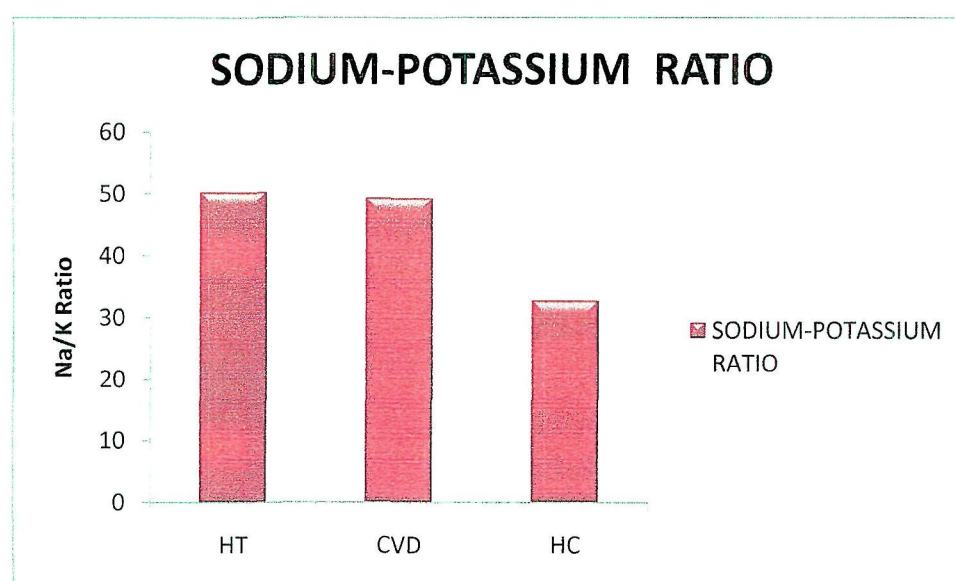
Sodium -Potassium ratio in the diet is a more important determinant of blood pressure than the amount of sodium consumed alone.

Na: K ratio is high - Hypertension is more prevalent

Table 4.4 Sodium- Potassium ratio in HT, CVD and HC

	HT	CVD	HC
SODIUM	155.6	157.7	137.2
POTASSIUM	3.1	3.2	4.2
SODIUM-POTASSIUM RATIO	50.19	49.28	32.67
p <0.05	Significant		

HT=Hypertensive Patients, CVD= Cardiovascular Disease Patients, HC= Healthy Controls



HT=Hypertensive Patients, CVD= Cardiovascular Disease Patients, HC= Healthy Controls

Fig 4.4 Sodium- Potassium ratio in HT, CVD and HC

Sodium Potassium ratio was found to be significantly higher ($p < 0.05$) in hypertensive (50.19) and cardiovascular disease patients (49.28) as compared to healthy controls (32.67). Thus present study supported that high sodium/potassium ratio is a strong indicator of increased risk of hypertension and cardiovascular diseases than levels of either sodium or potassium alone (Hooper *et al.*, 2002). The sodium-potassium balance influences blood pressure levels. The relative imbalance of this ratio is positively correlated with hypertension and heart disease (Androque and Madias, 2007). A fall in sodium consumption and increase in potassium consumption are useful in preventing and treating arterial hypertension (Karppanen, 1991).



SUMMARY AND CONCLUSIONS

5. SUMMARY AND CONCLUSIONS

High blood pressure or hypertension is a disease of the modern age. Hypertension is a major risk factor for stroke, myocardial infarction (heart attacks), heart failure, peripheral arterial disease and is a cause of chronic kidney disease. Even moderate elevation of arterial blood pressure is associated with a shortened life expectancy. Hypertension is the number one preventable risk factor for stroke, and significantly increases the risk for all cardiovascular disease outcomes including coronary artery disease and congestive heart failure. Sodium and potassium are essential dietary minerals and electrolytes. Normal body functioning depends on the right regulation of sodium and potassium both inside and outside of cells. Humans are prone to sodium overload and potassium depletion. This electrolyte imbalance is important in the pathogenesis of cardiovascular disease and sudden cardiac death. Sodium is the dominant environmental factor in the pathogenesis of primary hypertension and its associated cardiovascular risk. High sodium (salt) intake leads to hypertension and also increases the risk of heart disease. Potassium deficiency leads to high blood pressure problem. Serum sodium and potassium concentration determines the risk of hypertension and cardiovascular disease.

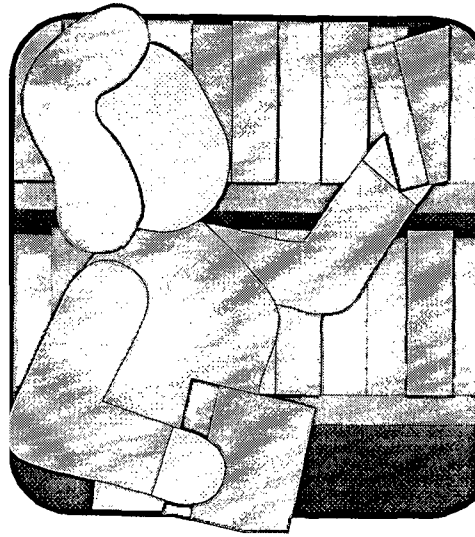
The present study “**Association of Sodium and Potassium Concentrations with Cardiovascular Diseases and Hypertension**” was carried out in the Department of Biology and Environmental Sciences during the year 2011-2012 with the following objectives:

1. To determine serum sodium and potassium concentration in normal and hypertensive patients.
2. To correlate variations in the concentrations of sodium and potassium with hypertension and cardiovascular diseases.
- The data related to patients with hypertension and cardiovascular diseases were collected from hospitals and clinics in the Palampur region. All subjects were referred from the same geographic area and two sets were established: Group 1 included determination of sodium and potassium in healthy controls and patients with hypertension. Group 2 included the determination of sodium and potassium in healthy control group and patients with cardiovascular diseases.

- Serum sodium and potassium concentration determination was done with Atomic absorption Spectrophotometer PERKIN ELMER AANALYST 400 and Systronics Flame Photometer 129. Serum was collected after allowing the blood to clot at room temperature and the clot was then removed by centrifuging at 1000-2000 X g. The serum samples of hypertension, heart disease patients and healthy controls were analyzed by Atomic absorption spectrophotometer/flame photometric method for sodium and potassium. Emission wavelength of sodium and potassium is 589 nm and 766 nm respectively and sodium gives yellow flame color and potassium gives violet flame color.
- Different analytical techniques of statistics like mean, standard deviations, standard error, and test of significance were used to evaluate the significant difference in serum concentrations of sodium and potassium in patients with hypertension, cardiovascular diseases and healthy controls.
- The results showed significant association between serum sodium and hypertension and cardiovascular diseases. Mean serum sodium of hypertension (155.6 ± 0.943 mEq/ L) and cardiovascular disease patients (157.7 ± 1.086 mEq/L) showed significant variation ($p < 0.05$) as compared to healthy controls (137.2 ± 0.462 mEq/L). Serum sodium concentration was found to be much higher in patients of hypertension and cardiovascular diseases. Mean serum potassium of hypertension (3.1 ± 0.09 mEq/L) and cardiovascular disease patients (3.2 ± 0.08 mEq/L) also showed significant variation as compared to healthy controls (4.2 ± 0.09 mEq/L).
- Mean serum sodium and potassium concentration showed variation ($p < 0.05$) with age and sex. Significant difference in serum sodium and potassium were found between hypertensive male and female patients of different age groups. Serum sodium concentration was found to be higher in males as compared to females of same age group, In all groups, men have higher serum sodium as compared with women, indicated that men are less aware and receive less treatment for hypertension compared with women. Mean serum potassium also showed significant variation ($p < 0.05$) between hypertensive males and females of different age groups. Serum sodium and potassium concentration also varied with

age and sex in cardiovascular disease patients. Serum sodium was found to be higher in older patients whereas serum potassium concentration was found to be low in them.

Thus, in the present study the role of serum sodium and potassium was investigated in the development of Hypertension and Cardiovascular diseases and it was proved that both play very important role in the pathogenesis of the two diseases. It was also observed that age is also an important factor in the development of Hypertension and cardiovascular disease and these diseases also show variation with sex. The present study also depicted that sodium-potassium balance influences blood pressure levels. The relative imbalance of this ratio is positively correlated with hypertension and heart disease. Thus, serum electrolytes (sodium and potassium) assessment in blood serum can be used for monitoring patients suffering from hypertension and at increased risk of cardiovascular diseases.



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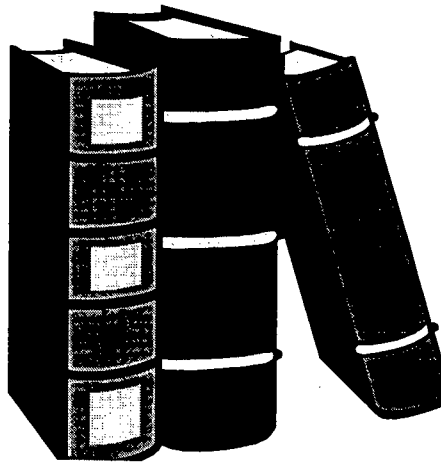
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APPENDICES

APPENDIX I

GROUP OF SUBJECTS	NORMOTENSIVE		HYPERTENSIVE	
	Number of subjects	Mean serum sodium(mEq/L)	Number of patients	Mean serum sodium(mEq/L)
Men under 40 years of age	19	138.6 $\pm$ 0.466	9	156.1 $\pm$ 0.901
Women under 40 age	9	138.8 $\pm$ 0.401	4	146.8 $\pm$ 0.551
Men 40-49 years of age group	4	139.8 $\pm$ 0.586	10	159.8 $\pm$ 0.731
Women 40-49 years	7	135.2 $\pm$ 0.576	6	155.7 $\pm$ 1.209
Men over 49 years of age	5	141.2 $\pm$ 0.635	13	164.1 $\pm$ 1.023
Women over 49 years of age	6	137.8 $\pm$ 0.342	8	161.2 $\pm$ 0.594
p <0.05	Significant			

Serum Sodium Concentration in Normotensives and Hypertensives on the Basis of Age and Sex

APPENDIX II

GROUP OF SUBJECTS	NORMOTENSIVE		HYPERTENSIVE	
	Number of subjects	Mean serum potassium(mEq/L)	Number of patients	Mean serum potassium(mEq/L)
Men under 40 years of age	19	3.8 ± 0.089	9	3.2 ± 0.096
Women under 40 years of age	9	4.8 ± 0.101	4	3.3 ± 0.097
Men 40-49 years of age group	4	4.2 ± 0.062	10	2.8 ± 0.075
Women 40-49 years of age	7	3.9 ± 0.093	6	3.1 ± 0.088
Men over 49 years of age	5	4.5 ± 0.054	13	3.1 ± 0.091
Women over 49 years of age	6	4.1 ± 0.063	8	3.6 ± 0.097
p < 0.05	Significant			

Serum Potassium Concentration in Normotensives and Hypertensives on the Basis of Age and Sex

APPENDIX III

GROUP OF SUBJECTS	HEALTHY CONTROLS		CARDIOVASCULAR DISEASE PATIENTS	
	Number of subjects	Mean serum sodium(mEq/L)	Number of patients	Mean serum sodium(mEq/L)
Men under 40 years of age	19	138.6 ± 0.466	9	152.3 ± 0.540
Women under 40 years of age	9	138.8 ± 0.401	10	156.5 ± 0.698
Men 40-49 years of age group	4	139.8 ± 0.586	7	$154.2 \pm 1.07^*$
Women 40-49 years of age group	7	135.2 ± 0.576	8	$157.2 \pm 1.58^*$
Men over 49 years of age	5	141.2 ± 0.635	10	164.3 ± 0.927
Women over 49 years of age	6	137.8 ± 0.342	6	161.2 ± 1.07

*= significant ($p < 0.05$)

Serum Sodium Concentration in Healthy Controls and Cardiovascular Disease Patients on the Basis of Age and Sex

APPENDIX IV

GROUP OF SUBJECTS	HEALTHY CONTROLS		CARDIOVASCULAR DISEASE PATIENTS	
	Number of subjects	Mean serum Potassium (mEq/L)	Number of patients	Mean serum Potassium (mEq/L)
Men under 40 years of age	19	3.8 ± 0.089	9	$3.41 \pm 0.10^*$
Women under 40 years of age	4	4.8 ± 0.101	10	$3.14 \pm 0.059^*$
Men 40-49 years of age group	5	4.2 ± 0.062	7	3.21 ± 0.06
Women 40-49 years of age group	9	3.9 ± 0.093	8	3.91 ± 0.11
Men over 49 years of age	7	4.5 ± 0.054	10	$3.07 \pm 0.058^*$
Women over 49 years of age	6	4.1 ± 0.063	6	$2.93 \pm 0.084^*$

*= significant ($p < 0.05$)

Serum Potassium Concentration in Healthy Controls and Cardiovascular Disease Patients on the Basis of Age and Sex

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CLASS	SCHOOL/UNIV	YEAR OF PASSING	BOARD	PERCENTAGE	DIVISION
10 th	K.V NO 1 FEROZEPUR CANTT	2004	C.B.S.E	65.00%	1 st
12 th	K.V NO 1 FEROZEPUR CANTT	2006	C.B.SE	74.00%	1 st
B.Sc	G.G.D.S.D COLLEGE RAJPUR	2009	H.P.U	74.40%	1 st
B.Ed	K.L.B.D.A.V COLLEGE	2010	H.P.U	70.81%	1 st
M.Sc BIOLOGY	CSKHPKV PALAMPUR	2012	H.P.U	75.70%	1 st