Evaluation of the relationship between serum lipid profile and blood pressure in hypertensive patients

Thesis Submitted to Vidyasagar University for the Partial Fulfillment of the Degree of Bachelor of Medical Laboratory Technology (BMLT)

Submitted by

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Declaration

I do hereby declare that the present Master thesis entitled **"Evaluation of the relationship between serum lipid profile and blood pressure in hypertensive patients"** embodies the original research work carried out by me in the Department of Biological Sciences, Midnapore City College, Paschim Medinipur, West Bengal, India under the supervision of Mr. Surya Kanta Dey, Assistant Professor, Department of Paramedical & Allied Health Sciences, Midnapore City College. Whenever I have used materials (data, theoretical analysis, and text) from other sources, I have given due credit to them by citing them in the text of the thesis and giving their details in the references. I have followed the guidelines provided by the Institute in writing the thesis. I further declare that the results of this work have not been previously submitted for any other degree or Diploma or fellowship.

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Dedicated to my Parents and Teachers

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ABSTRACT

Arterial hypertension and dyslipidemia are two of the most prevalent cardiovascular risk factors in the general population and their relationship has become a central focus for cardiovascular disease prevention. The objectives of this study were to evaluate the differences of lipid profile, blood pressure (BP) profile and the influence of risk factors in a group of patients with essential arterial hypertension. A total of 148 human volunteers aged between 30–70 years of either sex, visiting different hospitals and clinics of were included in the study. They were considered hypertensive if systolic blood pressure was ≥140 mm Hg or diastolic blood pressure was ≥ 90 mm Hg or the subjects were currently using antihypertensive medication. The results showed that the mean systolic blood pressure (SBP) of hypertensive males and females were 147.56 ± 20.62 and 142.96 ± 19.01 mm of Hg and mean diastolic blood pressure (DBP) was 93.1 ± 10.52 and 92.85 ± 12.51 mm of Hg respectively. Among Hypertensives, 37.23% of male and 22.22% of female were in the 2nd stage of Hypertension. Our result also suggested that the mean Systolic blood pressure in male was significantly higher than female. This may be due to change in lifestyle and diet. On the other hand, the value of TC and LDL were increased significantly in female than male. In conclusion, dyslipidemia is associated with hypertension and hypertensive patients need measurement of blood pressure and lipid profile at regular intervals to prevent cardiovascular diseases.

Keywords: Lipid Profile, Hypertension, Cholesterol, LDA, HDL, Triglyceride

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Chapter 1: Introduction

INTRODUCTION

Globally, hypertension has become one of the major health problems and a most common risk factor for cardio-vascular disease (CVD) (Kearney et al., 2005). The prevalence of hypertension is increasing day by day worldwide, especially in the developing countries, due to rapid urbanization, unhealthy diet, and lifestyle changes have lead to an increased rate of CVD in Southeast Asia, including India (Joshi et al., 2007). According to World Health Organization (WHO) report, India by 2020 CVDs will be the largest cause of disability and death. Around 2.6 million people in India are predicted to die due to coronary heart diseases by 2020 (Butola et al., 2016).

Hypertension and dyslipidemia are associated with oxidative stress and are major causes of cardiovascular disease amounting to 30% of global death rate (Reza et al., 2014). It is widely accepted that cardiovascular disease is associated with hypertension and increased blood levels of low-density lipoprotein (LDL), total cholesterol (TC), and triglycerides. In contrast, a low level of high density lipoprotein (HDL) is a risk factor for mortality from cardiovascular disease (Criqui et al., 1993). The blood pressure however, is not the only determinant of cardiovascular damage and the propensity of hypertensive patients to develop target organ damage is markedly influenced by coexisting risk factors such as age, sex, smoking, obesity, diabetes, dyslipidemia and others. Among these factors lipoproteins are fundamental to the atherosclerotic process and greatly affect the impact of hypertension on development of target organ damage and therefore on cardiovascular morbidity and mortality (Srinivaspai et al., 2014).

History of hypertension

The modern history of hypertension begins with the understanding of the cardiovascular system with the work of physician William Harvey (1578–1657), who described the circulation of blood in his book "De motu cordis". The English clergyman Stephen Hales made the first published measurement of blood pressure in 1733. (Haynes, 1998) Descriptions of hypertension as a disease came among others from Thomas Young in 1808 and especially Richard Bright in 1836. The first report of elevated blood pressure in a person without evidence of kidney disease was made by Frederick Akbar Mahomed (1849–1884).

The concept of essential hypertension ('hypertonie essential') was introduced in 1925 by the physiologist Otto Frank to describe elevated blood pressure for which no cause could be found.

In 1928, the term malignant hypertension was coined by physicians from the Mayo Clinic to describe a syndrome of very high blood pressure, severe retinopathy and adequate kidney function which usually resulted in death within a year from strokes, heart failure or kidney failure (Franklin et al., 199). Consequently, hypertension was often classified into "malignant" and "benign". In 1931, John Hay, Professor of Medicine at Liverpool University, wrote that "there is some truth in the saying that the greatest danger to a man with a high blood pressure lies in its discovery, because then some fool is certain to try and reduce it" (Hansson et al., 1998).

Hypertension is defined as an abnormal elevation in diastolic pressure and/or systolic pressure; mean arterial pressure is also elevated in hypertension, but it is not usually measured in people. In past years, the diastolic value was emphasized in assessing hypertension. However, elevations in systolic pressure ("systolic hypertension") are also associated with increased incidence of coronary and cerebrovascular disease (e.g., stroke). Therefore, we now recognize that both systolic and diastolic pressure values are important to note. According to the latest U.S. national guideline (Hemmelgarn et al., 2006). the following represents different stages of hypertension:

Classification	Systolic (mmHg)	Diastolic (mmHg)
Normal	<120	<80
Prehypertension	120-139	80-89
Stage 1	140-159	90-99
Stage 2	>160	

Symptoms of high blood pressure

Although patients with isolated hypertension are usually asymptomatic, occasionally they have symptoms such as Dizziness, Headache (especially pulsating headaches behind the eyes that occur early in the morning), Blurred vision, Facial flushing or tinnitus (ringing sound in the ears). Hypertension which is very severe with a systolic blood pressure (SBP) >240 mmHg or diastolic blood pressure (DBP) >120 mmHg is called accelerated hypertension. Accelerated hypertension is associated with confusion, visual disturbances, nausea and vomiting. When hypertension causes increased intracranial pressure (pressure exerted by the cranium on the brain tissue and brain fluid), it is called malignant hypertension or hypertensive crisis and is a medical emergency that requires immediate reduction of the blood pressure (Galie et al., 2004).

Types of high blood pressure

There are two main types of high blood pressure:

Essential (primary) hypertension

- The main form of high blood pressure – accounts for around 90–95% of cases
- Has no single identifiable cause
- Potential causes include genetic and environmental factor

Secondary hypertension

- Rare forms of high blood pressure
- Caused by another medical condition or treatment
- Causes include kidney problems (renovascular hypertension), adrenal gland tumors, thyroid disease, and narrowing of the aorta (the main artery that takes blood from the heart to the rest of the body)
- Isolated systolic hypertension – the systolic pressure (top number) is raised but the diastolic pressure is normal
- Isolated diastolic hypertension – the diastolic pressure (bottom number) is raised but the systolic pressure is normal
- White coat hypertension – where the blood pressure is raised due to the stress of a visit to the doctor or nurse

Pathophysiology

Hypertension is a chronic elevation of blood pressure that, in the long-term, causes end-organ damage and results in increased morbidity and mortality (Hemmelgarn et al., 2006). Blood pressure is the product of cardiac output and systemic vascular resistance vascular tone may be elevated because of increased α-adrenoceptor stimulation or increased release of peptides such as Angitension or endothelins. The final pathway is an increase in cytosolic calcium in vascular smooth muscle causing vasoconstriction. Several growth factors, including Angitension and endothelins, because an increase in vascular smooth muscle mass termed vascular remodeling (Daskalopoulou et al., 2015). with ageing, stiffening of the aorta and elastic arteries increases the pulse pressure. The autonomic nervous system plays an important role in the control of blood pressure. In hypertensive patients, both increased release of, and enhanced peripheral sensitivity to, norepinephrine can be found. In addition, there is increased responsiveness to stressful stimuli. Another feature of arterial hypertension is a resetting of the baroreflexes and

decreased baroreceptor sensitivity. The renin–angiotensin system is involved at least in some forms of hypertension (e.g. renovascular hypertension) and is suppressed in the presence of primary hyperaldosteronism. Elderly or black patients tend to have low-renin hypertension

Relationship between lipid profile and blood pressure

Elevated blood pressure (BP) values represent the primary world-wide factors that contribute to premature death and increase in disability-adjusted life years (Forouzanfar et al., 2017). Monitoring of office BP and out-of-office BP have been proven to be correlated with the incidence of important cardiovascular diseases (CVD) (hemorrhagic stroke, ischemic stroke, myocardial infarction, sudden death, heart failure, and peripheral artery disease), as well as end-stage renal disease (Chobanian et al., 2003). Furthermore, there is increasingly more evidence that links hypertension with an increasing risk of developing atrial fibrillation, cognitive decline and dementia (Mayr et al., 2010).

Hypercholesterolemia in humans usually involves an elevation in the plasma concentration of low-density lipoprotein cholesterol (LDL-C) and/or its defective clearance (Checovich et al., 1988). The levels of serum triglycerides and LDL-C as weight increases but the high-density lipoprotein cholesterol (HDL-C) falls, thus amplifying the LDL-C/HDL-C ratio (4). Obesity has been accepted as an established risk factor for higher systolic and diastolic blood pressures. Sowers has shown that obesity, dyslipidaemia and hypertension are interrelated medical problems associated with an increased risk of cardiovascular diseases. Obesity markedly enhances the cardiovascular risk associated with other risk factors, such as hypertension (Berkey et al., 1988).

Chapter 2: Review of Literature

REVIEW AND LITERATURE

Cardiovascular diseases are the highest cause of death in the industrialized world, and many of these deaths may be work related. Hypertension is the most common of the cardio-vascular diseases which is the leading cause of morbidity and mortality in the industrial world. Stress, tension, smoking, liquors, insufficient rest, metabolic disorders, excessive consumption of tea or coffee, emotional disturbance etc. are also associated with high blood pressure. Several previous studies showed the relation between hyperlipidemia and hypertension. An excessive daily intake of saturated fats, cholesterol, and other sources of calories and subsequent disturbance of lipid profile leading to hypertriglyceridemia and hypercholesterolemia are associated with obesity and, consequently, hypertension (Srivastava et al., 2016). Although dyslipidemia and hypertension occur together more often than can be explained by chance, few studies have carefully explored the nature of the relationship between plasma lipid levels and the risk of developing hypertension. A prospective study was conducted of 16130 middle-aged and older female health professionals in 1992 who provided baseline blood samples and had no history of high cholesterol level (no treatment or diagnosis) or hypertension (no treatment, diagnosis, or elevated blood pressure). Study found that in this large prospective cohort, atherogenic dyslipidemias were associated with the subsequent development of hypertension among healthy women (Sesso et al., 2005). A study was conducted to determine relationship of obesity with the blood pressure patterns and lipid parameters in preview of its unique local diet patterns. A total of 200 non-diabetic human subjects of either sex were included in the study. They were categorized on the basis of body mass index (BMI) as obese and non-obese. This study found out that the mean BMI was higher in subjects consuming saturated fats as compared to those using unsaturated the means SBP and DBP were also higher in subjects consuming saturated fats. Mean LDL-C showed a higher value for individuals using saturated fats than those consuming unsaturated ones but the difference was non-significant. Same was true for HDL-C, TC and TG (Akhtar et al., 2006).

A cross-sectional study was carried out among 234 participants including 159 hypertensive patients and 75 normotensive controls from January to December 2012 in the National Centre for Control of Rheumatic Fever and Heart Disease in Dhaka, Bangladesh. The study suggested that hypertensive patients in Bangladesh have a close association with dyslipidemia and need

measurement of blood pressure and lipid profile at regular intervals to prevent cardiovascular disease, stroke, and other comorbidities (Choudhury et al., 2014). Hypertension and dyslipidemia are associated with oxidative stress and are major causes of cardiovascular disease. A study was conducted to assess of Serum Lipid Profile among Hypertensive patients in Uttarakhand. Among 150 hypertensive patients (106 males and 44 females), maximum hypertensives 79 (52.7%) were in the age group of 50 to 70 years and 132 (88.0%) of them were in the 2nd stage of Hypertension. Serum levels of total cholesterol, triglyceride, HDL-C and LDL-C in hypertensive subjects were 190.50±32.84, 225.94±86.72, 40.10±4.23 and 43.05±9.50 mg/dL respectively. The study concluded that dyslipidemia is associated with hypertension and hypertensive patients need measurement of blood pressure and lipid profile at regular intervals to prevent cardiovascular diseases (Butola et al., 2016).

A recent study was Evaluated the lipid profiles and hematological parameters in hypertensive patients. Laboratory-based cross-sectional study was conducted in 100 eligible hypertensive patients at the hospital. The mean serum levels of triglyceride, total cholesterol, and low-density lipoprotein were significantly higher than their respective cut-off values in the hypertensive patients. Besides, 54%, 52%, 35%, and 11% of the hypertensive patients had abnormal low-density lipoprotein, total cholesterol, triglyceride, and high-density lipoprotein levels, respectively. Higher levels of low-density lipoprotein, hemoglobin, and red blood cell count were observed in the hypertensive patients whose blood pressure had been poorly controlled than the controlled ones. The study highlighted that hypertensive patients had a high prevalence of lipid profile abnormalities and poorly controlled blood pressure which synergize in accelerating other cardiovascular diseases (Gebrie et al., 2018). Relationship between lipid profile and blood pressure in hypertensive patients was established by Haba et al., 2019. They studied the cardiovascular risk factor profile, with specific accent on the lipid parameters, left ventricular mass index (LVMI) and the values of systolic and diastolic BP (SBP, DBP) at hospital admission and discharge in non-acute setting. The results showed that admission BP was better correlated with hypercholesterolemia than BP at discharge, especially total cholesterol and HDL. All lipid markers were increased in patients with higher grades of arterial hypertension, total cholesterol having the best statistical significance (149.38 ± 40.04 – grade 1 vs. 197.29 ± 54.75 – grade 2 vs. 187.88 ± 44.29 mg/dl – grade 3, p=0.015). However, LVMI was not significantly different according to BP grade and did not correlate with lipid markers.

Chapter 3: Aim and Objectives

AIMS AND OBJECTIVE

The present study was aimed to assess the Serum lipid profile in hypertensive patients and find out its relation between Serum lipid profile and hypertension.

The objectives of the study are

1. To assess the serum lipid profile of hypertensive patients.
2. To find out the correlation between Serum lipid profile and hypertension.

Chapter 4: Materials and Methods

MATERIALS AND METHODS

A total of 148 human volunteers aged between 30–70 years of either sex, visiting different hospitals and clinics of were included in the study.

Inclusion criteria

They were considered hypertensive if systolic blood pressure was ≥140 mm Hg or diastolic blood pressure was ≥ 90 mm Hg or the subjects were currently using antihypertensive medication.

Exclusion criteria

acute onset of CVD, other acute medical problems or secondary hypertension.

Type 2 diabetes between, chronic kidney disease (CKD), Cancer or other diseases

Blood pressure measurement

Blood pressure was measured after the subject had rested for at least 5 minutes from right arm placed at the heart level by a physician. Two measurements were taken by a mercury sphygmomanometer with at least 5 minutes between successive measurements. The mean of two measurements of Korotkoff phase I was recorded for systolic blood pressure (SBP). The mean of two values of korotkoff phase IV was recorded for diastolic pressure (DBP). Hypertension was classified according to JNC-8 Criteria: (Dipiro et al., 2014).

Hypertension	Systolic BP (mm of Hg)		Diastolic BP (mm of Hg)
Stage 1	140 -159	or	90 -99
Stage 2	≥160	or	≥100

Biochemical analysis

Venous blood was collected in the morning after an overnight fast and serum was used for the biochemical tests. Lipid parameters (TC, TG, LDL-C and HDL-C) were estimated by enzymatic colorimetric test (Williams et al., 2018). Hypercholesterolemia was defined as fasting total serum cholesterol and triglyceride of greater than or equal to 200mg/dl and 150 respectively. Blood concentration of LDL (low-density lipoprotein cholesterol) equal or above

150mg/dl and blood concentration of HDL (high-density lipoprotein cholesterol) under 40mg/dl respectively, were considered to be undesirable.

Statistical analysis

The statistical significance and multigroup comparisons of the data were analyzed by using one and one-way analysis of variance (ANOVA), followed by a Tukey post hoc test using Origins 8 (OriginLab, Northampton,USA). Data are presented as means ± standard deviation (SD). Statistical significance was considered at $p < 0.05$.

Chapter 5: Results

RESULTS

In the present study, out of 148 hypertensive patients, 94 were males and 54 females. Maximum Hypertensives patients were found in the age group of 50 to 70 years (Table 1).

Table 1: Age group wise distribution of hypertensive patients

Age Group (Years)	Male (%)	Female (%)
30-50	43.07	42.5
50-70	78.57	66.66

The mean systolic blood pressure (SBP) of hypertensive males and females were 147.56 ± 20.62 and 142.96 ± 19.01 mm of Hg and mean diastolic blood pressure (DBP) was 93.1 ± 10.52 and 92.85 ± 12.51 mm of Hg respectively (Table 2). Among Hypertensives, 37.23% of male and 22.22% of female were in the 2nd stage of Hypertension as shown in Table 3.

Table 2: Blood Pressure Distribution of Hypertensive Patients.

Category	Male (n=94)		Female (n=54)	
	Mean (mm Hg)	± SD	Mean (mm Hg)	± SD
Systolic BP	147.56	20.62	142.96	19.01
Diastolic BP	93.1	10.52	92.85	12.51

Table 3: Distribution of Patients according to Hypertension Stages.

Hypertension	Male % (n=94)	Female % (n=54)
Stage 1	18.08	31.48
Stage 2	37.23	22.22

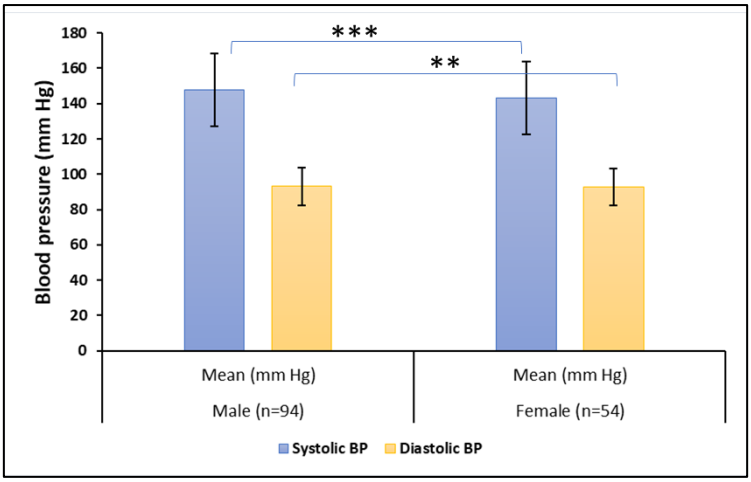

Figure 1. Representation of SBP and DBP in male and female

Analysis of lipid profile

Serum levels of total cholesterol (TC), triglyceride (TG), LDL and HDL in hypertensive male subject were 210.85 ± 45. 190.7± 79.46, 128.17± 42.22 and 49.03± 10.44 mg/dL respectively while in female hypertensives the results were 216.48 ± 49.38, 160.38 ± 70.1, 136.61 ± 39.26 and 51.04 ± 8.75 mg/dL respectively. (Table 4)

In normotensive subjects (Control), TC, TG, LDL and HDL were found 171±6.2, 127±11.2, and 110.3±6.3 and 38.55±6.28 mg/dL, respectively in male and 179.06±7.38, 133.8±14.02, 120.18±8.06 and 41.08±7.11 mg/dL.

Table 4: Lipid Profile of Hypertensive Patients according to Sex.

Lipid Profile	Male (n=94)		Female (n=54)	
	Mean (mg/dL)	± SD	Mean (mg/dL)	± SD
TC	210.85	45.64	216.48	49.38
TG	190.7	79.46	160.38	70.1
LDL	128.17	42.22	136.61	39.26
HDL	49.03	10.44	51.04	8.75

Table 5. Relationship between total cholesterol and SBP, respectively DBP in male and female.

Systolic BP (mm Hg)	Male (n=94)		Female (n=54)	
	r value	P value	r value	P value
TC (mg/dL)	+ 0.23035	≤ 0.026	+ 0.07185	≤ 0.605

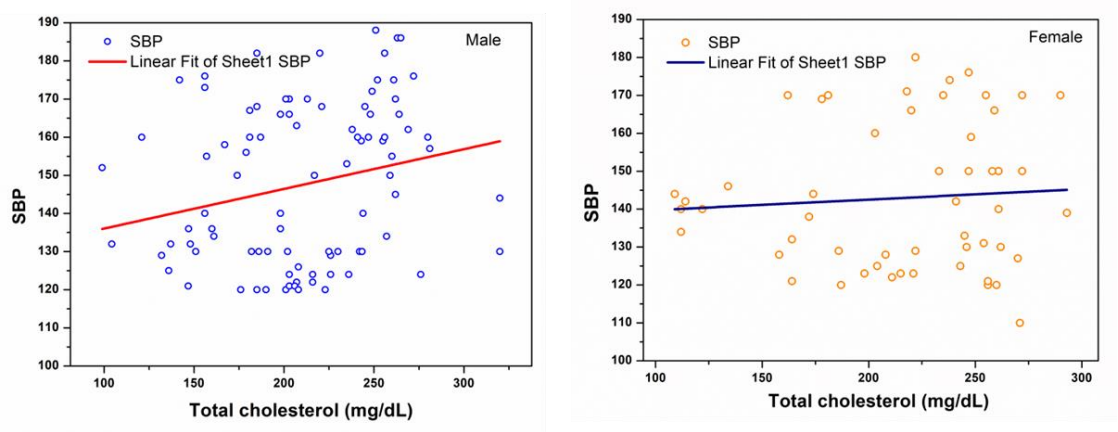

Figure 2. Relationship between total cholesterol and SBP, respectively DBP in male and female

Correlation between SBP and TC in both sexes was evaluated. Results showed a strong positive correlation between SBP and TC was found in male than female with r value was + 0.23035 in male and + 0.07185 in female respectively.

Chapter 6: Discussion

DISCUSSION

This study provides evidence that baseline levels of lipids, particularly total cholesterol and HDL, are associated with increased levels of arterial hypertension, expressed by higher values of BP or the grade of arterial hypertension. Though there is a lot of research over this topic, the precise biological mechanism by which lipids may give rise to elevations in BP still present some evidence gaps. Genetic and cross-sectional studies suggested a connection between dyslipidemia and hypertension. Hypertensive individuals have a higher prevalence of dyslipidemia and 12% of subjects with early-onset hypertension have an increased frequency of lipid disorders (Saquib et al., 2012). At first, smooth muscle cell hypertrophy and collagen deposition come as a consequence to high cholesterol levels leading to arterial stiffness translated to elevated systolic BP (Anjum et al., 2013).

In addition, dyslipidemia leads to endothelial dysfunction and improper vasoregulation, as nitric oxide production release and subsequent activity being reduced among those with high total cholesterol and low HDL levels. Furthermore, dyslipidemia has been associated with increased circulating levels of endothelin-1 which inturn has been linked with hypertension [9]. In addition, dyslipidemia may cause damage to the renal microvasculature with the downstream effect of hypertension (Karthikeyan et al., 2009). Castelli et al from the Framingham study shows that patients with high blood pressure have high values of cholesterol. More than half of men and women in the study had abnormal lipid profile. Utpal kumar et al found that total cholesterol, triglycerides and VLDL are increased in hypertension patients compard to healthy controls. The lipid levels in smokers with hypertension is compared to non-smokers with hypertension. In smokers the values of total cholesterol and LDL are high which is statistically very significant. The LDL to HDL ratio and total cholesterol to HDL ratio is also high in smokers with hypertension which is statistically very significant. The HDL, triglycerides and VLDL are not statistically significant (Schaeffner et al., 2003).

These results are consistent to the findings of our study, which reported a more significant correlation between HDL levels and the BP values. However, the severity of the disease expressed by the hypertension grade correlated only with the total cholesterol levels, as high cholesterol levels were more frequent in patients with satge2 hypertension. (Nohria et al., 2003). Furthermore, a recent study showed that high levels of oxidized LDL are strongly correlated

with increases in decanoyl carnitine and lysoPC (C14:0) which are relevant metabolites for predicting the risk of developing diabetes. Our result suggested that the mean Systolic blood pressure in male was significantly higher than female. This may be due to change in lifestyle and diet. On the other hand, the value of TC and LDL were increased significantly in female than male. Correlation between SBP and TC in both sexes was evaluated. Results showed a strong positive correlation between SBP and TC was found in male than female with r value was + 0.23035 in male and + 0.07185 in female respectively. This may be due to repeated pregnancies resulting in fat deposition leading to higher levels of cholesterol and triglycerides in females. Also, females included in the study were mostly housewives doing less physical work. The limitation of this study was small sample size and the control group was selected purposively, not age and sex matched. In addition, we could not compare the effects of lipid profile variation due to diet, physical activity, medication, or other factors.

Chapter 7: Conclusion

CONCLUSION

The results of this study demonstrate that patients with hypertension are more likely than normotensive patients to exhibit dyslipidemia, including elevated TC, LDL, TG, and reduced HDL cholesterol levels. Our results suggest that elevated BP may predict certain disturbances in lipoprotein metabolism. This association will help to develop future strategies for preventing both hypertension and dyslipidemia through proper lifestyle changes or medical management or by the combination of both. Hypertensive patients need measurement of BP and lipid profile at regular intervals throughout their primary health care to prevent CVD and stroke.

Chapter 8: Future scope

FUTURE SCOPE

This study did not consider confounders such as insulin resistance, endothelial disfunction, previous statin treatment or other relevant biological pathways that may affect lipid and BP levels. On the basis of this preliminary study, the future scope of this study should be evaluated as follows

- As we found a strong relationship between hypertension and high cholesterol, an extensive study should be constructed to find out the interrelationship between life style and diet of hypertensive patients with their lipid profile.
- Need to establish the root cause of increased cholesterol in hypertensive patients and lower the risk of heart disease.

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