PREVALENCE OF DYSLIPIDEMIC HYPERTENSION IN A SUBSET OF KASHMIRI (NORTH INDIA) POPULATION

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ABSTRACT

Worldwide studies conducted on different populations have suggested a positive association between dyslipidemia and hypertension, with significant proportion of populations suffering from both ie dyslipidemic hypertension, most often possible mechanism being insulin resistance and endothelial dysfunctioning. The present study aimed to determine prevalence of dyslipidemic hypertension and to establish, if any, relationship between blood pressure and serum lipid levels across the range of blood pressure categories including prehypertension in a subset of Kashmiri population. A total of 100 patients and 50 control subjects from Kashmiri population were included in the present study. The level of TG and total cholesterol, LDL, HDL and VLDL in serum samples was estimated by enzymatic colorometric method on Hitachi 912 (Boehringer Mannheim system). Statistical analysis was carried out by students “t” test using ANOVA software and the results were considered statistically significance when p value ≤0.05. In our study overall 14.4% of total kashmiri population (i.e.72% of hypertensive kashmiri population) suffer from dyslipidemic hypertension. Significantly elevated total levels of serum TG (204.9mg/dl Vs 139.2mg/dl (p=000), total Cholesterol (175.1mg/dl Vs 147.2 mg/dl) (p=0.002), VLDL-cholesterol (41.0mg/dl Vs 28.9mg/dl) (p≤0.0001) LDL-cholesterol (181.3 mg/dl Vs 130.0 mg/dl) (p≤0.0001) and decreased level of HDL-cholesterol (34.8mg/dl Vs 46.1 mg/dl) (p≤0.0001) were found in hypertensive’s when compared with normotensive’s. Within lipid profile, greater percentage of hypertensive’s compared to normotensives show elevated levels of TG (51% Vs 18%) followed by cholesterol (49%Vs 21%) or LDL cholesterol(45% Vs 22%). Low HDL was also found in 44% of hypertensives compared to only 12% in normotensive’s.
The findings of the present study show slight variations when compared with rest of the India but is in complete agreement with certain Muslim dominant areas with which we share common dietary habits and cultural practices. **Conclusion:** Our study reveals a positive association between blood pressure and dyslipidemia in Kashmiri population. 72% of the hypertensive in our population shows dyslipidemia too. Since the treatment of dyslipidemia and hypertension alone is different from the treatment of dyslipidemic hypertension which may involve reversal of insulin resistance. The findings of the present study, therefore, may provide a rationale for pharmacotherapy in a subset of hypertensive people with dyslipidemic hypertension.

**ABBREVIATION:** LDL=low density lipoproteins; HDL=high density lipoprotein; VLDL=very low density lipoprotein TG=Triglycerides.

**INTRODUCTION**

Hypertension is a common, asymptomatic, readily detectable usually easily treatable disease that leads to lethal complications if left untreated.\(^1\) A recent estimate suggests that world over approximately 1 billion adults have hypertension (333 million in economically developed and 639 million in economically developing countries).\(^2\) Hypertension is probably the most important public health problem in developed countries with over 50 million adults (29%) having hypertension (defined BP=140/90) in United States alone.\(^1,2\) The prevalence of hypertension in India ranges from 20-40% in urban adults and 12-17% among rural adults.\(^3\) Hypertension can be classified as essential (primary) (unknown medical cause) or secondary (such as Renal Artery Stenosis or tumors pheochromocytoma, paraganglioma).

Hypertension is a multifactorial trait that results from the net effect of environmental and genetic factors.\(^2\) Factors that may contribute to hypertension include excess dietary salt or alcohol intake, stress, aging, genetic susceptibility, physical inactivity, diet rich in saturated fats and family history. Dyslipidemia or disordered lipid profile characterized by elevated total cholesterol >200mg/dl, LDL Cholesterol >130mg/dl, TG >200mg/dl, Total cholesterol/HDL =4.5 and low HDL =<40mg/dl has been associated with hypertension.\(^4\) The interrelationship of elevated circulating triglycerides, low HDL cholesterol, central body fat distribution, diabetes mellitus, and hypertension is postulated to be explained by insulin resistance and grouped as Syndrome X.\(^5-7\) Insulin resistance by promoting fat utilization for energy increases fatty acid accumulation, causing dyslipidemia.\(^7,8\)
A growing body of evidences indicates a positive relation between disordered lipid profile, marked by increased lipid peroxides like malondialdehyde, and endothelial dysfunction [9]. Dysordered lipid profile has been also reported in pregnancy induced hypertension (PIH) with a prevalence of 15.2%. The finding that serum lipids increases during pregnancy with 2 fold further increase during pregnancy induced hypertension (PIH), suggests a positive association between dyslipidemia and hypertension.[9]

The relevance of persistent elevated hypertension and hyperlipidemia/dyslipidemia, especially in younger age group, in predicting cardiovascular risk is gaining increasing recognition and in that respect lipid profile has been the most intensively investigated in hypertensive patients in clinical studies.[8] The present study is a preliminary attempt to establish the prevalence of dyslipidimic hypertension (ie patient suffering from both hypertension and dyslipidemia) in the Kashmiri population which indirectly reflects the individuals or the proportion of our population that eventually are at risk of developing cardiovascular disease.

**MATERIALS AND METHODS**

Patients attending the Cardiology Clinic of Sher-i-Kashmir Institute of Medical Sciences (SKIMS) for the management of hypertension were recruited for this study with prior informed consent. The acceptance for the present work was taken from our Institutional (SKIMS) ethical committee and the procedures adopted in the study were in accordance with Helsinki Declaration (1964) of the World Medical Association. In total, 100 patients and 50 healthy control subjects with descriptive features given in Table 1 were included in the present study. Patients with stroke, and renal diseases were excluded from this study. The patients under study were grouped according to JNC 7 classification of hypertension (2003) as pre-hypertensive [defined BP=130-139/85-89mmHg], hypertensive stage I [defined BP=140-159/90-99 mmHg] and hypertensive Stage II [defined BP =160/>100mmHg].[10] The patients under study were grouped as Dyslipidemic whose lipid profile is characterized by either elevated total cholesterol>200mg/dl or LDL Cholesterol>130mg/dl or TG>200mg/dl or Total cholesterol/HDL =4.5 or lowHDL =<40mg/dl or combination of these parameters. The controls subjects under study were randomly selected age and sex matched healthy people from the Kashmir population that clinically were found devoid of hypertension or dyslipidemia or any other disease that affect these parameters.
Serum was separated from the blood samples drawn from patient and control subjects by centrifugation at 3000rpm, and stored frozen at -70°C until analysis. The level of TG and total cholesterol in serum samples was estimated by enzymatic colorometric method on Hitachi 912 (Boehringer Mannhum system). The assay for TG estimation is based on principle where complete enzymatic hydrolysis of TG by lipase produces glycerol, which in presence of ATP and enzyme glycerol kinase is converted to glycerol-3-phosphate which in presence of molecular O₂ and glycerol phosphate oxidase (GPO) is converted to H₂O₂. The H₂O₂ produced in presence of 4amino-phenazone and chlorophenol is converted to a chromogen (4-p-benzaquinone-mono iminophenazone) read at 700nm.[11] The calibration was carried out using quality control sera.

Total cholesterol in serum samples was estimated by enzymatic colorometric method on Hitachi 912 (Boehringer Mannhum system).[12] The assay involves enzymatic conversion of cholesterol esters and cholesterol in presence of molecular O₂ to the production of H₂O₂, which in presence of 4amino-phenazone and chlorophenol is converted to a chromogen (4-p-benzaquinone-mono iminophenazone) read at 700nm. The calibration was carried out using quality control sera.

The level of HDL cholesterol in serum samples was estimated by phosphotungstic acid and magnesium chloride method.[13] LDL cholesterol, VLDL and chyomicrons was precipitated from the serum using phosphotungstic acid and MgCl₂, leaving HDL in the supernatant. The HDL from the supernatant was estimated as total cholesterol estimation. The quality control was established using precilip EL and precinorm. The level of LDL and VLDL was calculated by Friedwalds formulae: LDL=TOTAL Cholesterol-[HDL+TG/5], where TG/5 represents cholesterol contained in VLDL.[14]

**Statistical Analysis**

The total serum lipid profile were expressed as mean ±SD. Standard unpaired students “T” test was used for comparison of lipid levels between prehypertensives, hypertenives and normotensive control subjects. Statistical analysis was carried out by ANOVA software and results were considered significant when p<0.05.

**RESULTS**

Total 80 hypertensive (42.5% M and 57.5%F) mean age group of 54.5±11.2yrs; 20 prehypertensive (50%M and 50% F) mean age group of 50.7 ±11.1yrs and 50 normotensive
mean age group of 50±10.8 years were included in the study (Table: 1). The mean total cholesterol, TG, LDL and HDL in hypertensive, prehypertensive and normotensive subjects is given in (Table 2). In our study 72% (72/16,00000x100=115200) of hypertensive’s show dislipidemic too characterized by either cholesterol >200mg/dl or LDL >100mg/dl or TG>150mg/dl or HDL <40mg/dl or combination of them compared to only 23.3% among normotensives. Assuming a prevalence of hypertension 20% in Kashmir (Northern India), with a total population of 80 lakhs, the present study reveals dyslipidemic hypertension in 72% of hypertensives (72/16,00000x100=115200) which amounts to overall 14.4% (115200/80,00000x100) of a subset of Kashmiri population.

The estimation of cholesterol level in 100 patients and 50 control subjects, revealed significantly high level of mean total cholesterol in hypertensives (175±40.6mg/L) compared to control subjects (147.2±61.9 mg/dl) (p<0.002) (Table 2). Also the total cholesterol mean was found higher, though not statistically significant, in prehypertensive subjects (166.9±57.8mg/dl) as compared to normotensive (147.2±61.9mg/dl) (p=0.147) subjects. The overall total cholesterol mean was significantly different between hypertensive, prehypertensive and normotensive (p=0.011) (Table 2). The serum cholesterol was >200mg/dl in 49% of hypertensives, 37% of prehypertensives as compared to only 21% of normotensive subjects, which is statistically significant (p=0.011).

Similarly statistically significant difference in levels of TG was found in hypertensive (204-9±125.1 mg/dl) (p<0.0001) when compared with normotensive subjects (139.2±62 mg/dl). But was found insignificant when compared between hypertensive (204.9±125.1) and prehypertensive (186.2±121mg/dl) (p=0.487) and between pre- hypertensive (186.2±121mg/dl) and normotensive subjects (139.2±62 mg/dl) (p=0.100). The overall mean total TG levels is significantly different in hypertensive, prehypertensives and normotensives (p=0.003). TG levels >200mg/dl was found in 51% of hypertensive’s, 39% of prehypertensives as compared to only 18% of normotensive subjects, which is again statistically significant (p=0.003).

The difference in mean total level of VLDL between hypertensive (41.0±25.1 mg/dl) and normotensive (28.9±14.8 mg/dl) was found significant (p=0.002). Difference in levels of VLDL, though not statistically significant, was also found between prehypertensive and normotensive subjects (p=0.154) and between hypertensive and prehypertensives (p=0.496).
The overall mean total VLDL level between hypertensive, prehypertensive and normotensive subjects is statistically significant (p=0.011).

Statistically significant difference was also found in mean total LDL level between hypertensives (181.3±62.4 mg/dl) and normotensives (130±74.2 mg/dl) (p=0.00) as well as between prehypertensive (169.8±80.3 mg/dl) and normotensives (130±74.2) (p=0.030). The overall mean total LDL levels between three group is statistically significant (p=0.000). Serum LDL was found >130mg/dl in 45% of hypertensives, in 31% of prehypertensives while as only 22% of normotensives had LDL>130mg/dl, which is statistically significant (p=0.00).

Statistically significant difference in levels of HDL was also found between hypertensive (34.8±8.4mg/dl) and normotensives (46.1±8.4 mg/dl) (p=0.000) as well as between prehypertensives (37.0±9.7 mg/dl) and normotensives (46.1±8.4 mg/dl) (p=0.000).The overall mean total HDL levels between three groups is statistically significant (p=0.000).

Low HDL level (<40mg/dl) was found in 44% of hypertensives, 29% of prehypertensives compared to only 12% of normotensives.

**Table 1: Descriptive characteristics of patients and control groups**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Hypertensive n=80</th>
<th>Prehypertensive n=20</th>
<th>Control n=50</th>
<th>t</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>34 (42.5%)</td>
<td>10 (50%)</td>
<td>26 (52%)</td>
<td></td>
<td>0.544(NS)</td>
</tr>
<tr>
<td>Female</td>
<td>46 (57.5%)</td>
<td>10 (50%)</td>
<td>24 (48%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age in Years Mean ±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤35</td>
<td>54.5±11.2</td>
<td>50.7±11.1</td>
<td>50±10.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;35</td>
<td>17(%)</td>
<td>7</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>63(%)</td>
<td>13</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SBP (mmHg) Mean ±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>143.3±10.15</td>
<td>132±8.15</td>
<td>118.41±5.42</td>
<td>1.385</td>
<td>0.168</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.244</td>
<td>0.026</td>
<td></td>
</tr>
<tr>
<td>DBP(mmHg) Mean ±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.824</td>
</tr>
<tr>
<td></td>
<td>85.21±4.15</td>
<td>85.56±4.32</td>
<td>77.43±3.40</td>
<td>5.625</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.244</td>
<td>0.026</td>
<td></td>
</tr>
</tbody>
</table>

JNC 7 classification of hypertension,(2003).

Values are expressed as mean±1 SD or percent, unless otherwise specified.

“n” Represents the number of Subjects; SD= Standard Deviation; SBP= Systolic Blood Pressure. DBP= Diastolic Blood Pressure. Superscripted alphabets a, b, and c represents the respective significant differences determined by students t-test between hypertensives and prehypertensives; hypertensives and normal and prehypertensives and normal subjects.
Table: 2 Lipid profile (in mg/dl) in patients with different grades of Hypertension compared to controls

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Patient</th>
<th>Control</th>
<th>t</th>
<th>P-value</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypertensive</td>
<td>Prehypertensive</td>
<td>n=80</td>
<td>n=20</td>
<td>n=50</td>
</tr>
<tr>
<td>Cholesterol(mg/dl) Mean ±SD</td>
<td>175.1±40.6</td>
<td>166.9±57.8</td>
<td>147.2±61.9</td>
<td>8.287</td>
<td>27.91</td>
</tr>
<tr>
<td>Triglycerides (TG)(mg/dl) Mean ±SD</td>
<td>204.9±125</td>
<td>186.2±121</td>
<td>139.2±62</td>
<td>18.73</td>
<td>65.73</td>
</tr>
<tr>
<td>VLDL(mg/dl) Mean ±SD</td>
<td>41.0±25.1</td>
<td>37.2 ±24.2</td>
<td>28.9±14.8</td>
<td>3.76</td>
<td>12.14</td>
</tr>
<tr>
<td>LDL(mg/dl) Mean ±SD</td>
<td>181.3±62.4</td>
<td>169.8 ±80.3</td>
<td>130.0±74.2</td>
<td>11.52</td>
<td>51.30</td>
</tr>
<tr>
<td>HDL(mg/dl) Mean ±SD</td>
<td>34.8±8.4</td>
<td>37.0±9.7</td>
<td>46.1±8.4</td>
<td>2.187</td>
<td>11.29</td>
</tr>
</tbody>
</table>

Values are expressed as mean±1 SD or percent, unless otherwise specified.

“n” Represents the number of Subjects; SD= Standard Deviation; Superscripted alphabets a, b, and c represents the respective significant differences determined by students t-test between hypertensives and prehypertensives; hypertensives and normal and prehypertensives and normal subjects.

DISCUSSION

In the present study the estimation of serum lipid levels in hypertensives, prehypertensives and normotensives revealed dyslipidemic hypertension in 72% of hypertensive which amounts to overall 14.4% of a subset of Kashmiri population. This prevalence is comparable to that found in two communities of southeastern New England.[15] Further the difference in lipid profile was higher among hypertension than pre-hypertensives when compared with normotensives. Similar Association between hypertension and lipid levels were also reported in a large age adjusted case control studies carried out by Karee etal (1991).[41] Rajeev Gupta (2001)[8] Catherine E, [16] Johnson M .L (2004).[17] The result of our study is also in good agreement with the studies carried out in Stockholm,[18]; in US[19]; in Nigeria.[20] Within lipid profile, maximum percentage deviation in hypertensives Vs normotensives was observed in TG levels (51% Vs 18% ) and HDL (45% Vs 12%) followed by Cholesterol (49% Vs 21%) and LDL (45% Vs 22%). Similar association, except for TG levels, was also reported in a large retrospective study carried out by Jogleker, S.J and Nanivadekar A.S (1996)[9] in India.
on patients who attended Apollo hospital for the management of hypertension where 51% of patients showed cholesterol >200mg/dl, 37% had LDL>130mg/dl, 11% had elevated ratio of total cho/HDL >4.5, 30% TG>200mg/dl.

The findings of the present study, ie greater proportion of hypertensive patients from our population having higher TG levels compared to rest of India where Cholesterol levels are higher in significant proportion of hypertensive population, could be associated to different ethnicity, dietary habits and cultural practices of kashmiri population from rest of India. However, this finding of our study, is in good agreement with the study carried out in Bangladesh, a Muslim dominated area, by Shahadat H, et al.,(1999) ; and by Saha M S (2006). [21,22] Kashmir being Muslim dominated area, share dietary habits (like heavy consumption of red meat) and cultural practices (marriage/functional ceremonies) with Muslim dominated populations of Southeast Asia, as substantiated by the findings of the present study which is in good agreement with other Muslim dominated populations.

Various studies conducted worldwide including present one suggest a possible biological interaction between hypertension and dyslipidemia. [19] However the exact mechanisms that may account for the observed relationship between hypertension and dislipidemia are obscure but certainly include insulin resistance (also grouped as Syndrome X) [6,7] and endothelial dysfunction, common features in the pathogenesis of both the conditions. [4] Insulin resistance causes dislipidemia by promoting fat utilization for energy purposes, and hypertension may decrease insulin sensitivity by affecting sympathetic nervous activity, or alternatively influencing function of biological membranes depending upon plasma fatty acid and lipoprotein concentrations. [5-7, 23, 24] The correlation between the two is further supported by the fact that lipid lowering agents like statins and fibrates also lowers blood pressure by affecting arterial wall structure and hence pulse wave velocity. [25,26] Hypertension and dislipidemia may be, therefore, considered independent risk factors that contribute synergistically to the development of Cardiovascular disease. Further, the life style strategies employed for the management of hypertension and dislipidemia alone share remarkable similarities. Both aim to reduce saturated fat intake, increase fruit and fiber intake, improve exercise tolerance and stop smoking. However the treatment of dyslipidemia and hypertension alone is different from the treatment of dyslipidemic hypertension which may involve insulin resistance as well. The finding of this study, therefore, may provide a rationale for pharmacotherapy, in a broader subset of people with dyslipidemic hypertension.
CONCLUSION
The findings of the present study suggest estimation of lipid levels in hypertensives as an essential/potential tool for early identification of individuals with dyslipidemic hypertension. Since treatment of dyslipedemia and hypertension alone is different from treatment of dyslipidemic hypertension, the finding of this study, prevalence of dyslipidemic hypertension, therefore, provide a rationale for pharmacotherapy, in a broader subset of people with dyslipidemic hypertension.

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