

## The impact of hypertension on lipid parameters in type 2 diabetes

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### Abstract

**Objective:** To study the effect of hypertension on lipid levels in patients with type 2 diabetes mellitus.

**Methods:** This prospective, observational study was conducted at 1 Mountain Medical Battalion, Bagh, Azad Kashmir, from May 2012 to April 2015, and comprised adult type 2 diabetics. Patients already on lipid-lowering agents, hypothyroidism, nephrotic syndrome, unwilling patients and those who had serum triglycerides >4.5mmol/l were excluded. Blood pressure was measured twice in sitting position. Amongst hypertensive patients, blood pressure  $\leq$ 140/90mmHg reflected good control. Serum total cholesterol, triglyceride and high-density lipoproteins were measured using enzymatic calorimetric method. Friedewald equation was used to calculate low-density lipoprotein levels. Subjects were divided into three groups: those without hypertension; those with hypertension but good blood pressure control; and hypertensives with poor blood pressure control. SPSS 20 was used for data analysis.

**Results:** Of the 322 patients, 129(40.06%) were women and 193(59.94%) were men. The overall mean age was  $51.42 \pm 10.93$  years. Hypertension was seen in 144(44.72%) patients. Blood pressure was well controlled in 46(31.94%) hypertensive patients. Among patients without hypertension and those with good or poorly controlled blood pressure, the mean values for serum total cholesterol were  $181.08 \pm 32.05$ ,  $186.87 \pm 39.00$ ,  $185.33 \pm 35.55$  mg/dl, triglycerides were  $172.57 \pm 80.53$ ,  $187.61 \pm 81.42$ ,  $183.19 \pm 74.34$  mg/dl, high-density lipoproteins were  $40.54 \pm 12.36$ ,  $37.06 \pm 8.80$ ,  $40.15 \pm 12.35$  mg/dl and low-density lipoproteins were  $105.79 \pm 29.73$ ,  $110.81 \pm 31.66$ ,  $106.56 \pm 35.16$  mg/dl. The number of patients with abnormalities of total cholesterol was 44(26.83%), 13(28.26%), 33(29.46%), triglycerides was 83(50.61%), 30(65.22%), 66(58.93%), high-density lipoproteins was 119(72.56%), 39(84.78%), 93(83.04%) and low-density lipoproteins was 90(54.88%), 29(63.04%) and 59(52.68%), respectively.

**Conclusion:** Hypertension did not worsen diabetic dyslipidaemia.

**Keywords:** Dyslipidaemia, Metabolic syndrome X, Risk factors, Pakistan. (JPMA 66: 1262; 2016)

### Introduction

The prevalence of coronary heart disease (CHD) is continuously increasing. Nearly 27% of Pakistanis aged 40 years or above have CHD.<sup>1</sup> Hypertension and dyslipidaemia are two of the several major risk factors. The relationship between dyslipidaemia and hypertension is complex. It is believed that dyslipidaemia may lead to the development of hypertension by causing endothelial dysfunction.<sup>2</sup> Moreover, the co-existence of these two risk factors exerts more than an additive impact on the vascular endothelium, resulting in heightened atherosclerosis and thus CHD.<sup>3</sup>

Type 2 diabetes mellitus (T2DM) is another important risk factor for CHD, often labelled as a CHD risk equivalent. In patients with diabetes, hypertension is often seen as a component of the well-known metabolic syndrome. High blood pressure (BP) portends an increased risk of diabetic micro- as well as macrovascular complications. Co-

existent hypertension increases mortality by 7.2 times in diabetics.<sup>4</sup> In such patients, targeting hypertension and dyslipidaemia reduces cardiovascular risk beyond the level achieved by lowering blood glucose levels only.<sup>5</sup> It has even been suggested that controlling blood pressure with intensive pharmacological treatment may be even more important in reducing cardiovascular risk than blood glucose control.<sup>6</sup>

Both diabetes and hypertension are known to be associated with lipid abnormalities. Almost 50% diabetics have dyslipidaemia.<sup>7</sup> This is characterised by elevated plasma triglycerides (TG) levels, low high-density lipoproteins (HDL) cholesterol levels and increased concentration of small dense low-density lipoproteins (LDL) cholesterol. Similarly, dyslipidaemia has been reported in 50% to 80% of hypertensive patients.<sup>8</sup> Given the effects of both these disorders on lipid parameters individually, it may be presumed that the impact of co-existent diseases would be far greater. However, this has not been studied adequately on our local population. The current study was carried out to determine the effect of hypertension on lipid levels in patients with T2DM.

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## Patients and Methods

This prospective, observational study was carried out at 1 Mountain Medical Battalion, Bagh, Azad Kashmir, from May 2012 to April 2015. Approval of the research protocol was obtained from the institutional ethics review committee. Patients with T2DM, aged 30 or above, presenting to medical outdoor clinic for the first time during the study period were analysed for eligibility. Patients already on lipid-lowering agents, had hypothyroidism, nephrotic syndrome, or serum triglyceride (TG) >398 mg/dl or those who were unwilling to participate were excluded. All those fulfilling the selection criteria were enrolled after obtaining informed written consent from them. Demographic data was noted down. History of hypertension as well as the use of any antihypertensive drugs was obtained. Any of these two features was used to define essential hypertension. Blood pressure was measured twice in sitting position with a mercurial sphygmomanometer using the standard technique and mean value was calculated. Blood pressure  $\leq$ 140/90mmHg reflected good control of hypertension. Height and weight were recorded to calculate body mass index (BMI). Waist circumference was also measured at the level of iliac crest. Venous whole blood samples were

collected after 12 hours' fast for estimation of serum total cholesterol, TG and HDL cholesterol with Merck Microlab-300 Automated Clinical Chemistry Analyser using enzymatic calorimetric method. Friedewald equation was used to calculate LDL cholesterol levels. Upper limits of normal level for different lipid fractions were taken as: total cholesterol= 200.00 mg/dl, TG= 150 mg/dl, LDL cholesterol= 100mg/dl. HDL cholesterol was considered abnormal if it was <40mg/dl in men and <50mg/dl in women.

SPSS 20 was used for data analysis. Patients with diabetes were divided into three groups: those without hypertension, those with good control of blood pressure and those with poor control of blood pressure. Means of the different lipid fractions were compared between the three groups using one-way analysis of variance (ANOVA). Proportions of patients with abnormalities in lipid fractions were compared using chi-square test. A p-value of  $\leq$ 0.05 was considered significant.

## Results

Of the 322 patients, 129(40.06%) were women and 193(59.94%) were men. The overall mean age was 51.42 $\pm$ 10.93 years. Hypertension was seen in 144(44.72%)

**Table-1:** Baseline characteristics of study population.

Variable	Total (n=322)	Diabetes without hypertension (n= 178)	Diabetes with hypertension (n=144)	p
Age (years)	51.42 $\pm$ 10.93	49.62 $\pm$ 10.98	53.63 $\pm$ 10.49	0.001
Gender (males: females)	129: 193	83: 95	46: 98	0.008**
Education (years)@	5 (0- 16)	5 (0- 16)	0 (0- 16)	0.008*
Duration of diabetes (years)@	3 (0- 30)	3 (0- 30)	4 (0- 30)	0.262*
Current smokers (number)	28 (8.70%)	21 (11.80%)	7 (4.86%)	0.028**
BMI (kg/m <sup>2</sup> )	26.17 $\pm$ 4.78	25.53 $\pm$ 4.79	26.95 $\pm$ 4.67	0.008
Waist circumference (cm)	99.10 $\pm$ 11.17	97.56 $\pm$ 10.92	101.00 $\pm$ 11.22	0.006
Systolic BP (mmHg)	140.51 $\pm$ 26.37	127.75 $\pm$ 19.08	154.28 $\pm$ 25.63	<0.001
Diastolic BP (mmHg)	85.68 $\pm$ 11.20	80.65 $\pm$ 9.28	91.91 $\pm$ 10.21	<0.001
Plasma glucose fasting (mg/dl)	182.52 $\pm$ 75.24	187.56 $\pm$ 78.84	175.50 $\pm$ 70.38	0.123

\*Mann-Whitney U test

\*\*Chi square test, @median and range

BP: Blood pressure. BMI: Body mass index.

**Table-2:** Comparison of mean lipid levels.

Variable	Total	Without hypertension (n=178)	Well controlled hypertension (n= 46)	Poorly controlled hypertension (n= 98)	p
Serum total cholesterol (mg/dl)	183.78 $\pm$ 35.16	181.08 $\pm$ 32.05	186.87 $\pm$ 39.00	185.33 $\pm$ 35.55	0.480
Serum TG (mg/dl)	179.65 $\pm$ 78.76	172.57 $\pm$ 80.53	187.61 $\pm$ 81.42	183.19 $\pm$ 74.34	0.376
Serum HDL-C (mg/dl)	39.00 $\pm$ 11.58	40.54 $\pm$ 12.36	37.06 $\pm$ 8.80	40.15 $\pm$ 12.35	0.257
Serum LDL-C (mg/dl)	108.49 $\pm$ 30.89	105.79 $\pm$ 29.73	110.81 $\pm$ 31.66	106.56 $\pm$ 35.16	0.636

TG: Triglycerides.

HDL-C: High-density lipoproteins cholesterol.

LDL-C: Low-density lipoproteins cholesterol.

**Table-3:** Proportions of patients with abnormal lipid fractions.

Variable	Diabetes without hypertension (n=178)	Well controlled hypertension (n= 46)	Poorly controlled hypertension (n=98)	p
Serum total cholesterol	44 (26.83%)	13 (28.26%)	33 (29.46%)	0.890
Serum TG	83 (50.61%)	30 (65.22%)	66 (58.93%)	0.144
Serum HDL-C	119 (72.56%)	39 (84.78%)	93 (83.04%)	0.058
Serum LDL-C	90 (54.88%)	29 (63.04%)	59 (52.68%)	0.487

TG: Triglycerides.

HDL-C: High-density lipoproteins cholesterol.

LDL-C: Low-density lipoproteins cholesterol.

patients, 46(31.94%) of whom had a good control of blood pressure; the remaining 178(55.28%) patients did not have hypertension ( $p=0.008$ ). Moreover, 28(8.7%) of the participants were smokers. The overall mean BMI was  $26.17\pm 4.78$  kg/m<sup>2</sup> and waist circumference was  $99.10\pm 11.17$  cm. The mean systolic and diastolic BP values were  $140.51\pm 26.37$  mmHg and  $85.68\pm 11.20$  mmHg (Table-1).

Of those who had hypertension, the condition of 46(31.94%) was well controlled while that of 98(68.05%) was poorly controlled. The mean serum total cholesterol was  $181.08\pm 32.05$ mg/dl among patients without hypertension,  $186.87\pm 39.00$ mg/dl among those with well-controlled hypertension and  $185.33\pm 35.55$ mg/dl among those with poorly controlled hypertension ( $p=0.480$ ). The mean serum TG level was  $172.57\pm 80.53$ ,  $187.61\pm 81.42$  and  $183.19\pm 74.34$  mg/dl ( $p=0.376$ ) in the three groups. The mean serum HDL and LDL levels were  $40.54\pm 12.36$  and  $105.79\pm 29.73$  mg/dl respectively, among patients who had hypertension;  $37.06\pm 8.80$  and  $110.81\pm 31.66$  mg/dl among those with well-controlled hypertension; and  $40.15\pm 12.35$  and  $106.56\pm 35.16$  mg/dl among those with poorly controlled hypertension (Table-2).

Moreover, 44(26.83%) patients who had diabetes without hypertension, 13(28.26%) with well-controlled hypertension and 33(29.46%) with poorly controlled hypertension had abnormal serum total cholesterol level ( $p=0.890$ ). The number of participants who had abnormal serum TG level was 83(50.61%), 30(65.22%) and 66(58.93%) in the three groups, respectively ( $p=0.144$ ). Besides, abnormal serum HDL level was seen in 119(72.56%) patients in the first group, 39(84.78%) in the second and 93(83.04%) in the third ( $p=0.058$ ), whereas 90(54.88%), 29(63.04%) and 59(52.68%) patients had abnormal LDL level ( $p=0.487$ ).

The number of patients with abnormalities of different lipid fractions were similar in the three groups (Table-3).

## Discussion

Atherosclerosis occurs at a faster rate in diabetic patients.

Coronary arteries are an important site, and thus these patients are more prone to developing CHD. Hypertension frequently co-exists with diabetes. In an earlier study, we found that 40% of diabetic patients were hypertensive as well.<sup>9</sup> This association adds to the CHD risk. Indeed, lowering blood pressure in patients with diabetes can reduce overall mortality as well as deaths from cardiovascular events and stroke.<sup>10</sup>

The main finding of this study is that co-existent hypertension does not worsen dyslipidaemia in patients with T2DM. Our results are in keeping with the results of a study done by Tedesco et al.<sup>11</sup> There was no significant difference in total cholesterol, TG and HDL levels amongst hypertensive and normotensive diabetics. Similarly, a study done on Nigerians concluded that concurrent hypertension and T2DM does not result in a more severe dyslipidaemia than when either of the two conditions occurs alone.<sup>12</sup> Proportions of diabetic patients with dyslipidaemia were the same in hypertensive and normotensive groups (82.8% vs. 81.5%) in a study done in India.<sup>13</sup>

Contrasting results have also been reported in some previous studies. Prevalence of dyslipidaemia was higher amongst hypertensive diabetics from Ghana when compared to those without hypertension.<sup>14</sup> Amongst a Pakistani diabetic cohort, patients with hypertension had significantly higher non-HDL-C and lower HDL-C in contrast to normotensive patients.<sup>15</sup> In a study done in Nigeria, hypertensive diabetics had higher serum total cholesterol, TG and LDL-C as well as lower HDL-C as compared to normotensive diabetics.<sup>16</sup> A study done in Macedonia revealed that diabetic hypertensive patients with good control of blood pressure had lower serum total cholesterol, TG, LDL-C, and higher HDL-C, as compared to those having uncontrolled blood pressures.<sup>17</sup>

Many studies have also reported variable effects of hypertension on different lipid fractions in diabetic patients. Alatab et al. found higher serum LDL-C and total cholesterol levels in hypertensive diabetics from

Iran as compared to normotensive diabetics, but the difference in TG and HDL was not statistically significant.<sup>18</sup> In an Indian study done by Salman et al., HDL was lower and TG higher but hypertension did not affect total cholesterol and LDL levels.<sup>19</sup> Total cholesterol and LDL were higher in hypertensive diabetics, as compared to normotensive diabetics, but TG levels were the same in the two groups in a study done on an African population.<sup>20</sup> Similarly, in a Bangladesh study, total cholesterol and LDL-C were found to be higher in hypertensive diabetics but there were no differences in levels of HDL and TG.<sup>21</sup> However, the results of that study should be interpreted cautiously because of the very small sample size that did not provide adequate power to assess the differences.

Another important finding of the current study is the absence of improvement in lipid parameters with good control of blood pressure. This is in contrast to the Spanish multicentre LIPICAP-PA study where LDL-C control was better in those with good control of blood pressure (43% vs. 22.4%).<sup>22</sup> Conflicting results may partially be attributable to a shortcoming of our study design. In this cross-sectional study, control of blood pressure was assessed on the basis of readings taken on a single day only. This information might not be a totally reliable marker of control in the longer run. Nevertheless, since controlling blood pressure alone did not improve lipid profile amongst our patients, additional measures including dietary and pharmacological treatment are required to lower lipids. Use of statins is all the more important because they have antihypertensive effects as well.<sup>23</sup>

The main strength of this study is the inclusion of all patients satisfying the selection criteria, so that the results are truly reflective of patient population visiting this healthcare set-up. Smoking modifies serum lipid levels, may lead to insulin resistance and can lower serum HDL-C levels.<sup>24</sup> In our study, a greater proportion of normotensive patients were current smokers as compared to hypertensive patients. This factor could not be taken care of. There are a few other limitations of this study. We did not study the influence on other confounding factors such as physical activity, dietary habits, oral hypoglycaemic agents and antihypertensive medications on lipid parameters in either of the two groups.

## Conclusion

Hypertension super-imposed on diabetes did not aggravate dyslipidaemia seen with diabetes alone.

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