



Original Research Paper

Study of Blood Pressure and Lipid Profile in Uncontrolled Diabetes Mellitus

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ABSTRACT

Hypertension and Dyslipidemia are common accompaniments of Diabetes Mellitus and are major risk factors for cardiovascular diseases. This is a study of hypertension and lipid profile in 35 subjects with uncontrolled diabetes in comparison with an equal number of apparently normal subjects. Levels of HbA1C above 7% is taken as a marker of uncontrolled DM. Study was done in the diabetic clinic under the department of General Medicine. On analysis of the data, the mean values of systolic and diastolic BP are found to be significantly higher in diabetic patients compared to normal control group. Also a significantly high the value is obtained for total cholesterol, serum Triglyceride and VLDL in the diabetic group. No significant difference in HDL or LDL was obtained between the groups. This may be because some of the patients were on lipid lowering drugs. Even then the presence of significant dyslipidemia increased BP in patients with poorly controlled diabetes shows their increased cardiovascular risk.

Keywords: Blood Pressure, Lipid Profile, Glycemic control, Diabetes Mellitus.

INTRODUCTION

Diabetes mellitus (DM) is a chronic progressive disease occurring due to the reduced production of insulin by pancreas or due to the inability of the body to properly utilise the insulin it produces. This leads to excessive blood glucose level (hyperglycemia). In the long run the condition will cause complications involving multiple organs. The worldwide prevalence of DM has risen dramatically over the past two decades. King H et al estimated that the number of persons with diabetes was 150 million in 2000 and this is expected to double by 2025^[1]. With over 20

million diabetic subjects India leads the world in the number of individuals with Diabetes.

Hypertension is a common accompaniment of DM. Hypertension and diabetes are two of the leading risk factors for atherosclerosis and its complications. There is a substantial overlap between the etiology and disease mechanisms of these two conditions. Hypertension affects approximately 70% of patients with DM and is about twice as common in diabetics than those without diabetes^[2]. The UK prospective diabetic study showed that BP control helps to avoid cardiovascular complications in patients with Type 2DM.

Dyslipidemia is another major risk factor for cardiovascular diseases in Diabetes. A characteristic pattern termed diabetic dyslipidemia consists of low blood levels of High Density Lipoprotein (HDL), increased triglycerides (TG) and increase in small dense LDL cholesterol. The Low Density Lipoproteins (LDL) are converted into smaller perhaps more atherogenic lipoproteins termed small dense LDL cholesterol. These changes are also a feature of the insulin resistance syndrome which underlies many cases of type 2 diabetes.

Here an attempt is made to study Blood Pressure and lipid profile of patients with uncontrolled Diabetes Mellitus in comparison with apparently normal control group.

METHODS

Study Design: Hospital based cross sectional study

Study Setting: Individuals attending the diabetic clinic under the Department of General Medicine as cases and age and sex matched normal people accompanying the patients as controls.

Biochemical investigations done in the department of Biochemistry.

Study Period: 1 year

Study Population: 35 diabetic patients and 35 apparently normal individuals satisfying the inclusion and exclusion criteria

Inclusion Criteria: Diabetic patients of both sexes with glycated Haemoglobin (HbA1c) level more than 7%.

Exclusion Criteria

- 1) Past history of Stroke or Coronary artery disease.
- 2) Patients treated for other heat diseases.

The study started after getting permission from human ethical committee and review board of the institution. A written informed consent was obtained from all the subjects included in the study. Patient details and past history was obtained by oral questionnaire, clinical examination, from case records and by discussing with the treating physician. BP was checked in the right upper limb in sitting position. Biochemical parameters such as RBS, HbA1C, serum cholest-

erol, serum triglyceride, LDL, HDL and VLDL were measured.

The target level of HbA1C recommended by American Diabetic Association for diabetics under treatment is less than 7%^[3]. So in this study patients with HbA1C more than 7% was taken to have uncontrolled diabetes.

Lipid profile in diabetic and non-diabetic group was compared by taking cut-off values of serum cholesterol as 200 mg/dl, serum triglyceride as 150 mg/dl, LDL as 130 mg/dl, HDL as 40mg/dl and VLDL as 30 mg/dl as per Adult Treatment Panel III (ATP criteria III)^[4]. For finding the association of diabetic status with blood pressure, cut-off value of systolic BP (SBP) was taken as 120 mm Hg and that for diastolic BP (DBP) as 90 mm Hg as per JNC 7 criteria (7th report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of high BP).

STATISTICAL ANALYSIS

The data were entered into a computer using the package Microsoft Excel. For analysis, statistical package for social sciences (SPSS) version 17 was used. Continuous variables were expressed as mean \pm standard deviation and qualitative data was expressed as percentage. Independent t test was used for comparing quantitative data between groups. Categorical variables were compared using chi square test. All p values were 2 tailed and a 'p' value of <0.05 was considered statistically significant.

RESULTS

1. Blood Pressure and Diabetes

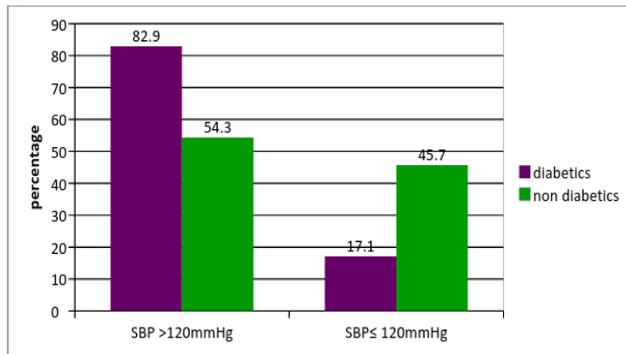
Table 1: Meansystolicand diastolic blood pressure in uncontrolled diabetics and non diabetic group

Variable	Category	N	mean	SD	t	P
Systolic BP	Diabetic	35	137.7	17.2	3.760	< 0.001*
	Non diabetic	35	125.3	9.5		
Diastolic BP	Diabetic	35	85.4	6.9	3.064	0.003*
	Non diabetic	35	80.9	5.4		

Mean systolic blood pressure in the diabetic patients was 137.7 mm of Hg and that in the non

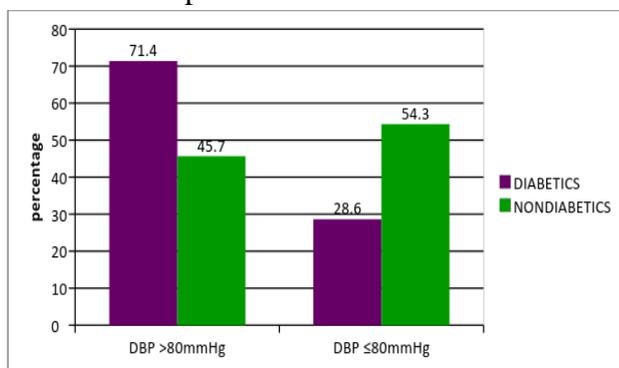
diabetic group was 125.3 mm of Hg. ‘t’ test showed that the difference was statistically significant. Mean diastolic blood pressure in the diabetic subjects was 85.4 mmHg and in non diabetic comparison group it was 80.9 mmHg. This difference was also statistically significant (p= 0.003).

Figure 1: Comparison of diabetic status with systolic BP



Among diabetic cases, 82.9% were having high systolic BP (>120 mmHg) while in the comparison group only 54.3% were having high value (Fig:1). This difference in proportion was found to be statistically significant (p= 0.010). Among diabetic cases, 71.4% were having high diastolic BP (>80 mmHg) while in the comparison group only 45.7% were having high value (Fig:2). This difference in proportion was also found to be statistically significant (p= 0.029).

Figure 2: Comparison of diabetic status with diastolic blood pressure



2 Lipid profile and Diabetes

Table 2: Mean lipid profile in uncontrolled diabetic and non diabetic subjects

	Category	N	Mean	sd	t	P
Serum cholesterol	Diabetic	35	207.9	46.0	2.197	0.031*
	Non diabetic	35	184.9	41.6		
Serum triglyceride	Diabetic	35	150.4	59.0	3.510	0.001*
	Non diabetic	35	105.3	47.7		
HDL	Diabetic	35	43.9	5.8	1.303	0.197
	Non diabetic	35	41.3	9.8		
LDL	Diabetic	35	136.6	29.5	1.556	0.124
	Non diabetic	35	124.9	33.5		
VLDL	Diabetic	35	30.0	11.8	3.300	0.002*
	Non diabetic	35	21.6	9.3		

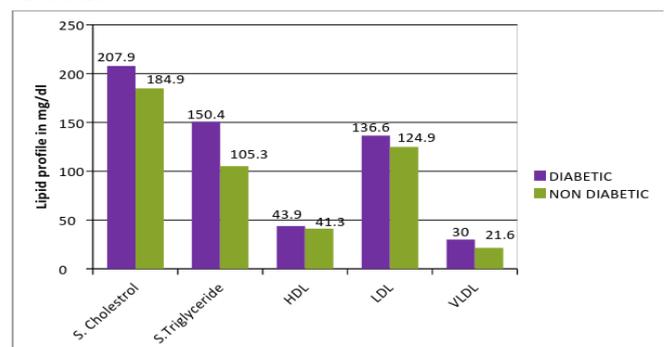
Mean **Total Cholesterol (TC)** in the diabetic patients was 207.9 ± 46 mg/dl and in the non diabetic comparison group it was 184.9± 41.6 mg/dl. Student t test showed the difference to be statistically significant.

Mean **Serum triglyceride** in the diabetic patients was 150.4 ± 59 mg/dl and in the non diabetic group it was 105.3± 47 mg/dl .Student t test showed the difference to be statistically significant (p= 0.001) .

Mean **VLDL** in diabetic patients was 30±11.8mg/dl while in non diabetic comparison group it was 21.6 ± 9.3mg/dl. The difference was statistically significant (p=0.002).

However there were no statistically significant differences between the mean values of high density lipoprotein (HDL) and low density lipoprotein (LDL) between diabetic patients and non diabetic comparison group.

Figure 3.Mean lipid profile in diabetics and non diabetics



Out of the total, 60% (n=21) of diabetics were having a higher T. cholesterol ie >200mg/dl²³³ while in non diabetic subjects only 31.4% (n=11) were having increased total cholesterol. This difference in proportion was found to be statistically significant (p=0.016) (Table 3)

A significantly high proportion of diabetics (37%, n=13) were having increased s. triglyceride levels (>150mg/dl) as compared with non diabetic individuals (2.9%,n=1).

Among diabetic cases, 54.3% were having high LDL (>130mg/dl) while in the comparison group only 31.4% were having high values. This difference in proportion was found to be statistically significant (p= 0.053).

Table 3: Comparison of lipid profile in diabetic and non diabetic subjects

Variables	Category	Diabetics	Non diabetics	P value
S.Cholest erol	> 200	21 (60%)	11 (31.4%)	0.016*
	≤ 200	14 (40%)	24 (68.6%)	
S.Triglyc eride	> 150	13 (37.1%)	1 (2.9%)	< 0.001*
	≤ 150	22 (62.9%)	34 (97.1%)	
LDL	>130	19 (54.3%)	11 (31.4%)	0.053*
	≤ 130	16 (45.7%)	24 (68.6%)	
HDL	> 40	24 (68.6%)	24 (68.6%)	1.000
	≤ 40	11 (31.4%)	11 (31.4%)	
VLDL	> 30	12 (34.3%)	1 (2.9%)	0.001*
	≤ 30	23 (65.7%)	34 (97.1%)	

A significantly high proportion of diabetics (34.3%, n=12) were having increased VLDL levels (>30mg/dl) as compared to non diabetic individuals (2.9%, n=1).

No significant difference in proportion of HDL values were found between the two groups.

DISCUSSION

1 Diabetes and Blood pressure

Diabetes mellitus and high blood pressure are closely related diseases. They occur together so frequently that they are considered to be co

morbidities. The common denominator in target organ disease is the vascular tree. They share certain physiological traits. The effects caused by each disease tend to make the other disease more likely to occur. The effects include

- 1) **Increased fluid volume** - Diabetes increases the total amount of fluid in the body, which tends to raise blood pressure. Activation of Renin Angiotensin Aldosterone system (RAAS) results in salt retention, volume expansion and hypertension. Aldosterone also contributes to hypertension by enhancing sympathetic activity decreasing para sympathetic activity and reducing baroreceptor sensitivity^[5]
- 2) **Increased arterial stiffness** - Diabetes can decrease the ability of the blood vessels to stretch increasing the average BP^[6]
- 3) **Impaired insulin handling-** changes in the way the body produces and handles insulin can directly cause increase in BP^[7]
- 4) **Extra cellular matrix deposition-** Aldosterone causes increased extra cellular matrix deposition by glomerular cells leading to glomerulosclerosis and hypertension^[5]
- 5) **Increased autocrine or paracrine activity of angiotensin II (AT-II)** results in diminished action of insulin and insulin like growth factor-1 (IGF-1) signalling through the PI3K/PKB pathway, resulting in inhibition of mechanisms involved in their vasodilator and glucose transport properties^[8]

Gluko-Toxicity -- At high concentrations, glucose appears to have a direct toxic effect on endothelial cells, which may result in decreased endothelial-mediated vascular relaxation, increased constriction, promotion of vascular smooth muscle cell hyperplasia, and vascular remodeling.^[9] Enhanced expression of fibronectin and collagen IV in diabetics may further contribute to endothelial dysfunction^[10] The decreased elasticity of connective tissues in arterial walls may also be related, in part, to the increased

advanced glycosylation end products which occur in diabetic patients^[11]

The observation that diabetics are more prone for development of hypertension was confirmed by several studies. The prevalence of coexistent hypertension and diabetes varies across different racial, ethnic and social groups. Diabetes mellitus is an independent risk factor for coronary artery disease, and the risk is markedly increased when hypertension is present. Recent guidelines have recommended a target blood pressure (BP) level below 130/80mmHg to reduce these risks in patients with diabetes.^[12] In several studies^[13] it was found that the age- and sex-adjusted prevalence of hypertension among diabetic subjects was twice that of non diabetic subjects. Also control of hypertension is found to reduce incidence of cardiovascular complications and mortality in DM.

Diabetes and Dyslipidemia

The lipoprotein abnormalities commonly present in Type 2 diabetes include hypercholesterolemia, hypertriglyceridemia and reduced plasma HDL cholesterol. VLDL, which is the precursor of LDL and chylomicrons are also increased in diabetics.^[14] A number of diabetic patients in this study with proven dyslipidemia were also on cholesterol lowering medications. This would explain the absence of the typical diabetic dyslipidemia in the study population

Several factors are likely to be responsible for diabetic dyslipidemia. Effects of insulin on liver apoprotein production, regulation of lipoprotein lipase (LpL), actions of cholesteryl ester transfer protein (CETP), and peripheral actions of insulin on adipose tissue and muscle are examples. A number of studies using tracer kinetics in humans have demonstrated that liver production of apolipoprotein B (apoB), the major protein component of VLDL and LDL is increased in type 2 diabetes.^[15] Increased lipolysis in adipocytes due to poor insulin action results in increased fatty acid release from fat cells. The resultant increase in fatty acid transport to the liver, along with the increased apo B may cause an increase in VLDL

secretion and its eventual conversion to LDL.³⁰¹ By this, the normal degradation of apo B is prevented when lipid is added to the protein. Increased concentrations of plasma VLDL drive the exchange of triglyceride from VLDL for the cholesteryl esters in HDL. This can account for the etiology of hypertriglyceridemia and reduced HDL.^[16] Lipoprotein lipase (LpL) is the major enzyme responsible for conversion of triglyceride into free fatty acids. Several steps in the production of biologically active LpL may be altered in diabetes, including its cellular production^[17] and possibly its transport to endothelial cells.^[16] This results in reduced breakdown of triglycerides and hence its blood levels increases.

Compared with normal subjects, patients with type 2 diabetes have a slower clearance of chylomicrons from the blood. This is due to reduced activity of lipoprotein lipase which normally hydrolyzes the triglycerides within these particles.^[18] The American Diabetes Association has published clinical goals for lipoprotein levels in adults with diabetes. They are as follows: optimal LDL cholesterol levels less than 100 mg/dL, optimal HDL cholesterol levels more than 45mg/dL, and desirable triglyceride levels less than 200 mg/dL.^[19] Diabetic dyslipidemia is likely to be one of many reasons for the accelerated macrovascular disease in diabetic patients. Therefore treatment of lipid abnormalities has the potential to reduce cardiovascular events more than 50%. This leads to the expectation that treatment of elevated lipid levels will allow patients with diabetes to lead longer healthier lives.

Several studies have proved the association between glycemic control and lipid levels. Good glycemic control can yield a 10 to 15% decrease in LDL cholesterol concentration, lower TG levels and produce a favourable change in composition of LDL cholesterol particles^[20]. This would help in reducing the chance of cardiovascular risk.

CONCLUSION

A significantly increased presence of high BP and dyslipidemia even in patients on drugs points to the increased risk for cardiovascular diseases and the importance of meticulous management of these two conditions in diabetics. A prospective comparative study with well controlled diabetics may help in defining the role of glycemic control in reducing dyslipidemia and hypertension in DM.

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