RESEARCH ARTICLE

Correlation of Plasma Fibrinogen and Lipoproteins in Diabetic Hypertensive Patients

Niranjan Rachaiah[1], Vijay Malleshappa[2]
[1] Hassan Institute of Medical Sciences, Sri Chamaranjendra Hospital, Hassan
[2] Apollo BGS Hospitals, Kuvempunagar, Mysore
Correspondence to: Niranjan Rachaiah (drniranjanmr@gmail.com)

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ABSTRACT

Background: Diabetic hypertensive patients have higher cardiovascular morbidity and mortality than general population. Various risk factors like age, BMI (Body mass index), hypertension, smoking, dyslipidemia, etc. have been extensively studied, but still these together cannot explain increased cardiovascular morbidity and mortality in diabetes. Several studies have shown that fibrinogen is a powerful independent risk factor for cardiovascular disease. Hence fibrinogen levels and its correlation to lipoproteins in diabetic hypertensives were studied.

Objective: To estimate plasma fibrinogen levels in patients with type 2 diabetes mellitus and hypertension and to correlate plasma fibrinogen with Lipoproteins and also with BMI.

Materials and Methods: A Prospective cross sectional study conducted in a tertiary care hospital. Data collected by simple random sampling method and analysis of various parameters done by using chi square-test and correlated with pearson's correlation coefficient "r".

Results: The higher plasma fibrinogen levels were found in diabetic hypertensives (449.06 ± 131.26) when compared to controls. The mean total cholesterol, TG (triglycerides), LDL (Low density lipoprotein), VLDL (Very low density lipoprotein), HDL (High density lipoprotein) among cases were 195.82 ± 26.92 mg/dl, 243.62 ± 45.83 mg/dl, 104.15 ± 25.76 mg/dl, 48.72 ± 9.17 mg/dl, 38.21 ± 4.03 mg/dl respectively and the mean BMI of cases was 26.16 ± 5.36 kg/m^2. The plasma fibrinogen is positively correlated to BMI and total cholesterol levels which is statistically significant.

Conclusion: The plasma fibrinogen levels could potentially be considered for screening programs to identify people at high risk of vascular events.

Key Words: Plasma fibrinogen; Lipoproteins; Diabetic Hypertensive; BMI

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. Diabetes mellitus and hypertension are inter-related diseases that strongly predispose an individual to atherosclerotic cardiovascular disease.

The prevalence of coexisting hypertension and diabetes appears to be increasing in industrialized nations because of both hypertension and type 2 diabetes increases with age. Indeed, an estimated 35% to 75% of diabetic cardiovascular and renal complications can be attributed to hypertension.[1,2]

Mechanism contributing to systemic vascular disease in diabetes with hypertension are platelet adhesion and aggregation defects, coagulation and lipoprotein abnormalities, alterations in vascular endothelium, vascular smooth muscle abnormalities.[1] Plasma

fibrinogen is an important component of the coagulation cascade. Increasing evidence from epidemiological studies suggests that elevated plasma fibrinogen levels are associated with an increased risk of cardiovascular disorders, including ischemic heart disease, stroke and other thromboembolism.[3]

METHODS

Both outpatients and inpatients with diagnosis of type 2 diabetes mellitus with hypertension were selected by simple random sampling method during the period of June 2004 to June 2006 at Krishna Rajendra Hospital, Mysore, Karnataka, India. Twenty age and sex matched healthy group were taken as controls.

The diagnosis of diabetes mellitus as per the ADA (American Diabetes Association) criteria[4,5] and diagnosis of systemic hypertension according to Joint National Committee 7th report was done.[6]

Patients with abnormal lipid profile secondary to hypothyroidism, alcoholic liver disease, renal failure, nephrotic syndrome, and patients on drugs like glucocorticoids, estrogens and progesterons, and patients with history of familial dyslipidemia, pregnant women were excluded from the study.

Anthropometric parameters for obesity were measured as per WHO recommendations.[7] Fasting serum lipid profile were performed by using standard enzymatic techniques. LDL-cholesterol was calculated by using formula of Friedewald et al.[8] equation. Venous plasma glucose was measured by glucose oxidase method, Plasma fibrinogen was measured by Clauss method.

Ethical committee clearance and written informed consent were obtained.

Comparison of various parameters among male and female subjects with or without diabetes was performed by chi square-test. Correlation between two variables was done by Pearson's correlation coefficient "r". Analysis were done using SPSS +10.0 computer package for statistics.

RESULTS

In our study forty four out of 50 cases were known diabetics and 6 were newly detected diabetics with a mean duration of 9.38 years and mean duration of hypertension was 5.98 years. The mean height of the cases was 153 ± 7.6 cm and the mean weight was 61.68 ± 12.23 kg. The mean BMI of cases and controls were 26.16 ± 5.36 kg/m² and 22.79 ± 2.4 kg/m² respectively (Table 1).

Table-1: Body Mass Index (BMI) (weight/height²) among the Cases and Controls

BMI	Cases			Controls		
	Male	Female	Total	Male	Female	Total
< 18.5	0 (0%)	2 (4%)	2 (4%)	0 (0%)	2 (10%)	2 (10%)
18.5-24.9	11 (22%)	13 (26%)	24 (48%)	10 (50%)	3 (15%)	13 (65%)
25-29.9	4 (8%)	8 (16%)	12 (24%)	2 (40%)	3 (15%)	5 (25%)
≥ 30	3 (6%)	9 (18%)	12 (24%)	0 (0%)	0 (0%)	0 (0%)
Total	18 (36%)	32 (64%)	50 (100%)	12 (60%)	8 (40%)	20 (100%)
Mean ± SD	25.80± 4.14	26.36± 5.99	26.16± 5.36	23.54± 1.86	21.03± 2.77	22.79± 2.40

Table-2: Mean Lipoprotein Profile among the Cases and Controls

	Cases			Controls		
	Male	Female	Total	Male	Female	Total
Total cholesterol	192.02 ± 26.00	197.97 ± 27.38	195.82 ± 26.92	182.63 ± 32.19	177.29 ± 22.28	159.57 ± 25.24
Triglycerides	261.76 ± 46.20	233.41 ± 43.03	243.62 ± 45.83	153.22 ± 15.30	107.16 ± 44.01	168.58 ± 25.37
VLDL levels	52.36 ± 9.26	46.68 ± 8.60	48.72 ± 9.17	32.53 ± 6.097	21.44 ± 8.79	33.71 ± 5.07
HDL cholesterol	37.97 ± 4.58	38.34 ± 3.75	38.21 ± 4.03	44.84 ± 4.40	49.32 ± 4.45	44.51 ± 3.58
LDL cholesterol	89.53 ± 18.89	112.37 ± 25.68	104.15 ± 25.76	88.07 ± 17.56	103.28 ± 25.85	96.91 ± 25.64

Table-3: Plasma fibrinogen Pattern

Plasma fibrinogen	Cases			Controls		
	Male	Female	Total	Male	Female	Total
< 150	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
150-300	1 (2%)	7 (14%)	8 (16%)	11 (55%)	7 (35%)	18 (90%)
300-450	9 (18%)	7 (14%)	16 (32%)	1 (5%)	1 (5%)	2 (10%)
> 450	8 (16%)	18 (36%)	26 (52%)	0 (0%)	0 (0%)	0 (0%)
Total	18 (36%)	32 (64%)	50 (100%)	12 (60%)	8 (40%)	20 (100%)
Mean ± SD	433.80 ± 99.62	457.65 ± 146.90	449.06 ± 131.26	221.16 ± 72.33	229.90 ± 76.53	150.80 ± 15.28

In the present study the least and maximum waist circumference observed among female patients was 90 cm and 114 cm with a mean of 99.81 ± 7.25 cm.

The least and maximum waist circumference observed among male patients was 98 cm and 105 cm with a mean of 101.33 ± 2.16 cm. The mean waist circumference of cases and controls were 100.36 ± 5.95 cm and 89.6 ± 9.93 cm. All female cases had waist circumference greater than 88 cm and 16% of male cases had waist circumference greater than 102 cm.

The mean hip circumference among cases and controls were 101.20 ± 9.91 cm and 96.85 ± 7.92 cm.

The mean Waist/Hip ratio of cases and controls were 0.99 ± 0.6 and 0.92 ± 0.4 respectively.

The mean total cholesterol among cases and controls were 195.82 ± 26.92 mg/dl and 159.57 ± 25.24 mg/dl. All cases had serum triglyceride values more than 150 mg/dl and 88% of them had serum triglyceride values more than 200 mg/dl. (Table 2)

The mean plasma fibrinogen levels in cases and controls were 449.06 ± 131.26 mg/dl and 150.80 ± 15.28 mg/dl (Table 3). The minimum plasma fibrinogen in the present study was 188 mg/dl and the maximum was 688 mg/dl. The 52% of the study group had plasma fibrinogen levels greater than 450 mg/dl. All controls had normal plasma fibrinogen.

Elevated plasma fibrinogen level was observed among male and female diabetic hypertensives compared to male and female controls. The difference was statistically significant.

Plasma fibrinogen is positively correlated to BMI which is statistically significant (Table 4). The fibrinogen is also positively correlated to total cholesterol, triglycerides, LDL TC/HDL (Total cholesterol and High density lipoprotein) ratio and negatively correlated to HDL levels, but statistically significant correlation was found between plasma fibrinogen and total cholesterol (Table 5).

Table-4: Correlation Coefficient r between Plasma Fibrinogen and BMI

	Plasma Fibrinogen	Plasma Fibrinogen
	r-value	p-value
BMI	0.659	0.001

$p < 0.05$, statistically significant

Table-5: Correlation Coefficient r between Fibrinogen and Lipoproteins

	Plasma Fibrinogen	Plasma Fibrinogen
	r-value	p-value
TC	0.348	0.013
HDL	- 0.156	0.279
TC/HDL	0.208	0.148
TG	0.276	0.05
LDL	0.127	0.381

$p < 0.05$, statistically significant

DISCUSSION

As the age advances the occurrence of diabetes and hypertension increases, relating to this in the present study the mean age of male and female diabetic hypertensives is significantly higher than that of controls. Han et al.[9] and Sosenko et al.[10] also had the mean age in the same range. In our study the mean BMI of male diabetic hypertensives is 25.80 and female diabetic hypertensives is 26.36, suggesting that they are overweight and the mean waist circumference was significantly higher in male and female diabetic hypertensives than controls. It suggests presence of abdominal obesity in

diabetic hypertensive individuals were significant. Han et al.[9] study group also had the same range of overweight category with abdominal obesity. The presence of metabolic risk factors typically associated with obesity augmented risk for incidence of type 2 diabetes.[11] Hence Waist circumference may be taken as bedside marker for abdominal obesity and also it is a sensitive indicator for central obesity.

Several studies have shown that an increased volume of visceral fat in obese subjects is associated with dyslipidemia, characterized by increased TG and low plasma HDL concentrations.[12,13] Subhankar Chowdury et al.[14] and Hideki et al.[15] had a positive correlation between Body Mass Index and Total Cholesterol.

In our study the mean values of total cholesterol among male and female diabetic hypertensives and controls did not vary significantly, suggesting that diabetic dyslipidemias do not alter total cholesterol levels significantly. Similar results were observed by Sosenko et al.[10] who also had lower levels of HDL-C. In our study the mean values of HDL-C among male and female diabetic hypertensives were significantly lower than that of controls. So we can conclude the low HDL level in diabetics increases the risk of coronary artery disease.

The mean values of LDL were not different in diabetic hypertensives and controls, which is one of the features of diabetic dyslipidemia. However there will be increase in small dense LDL particles which makes it more atherogenic. Hyper-triglyceredemia is one of the features of diabetic dyslipidemia.

In our study the mean values of triglycerides were significantly higher in male and female diabetic hypertensives than controls. This is due to increase in the production of triacylglycerol and fatty acids in liver in diabetic hypertensives.
Inflammatory markers have emerged in the past few years as independent predictors of cardiovascular risk. The fibrinogen has been traditionally considered to be a hemostatic factor, but a recent analysis from the Cardiovascular Health Study showed elegantly that fibrinogen clusters with inflammatory and not with hemostatic factors.[16]

In our study population the mean plasma fibrinogen in diabetic hypertensives was significantly raised compared to controls. We found statistically significant positive correlation between plasma fibrinogen levels with total cholesterol and BMI. Similar results were observed by Barbara Glowinska et al.[17] and Anjula Jain et al.[18]

In summary, we demonstrated that in diabetic hypertensives, the inflammatory marker like plasma fibrinogen concentration is elevated and positively correlated with total cholesterol and BMI. Higher levels of plasma fibrinogen markedly increase the predictive power of high serum LDL cholesterol; conversely, low plasma fibrinogen levels are associated with low coronary risk, even when LDL is raised.[19]

Plasma fibrinogen being partly a modifiable risk factor and suitable lifestyle changes usually result in favourable decreases in plasma fibrinogen levels, although drug therapy has not been fully validated.[20]

As the diabetic hypertensives have higher fibrinogens levels and positively correlated with BMI and total cholesterol levels, the plasma fibrinogen needs to be emphasised in all diabetic hypertensives who are dyslipidemic.

CONCLUSION

Obesity is highly prevalent in diabetic hypertensives and a waist circumference measurement should be performed to assess better the individual's risk profile with reasonable goals of weight reduction. As the plasma fibrinogen concentration is elevated and positively correlated with total cholesterol and BMI, The plasma fibrinogen levels could potentially be considered for screening programs to identify people at high risk of vascular events.

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