World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Original Article

Plasma fibrinogen level, BMI and lipid profile in type 2 diabetes mellitus with hypertension

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Received: 07-12-2015 / Revised: 28-01-2016 / Accepted: 29-01-2016 / Published: 30-01-2016

ABSTRACT

Diabetic hypertensives have higher cardiovascular morbidity and mortality than general population. Various risk factors like age, BMI, 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. In the present study fibrinogen levels of 50 diabetic hypertensive subjects were estimated and its correlations with various parameters like BMI and lipid profile were studied. Higher plasma fibrinogen levels were found in diabetic hypertensives (449.06 ± 131.26). There was a significantly positive correlation between plasma fibrinogen and BMI ($p < 0.05$). There was a significantly positive correlation between BMI and total cholesterol levels ($p < 0.05$). Diabetic hypertensives have higher fibrinogens levels, which were related to BMI and total cholesterol level in a statistically significant manner.

Keywords: Diabetic hypertensives, plasma fibrinogen, lipid profile, total cholesterol, type 2 diabetes mellitus, body mass index

INTRODUCTION

Diabetes mellitus and hypertension are interrelated diseases that strongly predispose an individual to atherosclerotic cardiovascular disease. An estimated 3million Americans have both diabetes and hypertension [1]. Hypertension is about twice as frequent in individuals with diabetes as in those without diabetes. Lifestyle and genetic factors are important factors contributing to both hypertension and diabetes. Data obtained from death certificates show that hypertensive disease has been implicated in 4.4% of deaths coded to diabetes, and diabetes was involved in 10% of death coded to hypertensive disease. Indeed, an estimated 35% to 75% of diabetic cardiovascular and renal complications can be attributed to hypertension [2]. Primary hypertension accounts for the majority of hypertension in individuals with diabetes, particularly those with type 2 diabetes, who constitute more than 90% of people with a dual diagnosis of diabetes and hypertension [1]. Around 50% of all diabetic people whether type 1 or type 2 are dyslipidemic [3].The frequency is more with poorly controlled diabetics. Abnormal lipid levels and lipid metabolism are major contributors to macrovascular complications, coronary artery disease, cerebrovascular accidents and peripheral vascular disease. 75-80% of adult diabetic patient die due to these causes. Asians in general and Indians in particular are more prone to diabetes and coronary artery disease. These patients have 2-3 fold higher rate of coronary artery disease, a four-fold higher mortality rate during acute MI and 2 fold higher risk of post-MI morbidity than non-diabetic patients [4]. 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 [5].

It is important to recognize that the risk factors do not function in isolation. In fact, they frequently cluster in individual patients and possibly interact with each other. Although some of these risk factors cluster, others appear to be independent of each other. Furthermore, studies on these risk factors are usually either epidemiological descriptions of associations with coronary vascular disease or experimental studies focusing on a single risk factor

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These risk factors provide insights into the pathogenesis of coronary heart disease in diabetes. Many of the risk factors identified may reflect underlying inflammation, which may be either secondary to atherosclerosis itself or may represent a non-specific inflammatory response to infections, which are likely to be much more common in people with uncontrolled diabetes. Even if the origins of these risk factors are non-specific, they may be important, because they have the potential to enhance the coagulation and thrombotic disease, thus perpetuating the vascular disease or triggering vascular events [6].

With the above perspectives in mind, the present study was designed with an objective to correlate plasma fibrinogen with BMI and lipid profile parameters in patients with type 2 diabetes mellitus and hypertension and to estimate the plasma fibrinogen levels in those subjects.

MATERIALS AND METHODS

An observational cross-section study was taken up where the subjects were selected randomly among the patients with diagnosis of type 2 diabetes mellitus with hypertension (both outpatient and inpatient) attending K.R. Hospital, Mysore during the period from June 2004 to March 2006. The subjects who did not have type 2 diabetes mellitus and hypertension were considered as controls. The sample size was 70 with 50 cases and 20 controls. All patients with diagnosis of type 2 diabetes mellitus with hypertension (both old and new cases) were included in the study. Diagnosis of diabetes mellitus was as per the ADA 2005 criteria and Diagnosis of systemic hypertension was done according to Joint National Committee 7th report. Pregnant women, patients with abnormal lipid profile secondary to hypothyroidism, alcoholic liver disease, renal failure and nephrotic syndrome were excluded from the study. Patients on drugs like glucocorticoids, estrogens and progesterones and the subjects with history of familial dyslipidemia were also excluded from the study.

The anthropometric parameters of obesity such as height, weight, body mass index (BMI), waist circumference, hip circumference, waist-hip ratio (WHR) and blood pressure was recorded as per WHO recommendations [7]. Fasting serum lipid profile cholesterol and triglyceride measurements were performed by using standard enzymatic techniques: LDL-cholesterol was calculated by using formula of Friedewald et al [8]. Venous plasma glucose was measured by glucose oxidase method and plasma fibrinogen was measured by Clauss method.

All statistical analysis was done using SPSS +10.0 (Illianos, Chicago, USA). Comparison of various parameters among male and female subjects, with or without diabetes was performed by t-test. Correlation between two variables was done by Pearson's correlation coefficient.

RESULTS

The mean age of the study group was 55.80 ± 7.4 years and control group was 51.6 ± 6.57 years. 64% of cases were females as against 36% of males while 60% of controls were females as against 40% of males. 44 out of 50 cases were known diabetics and 6 were newly detected diabetics. Shortest duration of diabetes that was observed in the present study was 1 year and the longest duration was 22 years with a mean duration of 9.38 years. Shortest duration of hypertension that was observed in the present study was 1 year and the longest duration was 20 years with a mean duration of 5.98 years. **Figure-1** shows the comparison among the anthropometric measurements between cases and controls.

24% of the cases in the present study were observed to be in overweight category. 24% of the cases in the present study were observed to be in obese category. While 25% of controls in present study were observed to be in overweight category and none were obese. All female cases had waist circumference greater than 88 cms. 16% of male cases had waist circumference greater than 102 cms. **Table-1** shows the prevalence of generalized and central obesity in cases and controls.

Figure-2 shows the lipid profile compared between the cases and controls. All cases had serum triglyceride values more than 150 mg/dl and 88% of them had serum triglyceride values more than 200 mg/dl. All controls had serum triglyceride values less than 200 mg/dl and 65% of them had a serum triglyceride values less than 150 mg/dl. All cases had serum VLDL levels > 30 mg/dl. 60% of the controls had VLDL < 30 mg/dl. 64% of cases had low HDL levels (< 40 mg/dl) while all controls had normal HDL levels (40-60 mg/dl). 50% of cases had normal LDL-C levels (< 100 mg/dl), 28% of cases had above optimal LDL-C levels (100-129 mg/dl) and 22% of cases had borderline high LDL-C levels (130-159 mg/dl). While in controls, 75% had normal LDL-C levels, 15% had above optimal LDL-C levels and 10% had borderline high LDL-C levels.

60% of cases had normal cholesterol levels (< 200 mg/dl), 28% of cases had borderline high cholesterol levels (200-239) and 12% of cases had high cholesterol levels (≥ 240) while among

controls, 75% had normal cholesterol levels, 25% had borderline high cholesterol levels. 62% of cases had TC/HDL ratio greater than 5 whereas 95% of controls had TC/HDL ratio below 5. 52% of cases had plasma fibrinogen levels greater than 450 mg/dl but all the controls had normal plasma fibrinogen as shown in **Figure -3.**

On estimation of correlation coefficients (**Table-2**), Body Mass Index (BMI) is positively correlated to total cholesterol, TC-HDLC ratio, triglycerides and LDL-C and negatively correlated to HDL-C levels, but significant correlation was found between BMI, total cholesterol and TC/HDL-C. Plasma fibrinogen is positively correlated to BMI which is statistically significant.

DISCUSSION

The mean age of male and female diabetic hypertensives is significantly higher than that of controls. It suggests that as mean age in population advances, the number of people with diabetes and hypertension also increases [9, 10]. The mean weight values were not different in two groups, suggesting that it is a poor marker of body fat [9].The mean waist circumference was significantly higher in male and female diabetic hypertensives than controls. It suggests presence of abdominal obesity in diabetic hypertensives [9]. Waist circumference may be taken as bedside marker for abdominal obesity. It is a sensitive indicator for central obesity. The mean values of waist-hip ratio are significantly higher in male and female diabetic hypertensives than controls. It suggests that diabetic hypertensives have central obesity more commonly than controls. Waist-hip ratio is a sensitive indicator of central obesity.

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 [10].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 [10].Low HDL level in diabetics increases the risk of coronary artery disease. The mean values of LDL-C 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 [10]. The mean values of VLDL-C were significantly higher in diabetic hypertensives than controls. This is because of increased triglyceride production and VLDL is calculated by the formula
VLDL = triglycerides/5.

Hyper-triglyceridemia is one of the features of diabetic dyslipidemia. Hyper-triglyceridemia in diabetics is due to increase in the production of triacylglycerol and fatty acids in liver. Higher ratio of TCH/HDL increases the risk for coronary artery disease. Obesity is associated with increase in triglycerides, decreased HDL-C and high LDL-C. The elevated VLDL may be caused by increased hepatic FFA delivery, which increases triglycerides-synthesis. Low HDL-C and high LDL-C are indirect consequences of elevated triglycerides-rich VLDL. Genetic influences play a significant role in the expression of these abnormalities [3].

Plasma fibrinogen is an important component of the coagulation cascade, as well as a major determinant of blood viscosity and blood flow [4]. This increase in plasma fibrinogen levels may promote a prothrombotic or hypercoagulable state and may in part explain the risk of stroke and thromboembolism in conditions such as atrial fibrillation [5].

One of the major limitations of the present study is that the sample size is too small. The controls have been selected by simple random sampling. So the higher weight and height observed in the present study may not be significant. Common dyslipidemia encountered in Asian population is hyper-triglyceridemia. So hyper-triglyceridemia encountered in present study may not be significant. The lower body weight noted in the cases compared to controls may be due to diabetes itself and the same cannot be taken as significant. The normal plasma fibrinogen levels of Indian population are not studied.

In conclusion, diabetic hypertensives have higher plasma fibrinogen levels and it is significantly related to BMI and lipid profile parameters.

Table 1: Showing prevalence of various types of obesity

Types of obesity	Cases			Controls		
	Male	Female	Total	Male	Female	Total
Generalised obesity	3 (6%)	9 (18%)	12 (24%)	0	0	0
Central obesity	16 (32%)	30 (60%)	46 (92%)	1 (5%)	6 (30%)	7 (35%)

Table 2: Showing correlation coefficient between P. fibrinogen and lipid profile

	P. fibrinogen	p-value
TCh	0.348	0.013
HDL-C	- 0.156	0.279
TC/HDL C	0.208	0.148
TG	0.276	0.05
LDL-C	0.127	0.381

$p < 0.05$, statistically significant

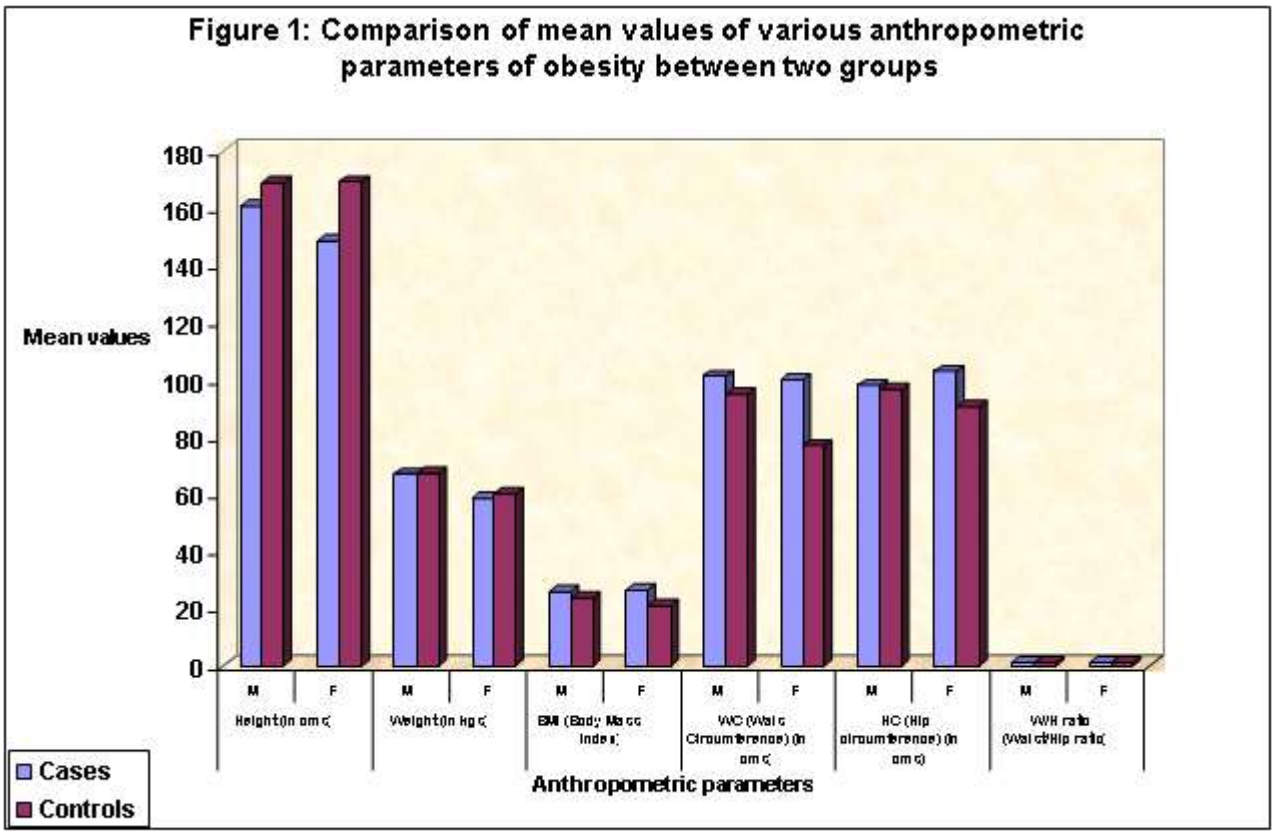


Figure 2: Comparison of mean values of fasting serum lipid profile between the two groups

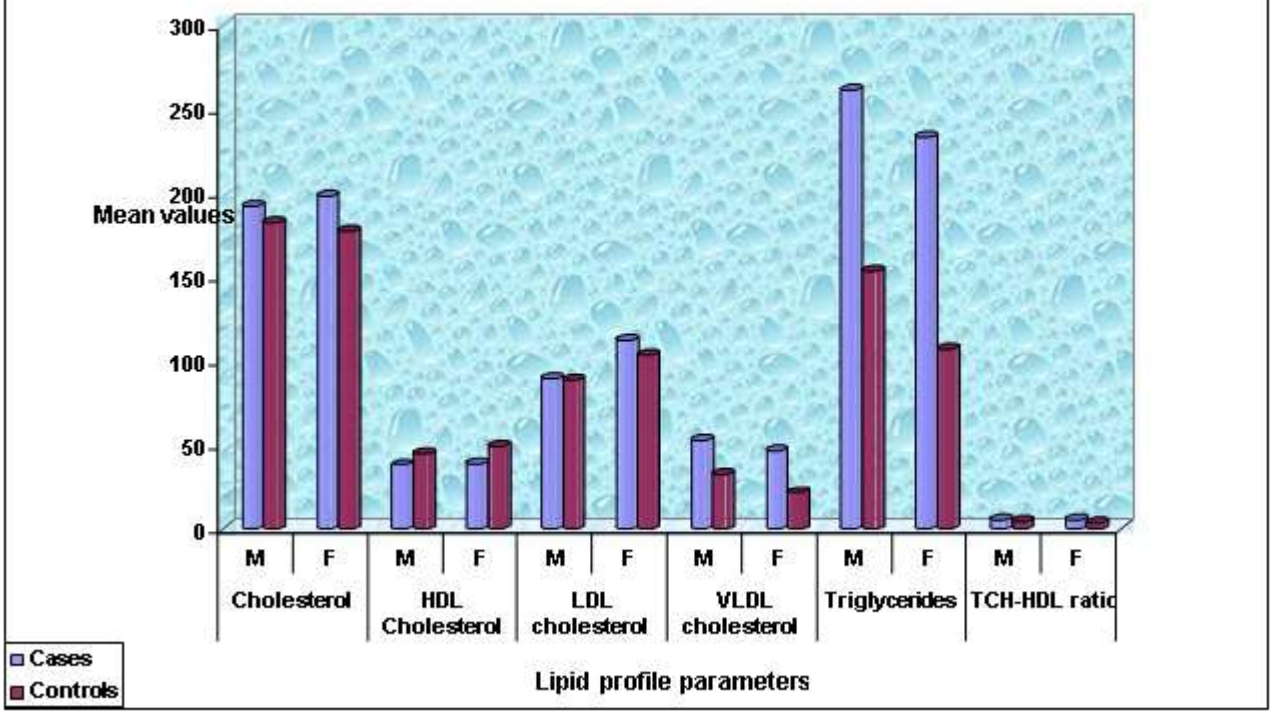
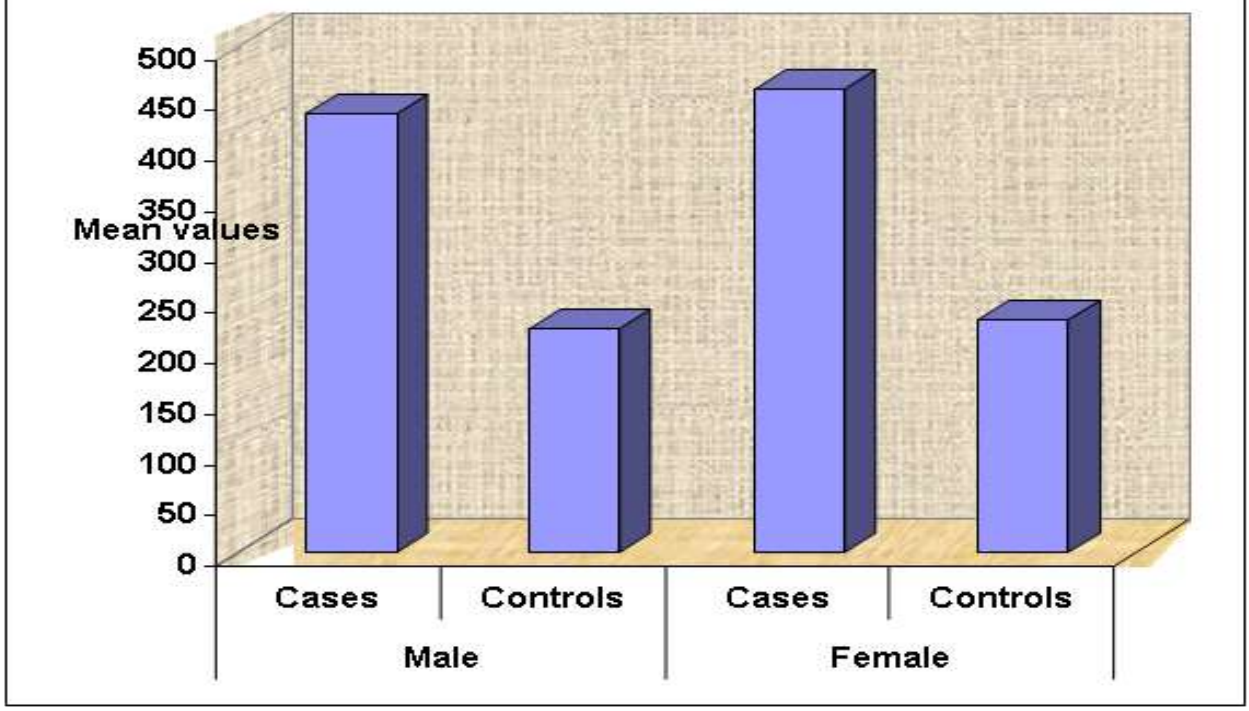


Figure 3: Comparison of mean values of plasma fibrinogen between two groups



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