ORIGINAL RESEARCH

A Correlative Study of Serum Fibrinogen Levels, BMI and Lipid Profile in Type 2 Diabetes Mellitus with Hypertension

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ABSTRACT
Aim: To estimate serum fibrinogen levels in patients with type 2 diabetes mellitus and hypertension and also to correlate serum fibrinogen with BMI and lipid profile parameters. **Material and Methods**: The present study was conducted on 135 patients at Narayana Medical College, NelloreduringMarch 2022 to December 2022. Patients are divided into a study group and acontrol group. **Results**: Higher serum fibrinogen levels were found in diabetic hypertensive patients (444.30 ± 63.58).There was a significant positive correlation between serum fibrinogen and BMI ($p<0.05$).There was a significant positive correlation between BMI and total cholesterol levels ($p< 0.05$). There was a significant positive correlation of serum fibrinogen with total cholesterol, TCH/HDL, and triglycerides. **Conclusion**: It can be concluded from the results that Type 2 Diabetics with hypertension have elevated fibrinogen levels related toBMI and total cholesterol, TCH/HDL and triglyceride levels in a statistically significantmanner.
Keywords: Body Mass Index, Fibrinogen, Total Cholesterol, Triglycerides.

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized byhyperglycemia resulting from defects in insulin secretion, insulin action, or both.The chronic hyperglycemia of diabetes is associated with long-termdamage/dysfunction and various organ's failure, especially the eyes, kidneys,nerves, heart, and blood vessels.Diabetes is an "Iceberg" disease. According to recent estimates, theprevalence of diabetes mellitus in adults is around 4% worldwide. It is projectedthat the disease prevalence will be 5.4% by the year 2025, with the global diabeticpopulation reaching 300 million. Of this, close to 77% of the global burden of disease is projected to occur in developing countries[1].

Type 2 Diabetes Mellitus forms 95% of all diabetics. An estimated 30million persons in the South East Asian region are affected at present. It isestimated that by the year 2025, there will be nearly 80 million diabetics in thisregion, the highest among all WHO regions. The greatest increase will be in India,i.e., from 19.4 million (1995) to 57.2 million by 2025. The prevalence of diabeticsin Indian adults was 2.4% in rural and 4-11.6% in urban dwellers[2]. The aim of the study was to estimate and correlate the serum fibrinogen levels, BMI and lipid profile intype 2 diabetes mellitus with hypertension.

MATERIAL AND METHODS

The patients diagnosed with type 2 Diabetes mellitus with hypertension coming to Narayana Medical College, NelloreduringMarch 2022 to December 2022. Controls were subjects who do not have type 2 diabetes mellitus and hypertension. 135 patients were selected randomly and divided into case (n=80) and control (n=55).

INCLUSION CRITERIA

1. All patients with a diagnosis of type 2 diabetes mellitus with hypertension.
2. Patients who are willing to participate in the study and have given written consent.

EXCLUSION CRITERIA

1. Type 1 Diabetes mellitus patients.
2. Patients with abnormal lipid profile secondary to hypothyroidism, alcoholic liver disease, renal failure and nephrotic syndrome.
3. Patients on drugs like Glucocorticoids, estrogens and progesterons.
4. Patients with a history of familial dyslipidemia.
5. Pregnant women.
6. Patients with a known history of coronary artery disease.

Method Followed

1. Anthropometric parameters of obesity as per WHO recommendations.
2. Fasting serum lipid profile cholesterol and triglyceride measurements were performed by using standard enzymatic techniques: LDL-cholesterol was calculated by using the formula of Friedewaldet al.[3]
3. Venous plasma glucose was measured by the glucose oxidase method.
4. Plasma fibrinogen was measured by the Clauss method.

MEASUREMENT PROTOCOLS

1. **Height:** It was measured against a vertical board with an attached metric rule, and a horizontal headboard was brought in contact with the uppermost point on the head. It was recorded barefoot, with a person standing on a flat surface and weight distributed evenly on both feet and heels together and the head positioned so that the line of vision is perpendicular to the body. The arms should be hanging freely by the sides, and the head, back, buttocks and heels should be in contact with the vertical board. The individual was asked to inhale deeply and maintained a fullyerect position. The topmost point on the head with sufficient pressure to compress the hair was taken as height to the nearest of 0.1 cm.[4]
2. **Weight:** Weight was recorded without footwear with light clothes worn on the body, standing straight on the center of the weighing machine with bodyweight evenly distributed between both feet by the ISI certified weighing machine to the nearest of 100 gms.[4]
3. **Body Mass Index:** Calculated as wt (kg)/ht^2(mt^2)
4. **Waist circumference:** It was measured in centimeters with a flexible measuring tape, midway between the inferior margin of the last rib and crest of the ilium in the horizontal plane, at the end of expiration, to the nearest of 0.1 cm. The tape should not compress the underlying soft tissues.[4]
5. **Hip circumference:** It was also measured in centimeters with a flexible measuring tape at the level of maximum extension of buttocks (greater trochanter) bilaterally in the horizontal plane with the subject standing with arms at the sides and feet together with light clothes over the body.[4]
6. **Waist-hip ratio** – WC/HC.
7. **Blood pressure:** After the initial screening, confirmation of hypertension diagnosis is based on the average of 2-3 readings taken at each of two or more visits at least one week apart. Preferably a standard mercury sphygmomanometer should be used.

STATISTICAL METHOD

Statistical analysis of our study was performed using the statistical software package of social science version 21(SPSS). The results of continuous variables are given as mean ± SD and proportion as a percentage. Comparison of various parameters among male and female subjects with or without diabetes and hypertension was performed by t-test. Correlation between two variables was done by Pearson's correlation coefficient and chi-square test. For all the tests, a 'p' value of <0.05 was considered statistical significance.

RESULTS

56.3% of cases were males against 43.8% of females. 67.3% of controls were males against 32.7% of females. The youngest case observed in the present study was 40 years old, and the oldest case observed in the present study was 84 years old. The study group's mean age was 59.06±10.34 years, and the control group was 55.6±9.98 years.Male diabetic hypertensiveshadhigher waist circumference, hipcircumference, waist-hip ratio, and BMI than the control group's males. Thedifference was statistically significant. Similar results were also seen between female diabetic hypertensives and female controls, as shown in Table 1. Though the table shows that controls had higher height and weight values than thecases, the BMI calculation shows that the cases were overweight or obesecompared to the controls. The lower weight in the cases may be due to diabetes.

Elevated levels of serum triglycerides, VLDL-cholesterol, LDL cholesterol, total cholesterol, TCH-HDL ratio and low levels of HDL-cholesterol were observedamong male and female diabetic hypertensives compared to male and femalecontrols. The difference was statistically significant (table 2).

All controls had normal serum fibrinogen. The mean serum fibrinogen levels in cases and controls were and 444.30±63.58 mg/dl and 223.91±25.38 mg/dl, respectively as shown in thetable 3.Elevated serum fibrinogen levels were observed among male and female diabetic hypertensives compared to male and

female controls. The differencewas statistically significant.

Body Mass Index (BMI) is positively correlated to total cholesterol, TC-HDLC ratio, triglycerides and LDL-C and negatively correlated to HDL-C levels. Still, asignificant correlation was found between BMI and total cholesterol, as shown in the table 4.

Serum fibrinogen was positively correlated to total cholesterol, TC/HDL-C, triglycerides and LDL-C, negatively correlated to HDL-C levels. A significantcorrelation was found between serum fibrinogen, total cholesterol, TCH/HDL-C andTriglycerides, as shown in Table 5.Serum fibrinogen is positively correlated to BMI, which is statisticallysignificant.

Table 1: Showing comparison of mean values of various anthropometricparameters of obesity between two groups

Parameters	Gender	Cases	Controls	P-value	Inference
Height (in cm)	Male	162.64 ± 6.523	168.22 ± 3.326	0.001	S
	Female	148.89 ± 3.270	162.17 ± 3.823	0.003	S
Weight (in Kgs)	Male	67.89 ± 8.454	68.19 ± 5.962	0.182	NS
	Female	59.91 ± 7.694	60.39 ± 7.437	0.218	NS
BMI (Body mass index) (kg/m^2)	Male	25.85 ± 4.337	24.13 ± 2.471	0.035	S
	Female	27.01 ± 3.195	23.07 ± 3.539	0.001	S
WC (Waist Circumference (in cm)	Male	101.20 ± 5.953	93.76 ± 7.584	0.000	S
	Female	99.97 ± 5.415	79.78 ± 2.315	0.000	S
HC (Hip circumference) (in cm)	Male	98.27 ± 2.263	97.08 ± 2.994	0.043	S
	Female	103.97 ± 5.685	93.89 ± 3.123	0.000	S
W/H ratio (Waist/Hip ratio)	Male	1.03 ± 0.081	0.97 ± 0.111	0.006	S
	Female	0.96 ± 0.039	0.85 ± 0.039	0.000	S

Table 2: Showing comparison of mean values of fasting serum lipid profilebetween two groups

Parameter	Gender	Cases (n=80)	Control (n=55)	P-value	Inference
Total Cholesterol	Male	190.64 ± 36.873	168.49 ± 17.958	0.002	S
	Female	197.34 ± 28.865	164.61 ± 26.255	0.000	S
HDL Cholesterol	Male	37.87 ± 4.143	45.38 ± 4.355	0.001	S
	Female	38.14 ± 3.607	49.11 ± 7.307	0.000	S
VLDL Cholesterol	Male	52.27 ± 12.992	30.70 ± 3.950	0.000	S
	Female	46.74 ± 12.120	21.56 ± 5.690	0.001	S
LDL Cholesterol	Male	100.51 ± 9.718	92.41 ± 17.517	0.010	S
	Female	112.46 ± 24.273	93.94 ± 26.928	0.014	S
Triglycerides	Male	261.53 ± 65.035	153.43 ± 19.867	0.000	S
	Female	233.66 ± 60.541	107.61 ± 28.049	0.000	S
TCH/ HDL ratio	Male	5.09 ± 1.104	3.73 ± 0.433	0.000	S
	Female	5.22 ± 0.944	3.39 ± 0.561	0.000	S

Table 3: Showing fibrinogen distribution

Serum Fibrinogen (mg/dl)	Cases			Controls		
	Male	Female	Total	Male	Female	Total
150 - 300	2 (2.5%)	1 (1.3%)	3 (3.8%)	37 (67.3%)	17 (30.9%)	54 (98.2%)
301 - 450	12 (15.0%)	9 (11.3%)	21 (26.3%)	0 (.0%)	1 (1.8%)	1 (1.8%)
> 450	31 (38.8%)	25 (31.3%)	56 (70.0%)	0 (.0%)	0 (.0%)	0 (.0%)
Total	45 (56.3%)	35 (43.8%)	80 (100.0%)	37 (67.3%)	18 (32.7%)	55 (100.0%)
Mean ± SD	433.87 ± 61.558	457.71 ± 64.512	444.30 ± 63.588	221.32 ± 19.284	229.22 ± 34.854	223.91 ± 25.384

Table 4: Showing correlation coefficient between BMI and lipid profile

	BMI	p-value	Inference
Total Cholesterol	0.196	0.023	P<0.05
HDL Cholesterol	-0.259	0.002	P<0.01
TCH/ HDL ratio	0.032	0.975	P>0.05
Triglycerides	0.042	0.626	P>0.05
LDL Cholesterol	0.003	0.712	P>0.05

Table 5: Showing correlation coefficient between Fibrinogen and lipid profile

	Fibrinogen	p-value	Inference
Total Cholesterol	0.319	0.000	P<0.001
HDL Cholesterol	-0.619	0.000	P<0.001
TCH/ HDL ratio	0.578	0.000	P<0.001
Triglycerides	0.595	0.000	P<0.001
LDL Cholesterol	0.165	0.058	P>0.05

DISCUSSION

A strong association of fibrinogen level with age has been found in our study.The level of fibrinogen rises with age. In the Lowe GDO study,[5] the mean fibrinogenconcentration increased steadily from 2.0 g/L in young adults to about 3.0 g/L in theelderly. The crude rate of increase in fibrinogen concentration was 1% per year overthe whole group.Plasma fibrinogen levels in men rise with age than in women. Bruno G et al study[6], Temelkovaet al[7], Lam TH et al[8], Om P. Ganda[9], Bruno y al[10] and Christophe Tribonilloy et al[11] were other studies in which age had been positivelyassociated with fibrinogen level. However, there was no association between ageand fibrinogen level in Raynand's E et al[12] studies.

The mean age of diabetic hypertensives in both men and women is far higher than controls. Ibehet al[13], Han et al[14] and Sosenko et al[15] have noted relatedobservations. It suggests that as the mean age in the population advances, thenumber of people with diabetes and hypertension also increases.

67.3% of controls were males against 32.7% of females, and 56.3% of caseswere males against 43.8% of females in our present study.The mean fibrinogen levels of females in this sample were higher than that ofmales. The fibrinogen concentration inGary TC Koet al[16], increased by 18.5 percent in his study of 101 diabetic participantsfrom 3.53 (1.06) g/L baseline to 3.97 (1.07) g/L. The increase was 15.5% in menand 9.5% in women, representing a change of 6.7% in men and 8.1% in women peryear, respectively.

The other studies which found higher fibrinogen values in females comparedto males were Balleisen L et al[17] study, Mariskaret al[18] study, William B Kannel et al[19] study and Folsom AR et at[20] study.

The mean BMI for males with diabetic hypertension is 25.85 kg/m^2, and forfemales with diabetic hypertension being 27.01 kg/m^2, with total mean in cases was26.36 kg/m^2, which was more than the mean of controls (23.78 kg/m^2). Ibeh at al[14] and Han et al[15] noted similar findings in their studies.In a study by StefaniaLamon- Fava et al[21], it is observed that increased BMIis associated with a three-fold increased risk of CAD than in subjects with low BMIand also reported the same in studies conducted by Manson JE et al.[22], Curb JD etal.[23], and Van Itallie TB[24].

The mean serum fibrinogen levels in diabetic hypertensives were significantly raisedcompared to controls. Similar results were observed by Barbara Glowinskaet al[25] andAnjula Jain et al[26].Mean Fibrogen was elevated in patients with diabetes mellitus compared withnon-diabetics in a Bruno et al. study with 1574 people with diabetes in northern Italy.Similarly, Jensen et al. reported a steady rise in the amount of fibrinogen incomplicated diabetics.[27]The mean value of fibrinogen was considerably higher inpatients with coronary artery disease than in controls. It appeared to be higher inpeople with diabetes than in non-diabetics in a study performed by Eriksson et al inthe Stockholm area.[28]

There was a positive correlation between Body Mass Index and TotalCholesterol, which was statistically significant. Similar results were observed by Subhankar Chowdury et al[29] and Hideki et al[30].In a study conducted by Om P. Gandaet al[31], BMI was significantlyand linearly associated with hypertension, fasting glucose levels, total serumcholesterol, VLDL and LDL cholesterol and inversely related HDL cholesterol, whichare the risk factors of CAD.

A positive correlation was found between serum fibrinogen levels and totalcholesterol, which was statistically significant. Similar results were observed byAnjula Jain et al[26], Barbara Glowinska et al[25] studies.In the present study, cholesterol level, serum triglyceride level, and LDL levelwere positively

correlated with fibrinogen, and HDL cholesterol was negativelycorrelated with fibrinogen. The Gary TC Koet al[16]analysis shows only changes in the plasmaconcentration of triglycerides to be in line with changes in fibrinogen levels.

Om P. Gandaet al[31] in their study, found a positive correlation of fibrinogenlevel with total cholesterol but not with triglycerides and HDL cholesterol. Resch KL[73] and Ernst E also found a positive correlation among plasmafibrinogen level, total cholesterol and LDL cholesterol.Our present study observed a negative correlation between serum fibrinogenlevel and HDL-cholesterol. Similar results were observed by Resch KLet al[32].

A significant positive correlation was found between serum fibrinogen andBMI. Similar results were observed by Anjula Jain et al[26] and Barbara Glowinska et al[25].In the study, there was a positive correlation between serum mean fibrinogenvalue and BMI. In the study of Ditschumit HH et al[33] found that obesity was independently related to mean fibrinogenlevel and fibrinogen level decreased after reduction of weight.Tribouilloyet al[11], in their study, found that fibrinogen levels were higher inthose who were obese with a BMI of more than 30 Kg/m^2.In the study of Balleisen Let al[17], the correlation between fibrinogen and body weight was more striking infemales than in males, irrespective of age and pill usage.

LIMITATIONS

1. The total number of patients studied was a small number. Only 80 cases and 55 controls have been studied.
2. The controls have been selected by simple random sampling. So the higher weight and height observed in the present study may not be significant.
3. 3. Common dyslipidemia encountered in the Asianpopulationis hypertriglyceridemia. So, hypertriglyceridemia encountered in the present studymay not be significant.
4. The lower body weight values noted in the cases compared to controls may be due to diabetes mellitus itself, and the same cannot be taken as significant.
5. The normal serum fibrinogen levels of the Indian population are not studied.

CONCLUSION

Anthropometric parameters of obesity were significantly higher in diabetichypertensives than controls.Most of the Diabetic hypertensive patients have a central obesity pattern.The dyslipidemia pattern seen in diabetic hypertensives is elevatedtriglycerides, VLDL-C, LDL-C, Total cholesterol and TC/HDL and decreasedHDL-C.Diabetic hypertensives have higher serum fibrinogen levels, and it issignificantly related to BMI and lipid profile parameters.

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