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Fibrinogen, CRP, Homocysteine, Estrogen Levels And Lipid Profile In Type 2 Diabetic Females With Family History Of Coronary Artery Disease In Relation To Low Socioeconomic Status In Urban Setup

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Abstract

Coronary Artery Disease (CAD) is narrowing/blockage of the coronary arteries caused due to atherosclerosis with high risk in both the sexes in urban environment and in females with positive family history of CAD. Fibrinogen, C-Reactive Protein (CRP), homocysteine, estrogen, lipid profile in type 2 diabetic females with CAD family history in relation to low socioeconomic status in urban setup was determined in 101 cases and compared with 102 normal healthy female controls without CAD family history over 8 months period. The study parameters including fasting blood glucose (FBG), HbA1c, fibrinogen, CRP, homocysteine, lipid profile - total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), very-low density lipoprotein (VLDL) and lipoprotein (a) - [Lp–a] were elevated with decreased high-density lipoprotein (HDL) – (p value <0.05) were statistically significant. Slight decrease in estrogen levels was noted (p value >0.05) – statistically not significant. High TC, TG, LDL, VLDL, Lp–a, and low HDL were seen in diabetics, due to lipolysis and gluconeogenesis at periphery and glucose release in blood. The elevated estrogen levels decreased all the above parameters and promoted HDL increase, commonly seen in pre-menopausal women. Increased fibrinogen, CRP, homocysteine in CAD occurred due to fragmentation of internal elastic lamina, disruption of elastic fibers, smooth muscle hyperplasia, atherosclerosis induced arterio-venous thrombosis and impaired production/acceleration of HDL catabolism in diabetics. Our study concluded existence of a relationship between type 2 diabetic females with CAD family history in urban environment with serum fibrinogen, CRP, homocysteine, estrogen, lipid profile but further large-scale studies should be undertaken.

Keywords: CAD – Coronary Artery Disease, CRP – C-Reactive Protein, FBG – Fasting Blood Glucose, HDL – High Density Lipoprotein, Lp-a – Lipoprotein (a), LDL – Low Density Lipoprotein, TC – Total Cholesterol, TG – Triglycerides, VLDL – Very-Low Density Lipoprotein.

Introduction

Coronary Artery Disease (CAD) is one of the most leading cause of mortality as well as morbidity among both men and women and accounted for above one third of total deaths worldwide. CAD is the narrowing or blockage of the coronary arteries caused by atherosclerosis. [1] Earlier, CAD was considered a disease predominantly affecting men and the women counterparts were neglected in the cardiovascular research programmes. [2] It accounted for 1 in 3 women deaths irrespective of race or

ethnicity. [1] Most women are unaware of the fact of their risk for CAD. [2]

The CAD prevalence in adults rose from 3% to 10% in urban Indians and in the rural population from 2% to 4% with similar rates in both men and women. [3] The lifetime risk of CAD development at 40 years of age is 50% for men and 33% for women and showed a positive relation in females with family history of CAD. [4] The prognosis and outcome for women is much worse than men post myocardial infarction, percutaneous coronary intervention and coronary artery bypass grafting. [2,5]

Numerous studies have shown the involvement of multiple risk factors and an interaction between genetic and environmental factors. Besides these factors, diabetes, glucose intolerance, central obesity, dyslipidemia associated with high levels of total cholesterol, triglycerides, LDL, VLDL, Lp-a, $HbA1_c$, FBG and decreased HDL have been implicated in the development of CAD process. [1,5] Increased levels of Fibrinogen, Homocysteine and CRP were reported with age advancement and were found to be independent risk factors associated with CAD development. [2,3] Estrogen plays a protective role in prevention of development of CAD in premenopausal women. [2,6] However the Hormone Replacement Therapy during postmenopausal period showed varied responses and needs further studies. [2,4]

There exists a strong association between development of diabetes and family history of CAD being present in sibling sisters than parents or brothers in diabetic females less than 55 years of age. Women with low literacy rate belonging to low socioeconomic status are more prone to develop diabetes when compared to their educated counterparts due to behavioral risk factors such as lack of nutritious food intake, obesity, alcohol consumption, smoking, physical inactivity, lack of exercise and poor stress management. [1,5] However, the relationship between fibrinogen, CRP, homocysteine, estrogen, lipid profile in females with family history of CAD in low socioeconomic status in urban environment and diabetes development is still under investigation. [1,2] The levels of various parameters showed conflicting results. [1-5]

Aims And Objectives:

To determine the serum levels of fibrinogen, CRP, homocysteine, estrogen and lipid profile in type 2 diabetic females with family history of CAD belonging to low socioeconomic status in an urban setup. To assess the above risk factors in women with family history of CAD and comparing them with normal healthy females of the same socioeconomic status.

Materials And Methods:

A hospital based cross sectional case control study was conducted on total of 101 type 2 diabetic female patients with family history of CAD belonging to low socioeconomic status in urban setup over a period of 8 months with convenient sampling of patients attending the medical out-patient department of Arunditi Institute of Medical Sciences, Gandimaisamma, Dundigal, Medchal, Hyderabad, Telangana, India. The patients were compared with 102 normal healthy age matched female controls without family history of CAD from low socioeconomic group.

Patients with hypertension, thyroid disorders, and any other chronic and infectious diseases and those who are on vitamin or mineral supplements, steroids were excluded from the study besides the patients who did not give voluntary consent, male patients of all age groups and female patients less than 35 years of age. Informed consent was taken and approval from ethics committee was also obtained. Detailed medical history and relevant clinical examinations were carried out in these patients.

Sample collection – Venous blood (5ml) was collected from antecubital vein using aseptic precautions into red capped plain vaccutainers for estimation of levels of fibrinogen, CRP, homocysteine, estrogen, lipid profile, $HbA1_c$ in purple capped vaccutainer and in grey capped vaccutainer for estimation of fasting blood glucose.

Various study parameters were estimated by the following methods in cases and controls –

1. Fibrinogen: Quantitative Turbidimetric immunoassay method on Chem-7 semi-autoanalyzer.

2. CRP: Immunoturbidimetric assay method on Erba Mannheim 200 auto analyzer.

3. Homocysteine: Enzymatic assay method on Chem-7 semi-autoanalyzer.

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4. Estrogen: CLIA method on Snibe hormone analyzer.

5. Lipid Profile: Enzymatic assay method on Erba Mannheim 200 auto analyzer.

6. Fasting Blood Glucose (FBG): GOD – POD method on Mannheim 200 auto analyzer.

7. $HbA1_c$: Immunoturbidimetric assay method on Erba Mannheim 200 auto analyzer.

All the analytes estimated are subjected to standard quality control (QC) guidelines. External Assurance Quality Scheme (EQAS) is under CMC Vellore. Internal Quality control is run twice daily with both first party controls (Cobas-PCC1, PCC2 and third-party controls (Randox)).

Results And Discussion:

The results obtained for mean and standard deviation of various parameters in controls and cases were tabulated as follows –

Table 1: Mean and Standard deviation of various parameters in controls and cases.

S. NO.	PARAMETER	MEAN &SD OF CONTROLS	MEAN & SD OF CASES	P - VALUE
1.	Age (Years)	45.29 ± 10.21	60.84 ± 10.32	<0.05*
2.	Fasting Blood Glucose (mg/dL)	110.29 ± 41.71	129.81 ± 49.00	<0.01*
3.	$HbA1_c$ (%)	6.14 ± 1.33	7.03 ± 2.3	<0.02*
4.	Fibrinogen (mg/dL)	4 ± 44.4	306.6 ± 0.65	<0.05*
5.	CRP (mg/dL))	0.438 ± 0.317	1.11 ± 1.41	<0.02*
6.	Homocysteine (umol/L)	6.53 ± 1.59	16.06 ± 1.34	<0.01*
7.	Estrogen (pg/mL)	22.7 ± 6.0	22.2 ± 4.9	>0.05**
8.	Total Cholesterol (mg/dL)	156.95 ± 27.68	271.41 ± 31.14	<0.01*
9.	Triglycerides (mg/dL)	175.19 ± 66.91	226.16 ± 78.59	<0.01*
10.	Low Density Lipoprotein (mg/dL)	101.08 ± 27.95	158.68 ± 30.19	<0.02*
11.	High Density Lipoprotein	42.24 ± 8.54	28.96 ± 9.69	<0.02*

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	(mg/dL)			
12.	Very-Low Density Lipoprotein (mg/dL)	33.52 ± 11.39	44.31 ± 16.30	<0.01*
13.	Lipoprotein (a) (mg/dL)	17.25 ± 8.03	50.11 ±36.13	<0.02*

In this study, the levels of fibrinogen, CRP, homocysteine, total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), very-low density lipoprotein (VLDL) and lipoprotein (a) – [Lp (a)] were significantly increased (P – value <0.05). High-density lipoproteins (HDL) levels were significantly decreased (P – value <0.05). Estrogen levels were slightly decreased and not significant statistically (P – value >0.05) in diabetic women as compared to their age matched controls of the same socioeconomic status.

In diabetic females, the fasting blood glucose and HbA1c were done and were found to be increased and in controls both the parameters were normal.

*P<0.05 is considered statistically significant.

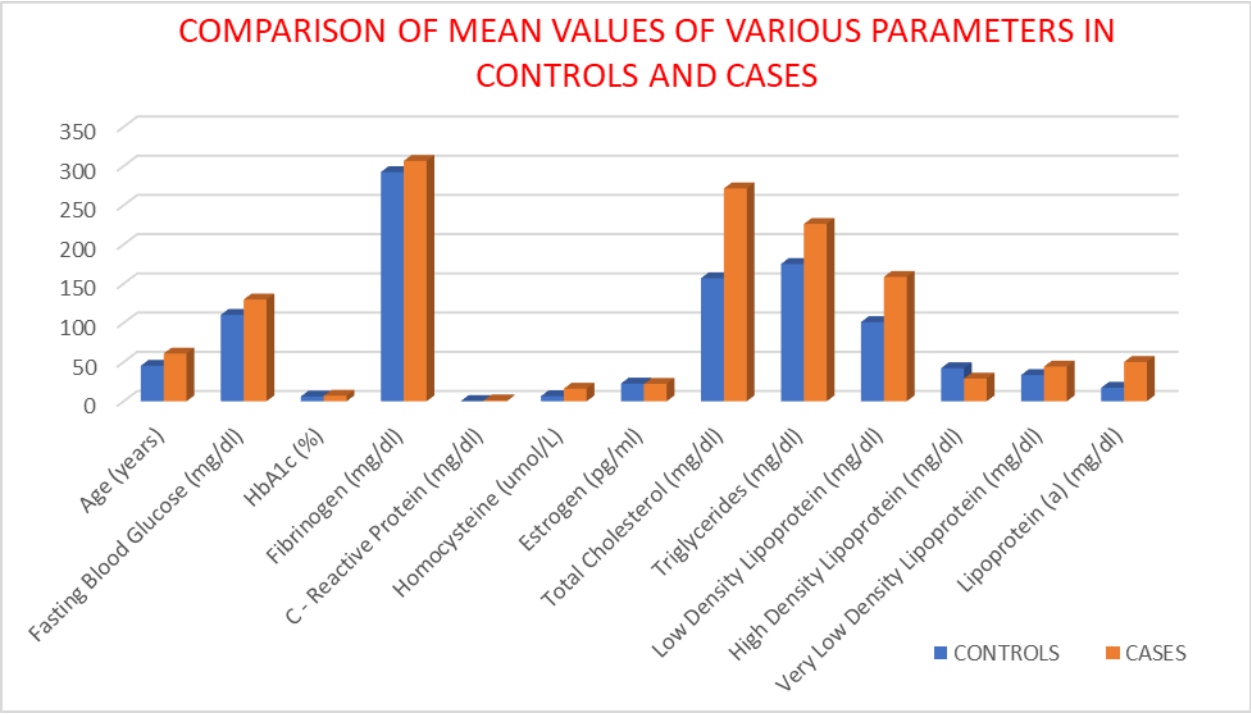
**indicates P>0.05 is not statistically significant.

Parameter values expressed as mean + SD.

The mean and standard deviation values of all the parameters in cases as well as control subjects were calculated and were represented in the graphical form as bar diagram using MS Excel Software.

The mean values were compared between the cases and normal healthy individuals. The P – Values were also calculated using student's paired T test to find out the statistical significance of various parameters.

Figure 1: Comparison of mean of various parameters in Controls and Cases.



Present study demonstrates that there exists a correlation between fibrinogen, CRP, homocysteine, estrogen, lipid profile and development of diabetes in women with positive family history of CAD in low socioeconomic status group in urban area. The FBG, HbA1c, along with fibrinogen, CRP, homocysteine,

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TC, TG, LDL, VLDL, Lp-a showed significant increase in study cases when compared to normal subjects. But the levels of HDL and estrogen in the cases were decreased when compared to their normal aged-matched controls. Other authors also found similar results according to their studies. [1-5]

A defect in coagulation leading to thrombosis may be a contributory factor for atherosclerosis as suggested by increase in the fibrinogen levels. [6] Fibrinogen itself is considered as an acute phase reactant and an independent risk factor for CAD and ischaemia. [7]

The acute phase protein CRP is a marker of systemic inflammation and its elevation in the blood suggests its role in the etiopathogenesis of atherosclerosis. [6]

Homocysteine is a risk factor for CAD due to its role as an inflammatory marker predisposing to disruption of the elastic fibers of the arterial wall, thrombosis, and hyperplasia of the smooth muscle.[6] These inflammatory markers may impair the production or accelerate the lipoprotein catabolism (HDL) that are protective against atherosclerotic process mostly seen in diabetics. [7]

Estrogen may have a role in the expression of endothelial nitric oxide synthase which is protective for atherosclerosis. However, in our study the levels of estrogen did not vary significantly in the study and control groups. Further-more, the increased level of estrogen is known to decrease all the above parameters and promote increase in levels of high-density lipoproteins which is the protective action of estrogen seen in pre-menopausal women and this action decreases with increase in age of the females. [8]

The dyslipidemia characterized by elevated levels of serum total cholesterol, triglycerides, low density lipoproteins, very-low density lipoproteins, lipoprotein (a) and low levels of high-density lipoproteins is mostly seen in diabetic individuals due to lipolysis. [9]

Increase in total cholesterol and LDL increases the risk of CAD, LDL being a strong predictor of mortality in women with CAD. A low concentration of HDL is a risk factor for CAD, compounded by an increase in LDL and triglyceride levels. This is called the lipid triad. [1]

The structure of lipoprotein (a) resembles plasminogen, and its levels are independent of other parameters of the lipid profile. Increased levels of lipoprotein (a), though being genetically influenced, are an independent risk factor for CAD. [2]

The levels of various parameters were decreased or increased as a result of the development of diabetes or these parameters in turn led to the development of diabetes in females with CAD family history in urban setup is not yet known.

Conclusion:

Our study concluded that the levels of fibrinogen, CRP, homocysteine, total cholesterol, triglycerides, low density lipoproteins, very-low density lipoproteins and lipoprotein (a) were significantly found on higher side and high-density lipoproteins were significantly decreased in type 2 diabetic females when compared to their normal counterparts. The estrogen levels were decreased marginally in cases than controls, but the decrease was not statistically significant.

Whether diabetes led to the development of abnormality in all the above parameters in women with family history of CAD or the parameters posed as risk factors contributing to the development of diabetes and impending CAD remain unknown for which large scale multi-centric population-based studies to establish the role of various parameters should be undertaken which would prove to be beneficial in future studies.

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