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RESEARCH ARTICLE

APOLIPOPROTEIN B / A1 RATIO AS RISK PREDICTOR OF ANGIOGRAPHICALLY PROVEN ATHEROSCLEROSIS

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Abstract

Background:-Apolipoproteins B and A-1 form major component of lipoproteins which are known to be involved in the pathogenesis of atherosclerosis. ApoB/Apo A-1 ratio reflects the balance between atherogenic and anti atherogenic particles thus reflecting the net atherogenic risk in such subjects.
Objectives:- To estimate serum Apo B and Apo A1 level and assess the role of their ratio apoB/apoA-1 as atherosclerosis risk predictor ofangiographically proven athrerosclerosis.
Material and Methods:-Study population consisted of angiographically documented 50 cases with coronary artery atherosclerosis and 50 controls without atherosclerosis of coronary artery. Serum lipid profile was measured on SYNCHRON CX-9 using standard kits. Serum apolipoprotein A and B were measured by immunoturbidemetric method on SYNCHRON CX-9using kits from SENTINEL.
Results:- Apo B/ Apo A1 ratio was significantly higher in cases than controls with p=0.008. No significant difference was found in conventional lipid markers of cases and controls.
Conclusion:- Apo B/ apo A1 ratio is a better atherosclerosis risk predictor than conventional lipid markers in angiographically proven atherosclerosis.

Introduction:-

Atherosclerosis is a chronic multifactorial diseasecharacterized by the atheromatous plaque on the vessel walls[1]. Manifestation of atherosclerosis varies according to vessel wall involved; CAD is one of the common manifestations of atherosclerosis. CAD which was earlier thought to be a disease of developed nations is now increasing in developing countries as well. It has become one of the leading causes of mortality and morbidity worldwide[2].To reduce morbidity and mortality efforts have been made to identify subjects at increased risk of CAD. Various diagnostic and prognostic markers of atherosclerosis have been studied and research is still being done in search of markers which could help in its early detection and management.

As atherosclerosis is a chronic multifactorial disease, dyslipidemia is one of the major risk factor known to play a significant role in the pathogenesis of atherosclerosis[3-5]. Lipoprotein LDL-C is considered atherogenic and HDL-C as anti atherogenic because of their role in the lipid transport[6-8]. Apo-B and apoA-1 arestructural and functional components of lipoprotein and are involved in lipid transport[9]. Apo B is involved in the transport of lipid from liver to the peripheral tissues[9-10] as it is the major apolipoprotein in Very Low Density, Intermediate Density and Low Density Lipoproteins[11]. Therefore, Apo B number indicates the total number of atherogenic particle.ApoA-1 is the major apolipoprotein involved in the transport of lipid from peripheral tissue to the liver as it forms major component of High Density Lipoprotein (HDL) particle and reflects the anti-atherogenic potential in HDL particles[12-13]. The ApoB/ApoA-1 ratio represents the balance between Apo B richatherogenic and Apo A-1 rich anti-

atherogenic particles. Since Apo ratio reflects the balance between atherogenic and antiatherogenic particles it is considered to be a better predictor of atherosclerosis risk.

Aim of our study was to assess the atherosclerosis risk predictive value of apo B, apo A-1 and (apo B/apo A-1) ratio in subjects with angiographically proven atherosclerosis.

Materials and methods:-

The study design was case-control study which was carried out jointly in the Department of Biochemistry, Lady Hardinge Medical College and Smt. SuchetaKriplani Hospital and Department of Cardiology, G.B. Pant Hospital, Delhi. With informed consent 100 subjects undergoing angiography were selected from Cardiology Department of G.B. Pant Hospital. Study population was selected on the basis of angiography; 50 subjects with atherosclerosis as proven by angiography were included as case and 50 subjects without atherosclerosis as proven by angiography were included as control group. Both the groups were age and sex matched. Study groups were subjected to detailed history with special reference to the atherosclerosis followed by clinical examination. Our study was approved by the Ethical Committee of Lady Hardinge Medical College.

The venous blood sample was collected from subjects under sterile conditions after overnight fasting. The blood samples for routine parameters were processed immediately for separation of serum and plasma. Routine parameters and lipid profile were measured by auto analyzer (SYNCHRON CX-9, Beckman Coulter) using standard reagents. Serum Apolipoprotein B and A1 were measured by immunoturbidimetric method (SENTINEL) on auto analyzer(SYNCHRON CX-9, Beckman Coulter).

Statistical analysis:-

Statistical analysis was performed by using SPSS version 20.0 software program. Continuous variables were expressed as mean ± S.D. The variables were compared with a normal distribution by unpaired 2-tailed Student's t-test. A value of $p \leq 0.05$ was considered statistically significant.

Results:-

Study groups were age and sex matched. Among various risk factors in study group, smoking was strongest and most prevalentrisk factor followed by hypertension.Significant difference was found in Apo B and Apo A1 ratio of two groups with $p \leq 0.008$. No significant difference was seen in the conventional lipid parameters of two groups. No significant difference was seen in serum Apo A-1 and Apo B level of two groups.

Discussion:-

Atherosclerosis is a chronic multifactorial disease of vessel wall characterized by atheromatous plaque[1]. Out of various risk factors dyslipidemia is one of major risk factor of atherosclerosis. Dyslipidemia characterized by increased LDL, TG and decreased HDLlevel is considered to be atherogenic[3-5]. Lipoproteins are known to play important role in the pathogenesis of atherosclerosis. LDL is an atherogenic lipoprotein involved in lipid transport from liver to the peripheral tissues or macrophages. HDL is an antiatherogenic lipoprotein involved in transport of lipid from peripheral tissue or macrophage to liver[14-17].Apo B and Apo A-1are the main apolipoproteins present in LDL and HDL respectively and are involved in the transport of lipid. Apo B is major apolipoprotein in Very Low Density, Intermediate Density and Low Density Lipoproteins, therefore, Apo B number indicates the total number of atherogenic particle. ApoB also serves as the ligand for the ApoB and apo E receptors thereby facilitating uptake of cholesterol in peripheral tissues and in the liver as reviewed[9,10,18]. ApoB may provoke atherogenesis since it can be entrapped in the arterial wall of the coronary arteries where it may be modified, oxidized and glucosylated and therefore also contribute in the process of plaque formation[18-20]. In this process ApoB containing LDL infiltrates the arterial wall and many factors like adhesion molecules, cytokines, and growth factors are involved in oxidation processes leading to inflammation and growth of plaques unless HDL bound ApoA-I can neutralize these processes. ApoB has been found to have a stronger relation with atherosclerosis risk than LDL-C in several other studies such as AMORIS[21] study, the INTERHEART study[22], MONIKA/KORA[23]and QUEBEC Cardiovascular study[24].These findings question the role of LDL as the primary variable for atherosclerosis risk evaluation and target for lipid-lowering therapy. In our study no significant difference was found in LDL-C which could be because most of subjects in our study groups were on statins. Also we didn't find any significant difference in ApoB of two groups.

ApoA-I forms major component of HDL-C and initiates the RCT process in peripheral tissues. ApoA-I has also many other functions beyond RCT since apoA-I is involved in anti-inflammation, anti-oxidation, anti-infectious activity, anti-protease activity, anti-apoptotic, and antithrombotic functions[25-27]. Many studies have shown an inverse relationship between apoA-I and CAD[25-27]. High apoA-I values have been found to correlate with low risk for MI in AMORIS[21]. No significant difference was found in HDL-C and Apo A-1 level of our study groups. Probably, because study subjects were divided into cases and controls on the basis of angiography and most of them were already on statins. This could be the probable reason for the lack of any significant difference in lipid profile of our study population.

Although various international guidelines have been using lipid ratios like TC/HDL-C and LDL-C/HDL-C to define CAD risk, these are not preferred nowadays because of limitations in their measurement. One reason why the lipid ratios are questioned as relevant risk markers is due to the fact that HDL-C is included in both numerator and denominator of the TC/HDL-C ratio. Another reason is that LDL-C most commonly is derived by the Friedewald[28] formula, HDL-C is involved as a factor for calculating LDL-C by Friedwald[28] formula and therefore also indirectly in the nominator and denominator of that ratio. Also Freidwald[28]'s formula cannot be used for TG > 400mg/dl. Therefore, these ratios are not preferred nowadays. Unlike lipoprotein, apolipoprotein does not have such analytical limitations, further their ratio (Apo B/Apo A-1) has been emerging as one the better marker of atherosclerosis risk. In our study we didn't find any significant difference in the lipid ratios of two study groups.

In our study we found significant difference in Apo B/Apo A1 ratio of the two study groups. Apo B/ Apo A1 ratio was significantly higher in angiographically proven atherosclerosis cases than controls indicating that it is the balance between the Apo B and Apo A1 rather their individual level which determines the overall atherogenicity of these particles. Our finding was supported by various studies such as INTERHEART[22]study showed Apo ratio as one of the strongest and the prevalent risk factor for MI. Other studies supporting such findings are Dutch EPIC-Norfolk[29] study, The German MONICA/Kora[23] Augsburg study, Swedish ULSAM[30]studies. They showed that the risk of MI increased in parallel with increasing values of the Apo-ratio.

Therefore, we conclude that Apo B/ Apo A1 ratio is a better atherosclerosis risk predictor than conventional lipid markers in angiographically proven atherosclerosis.

Table 1:-Characteristics of study groups.

	CASE (Mean ±S.D)	CONTROL (Mean ±S.D)	p value
Age	51.22 ± 7.6	48 ±7.2	0.105
Sex (M)	35 (70%)	33(66%)	0.668
(F)	15(30%)	17(34%)	
BMI	22.9 ± 3.4	22.5 ± 2.4	0.544
HYPERTENSION	22 (44%)	9 (18%)	0.005
SMOKING	30 (60%)	11 (22%)	0.000
F/H/O CAD	4 (8%)	3 (6%)	0.695

p value≤0.05 is considered statistically significant

Table 2:- Conventional lipid parameters in study groups.

PARAMETERS	**CASE (Mean ± S.D)**	**CONTROLS (Mean ± SD)**	**p value**
T.CHOL(mg/dl)	143.4 ± 42.30	142.14 ± 37.30	0.875
TG (mg/dl)	146.08 ± 67.67	134.36 ± 63.89	0.375
HDL (mg/dl)	41.700 ± 8.83	43.580 ± 12.55	0.389
LDL (mg/dl)	81.580 ± 37.57	77.940 ± 34.64	0.616
VLDL (mg/dl)	29.22 ± 13.51	26.84 ± 12.52	0.375
LDL/HDL	1.97 ± 0.80	1.82 ± 0.67	0.308
T CHOL/ HDL	3.58 ± 1.31	3.38 ± 0.89	0.382

p value≤0.05 is considered statistically significant.

Table 3:-Special lipid markers in study groups.

PARAMETERS	CASE (Mean ± S.D)	CONTROLS (Mean ± SD)	p value
Apo A-1	101.88 ±24.43	109.2 ±32.3	0.090
Apo B	91 ± 24.82	85.76 ± 26.49	0.306
Apo B/ Apo A-1	1.028 ±0.41	0.822 ±0.34	**0.008***

p value≤0.05 is considered statistically significant.

Conflict of interest:- Nil

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