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A STUDY OF SERUM APO LIPOPROTEIN A1, APO LIPOPROTEIN B AND LIPID PROFILE IN STROKE

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ABSTRACT

The Role of Serum Lipids, Lipoproteins and Lipoprotein related entities in the prediction of Stroke is not clear.

AIM: To study the relation between serum concentrations of Apo lipoprotein A1, Apo lipoprotein B, Apo B/Apo A1 ratio and Lipid profile in Stroke Cases and to compare them with healthy controls.

DESIGN: A total number of 100 subjects within 30 – 70 years were considered for the study. 50 subjects with Stroke (both clinically as well as radiologically proven cases) and 50 subjects with age and sex matched healthy individuals as controls.

MATERIAL AND METHODS: Apo B, Apo A1and ApoB/ApoA1 ratio, Total cholesterol, HDL,LDL cholesterol and Triglycerides were measured. Statistical analysis done with Student 't' test to compare the data between cases and controls. Diagnostic validity tests are conducted to assess the Diagnostic efficiency of Apo A1, Apo B and Apo B/Apo A1ratio.Significant results were obtained.

KEYWORDS : stroke, lipoproteins, cholestrol

INTRODUCTION

Stroke is a Global health problem and makes an important contribution to the morbidity, mortality and disability all over the world [1]. It is the leading cause of disability in adults and the second most common cause of death globally [2]. "Little stroke, big trouble" the theme speaks about the importance of Stroke as a critical warning sign of further more debilitating vascular events or death [3].Abnormal lipid profile parameters like Total Cholesterol (TC), Low Density Lipoprotein (LDL) cholesterol, High Density Lipoprotein (HDL) Cholesterol and Triglycerides (TG) are the probable risk factors for Ischaemic Stroke, largely due to their relation with Atherosclerosis. The apo lipoproteins are protein components of the Lipoproteins. Apo lipoprotein B (Apo B), reflects the concentration of potentially atherogenic Lipoproteins (LDL) and Apo lipoprotein A1(Apo A1) reflects the concentration of anti atherogenic particles (HDL), represent the additional Lipoprotein related entities that may indicate a vascular risk [4]. Dyslipidaemia, low Apo A1 and high Apo B are exclusively accepted as the risk factors for Coronary artery disease and stroke. In contrast, the correlation is not well established for Stroke [5]. So, the present study was planned to evaluate the relationship between Apo A1, Apo B and Lipid profile in Stroke

MATERIAL AND METHODS

A cross sectional study on the serum Apo A1, Apo B and Lipid profile in the Stroke subjects was carried out for a duration of 1year. A total number of 100 subjects within 30 – 70 years were considered for the study. 50 subjects with Stroke (both clinically as well as radiologically proven) were taken as the cases and 50 subjects age and sex matched healthy individuals were taken as the controls [Table/ Fig-1].

EXCLUSION CRITERIA-

- Patients with Liver Disease, Renal diseases, Sepsis, any sort of Malignancy were excluded from the study.
- Patients who were using drugs related with lipid profile alterations were excluded from the study.

All the cases and the controls were selected from Sree Balaji medical college and hospital, chennai-44 and the study was carried out in the Department of General Medicine. After obtaining the informed consents from the cases and the controls, about 6 ml of blood was drawn under aseptic precautions in sterile bulbs with overnight fasting for 12 hours early in the morning. The serum was separated by centrifugation and it was then used for the analysis.

Total cholesterol value was estimated by the Enzymatic Cholesterol oxidase Phenol aminoantipyrine method. HDL cholesterol value was estimated by the Enzymatic Cholesterol oxidase Phenol aminoantipyrine method after the precipitation of LDL, Very Low Density Lipoprotein (VLDL) Cholesterol and Chylomicrons values with phosphotungastate in the presence of divalent cations such as Magnesium. The triglycerides was estimated by the Enzymatic glycerol phosphate oxidase – Phenol aminoantipyrine method. LDL cholesterol value was estimated by using Friedewald's formula. Apo B and Apo A1 were estimated by an immunoturbidimetric method [6]. The estimationsof the values are done by using a Semiautoanalyzer (Erba). The statistical analysis was done by using Student's 't' test method. A "p" value of less than 0.05 was considered as statistically significant. Diagnostic validity tests were conducted to discriminate those with Stroke and those without the Stroke. The median values of the combined groups were used as the cut off for discriminating the cases from the Controls.

Table-1: Descriptive information on study subjects

No. of subjects		Controls (n=50)	Cases (n=50)
Age(years)	Mean±SD	58.5±10.8	61.9±7.1
	Range	40- 69	40-72
Gender	Male	31	34
	Female	19	16

RESULTS

The serum levels of Total cholestrol, LDL – C and Triglycerides were higher and HDL – C was lower in the Stroke cases than in the Controls and the difference was statistically significant with a p value of < 0.001 [Table/ Fig-2]. The serum levels of the Apo B and the Apo B / Apo A1 ratio were higher and Apo A1 was lower in the Cases as compared to the Controls. The difference was statistically significant with a p value of < 0.001 [Table/Fig-3].

For Apo A1, the cut off value was 114 mg/dl, for Apo B the cut off value was 144mg/dl and for the Apo B/Apo A1 ratio, the cut off value was 1.2. Apo B, Apo A1 and the Apo B/Apo A1 ratio had the highest Sensitivity, Specificity, Positive predictive value and Negative predictive value, with the diagnostic efficiencies for the Apo A1, the Apo B and the Apo B/Apo A1 ratio being 87%, 95% and 94% respectively [Table/Fig-4].

Table-2 Comparison of serum Total cholesterol, LDL, HDL and Triglycerides in cases and controls

Groups	n	TC (mg/dl)	LDL – C (mg/dl)	HDL – C (mg/dl)	TG (mg/dl)
Controls	50	188.0±36.9 (126-280)	113.0±38.3 (54- 226)	51.8±15.9 (25-82)	127.7±59.0 (56- 453)
Cases	50	274.3±28.8 (173-329)	203.7±28.8(173-329)	25.3±6.8 (10-42)	220.0±59.6 (116-499)
Mean diff		86.3	90.7	26.5	92.3
t value		13.08	12.82	10.87	7.78
p level		<0.001	<0.001	<0.001	<0.001

Table -3 : Comparison of serum Apo A1,Apo B and the ratio of Apo B/Apo A1 in cases and controls

Groups		**Apo B(mg/dl)**		**Apo A1(mg/dl)**		**ApoB/ApoA1**	
		Mean±SD	Range	Mean±SD	Range	Mean±SD	Range
Controls	50	106.4±29.8	112-196	158.9±39.6	86-266	0.71±0.27	0.31-1.58
Cases	50	190.8±39.7	138-296	87.1±23.6	41-145	2.39±0.96	1.1-5.0
Mean diff		84.4		71.7		1.68	
t -value		12.49		11.00		11.91	
p level		<0.001		<0.001		<0.001	

Table - 4: Diagnostic validity of Apo A1,Apo B and ApoB/ApoA1 ratio for discrimination of stroke subjects

	Apo B (>144mg/dl)	**Apo A1 (<114mg/dl)**	**ApoB/ApoA1 (>1.2)**
Sensitivity	96%	88%	98%
Specificity	94%	86%	96%
PPV	94%	86%	98%
NPV	95%	86%	96%
Diagnostic efficiency	95%	87%	94%

DISCUSSION

Atherosclerosis of the extracranial or the intracranial arteries accounts for significant proportions of causing stroke. Accordingly, the known contributors of atherosclerosis like cholesterol and its entities play an important role in its etiology of stroke [7]. Elevated total cholesterol and LDL cholesterol are described in terms of their effects on the pathogenesis of atherosclerosis. An association between carotid atherosclerosis and LDL – C has been found in many studies in the past [4]. It has also been shown that the elevated LDL – C levels in patients with are more susceptible to lipid peroxidation and that the products of lipid peroxidation are significantly associated with the risk of causing Stroke [9]. An inverse correlation has been found between the serum HDL – C levels and the risk of Stroke occurence. This can be explained by the anti atherogenic effects of HDL [11-12].The anti atherogenic effect of HDL can be further explained by several mechanisms like – its ability to transport cholesterol from the peripheral cells to the liver (a reverse cholesterol transport), its ability in preventing lipid peroxidation (antioxidant effects). its ability in limiting the expression of cytokines like TNF – α and interleukin – I (anti-inflammatory effects), its ability in inhibiting platelet activation and aggregation and its ability in improving the endothelial function by prostacyclin release and the release of the endothelium derived relaxing factor [11,12]. Higher HDL cholesterol levels are associated with less severe Stroke and a better outcome after the Stroke [10]. In the present study, the mean values of Apo B was higher, that of Apo A1 was lower and the Apo B /Apo A1 ratio was higher in the cases as compared to controls and the difference was statistically significant with a p value of < 0.001. The Apo B which is present in VLDL, IDL, large buoyant LDL and small dense LDL, reflects the total number of atherogenic particles. High Apo B levels may indicate an increased number of small dense LDL particles which easily oxidise and which promote an inflammatory response and help in the growth of plaques. The larger Apo B containing particles such as the VLDL and the IDL can enhance the risk of athero thrombosis by inhibiting fibrinolytic system and by stimulating the cytokine production and the inflammatory responses. Apo A1, the major protein in HDL, has a central role in the reverse cholesterol transport and in transferring the excess cholesterol from the peripheral cells back to the liver in the HDL particles.The Apo B /Apo A1 ratio reflects the balance of the cholesterol transport in a simplified way. The higher the values of the Apo B/Apo A1 ratio, the more cholesterol is likely to be deposited in the arterial wall, thereby provoking the process of atherogenesis and increasing the vascular risk. Therefore, the comparison of the apo lipoproteins with the lipoproteins shows that they both have similar forms of predictive abilities. This supports the finding that Apo B, Apo A1 and the Apo B/Apo A1 ratio represent and are the additional Lipoprotein related variables that estimate the risk for Stroke as well as the respective Cholesterol components.

A major reason of employing Apo lipoproteins to assess the risk of vascular events is:

- They are measured directly, in contrast with LDL – C, which is usually calculated by using Friedewald's formula.
- The measurements of the Apo lipoproteins are internationally standardised.
- The measurements of the Apo lipoproteins are accurate, with more precision and easily automated.
- They do not require fasting blood samples like lipid profile [4].

Hence, both the lipoproteins and Apo lipoproteins are used as the predictors of Stroke. They have a good sensitivity but they lack the specificity. Abnormal levels are reported in various physiological and pathological conditions like Pregnancy, Cardiovascular disease, and peripheral arterial diseases. Hence, while using the lipoproteins and the Apo lipoproteins in predicting the occurrence of Stroke, it is important to consider and to rule out the above clinical conditions.

CONCLUSION

The apo lipoproteins have good sensitivity, specificity and a high diagnostic accuracy than lipid parameters. So, the current study supports that Apo lipoprotein A1, Apo lipoprotein B and the Apo B/Apo A1 ratio can be used along with the traditional lipid profile measurements for better prediction of stroke. More extensive studies are required to assess the predictivity of the apo lipoproteins in indicating the risk of stroke in the patients with the history of Transient ischaemic attacks, in the patients with abnormal lipid levels and other risk factors.

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