

ASSOCIATION OF ANTICARDIOLIPIN ANTIBODIES LEVELS WITH INSTENT RESTENOSIS IN PATIENTS WITH CORONARY ARTERY DISEASE

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Abstract : Present study was conducted to evaluate the association of IgG anticardiolipin antibodies with instent restenosis in patients having undergone percutaneous intervention with bare metal or drug eluting stents. Coronary artery disease patients with stent placement at least 6 months prior were screened for eligibility. 26 satisfied the inclusion/exclusion criteria. 10 patients with symptoms of restenosis, confirmed on check angiography served as cases and 16 without symptoms of restenosis served as control. Unpaired t- test was applied to ascertain the significance of any difference between control and study groups. Antibody levels were estimated on ELISA reader. The mean (\pm SD) anticardiolipin antibodies levels in cases and controls were 11.8 \pm 5.1 GPL/U/ml and 14.3 \pm 10.2 GPL/U/ml, respectively. The difference was not statistically significant ($P>0.05$). In conclusion, we did not observe any significant correlation between the level of IgG aCL and instent restenosis.

Key words : instent restinosis anticardiolepin antibody
coronary artery disease patients

INTRODUCTION

Stents are increasingly being used by cardiologists to manage patients with CAD. Both bare metal stents (BMS) and drug eluting stents (DES) offer advantages over angioplasty. They induce a more predictable and satisfactory result, reduce the risk of the abrupt closure of the artery during the procedure and also decrease the chance of

restenosis by nearly 50% (1). However, in-stent restenosis remains a significant problem with the stents.

Several factors are known to be associated with the phenomenon of in-stent restenosis for e.g. elevated LDL levels, increased levels of plasminogen activator inhibitor-1, type-2 diabetes and enhanced platelet aggregability (2). An association of

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anticardiolipin antibodies (aCL) with coronary artery disease has been shown in several but not all studies (3, 4). These antibodies bind to acidic phospholipids on platelet membranes and promote aggregation, activation, degranulation and ultimately thrombocytopenia (5). They have also been shown to have an adverse impact on outcomes in Acute Coronary Syndromes (6).

The association of aCL antibody with instent restenosis has not been studied much. Therefore, the present study was conducted to evaluate the association of IgG aCL with instent restenosis in patients having undergone percutaneous intervention (PCI) with bare metal or drug eluting stents.

MATERIAL AND METHODS

The study was conducted by the Department of Physiology, GMCH in collaboration with the Departments of Cardiology and Pharmacology, PGIMER, Chandigarh.

Subjects

Coronary artery disease patients who underwent angioplasty with stent placement presenting to the Out Patient Department of Cardiology, Nehru Hospital, Postgraduate Institute of Medical Education & Research (PGIMER), Chandigarh, were screened for eligibility. Ten patients with restenosis after stent placement confirmed on check angiography served as cases and sixteen patients without restenosis but with stent placement served as controls. They were matched for gender, family history, history of smoking, hyperlipidemia and diabetes.

Inclusion criteria

1. 30–70 year old patients with angiographically proven (> 50% decrease in lumen diameter) or suspected to have restenosis based on investigations/signs and symptoms.
2. Stent placement must have been done at least six months prior to the enrolment in the study.
3. A control group of patients with stent duration at least one year but without stent restenosis.
4. Willing to give written informed consent.

Exclusion criteria

1. Presence of infectious and/or autoimmune diseases.
2. Presence of luminal thrombus before percutaneous intervention (PCI) as documented in patient's/hospital records.
3. Presence of active *Treponema pallidum* infection.
4. History of intake of drugs likely to alter the aCL levels (phenothiazines, hydralazine, procainamide or prednisone).

The following data were collected for each patient: Age, Sex, Height, Weight, Abdominal Circumference, BMI, Blood Pressure, Lipid Profile (by using Randox Kit), ECG, Urea/Creatinine, ECHO, Angiography site/length, Clinical history, Type and number of stent, Procedural Complications, Current Status: Any major adverse cardiac event, Any Insegment Restenosis, Previous/Ongoing medications.

After obtaining consent, 5 cc of blood was drawn from a peripheral vein in tubes. Serum was separated by centrifugation at 3000 rpm and stored at -20°C . Antibody levels were estimated using Orgentee Diagnostika, Gmbh Kit for IgG antibodies on ELISA reader (Lab System Company). Results were calculated after reading the optical density at 450 nm.

Statistical analysis

Continuous data was expressed as either mean (\pm S.D) and or Median (Range). Dichotomous data was expressed as percentage. A regression line was constructed in order to obtain the line of best fit for standards for ELISA. Unpaired t-test was applied to ascertain the significance of any difference between the control and the study groups. Chi-square test was used for dichotomous data in the demographic characteristic. $P < 0.05$ was considered statistically significant.

RESULTS

The study was conducted between May and August, 2006. A total of 56 patients were screened, 26 satisfied the inclusion/exclusion criteria and were considered for further evaluation. Out of 26 patients, 10 served as cases and 16 controls.

Out of 10 cases, 6 patients developed restenosis after one year of stent placement and 4 patient after more than one year of stent placement. The average duration of stent placement in control was more than 6 months. The two groups were similar in respect to most of the demographic variables evaluated (Table I).

TABLE I: Demographic characteristics of cases and controls.

Characteristic	Control (n=16)	Cases (n=10)	P value
Age in yrs (Mean \pm S.D.)	55.8 \pm 10.8	55.5 \pm 7.0	0.846
BMI in kg/m ²	23.8 \pm 4.5	25.4 \pm 4.6	0.295
SBP in mm of Hg	126.8 \pm 12.3	131.2 \pm 18.3	0.478
DBP in mm of Hg	78.6 \pm 11.2	84.2 \pm 10.6	0.223
Total chol. in mg/dl	150.5 \pm 43.5	152.4 \pm 32.1	0.906
HDL in mg/dl	40.3 \pm 5.4	38.7 \pm 15.0	0.757
LDL in mg/dl	86.7 \pm 40.5	84.1 \pm 27.6	0.864
TG in mg/dl	131.0 \pm 55.6	145.3 \pm 24.0	0.452
M/F	1/15	4/6	0.034
No of Vessels D/S	3/13	3/7	0.508
Stent (BMS/DES)	8/8	5/5	1.000
Smoker (Y/N)	7/9	6/4	0.927

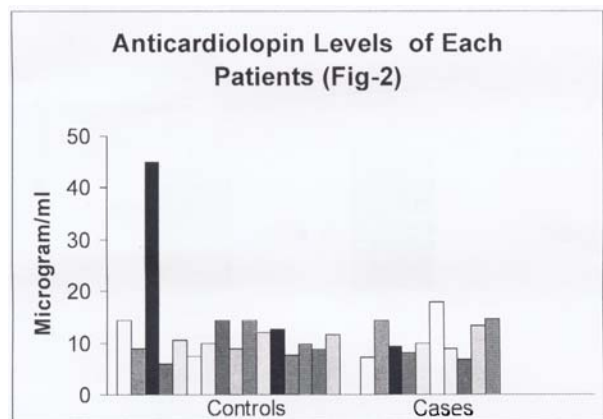


Fig. 1: Anticardiolipin levels of all patients included in the study.

The individual values of anticardiolipin levels are shown in Fig. 1. The mean (\pm SD) anticardiolipin levels in cases and controls were 11.8 ± 5.1 GPL/U/ml and 14.3 ± 10.2 GPL/U/ml, respectively (Fig. 2). The difference was not statistically significant ($P > 0.05$). The median values (range) for the two groups were 10.3 (5.9–45) and 9.6 (6.8–17.9) respectively for cases and controls.

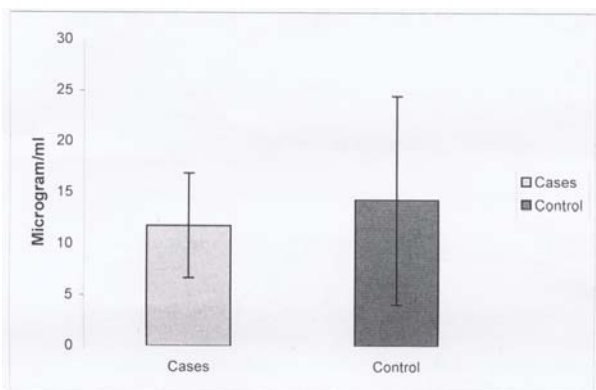


Fig. 2: Mean (\pm SD) aCL levels in cases and controls.

After adjusting for the demographic characteristics, the difference in the aCL levels continued to remain non-significant demonstrating the lack of effect of this variable on the outcomes.

DISCUSSION

Coronary restenosis is known to be the major limitation of PCI. Although stents have reduced restenosis as compared with balloon angioplasty, in-stent restenosis continues to occur in 40 to 45% of the patients (7). The occurrence of restenosis remains largely unpredictable for any particular patient, although powerful predictors of restenosis have been described that are helpful to characterize population of patients.

The association of anticardiolipin antibodies with CAD has been shown in several studies but remains controversial. Our study represents the first study to assess the association of anticardiolipin antibodies with in-stent restenosis in patients having undergone percutaneous intervention with Bare metal stent or Drug eluting stent.

In a study involving 74 males (34–87 years, mean 60) IgM and IgG-aCL in serum were determined in acute and chronic coronary artery disease. All patients underwent coronary angiography, patients with infectious and autoimmune diseases were excluded. 16 patients had CAD, 34 showed coronary stenosis with prior infarction, and 14 survived an acute MI, whereas 10 patients revealed no significant coronary narrowing (controls). The major risk factors were the same for all the groups. It was seen that neither the IgM nor the IgG anticardiolipin antibody levels showed any significant difference in four groups. The severity of coronary artery disease did not correlate to the level of anticardiolipin antibodies. Further, no correlation was found between elevated aCL and thrombocyte levels. Thus, showing that a higher anticardiolipin level does not appear to be a risk factor/marker for recurrent cardiovascular events (8).

On the other hand, in another study in patients with hyperlipidemia, to determine whether aCL IgG and IgM were independent risk factors for atherosclerotic vascular disease, it was seen that patients with atherosclerotic vascular disease events had lower HDL and higher aCL IgM levels. (9).

Anticardiolipin levels in previous studies have been seen to lie between 2.9 ± 5.5 to 9.6 ± 12.5 GPL/U/ml and values above 10 GPL/U/ml are associated with Acute Coronary Syndrome (10). In our study baseline values were already higher than 10 GPL/U/ml. These high baseline values would have decreased the chances of obtaining a significant difference between the cases and the controls.

The risk pattern profile for CAD in Indian

patients is different in many ways. For e.g. a large number of patients are lean and of younger age. It is possible that biomarkers such as CRP, aCL, fibrinogen etc which have been shown to be correlated in non-Asian population may not be of high relevance for Indian population.

Angiography was symptom driven in our study. It is well known that restenosis may even be silent. Had check angiography been done in the control group, it is likely that significant restenosis would have been present in some patients. However, check angiography at fixed intervals as is done in the West is not a routine practice in our country and therefore, may not have been ethically justified.

We also carried out a post-hoc analysis by deleting the outlier value in the control group. For these calculations, we imputed a single value with the mean value of the cases. Though the results continued to show a nonsignificant difference, there was a trend towards higher values in the cases. Since this analysis was not pre-specified, we cannot place too much emphasis on this.

In conclusion, our study has not shown any significant correlation between the level of IgG aCL and instent restenosis. However, since single point measurement of aCL was done and no follow-up could be done, further studies may be planned to shed more light on the status of aCL as a cardiovascular risk factor.

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