

Comparative Study to Evaluate the Anticardiolipin Antibody IgG in Pregnant and Non Pregnant Women with First Trimester Recurrent Abortions.

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Abstract: This study is an attempt to compare the prevalence of anticardiolipin antibodies in the pregnant (group 1) and non-pregnant (group 2) state in subjects with history of first trimester recurrent abortions; 72 healthy pregnant women were taken as controls (group 3); a total of 216 subjects were included; IgG anticardiolipin antibody (IgG acl) levels were measured by Elcsa technique. The presence of IgG acl were significantly higher in group1 (37.5%) as compared to group 2 (16.7%). These levels were negative or indeterminate in healthy controls.

INTRODUCTION

The recognition of and response to foreign antigens, amongst highly developed mammalian species, has been intensively studied. Advances in modern technology, especially involving recombinant DNA and advances in transplantation immunology have stimulated considerable interest in the immunologic aspects of pregnancy homograft. Many theories have been advanced to explain the lack of the rejection of fetus, such as: (1) maternal immunologic inertness, (2) the uterus, an immunologic privileged site, (3) antigenic immaturity of the fetus, (4) the functional absence of histocompatibility antigens on the trophoblast. Studies of immunologic parameters in pregnant women have been confined primarily to the measurement of total serum gamma globulin concentrations, antibody titers and fractional serum immunologic concentrations. Published data from various studies are contradicting, the total gamma globulin as determined by serum electrophoresis has generally been found to be decreased during pregnancy, where as immunochemical studies of fractional immunoglobulin concentration, have shown an increase in serum IgG level in one study¹; found unchanged in the other² and decreased in another study³. Substantial number (10%) of the human pregnancies terminate in spontaneous abortions leading to the emotional, physical as well as economical loss to the patient and the mankind. If the problem is recurrent in nature the trauma is manifold multiplied. In 50% of such cases the cause remains undiagnosed. Many of the answers to the problems plaguing the obstetricians caring for the patients of recurrent abortion will not be answered in the Petri dish or in the haematology laboratory is caused by immune alterations. In a large percentage (37%) of patients of recurrent abortions of unknown etiology, anticardiolipin antibody (acl) IgG has been diagnosed to be one of the culprits. Several studies^{4,5,6} have been done to find an association between anticardiolipin antibody and pregnant patients of recurrent abortions, but there is a paucity published literature comparing the presence of acl IgG in patients of first trimester recurrent abortions both in pregnant and non-pregnant state. The present study is an attempt to compare the prevalence of these antibodies in the pregnant and non-pregnant state in patients with history of first trimester recurrent abortions.

MATERIALS AND METHODS

The study population included 216 women with history of first

trimester recurrent abortions, pregnant group1 (72 subjects) and non-pregnant group 2, (72 subjects each, and from 72 healthy pregnant women (control) group 3 with good obstetric history, whose age ranged between 22 to 35 years; all patients in three groups were age matched and use of North Indian origin. History was taken from all the patients to rule out any drug intake (procainamide, anticoagulants etc.), which might lead to false positive results. Routine investigations and all other investigations, including TORCH test, VDRL, ultrasonography were performed to rule out any possible causes of recurrent abortions.

Sampling: Venous blood samples were obtained from pregnant women (group-1) with history of at least two recurrent abortions attending the antenatal clinic of Smt. Sucheta Kriplani Hospital, New Delhi. Additionally, venous samples were obtained from non-pregnant women (group-2) with history of two or more recurrent abortions attending the OPD clinics of the same hospital and also from healthy pregnant women with no history of any miscarriage taken as controls (group-3). The serum was separated and stored at -40 °C, until analysed for IgG acl levels.

Immunoglobulin measurement: Sera after collection were stored at -40°C were analyzed for anticardiolipin antibody(acl) IgG levels by ELISA technique, using BINDAZYME™. human Acl IgG Enzyme Immunoassay kit. All analyses in the present study were performed with the use of aliquots of the same specific antisera and same references were used for all studies. The same person conducted the tests throughout the study and analyses were performed on all samples at one time in order to avoid differences that could be attributed to day to day variability in the test procedure. Patients were classified into three levels of acl IgG presence, in line with the recommendation⁷ of Harris and Pierageli and the recommendation supplied with the Louisville standard (Table-1).

Table-1 : Interpretation for Anticardiolipin Antibody IgG

GPL Units/ml	Interpretation
<11 GPL	Negative
≥ 11 to < 20	Indeterminate
≥ 20 to 80	Low- Medium Positive
> 80 GPL	Strong Positive

The IgG acl was compared in group-1 and group-2 patients whereas group-3 patients served as controls.

Statistical analysis: The prevalence of IgG acl was statically compared

in the three groups.

RESULTS

When sera from 72 pregnant women (group-1) with age matched non-pregnant (group-2) women were studied under similar conditions, the prevalence of serum IgG aCl was observed to be less in group-2. The prevalence of IgG aCl in group-1 patients was 37.5% where as in group-2 patients was 16.7%, $p < 0.001$, significant (Table-2). In group-3 patients none of the patients had positive levels of IgG aCl. The levels were indeterminate in 16.7% of group-1, 25% of group-2 and 4.2% of group-3 patients and negative in 45.8%, 58.3% and 95.8% respectively. None of the patients in any of the groups had strongly positive levels of aCl IgG.

Table-2: Prevalence of Anticardiolipin antibody IgG

Inference	Group-1 (n=72) n(%)	Group-2 (n=72) n(%)	Group-3 (n=72) n(%)
Negative	33(45.8%)	42(58.3%)	69(95.8%)
Indeterminate	12(16.7%)	18(25%)	03(4.2%)
Low-medium positive	27(37.5%)	12(16.7%)	0
Strong positive	0	0	0

DISCUSSION

Recurrent pregnancy loss (rpl) has been associated with anticardiolipin antibodies^{4,5,6}. These antibodies reduce the growth of yolk sac and embryo and cause a maternal hypercoagulability leading to pregnancy loss in first trimester more so during the eighth and ninth weeks of pregnancy when the placenta replaces the yolk sac⁹.

Screening of these antibodies is mandatory in pregnant women with recurrent pregnancy loss for instituting efficient therapeutic regimen to achieve a successful pregnancy outcome⁶. The data obtained in the present study clearly indicate the presence of aCl IgG in patients with history first trimester recurrent abortions irrespective of the state of the patient pregnant or non-pregnant at the time of testing. Although the prevalence of aCl IgG was lower in the non-pregnant condition as compared to during pregnant state. This finding is in concurrence with a report¹⁰ that anticardiolipin antibodies decrease or may disappear in between pregnancies only to recur with increased activity in the subsequent pregnancy and lead to fetal loss but no numerical data has been reported. In conformity to our report, other researchers³ on a study of normal pregnancy have observed decrease in total serum IgG levels during second and third trimesters of pregnancy and post partum. This observation is also in keeping with a study¹¹ that has reported a post partum decrease in the B-cell count responsible for antibody mediated immunity. However, another worker¹² observed that the circulating B- cell levels during gestation remains unchanged. It had been suggested that maternal immune response is largely maintained during gestation, maternal susceptibility and the ability to combat the infection should be similar in both the pregnant and non-pregnant state.

The frequency of recurrent abortion in the presence of aCl antibodies is considerably increased. In a report¹³ it was observed that fetal death occurred in 10 of 13 (77%) patients with abnormal and in 2 of 37(5%) with normal aCl levels. A study on plasma aCl levels in post-menopausal (non pregnant) women in other diseases including myocardial infarction demonstrated high aCl levels as a risk factor. In another report⁹ aCl antibodies were associated with 743 post partum patients who had miscarried between 8 and 9 weeks of pregnancy. The finding in the present study that aCl IgG are positive during the non pregnant state in women with recurrent abortions in spite of the incidence being almost half when compared during the pregnancy, suggests that screening and treatment for these antibodies should be done as soon as the pregnancy is diagnosed or even pre conceptually. Treatment if not instituted can lead to abortions and fetal death in a huge percentage (96.8%) of pregnancies¹⁴. In the present study, 12 out of 72 (16.7%) patients of group-2 tested positive. This can be explained on the basis of a report¹⁰ which suggested that anticardiolipin antibodies may reduce in between pregnancies. Since women with aCl antibodies have a significant risk of adverse pregnancy outcome, the non pregnant patients with history of recurrent abortions even with slightly raised levels of these antibodies should be considered as high risk group. Early treatment of such patients may result in successful embryo implantation and provide protection against thrombosis of uteroplacental vessels thereby increasing the chances of successful pregnancy outcome. This may benefit these patients of recurrent pregnancy loss and the required treatment should be started pre-conceptually so as to increase the chance of successful outcome of their precious pregnancy.

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