RESEARCH PAPER | Medical Science | Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

Study of IgM anticardiolipin antibodies in pregnant ladies

KEYWORDS

Goel Neha	Tuli Anita
Professor, Department of Anatomy, Sudha Rustagi College of Dental Sciences and Research, Faridabad. Corresponding Author	Director,Professor and Head, Dept. of Anatomy, Lady Hardinge Medical College, New Delhi

ABSTRACT *Background : Abortion is termination of pregnancy by any means before the fetus is sufficiently developed to survive on its own. The growing recognition that in this group of patients there may be an immunologic basis aroused interest in research workers.The anticardiolipin antibodies (aCL) which are commonly associated with recurrent pregnancy loss are IgG and IgM. IgM antibody is the largest immunoglobulin and first to appear in an immune response. Women with phospholipid antibodies have a fetal loss of 90% when no specific treatment is given during pregnancy so this study was planned to find Anticardiolipin antibody levels (IgM) in patients of Abortions.Material/Methods: A total of 125 pregnant subjects were included in the study which includes study group (75 subjects) and a control group (50 subjects). Their blood was tested to assess the level of IgM aCL by enzyme-linked immunosorbent assay (ELISA). In the study group a total of 18 (24%) subjects were positive for raised IgM anticardiolipin antibodies. In the control group 2 (4%) subjects were positive for IgM anticardiolipin antibody all of whom had levels in the insignificantly positive range. Mean levels of anticardiolipin antibody IgM in control group was 2.57 ± 1.44 MPL units. p <0.001, highly significant. Result :Patients with increased IgM levels indicate a higher antibody burden with greater antigenic affinities explaining IgM mediated pregnancy wastage.*

Introduction

Abortion is termination of pregnancy by any means before the fetus is sufficiently developed to survive on its own. This corresponds to a gestational age of 20 weeks or a fetal weight of 500 gms. When abortion occurs spontaneously, the term miscarriage has been applied. The incidence of spontaneous abortion has commonly been quoted as 10% of all the pregnancies A number of immunologic and non-immunologic factors have been implicated as probable causes of abortions. Current methods of detection do not find any recognized causes in 40-50% of the patients with recurrent abortions [1]. The growing recognition that in this group of patients there may be an immunologic basis aroused interest in research workers. The antiphospholipid antibodies are gaining importance as potential causes of recurrent pregnancy loss and their presence in these is clearly documented.

The antiphospholipid antibodies were first detected by Wasserman in 1906.[2] The term antiphospholipid antibodies include three types of antibodies i.e. anticardiolipin (aCL), lupus anticoagulant and the antibodies causing false positive test for syphilis. The antiphoshoplipid antibodies are a diverse family of autoantibodies which share a common reactivity with negatively charged phospholipids. Although all three are associated independently with fetal loss, aCL are seen to have a definite edge over the other two.

The aCLs which are commonly associated with recurrent pregnancy loss are IgG and IgM. [3] These immunoglobulins are serum glycoproteins that are produced by plasma cells in response to antigens.

IgM antibody is the largest immunoglobulin and first to appear in an immune response. [4] It constitutes approximately 10% of normal immunoglobulins. High level of IgM anticardiolipin appear to be more distributed than IgG anticardiolipin antibodies and have been found in autoimmune, drug induced and infectious disorders including some patients with syphilis.

The antiphospholipid antibodies act via myriad of prothrombotic mechanisms [5] to bring about thrombosis and infarction of the placental vasculature, thereby causing fetal compromise and death. The antibodies might affect platelet membranes leading to subtle and sometimes non-subtle changes in platelet function. [6] The antibodies might damage the endothelial cell membranes, leading to decreased prostacyclin release. Prostacyclin is a vasodilator which prevents platelet aggregation. Any decrease in the former leads to increased thrombosis.[7] Women with phospholipid antibodies have a fetal loss of 90% when no specific treatment is given during pregnancy so this study was planned to find Anticardiolipin antibody levels (IgM) in patients of Abortions

MATERIALS AND METHODS

The study was conducted in the Department of Anatomy and the subjects for the study were obtained from the Department of Obstetrics and Gynaecology of Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital and Kalawati-Saran Children's Hospital. New Delhi. A total of 125 subjects were taken for the study.

A total of 125 pregnant subjects were included in the study which includes study group (75 subjects) and a control group (50 subjects). Subjects in the Study group included patients with a history of two or more first trimester or second trimester spontaneous abortions who were otherwise healthy without any obvious medical or surgical cause for the pregnancy loss. Control group included subjects in similar age groups but without any history of recurrent spontaneous abortions and with one or more live births.

Subjects in which some medical disorder or a congenital anomaly was responsible for the abortions, were excluded

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

from the study. An informed content was obtained from the volunteers. A detailed history was obtained from the patients which included parity, detailed obstetric history including the time and reason (if known) for the previous spontaneous abortions. Also past history of any autoimmune diseases , drug intake (Chlorpromazine, procainamide etc.) or bleeding disorders were ruled out.

A detailed clinical & obstetric history was taken with reference to age , gravidity, parity ,date of last menstrual period (LMP) ,detailed history including the time and reason for the previous spontaneous abortions. History of present pregnancy with regard to fever, drug intake radiation exposure, blurring of vision, headache and pedal edema was taken. Any history of autoimmune disease, history of bleeding tendencies was also taken into account.

Blood from the patients were collected to assess the presence of anticardiolipin antibodies (IgM) by Enzyme linked immunesorbent assay (ELISA) technique [8,9] using the ELISA kit of Varelisa . Blood levels of IgM, anticardiolipin antibodies are reported in MPL units/ ml.

Interpretation of Results as per the manufacturer's advice in the kit

Negative	< 6 MPL-U/ml
Equivocal	6-10 MPL-U/ml
Positive	> 10 MPL-U/ml

Values above 10 MPL-U/ml were interpreted as significantly different that expected within a normal population.

Observations :
Mean age of study group = 23.57 ± 3.09 yrs. Mean age of control group = 23.57 ± 2.081 yrs. P > 0.05, not significant (ages of both groups were comparable). Mean gravidity in study group = 3.65 ± 0.078. Mean gravidity in control group = 2.72 ± 0.99 .

Table 1 : Distribution of patients according to number of abortions.

Number of Abortions	Study Group n = 75 No. (%)	Control Group n = 50 No. (%)
0	0	50 (100)
1	0	0
2	46 (61.3)	0
3	25 (33.33)	0
4	2 (2.66)	0
5	2 (2.66)	0

Mean number of abortions in study group was 2.49 (Range 2-5).

Table 2. Distribution of patients according to anticardiolipin antibody levels (IgM).

IgM (Anticardiolipin Antibody)	Study Group n = 75 No. (%)	Control Group n = 50 No. (%)
Significantly positive (PS)	8 (10.7)	0
Insignificantly Positive (PI)	10 (13.3)	2 (4)
Negative (N)	57 (76)	48 (96)

In the study group a total of 18 (24%) subjects were positive for raised IgM anticardiolipin antibodies. Out of whom 8 (10.7%) subjects had significantly raised and 10 (13.3%) had insignificantly raised levels of IgM aCL. Mean levels of anticardiolipin antibody IgM in study group was 5.83 ± 4.47 MPL units. In the control group 2 (4%) subjects were positive for IgM anticardiolipin antibodies all of whom had levels in the insignificantly positive range. Mean levels of anticardiolipin antibody IgM in control group was 2.57 ± 1.44 MPL units. p <0.001, highly significant.

Discussion
The antiphospholipid antibodies have pathogenetic relevance of wide spread acceptance because of the association of these antibodies with thrombosis in patients with systemic lupus erythematosus and in normal individuals. Several intermediary thrombotic mechanisms have been suggested as causative, perhaps the most rational suggestion concerning pathogenesis to date is that some antiphospholipids possess a critical property that promotes thrombosis upon interaction with platelet or endothelial membrane phospholipids.

This study was conducted in the Department of Anatomy in collaboration with the Department of Obstetrics and Gynecology of Lady Hardinge Medical College and associated Hospitals.

In the present study pregnant patients with a history of two or more spontaneous first or second trimester abortions were included and were compared with patients without any history of abortion or pregnancy loss and at least one previous live birth.

The mean age of the subjects in our study group was 23.57 ± 3.09 years and that in the control group was 22.88 12.81 years (p > .05, not significant). There was no significant correlation of recurrent abortions with any particular age group. Maximum number of patients (62.7%) in our trial were in the age group of 21-25 years whereas in a study conducted by Parazzini et al (1991) [10] maximum number of patients ie. 38 percent each were in the age groups 25-29 and 30-34 years. Similarly the mean age reported by Unander et al (1987) [11] was 31.0 ± 4.6 which was much higher than that observed in our study. The lower age of patients observed in our study was probably due to early marriages in country.

The mean gravidity of the patients in our study group was 3.65 ± 0.78 with range of 3-6 and that in the control group was 2.72 ± 0.99 ranging between 2-6. In the study group 49.3% and 40% of the patients respectively were third fourth gravida and none of the patients were below gravida three. In the control group however, maximum number of patients i.e 56% were gravida two. Mean gravidity of 3.65 ± 0.78 in our present study, nearly conforms with the gravidity of 3.9 as reported by Cowchock et al (1986) [12] despite the lower age up of patients in our study.

In the present study 85.33% of the cases were primary abortors which was twice as high compared to the findings reported by Cowchock (1986), and Maclean et al (1994) who in different researches reported primary abortions in 49% and 48% of the patients.

In the patients in our study group 61.3% had two spontaneous abortions whereas 38.7% of the patients had three or more miscarriages compared to the findings of Maclean et al (1994) [13] who reported 47% of the patients with two & 53% with three or more previous miscarriages.

Volume : 5 | Issue : 10 | October 2015 | ISSN - 2249-555X

Mean number of abortions in the study group was 2.49 with a range of 2 to 5 abortions as compared to a mean of 3.4 abortions (range 2-11) reported by Cowchock et al (1986) in a study on 61 patients of recurrent spontaneous abortions. However no correlation was observed between the number of abortions and the prevalence of anticardiolipin antibodies.

Prevalence of IgM anticardiolipin antibodies :

The prevalence of raised anticardiolipin antibodies (IgM) was found in 10.7% of the study group of patients with mean levels of 5.83 ± 4.47 MPL units. Findings were comparable to those of Unander et al (1987) and Parazzini et al (1991) who reported 7% and 12% prevalence of IgM anticardiolipin antibodies in cases of recurrent spontaneous abortions. Silver et al (1996) in a study reported raised IgM anticardiolipin antibodies in 20.4% of the women who underwent clinically indicated testing for antiphospholipid antibodies. In our study it was observed to be prevalent in half the percentage compared to the findings of Silver et al (1996). [14,15]

Table 3 : Prevalence of IgM anticardiolipin antibody as reported by different authors

Authors Name	Prevalence
Cowchock et al (1986)	9.8%
Unander et al (1987)	7%
Parazzini et al (1991)	12%
Maclean et al (1994)	1.6%
Sliver et al (1996)	20.4%
Present study (2002)	10.7%

Five of the eight patients ie. 62.5 percent with increased levels of IgM anticardiolipin antibodies in our study had some other infection also (such as toxoplasmosis, cytomegalovirus and tuberculosis) suggesting the polyclonal finding of IgM. This proves the findings reported by Lockwood et al (1989) that there is polyclonal binding of IgM.

In our study prevalence of increased IgM anticardiolipin antibody in patients with explained recurrent abortion was 83.3% (i.e. five out of six patients). In patients with unexplained recurrent abortion the prevalence of IgM cardiolipin antibody was 4.35% ie. (3 of 69 patients) which is in comparison to the observation of 7% as reported by Unander et al (1987).

Patients with increased IgM levels indicate a higher antibody burden with greater antigenic affinities explaining IgM mediated pregnancy wastage.

REFERENCE

1. Harger JH, Archer DF, Marchese SG (1983). Etiology of recurrent abortion and outcome of subsequent pregnancies. Obstet Gynecol; 62; 574. 2. Wasserman (1906). Antiphospholipid antibodies first detected by Wasserman in 1906 — quoted by Kumar P, Basu J (1997). Prevalence of anticardiolipin antibodies in women with poor obstetric outcome. A pilot study. Obs Gynae today 1; 2; 808-809. 3. Barbui T, Cortelazzo S, Galli M, Parazzini F, Rossi E, Radici E (1988). Antiphospholipid antibodies in early repeated abortions : a case— controlled study. Fertil Steril 50; 589-592. 4. Beer AE, Quebbeman JF, Ayers JWT, Haines RF (1981). Major histocompatibility complex antigens, maternal and paternal immune responses, and chronic habitual abortions in humans. Am J Obstet Gynecol 141; 987. 5. Boey ML, Colaco CB. Gharavi AE, Elkon KB, Loizou S. Hughes GRV (1983). Thrombosis in systemic lupus erythematosus : striking association with the presence of circulating lupus anticoagulant. British Medical Journal; 287: 1021-1023 6. Hughes GRV, Harris EN, Gharavi AE (1986). The Anticardiolipin Syndrome. J. Rheumatology; 13; 486-489 7. Carreras LO, Machin SJ, Deaman R (1981). Arterial thrombosis, Intrauterine death and lupus anticoagulant, detection of immunoglobulin interfering with prostacyclin formation. Lancet 1; 244-246. 8. Engvall E, Perlmann P (1971). Enzyme linked immunosorbent assay (ELISA): Quantitative assay of IgG. Immunochem: 8; 871. 9. Loizou S. Mc Crea JD, Rudge AC, Reynolds R, Boyle CC, Harris EN (1985). Measurement of anticardiolipin antibodies by an enzyme linked immunosorbent assay (ELISA). Standardization and quantitation of results. Clin Exp Immunol; 62; 738-745. 10. Parazzini F, Acaia B, Faden D, Lovotti M, Marelli G (1991).Antiphospholipid antibodies and recurrent abortion. Obstet Gynecol; 77; 854858. 11. Unander AM, Norberg R, Hahn L, Arfors L (1987). Anticardiolipin antibodies and complement in ninety-nine women with habitual abortion. Am J Obstet Gynecol; 156; 114-119. 12. Cowchock FS, Reese EA, Balaban D, Brauch DW, Plouffe L (1992). Repeated fetal losses associated with antiphospholipid antibodies. A collaborative randomized trial comparing prednisone with lowdose heparin treatment. Am J Obstet Gynecol; 166; 1318-1323. 13. Maclean MA, Cumming GP, McCall F, Walker ID, Walker JJ (1994). The prevalence of lupus anticoagulant and anticardiolipin antibodies in women with a history of first trimester miscarriages. British J Obstet Gynecol; 101; 103-106. 14. Silver RK. Macgreger SN, Sholl JS, Hobart JM, Neeshof MG, Ragin A (1993). Comparative trial of prednisone plus aspirin versus aspirin alone in the treatment of anticardiolipin antibody positive obstetric patients. Am J Obstet Gynecol. 169; 1411-1417. 15. 113. Silver RM, Draper ML. Scott JR, Lyon JL, Reading J, Branch DW (1994). Clinical consequences of Antiphospholipid Antibodies : An Historic Cohort study. Obstet Gynecol 83; 372-377.