Plasma Cardiolipin in Postmenopausal Women in Mauritius

S Bedadun[1] *and AH Subratty*[1]

ABSTRACT

Data concerning the relationship between anti-cardiolipin antibodies and several diseases including myocardial infarction are not readily available for Mauritius. Anticardiolipin antibodies were measured using commercially available ELISA kits. Haematological profiles were measured using a Coulter Counter in the study population. Our study revealed significantly higher IgG and IgA levels as well as a strong correlation between decreased platelet levels and increased anticardiolipin status in the women during postmenopause. It is concluded that abnormal cardiolipin level could be an important risk factor for cardiovascular accidents among postmenopausal women in Mauritius. (*Afr J Reprod Health* 2001; 5[2]:135-138)

RÉSUMÉ

Cardiolipine du plasma chez les post ménopausées à Maurice. Les données concernant le rapport entre les anticorps anticardiolipides et plusieurs maladies y compris l'infarctus du myocarde ne sont pas facilement disponibles pour Maurice. Les anticorps anticardiolipides ont été mesurés à l'aide des trusses ELISA qui sont disponibles à titre commercial. Des profils hématologiques ont été mesurés à l'aide d'un compteur de Coulter chez la population étudiée. L'étude a révélé de manière significative des niveaux plus élevés de IgG et IgA aussi bien qu'une forte corrélation entre les niveaux inférieurs de plaquettes et le statut élevé d'anticardiolipide chez les femmes au cours de la ménopausées. L'étude conclut que le niveau anormal cardiolipide peut être un facteur important de risque pour les accidents cardiovasculaires chez les post ménopausées à Maurice. (*Rev Afr Santé Reprod* 2001; 5[2]:135-138)

KEY WORDS: *Plasma, cardiolipin, postmenopause, Mauritius*

[1]*Department of Health & Medical Sciences, Faculty of Science, University of Mauritius, Reduit, Mauritius.*

Correspondence: *Dr A.H. Subratty, Associate Professor, Department of Health & Medical Sciences, Faculty of Science, University of Mauritius, Reduit, Mauritius. E-mail: subratty@uom.ac.mu*

Introduction

Antiphospholipid antibodies (APL) are a heterogeneous group of circulating autoantibodies directed against negatively charged phospholipid components of cell membranes. Cardiolipin (diphosphatidyl glycerol) is a highly conserved phospholipid component of the mitochondrial membrane. The physiological role and nutritional sensitivity of this phospholipid class historically have been overlooked or poorly understood. Research has indicated that this phospholipid is not only responsible for a great many biochemical and physiological functions. However, far from being resistant to a dietary modification, it proves to be one of the phospholipid classes most sensitive to dietary fatty acids.[1] Their presence is associated with repeated episodes of venous or arterial thrombosis, recurrent fetal loss, and thrombocytopenia.[2] Anticardiolipin (ACL) antibodies levels[3] and thrombocytopenia[4] have been reported to correlate in patients with systemic lupus erythromatous (SLE)[5] and chronic autoimmune thrombocytopenic purpura.[6] These findings suggest that such antibodies cross-react with platelet phospholipids and may lead to platelet destruction.[7]

Hamsten et al[8] have observed an increased prevalence of patients with elevated anticardiolipin antibody levels in their sera in a highly selected series of young patients with myocardial infarction. In addition, high levels of anticardiolipin antibodies, usually of the IgG class, serve as an indication of a high risk for recurrent cardiovascular events. Klemp et al[9] have reported an association between elevated levels of ACL antibodies and ischaemic heart diseases, as well as with coronary heart diseases. Recent studies[10] have led to the conclusion that anticardiolipin antibody levels are significantly higher in patients developing a cardiac end point than in normal subjects.

The present study was conducted to investigate whether abnormal plasma ACL antibodies could be a risk factor for the genesis of thrombocytopenia by causing platelet aggregation in postmenopausal women.

Materials and Methods

Fifty women who had reached menopause for at least one year before the study and sixteen female participants who had not yet reached menopause constituted the study group. Criteria for inclusion also included (a) no known liver disease; and (b) no congestive heart failure. Oral consent was obtained from all participants prior to entry into the study.

Upon inclusion in the study, venous blood was collected from each individual using 10ml disposable syringes. Whole blood collected in EDTA tubes were used for determination of haematological parameters using an automatic Coulter Counter.

Serum obtained after centrifugation of whole blood was used for cardiolipin-binding antibodies (IgM, IgA & IgG) assays using commercially available ELISA kits (Cambridge Life Sciences, UK). Data on the occurrence of these antibodies are reported elsewhere.[11] Serum samples were analysed in duplicates. The tests were standardised using reference sera.

Results

Statistical Analysis

Differences in variables were estimated using either Student's t-test or ANOVA. The χ^2 test was applied to class variables. A logistic regression analysis was used to study the associations between ACL antibody levels and postmenopause. The joint effects of the antibody and other risk factors (red blood cell count, white blood cell count, age and platelets) were also studied. All data manipulation was performed using *Microsoft-Excel*.

The mean levels of ACL antibodies, IgG and IgA were significantly higher in postmenopausal than premenopausal women ($p < 0.05$). However, no significant changes were detected for IgM levels among the two study groups (Table 1). No significant association ($p < 0.05$) was also noted between ACL antibodies and the haematological parameters (Table 2). A strong correlation was observed between platelets and anticardiolipin antibodies (24±83 U/ml, $r = 0.8$) between the study populations.

Table 1 **Serum Anticardiolipin Antibody Levels in Women**

Anticardiolipin type	Premenopausal women (n = 16)	Postmenopausal women (n = 50)	Statistics
IgG (μ/ml)	0.27±0.11	0.36±0.15	S
IgM (μ/ml)	0.24±0.05	0.28±0.13	NS
IgA (μ/ml)	0.17±0.06	0.22±0.10	S

Table 2 **Haematological Profiles Monitored for the Study Populations**

Haematological parameters	Premenopausal ($\bar{x}$ ± SD)	Postmenopausal ($\bar{x}$ ± SD)	Statistics
Hb (g%)	0.11±4.1	11.0±2.8	NS
RBC (mmol/l)	4.8±0.64	4.5±0.6	NS
HCT (%)	33.0±5.6	37.3±4.3	S
MCV (μm/mm^3)	78.6±9.2	79.3±10.8	NS
MCHC (s/dl)	28.9±3.5	29.4±2.5	NS
MCHC (g/dl)	33.4±3.5	33.8±2.5	NS
Platelets (THSD/mm^3)	241.1±40.0	214.8±83.1	S
WBC (THSD/mm^3)	7.9±1.7	8.3±1.8	S
%Lymphocytes (THSD/mm)	28.7±6.6	30.6±8.5	NS

Discussion

In the present study, certain types of ACL antibody levels were significantly higher in women who have reached menopause than in the control subjects. The possible reasons for detection of higher levels of these antibodies, in particular IgG, in postmenopausal women could be that (i) the binding site of anticardiolipin antibody IgG possibly has a higher affinity for the corresponding (cardiolipin) than those of IgM and IgA types. The IgG type is most sensitive to the cardiolipin binding antigens, compared with the other two, or (ii) anticardiolipin antibody of the IgG class has greater potential to combat pathological rise of cardiolipin antigens since it is the main antibody involved in the body's immune response mechanism against antigens. Our observations also showed that the levels of anticardiolipin antibodies varied significantly among individuals of different ages. In the postmenopausal group, there were certain younger women who had a higher level of ACL antibodies in their sera than older subjects within the same study population. Hence, it would appear that there is no fixed trend in the rise of these antiphospholipid antibodies with age. Thus, factors other than age could be responsible for findings of abnormally high ACL antibodies in postmenopausal women.

Significant decrease in platelet levels could be explained due to the fact that naturally occurring ACL antibodies are able to bind to negative phospholipid acidic charges present on platelets and may thus lead to their clumping and destruction.[7] It is known that plasma protein β2-glycoprotein (β2 GP1) acts as a blood anticoagulant by binding to negatively charged phospholipids, namely cardiolipin, and also inhibits adenosine-induced aggregation of human blood platelets. The phospholipid-β2 GP1 complex acts as an antigen for ACL antibodies, which eventually block the anticoagulant effect of β2 GP1 and induce hypercoagulation and thrombus formation. These possible risks of thromboembolic events in postmenopausal women could arise because of disruption of endothelial cells that produce the platelet anti-aggregatory eicasanoid product, PGI_2. Thus, the gradual decrease of platelet levels in the circulating blood of postmenopausal women can be one of major threats for later pseudothrombocytopenia events. This can lead to venous or arterial thrombosis,[4] thus blocking the blood vessels by the clumps of agglomerated platelets. Platelet clumping and destruction by autoimmune antibodies is one of the main factors leading to arterial/venous thrombosis and coronary artery thrombosis.

In conclusion, there is a lot to gain by screening women for anticardiolipin antibodies, considering the vascular, renal, obstetric, neurological and pulmonary complications arising from these antibodies. However, a larger group of African women should be studied to find out whether African women are at risk of developing anticardiolipin antibodies.

REFERENCES

1. Berger A and German B. Biochemistry of cardiolipin: sensitive to dietary fatty acids. *Advances in Food and Nutritional Research* 1992; 37: 300–302.
2. Triplett A. Antiphospholipid antibody and thrombosis: a consequence, coincidence, or cause? *Plathological Medicine* 1993; 117: 78–79.
3. Maclean MA and Cumming GP. The prevalence of lupus anticoagulant and anticardiolipin antibodies in women with a history of first trimester miscarriages. *Br J Obs & Gyn* 1994; 75: 390–396.
4. Ronbey RA and Pratt CW. Thrombosis and lupus anticoagulant activity induced by autoimmune antiphospholipid antibodies is dependent upon beta-2-glycoprotein. *Int J Clin Res* 1992; 90: 361–365.
5. Namura S and Yanabu M. Antiphospholipid antibodies bind to platelet microparticles in idiopathic (autoimmune) diseases. *Medical and Scientific Research* 1988; 16: 437–456.
6. Outi V and Matti M. Anticardiolipin antibodies and the risk of myocardial infarction. *Clin Inv & Rep* 1992; 3: 44–89.
7. Martinuzzo M and Maclouf J. Antiphospholipid antibodies enhance thrombin-induced platelet activation and thromboxane formation. *Thrombosis Haematosis* 1993; 70: 117– 25.
8. Hamsten A and Norberg R. Antibodies to cardiolipin in survivors of myocardial infarction; association with recurrent cardiovascular events. *Lancet* 1986; 1: 113–116.
9. Klemp PR. Cooper RC and Strahs FJ. Anticardiolipin in ischaemic disorders. *Clinical Immunology* 1988; 254–257.
10. Vaarala O and Alftham G. Cross-reaction between antibodies to oxidised low-density lipoprotein and cardiolipin in systemic lupus erythromatosus. *Lancet* 1983; ii: 211.
11. Hughes GR. Standardising the anticardiolipin antibody test. *Lancet* 1987; 1: 277–273.