

Prevalence of Anticardiolipin Antibodies in Pregnancies with History of Repeated Miscarriages

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Abstract: *Aim:* This study aimed at evaluating the prevalence of high anticardiolipin antibody and lupus anticoagulant levels in women with histories of at least two miscarriages.

Methods: The presence of high anticardiolipin antibody and lupus anticoagulant levels were evaluated in 52 patients with ages between 17 and 41 (mean 26.7 years old) who had histories of repeated miscarriages.

Results: High anticardiolipin antibody levels were identified in 55.77% and lupus anticoagulant levels in 2% of the individuals.

Conclusion: In conclusion, women who suffer from repeated miscarriages present with a high prevalence of anticardiolipin antibodies. Further studies on this issue are crucial as these antibodies are associated with hypercoagulability and thus increased the risk of thromboembolic events.

Keywords: Repetitive miscarriage, thromboembolism, anticardiolipin antibodies, lupus, anticoagulant.

INTRODUCTION

Antiphospholipid syndrome (APS), in relation to pregnancy, is characterized by the presence of antiphospholipid autoantibodies in association with repeated fetal loss and complications such as pre-eclampsia, retarded fetal growth or placental insufficiency [1, 2]. This syndrome constitutes a heterogeneous group of circulating antibodies against anionic phospholipids with the most important ones being Anticardiolipin Antibodies (ACA), a positive Venereal Disease Research Laboratory test (VDRL) and lupus anticoagulants [2, 3]. False-positive VDRL results do not constitute diagnostic criteria for the syndrome due to the low sensitivity and specificity of the test. However, high levels in pregnant women should serve as a warning of the presence of antiphospholipid antibodies [4].

In pregnant women, an APS rate from 0.2% to 2% is similar to the frequency in the general population [5], however, this syndrome is responsible for about 10% of the cases of repeated miscarriages [6, 7].

Several publications have associated APS with retarded intrauterine growth [8, 9] and others with pre-eclampsia [5, 10] although this latter correlation remains controversial [11, 12].

Antibodies of this syndrome can inhibit placental anticoagulant protein by binding to phospholipids, thereby leading to thrombosis [13], and also by influencing the production of gonadotropin [14]. The β 2 glycoproteins act as a cofactor in the binding of antiphospholipid antibodies to anionic phospholipids, thus functioning as a natural anticoagulant and therefore any interference in this system may result in thrombosis [15]. In an animal model, spontaneous miscarriages were observed with passive transfer of purified anticardiolipin IgG [1, 16].

Treatment using heparin, aspirin or intravenous immunoglobulins reduces the rate of fetal loss. Risk of pre-eclampsia and placental insufficiency occurs in around 50% of non-treated patients and the success rate of prophylactic treatment using heparin and aspirin is approximately 70% [1]. The reduction of these symptoms with the normalization of the levels of ACA is associated to an improvement in the survival rate of fetuses during pregnancy [17].

This current study aimed at evaluating the prevalence of high ACA and lupus anticoagulant levels in women who had suffered two or more miscarriages.

METHODS

In a retrospective study, 52 consecutive pregnant women who had suffered from two or more miscarriages were evaluated in a teaching hospital in São José do Rio Preto, São Paulo, Brazil, in a period from April 1988 to November 2003. Their ages ranged from 17 to 41 years old with a mean of 26.7 years. Inclusion criteria were a history of multiple miscarriages (2 or more) and positive results for ACA tests.

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No patient had a history of rheumatologic disease before pregnancy. Patients who suffered not more than one miscarriage were excluded from the study. Evaluation of the ACA was achieved by Enzyme-Linked Immunosorbent Assay (ELISA – Quanta Lite™ ACA IgG/IgM INOVA Diagnostics). Lupus anticoagulant was investigated using the activated partial thromboplastin time (aPTT) prolonged by the presence of an inhibitor. For statistical analysis, simple percentages and the Fisher exact test were utilized with an alpha error of 5% (p -value < 0.05) were considered acceptable.

The study was approved by the Ethics Committee of the Medical School in São Jose do Rio Preto, Brazil (FAMERP).

RESULTS

Abnormally high ACA levels were detected in 55.77% of the women and lupus anticoagulant in 2%.

High IgM ACA levels were found in 41.1% of the cases, high IgG ACA in 17.6% and high levels for both IgM and IgG ACA were identified in 38.2% of the cases. There was no significant difference between the number of patients with high IgG and IgM immunoglobulin levels when analyzed using the Fisher exact test (p -value < 0.09).

DISCUSSION

High ACA levels are harmful to the normal evolution of gestation and can affect both mother and child. Diagnosis and prophylactic treatment can improve the outcome of the pregnancy [1, 18]. The current study detected an abnormally high rate of pregnant women who had suffered repeated miscarriages with high serum levels of these antibodies. The prevalence of lupus anticoagulant (2%) was lower than the rate of ACA (55.7%). Thus, it is important to highlight this high prevalence as venous thromboembolism has been identified as one of the commonest causes of maternal death [19, 20]. This should be seen as a warning about the necessity to investigate hypercoagulability states during pregnancy particularly in respect to antiphospholipid antibodies. We should continue to be aware of maternal complications other than miscarriages. Some published investigations did not identify any association between antiphospholipid antibodies and repeated miscarriages [21, 22], but other studies did [23, 24]. This demonstrates the need for further studies using larger number of individual and standardization of the investigational methods. Gestation and puerperium are associated with thromboembolism [25, 26], thus an association of risk factors in maternal thromboembolism is implicated.

In the evolution of these patients it is observed that the ACA levels may vary, and even may become negative. In this group, three patients had a history of thrombotic events; two deep venous thrombosis and one myocardial infarction. Thrombotic events are associated with the syndrome and physicians should be watchful about this possibility.

The prevalence of patients with high levels of these antibodies in the current study is within the range cited by other studies, as publications have reported a prevalence of these antibodies in from 15 to 59.1% of cases [26-28]. This variation is due to the different methods employed to

measure the antibodies and so there is a true necessity of standardization.

Another warning is related to the possibility of false-positive VDRL results and their interpretation that can cause psychological instability within the family [29].

CONCLUSION

In conclusion, individuals suffering from repeated miscarriages are frequently present with antiphospholipid antibody syndrome. These data indicate the necessity of a systemic investigation of these antibodies in pregnant women.

COMPETING INTERESTS

The authors declare that they have no competing interests (political, personal, religious, ideological, academic, intellectual, commercial or any other) in relation to this manuscript.

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