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Brief Report

Evaluation of Antiphospholipid Antibodies and Activated Partial Thromboplastin Time in Women with Adverse Outcome of Pregnancy

Sariyeh Golmahammad Iou[1], Nader Pashapour[1], Mahnaz khalili[2], Farzaneh Broomand[1], Fatemeh Bahadori[3]

Abstract

Adverse outcome of pregnancy is a potentially dangerous complication of conception and affects 15-20% of pregnancies. According to recent studies increased level of blood antiphospholipids antibodies, if accompanied by predisposing factors, can be an adverse event in human pregnancy. The aim of the present study was to compare the maternal serum levels of anticardiolipin and antiphosphatidyl serine, and partial thromboplastin time between patients with adverse outcome of pregnancy and matched subjects with normal pregnancy. Serum levels of anticardiolipin and antiphosphatidyl serine and activated partial thromboplastin time were measured in 150 women with adverse pregnancy outcome and 150 matched women with normal pregnancy after a gestational age of 10 weeks. Data on maternal age, age of pregnancy, serum levels of anticardiolipin and antiphosphatidyl serine, and activated partial thromboplastin time were collected and compared by Student's t or χ^2 tests. The age of mothers in the two groups were 25.86±5.90 and 27.09±5.63 years (P=0.67), and the age of pregnancies were 29.34±5.12 and 28.17±7.03 (P=0.1) weeks in the control and patient groups, respectively. Positive levels of serum anticardiolipin and antiphosphatidyl serine antibodies, and activated partial thromboplastin time for the control and patient groups were 14.3% versus 85.7% (P=0.002), 15.2 % versus 84.8 % (P=0.003), and 23.1 % versus 76.9% (P=0.001), respectively. The findings suggest that positive levels of serum antiphospholipids are associated with adverse outcome of pregnancy in the study population.

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Keywords ● Activated partial thromboplastin time ● phosphatidyl serines ● anticardiolipin ● normal pregnancy

[1]Departments of Gynecology,
[2]Immunology, [3]Perinatology,
Faculty of Medicine,
Urmia University of Medical Sciences,
Urmia, Iran.

Correspondence:
Nader Pashapour MD,
Department of Neonatology,
Faculty of medicine,
Urmia University of Medical Sciences,
Urmia, Iran.
Tel: +98 441 3466400
Fax: +98 441 2780801
Email: npashapor@yahoo.com
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Introduction

Adverse outcomes of pregnancy are potentially dangerous complications of conception that affects 15-20% of pregnancies.[1] Recent studies revealed a significant association between adverse outcome of pregnancy and the presence of anticardiolipin antibody (ACA) if accompanied by prolonged activated partial thromboplastin time (aPTT).[2] Also, it is well-known that there are disparities between developed and developing countries in terms of maternal and infantile mortalities, stillbirths and low birth weights.[3]

Recent studies have revealed that for the impact of antiphospholipid (APL) antibody on embryo, a second hit such as infection, trauma, or environment factors is necessary.[4] Controversial results of the previous studies about the association of APL with adverse outcome of pregnancy might be justified by the findings of a recent study demonstrating that other factors like infection and environment along with APL were acted as an inciting factor for adverse outcome of pregnancy.[5]

We assumed that APL antibodies alongside aPTT and a second hit may play a role in adverse outcome of pregnancy with unknown etiology including intrauterine growth retardation (IUGR), fetal death, and preeclampsia. We tried to find out whether there was a correlation between the adverse outcome of pregnancy and the serum levels of two antiphospholipids antibodies alongside aPTT in affected women in the region that the study was performed. This was carried out by comparing blood concentrations of ACA, antiphosphatidyl serine and aPTT in four types of complicated pregnancies with those of matched normally delivered pregnancies. To the best of our knowledge, this is the first study in this field that measures serum concentrations of two antiphospholipid antibodies and aPTT simultaneously.

Patients and Methods

The present study was approved by Ethical Committee of Urmia University of Medical Sciences. The study samples were 300 women including a case and a control groups referring to Kosar Obstetrics Hospital affiliated to Urmia University of Medical Sciences. A written informed consent was obtained from each participant in the study. Adverse outcome of pregnancy was defined as all conceptions concluded to IUGR, fetal death, abortion and preeclampsia. Preeclampsia was defined as new onset of hypertension after 20 weeks of gestation with high systolic (≥140 mmHg) and diastolic (≥90 mmHg) blood pressures, and proteinuria (300 mg/24 h). Intrauterine growth retardation, fetal death, and abortion were documented and established by history, clinical examination and sonography. Considering a power of 80% and an alpha value of 0.05, and a minimum detectable change of 16-20% for serum antiphospholipid in aborted group and 5% for normal delivery group,[6] a sample size of 139 was calculated for each group. The minimum detectable changes were obtained from a previous study. One hundred and fifty pregnant women with pregnancy complications and the same number of healthy pregnant women were enrolled in the study. Inclusion criteria for the patients group were the presence of IUGR, and a history of two or more fetal death, abortion, IUGR, fetal death or preeclampsia with gestational age of less than 34 weeks. Patients with a history of uterine anomaly, diabetes mellitus, thyroid disease, aspirin, heparin or corticosteroid intake, embryo anomalies, chronic systemic disease including lupus, autoimmune, hypertension, asthma, and cardiopulmonary diseases were excluded from the study.

At the time of admission to the hospital, 5 ml venous blood samples were collected, and their sera were isolated by centrifugation and stored at -60˚C until analysis. Serum levels of anticardiolipin, antiphosphatidyl serine and aPTT were measured by ELIZA using kits of Genesis (England), Immuno-biological laboratory (IBL) (Germany) and Biopol (USA) for phosphatidyl serine, anticardiolipin and aPTT respectively.

Tests were considered positive if the values for serum levels of ACL and antiphospholipid were higher than 11 Mmol/U/ML and the value for aPTT were more than 35".

Statistical Analysis

Comparison of quantitative and qualitative data between the two groups was performed by Student's t and χ^2 tests, respectively. A P value of ≤0.05 was considered as statistically significant. Statistical Package for Social Sciences was used for data analysis.

Results

The total number of the study samples was 300 with equal number (n=150) in each group.

There was no significant (P=0.67) difference between the age of participants in patient group (25.86±5.90 years) and that of the control group (27.09±5.63 years). Moreover, there was no significant (P=0.1) difference between the age of pregnancies in the control (29.34±5.12 weeks) and that of the patients (28.17±7.03 weeks) groups (table 1).

Table 1: The ages (in years) of the patients and the age (in weeks) of their pregnancy.

	Group	Number	Mean±SD
Age of the patients (years)	Control	150	25.86±5.90
	Case	150	27.09±5.63
Age of patients' pregnancy (weeks)	Control	150	29.34±5.15
	Case	150	28.17±7.03

There was a significant (P=0.003) difference between the number of positive cases for

antiphosphatidyl serine in the control group (n=5, 3.3%) and the case group (n=28, 18.7%). Of cases with positive antiphosphatidyl serine levels, 15.2 % and 84.8 % were from the control and patient groups, respectively. There was significant (P=0.002) difference between the number of positive cases for anticardiolipin antibody in the control group (n=10, 6.7%) and the case group (n=60, 40 %). Of cases with positive serum anticardiolipin levels, 14.3% and 85.7% were from the control and patient groups, respectively.

There was significant (P=0.001) difference between the number of cases with abnormal results for aPTT test in the control group (n=8, 6%) and the case group (n=30, 20%). Of cases with abnormal aPTT test, 23.1% and 76.9% were from the control and patient groups, respectively (table 2).

Discussion

The mean maternal age and age of pregnancy were not significantly different between the control and patient groups (table 1). Regarding serum positive test for anticardiolipin and antiphosphatidyl serine antibody, there was significant difference between the patients with adverse outcome of pregnancy and those with normal delivery controls (P=0.002 and P=0.003, respectively). To determine the role of antiphospholipids antibodies in predicting the adverse pregnancy outcome, a study was conducted on 95 women in Colorado, the results of which similarly revealed that the elevated levels of anticardiolipin antibody in women increased the rate of fetal loss.[6] Another research in this field was conducted on 25 women with a history of fetal loss in Sultan Qaboos University. The authors, after a retrospective review of the above-mentioned cases, suggested that the presence of anticardiolipin antibody appeared to increase the risk of abortion.[7]

We observed positive anticardiolipin antibody test in 10 and 60 cases of control and patients groups, respectively (P=0.002). However, the results of a study, which was carried out in Sari (North of Iran), showed a different conclusion from that of our research. In that study, researcher commented that the prevalence of anticardiolipin antibody in patients was not significant, and it was not the cause of recurrent abortion and fetal deaths.[8]

In contrast with the above–mentioned study,[8] another study, which revealed that approximately one third of women with Antiphospholipid antibody syndrome (APS) developed preeclampsia during pregnancy, suggested that APS was associated with adverse pregnancy outcomes including preeclampsia, recurrent early pregnancy loss, fetal death, and intrauterine growth restriction.[9]

Considering the values of aPTT, the results of our study revealed that there was a significant (P=0.001) difference between the patients with adverse outcome of pregnancy and normal delivery controls. Consistent with the results of the present study, a study about the relation of coagulopathy and adverse outcome of delivery concluded that delivery complications associated with coagulopathy occurred in 11% of women with IUGR, and were associated with preexisting preeclampsia/hemolysis, elevated liver enzymes, and low blood platelets counts (HELLP), uterine rupture, or an acute clinical problem in most cases.[10] On the other hand, another study evaluated the efficacy of prophylaxis using low-dose non-fractioned heparin and aspirin in the prevention of IUGR and low birth weights in patients suffering from antiphospholipid antibody syndrome.[11]

Kramer,[3] and Nodler and colleague,[12] argued that older age and white race lacking Medicaid predispose women to the elevation of antiphospholipid antibody titers. However, there was no significant difference between the

Table 2: The frequencies of positive tests for activated partial thromboplastin time, and serum levels of anticardiolipin antibody and antiphosphadyl of the control and case groups.

Test		Control group	Case group				No.	P value
			Abortion	Fetal death	Preeclampsia	IUGR		
Activated partial thromboplastine time	negative	141	4	59	45	12	261	
	positive	9	1	18	10	1	39	0.001
Total		150	5	77	55	13	300	
Anticardiolipin Antibody	negative	140	1	46	32	11	230	
	positive	10	4	31	23	2	70	0.002
Total		150	5	77	55	13	300	
Antiphosphadyl serine	negative	145	4	65	42	11	267	
	positive	5	1	12	13	2	33	0.003
Total		150	5	77	55	13	300	

age of the control (25.86 years) and case (27.09 years) groups (table 1). It might worth mentioning that the current study was carried out using samples from a developing region.

Today, the role of APL in adverse outcome of pregnancy is recognized. However, the controversy between the results of previous studies and the present study may be justified by the findings of Vega et al. [4] It has been pointed out that for the impact of APL on embryo, a second hit like infection, trauma, and environmental factors are necessary.[5,13]

Conclusion

The elevated serum levels of antiphosholipids including ACA and antiphosphatidyl serine antibodies, and activated partial thromboplastin time were significantly higher in the patients' group than those in the control group. In order to determine the role of serum antiphosholipids in the adverse outcome of pregnancy more studies, which examines the impact of a second hit, are necessary.

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Conflict of Interest: None declared

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