



Association between Antiphospholipid Antibodies (APLA) and Preeclampsia (PE) in Females Presenting for Antenatal Check-Up

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ABSTRACT

Introduction: APLA have been associated with a number of obstetric complications however their role in the pathogenesis of preeclampsia has remained an issue of controversy. There is a lack of information on APLA in pre-eclamptic women.

Objective: To assess the association between antiphospholipid antibodies (APLA) and preeclampsia (PE) in females presenting for antenatal check-up.

Materials and Methods: This Case Control study was conducted in Services Institute of Lahore. After approval from hospital ethical committee, 200 females, fulfilling the inclusion criteria were included in the study from OPD of Department of Obstetrics & Gynecology. Informed consent was obtained. Demographic information was also recorded. The females were divided in two groups on the basis of presence or absence of PE i.e. cases and controls.

Results: The mean age of the patients among cases was 27.60 ± 4.96 years the minimum age was 20 years and maximum was 35 years whereas among controls the mean age of the patients was 27.94 ± 4.13 years the minimum age was 20 years and maximum was 35 years. The mean gestational age among cases was 27.46 ± 4.72 weeks the minimum gestational age was 20 weeks and maximum was 35 weeks on the other side the mean gestational age among controls was 27.25 ± 4.74 weeks the minimum gestational age was 20 weeks the maximum was 35 weeks. There was significant association between preeclampsia and APLA as the p-value was significant (p-value=0.007).

Conclusion: Results of this study showed a significant association and significant risk between APLA and preeclampsia. Therefore a routine assay of APLA in women at risk of preeclampsia should be done. However APLA testing should be considered in women with early onset severe preeclampsia, especially when additional clinical features of APS are present.

KEY WORDS: Antiphospholipid Antibodies (APLA), Antenatal Check-up, Preeclampsia (PE)

INTRODUCTION

Antiphospholipid antibodies (APLA) are a group of auto-antibodies that have the ability to bind to cardiolipin alone, to cardiolipin complexed to a cofactor or to a cofactor alone. APLA are found in up to 5% of healthy subjects in the general population. The prevalence of APLA in the low risk obstetrical population ranges from 1-9%.¹ APLA promote activation of endothelial cells, monocytes, and platelets; and overproduction of tissue factor and thromboxane A₂. Complement activation might have a central pathogenetic role.²

Antiphospholipid syndrome (APS) is associated with adverse pregnancy outcomes including preeclampsia, recurrent early pregnancy loss, fetal death, and intrauterine growth restriction. Approximately one third of women with APS will develop preeclampsia during pregnancy.^{3,4} Antiphospholipid syndrome was first described 27 years ago in patients with systemic lupus erythematosus (SLE) and positive anticardiolipin antibodies, who presented with a clotting syndrome that affected arteries and veins. Female patients had a high risk of recurrent miscarriage and late fetal loss.⁵ Current evidence does not justify inclusion of preeclampsia as a major criterion for APS, but preeclampsia could reasonably be included as a secondary or minor criterion in diagnosis when a patient has other clinical features of APS.³

The presence of antiphospholipid antibodies (APLA) especially anticardiolipin antibodies increased pregnancy risk, as 59.1% IgG or IgM antibodies to one of the six phospholipids (cardiolipin, APS, API, APE, phosphoglycerol and phosphatidic acid) were seen as compared to controls (4.6%).⁶ Benedict et al., also found that insignificant difference observed between preeclamptic and control



females for presence of APLA i.e. 10% in preeclampsia group and 0% in control group.⁷ Dreyfus reported no association between antiphospholipid antibodies and preeclampsia. The OR for the association was 0.95 (95% CI 0.45, 2.61). APLA were detected 4.4% (8/180) PE women and in 5.3% (19/360) controls.⁸

Rationale of this study is to determine the association of APLA with PE in females presenting in a tertiary care setting for antenatal check-up. Literature has showed that there is significant association between APLA and PE but there are also contradictions present regarding association of APLA with PE. So we planned this study to find whether there is any impact of APLA for development of PE. Moreover, not much data is available and no local data was found in literature. So we aimed to conduct this study to find local magnitudes and can be able to detect increase in APLA in pregnant females in early gestational age and can prevent PE.

OBJECTIVE

To assess the association between antiphospholipid antibodies (APLA) and preeclampsia (PE) in females presenting for antenatal check-up.

MATERIALS AND METHODS

This Case Control study was conducted in Services Institute of medical sciences, Lahore. The data was collected through Non-probability consecutive sampling technique.

Sample Size

A sample size of 200 (100 in each group) with 80% power of test and 5% level of significance and taking expected percentage of APLA i.e.10% in females having PE and 0% in females without PE.

Inclusion Criteria

- Age of patient between 20-35 years of any parity
- Singleton pregnancy of gestational age ≥ 20 weeks (on USG)
- **CASES**
Females with PE (as per operational definition)
- **CONTROL**
Females without PE presenting for antenatal routine checkup

Exclusion Criteria

- Females with chronic hypertension (BP $\geq 140/90$ mmHg) before pregnancy
- Females with chronic or gestational diabetes (BSR > 200 mg/dl)
- Females with recurrent spontaneous miscarriages, history of deep vein thrombosis and autoimmune disease
- Females on anticoagulant therapy and coagulation factor deficiencies in pre-pregnancy
- Females with infectious diseases (HIV inclusive) and malignancies (on medical record)

Data Collection Procedure

After approval from hospital ethical committee, 200 females, fulfilling the inclusion criteria were included in the study from OPD of Department of Obstetrics & Gynecology. Informed consent was obtained. Demographic information (name, age, gestational age, parity and address) was also recorded. The females were divided in two groups on the basis of presence or absence of PE i.e. cases and controls. Blood sample of 12mls were collected from the antecubital vein of each of the study subject and was sent to the laboratory of the hospital to assess APLA (as per operational definition). Reports were assessed to label APLA positive or negative. All this information was recorded on proforma (attached).

Data Analysis

Data was analyzed in SPSS version 20. Mean \pm SD was calculated for age and gestational age. Frequency was measured for parity. Odds Ratio was calculated to measure association between APLA and PE. OR > 1 was considered statistically significant. Data was stratified for age and parity. Post stratification OR was calculated. OR > 1 was considered significant.



RESULTS

Mean age of the patients among cases was 27.60 ± 4.96 years the minimum age was 20 years and maximum was 35 years whereas among controls the mean age of the patients was 27.94 ± 4.13 years the minimum age was 20 years and maximum was 35 years. (Table-1)

Table-1: Descriptive statistics for age

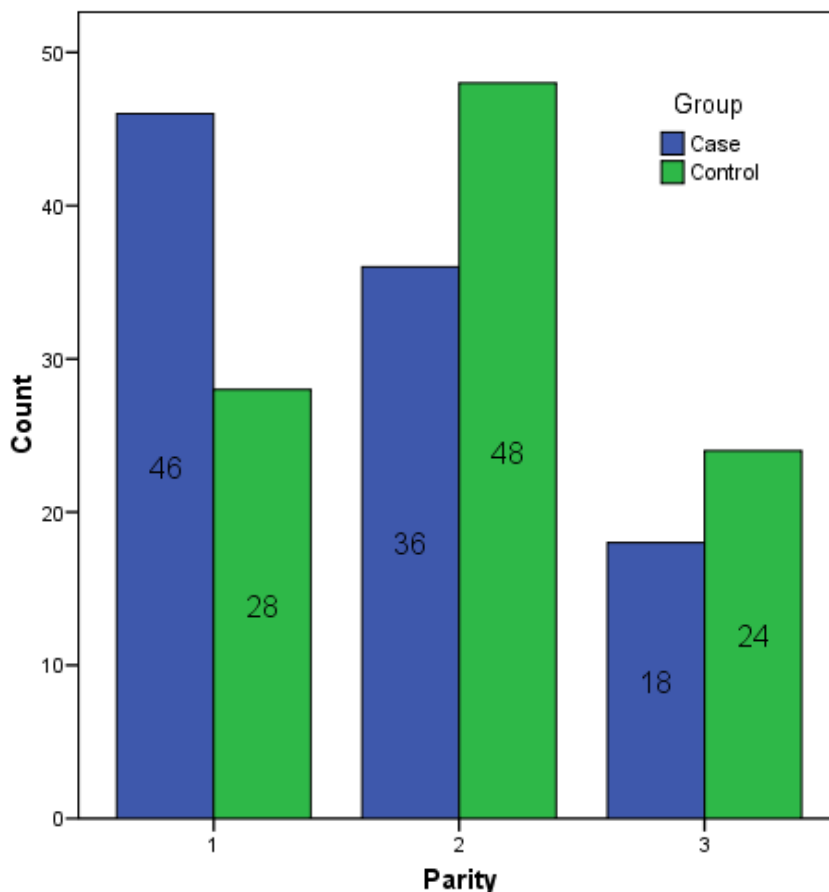
	Cases	Controls
n	100	100
Mean	27.60	27.94
Std. Deviation	4.96	4.139
Minimum	20	20
Maximum	35	35

Cases: Females with PE (as per operational definition)

Control: Females without PE presenting for antenatal routine checkup

The mean gestational age among cases was 27.46 ± 4.72 weeks the minimum gestational age was 20 weeks and maximum was 35 weeks on the other side the mean gestational age among controls was 27.25 ± 4.74 weeks the minimum gestational age was 20 weeks the maximum was 35 weeks. Among cases there were 46() women whose parity was 1, 36 women’s parity was 2 and 18 women’s parity was 3 whereas among controls there were 28 () women’s whose parity was 1, 48 women’s parity was 2 and 24 women’s parity was 2.

Graph-1: Parity Status of Women





Among cases there were 17 (17%) women in which Antiphospholipid antibodies were present where as in 83 (83%) APLA was absent, among controls there were 5(5%) women in which Antiphospholipid antibodies were present where as among 95 (95%) APLA was absent. There was significant association between preeclampsia and Antiphospholipid antibodies (APLA) as the p-value was significant (p-value=0.007). The odds ratio is 3.89 which means there are 3.89 time more odds of having preeclampsia if APLA is present in women. (OR=3.89)

Table-2: Association between APLA & preeclampsia

		Group		Total
		Case	Control	
APLA	Present	17(17%)	5(5%)	22
	Absent	83(83%)	95(95%)	178
Total		100	100	200

There was significant association between APLA and preeclampsia in the age group of 20-28 years as the p-value was significant. (p-value= 0.041) there are 3.34 times more odds of developing preeclampsia in this age group if patient have APLA (OR=3.34) whereas in the age group of 29-36 years there was no significant association between APLA and preeclampsia as the p-value was not significant (p-value=0.066) there are 5.87 times more Odds of developing preeclampsia is the APLA is present in patient.

Table-3: Association between APLA and preeclampsia stratified for age groups

		Age Groups			
		20-28 Years		29-36 Years	
		Case	Control	Case	Control
APLA	Present	12(%)	4(%)	5(%)	1(%)
	Absent	43(%)	48(%)	40(%)	47(%)
Total		55	52	45	48
Chi-Square Test		4.19		3.38	
p-value		0.041		0.066	
Odds Ratio		3.34		5.87	

There was no significant association between APLA and preeclampsia among the women whose party was 1 but there were 4.08 times more odds of developing Preeclampsia among those women in which APLA was present where as among women whose parity was 2 there was also no significant association between preeclampsia and APLA and there were 2.09 times more odds of developing preeclampsia if the APLA was present lastly women with parity 3 there was no significant association between Preeclampsia and APLA and there were 4.6 times more odds of developing preeclampsia if APLA was present.

Table-4: Association between APLA & Preeclampsia Stratified For Parity

		Parity					
		1		2		3	
		Case	Control	Case	Control	Case	Control
APLA	Present	11(%)	2(%)	3(%)	2(%)	3(%)	1(%)
	Absent	35(%)	26(%)	33(%)	46(%)	15(%)	23(%)
Total		46	28	36	48	18	24
Chi-Square Test		3.38		0.63		1.88	
p-value		0.066		0.24		0.17	
Odds Ratio		4.08		2.09		4.6	



DISCUSSION

APLA constitute a heterogeneous group of circulating antibodies against anionic phospholipids with the most important ones being anticardiolipin antibodies, anti- β 2-glycoprotein I (β 2 GP I) and lupus anticoagulants.⁸⁵ In relation to pregnancy, they are associated with recurrent fetal loss and complications such as preeclampsia retarded fetal growth or placental insufficiency.⁹

Preeclampsia is defined as the onset of proteinuric hypertension after 20 weeks of pregnancy; a systemic disease of the later stages of pregnancy that affects about 5 - 10% of all pregnancies¹⁰ and is the most common, yet least understood disorder of pregnancy. It is a rapidly progressive condition characterized by high blood pressure, platelet aggregation, swelling of the lower extremities and protein in urine.¹¹ It is one of the most dangerous complications of pregnancy, and it remains an important cause of foeto-maternal morbidity and mortality, particularly in developing countries where it accounts for a significant cause of maternal deaths.¹²

The role of APLA in the aetiopathogenesis of obstetric complications such as recurrent spontaneous miscarriages has been well established. Women with APS are known to have increased risk of developing preeclampsia however the role of APLA in preeclampsia in general is still unclear.¹³

Preeclampsia generally is associated with serious maternal and fetal complications such as DIC, abruptio placenta, maternal deaths and adverse fetal outcome.¹⁴ APLA positivity may not be accountable for the adverse events. Several publications have associated antiphospholipid antibodies with miscarriage-ages, retarded intrauterine growth and others with preeclampsia although this latter correlation remains controversial.¹⁵⁻¹⁸

In this study women who had preeclampsia among them 17(17%) were positive for APLA and among control only 5(5%) women were positive for APLA. However a statistically significant association was seen between preeclampsia and APLA. i.e. (p-value=0.007) Women with preeclampsia had OR=3.89 times more chances of having APLA positive in them.

CONCLUSION

Results of this study showed a significant association and significant risk between APLA and preeclampsia. Therefore a routine assay of APLA in women at risk of preeclampsia should be done. However APLA testing should be considered in women with early onset severe preeclampsia, especially when additional clinical features of APS are present

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PROFORMA

Association of Antiphospholipid Antibodies (APLA) with Preeclampsia (PE) in females presenting for Antenatal Check-up

Case#: _____ Date: _____
Reg. no: _____
Name: _____ W/O: _____
Age: _____ Gestational age: _____
Parity: _____
Address: _____

Study group: **Case (with PE)** **Control (without PE)**
 APLA: **Positive** **Negative**

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