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

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Abstract

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

Method: After ethical committee approval and informed consent 200 obstetric patients fulfilling inclusion criteria were included in this case control study from OPD of unit 2 Obstetrics and Gynecology Department of Lady Willingdon Hospital Lahore. Demographic record was maintained and two groups were created, case and control on the presence or absence of PE

Results: mean age of case group was 27.60±4.96 ranging from 20 to 35 years while mean age of control group was 27.94±4.13 also ranging from 20 to 35 years Mean gestational age of case group was27.46± 4.72 weeks ranging 20 to 35 weeks while mean gestational age of control group was 27.25± 4.74 weeks, ranging 20 to 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. obstetric patients with a high risk of preeclampsia, must have routine APLA assay.in women with early onset pre-eclampsia APLA should routinely be tested. When other clinical features are suggestive of APs.

Keywords: antiphospholipid antibodies (APLA), preeclampsia (PE), antenatal check-up

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Introduction

A group of antibodies called as Antiphospholipid antibodies (APLA) either binds to only cardiolipin or to a cofactor complexed cardiolipin or to a cofactor only. Incidence of APLA is about 5% in healthy people of the population. In low risk pregnant women prevalence of APLA ranges from 1-9%.[1] Antiphospholipid syndrome is an autoimmune condition characterized by a hypercoaguable state which causes many obstetric complications such as recurrent pregnancy loss, Intrauterine growth restriction, fetal demise and hypertensive disorders of pregnancy.[2,3] One third obstetric population with APS develops preeclampsia.[3,4]

APS was reported 27 years back in patients with systemic lupus erythematosus (SLE) and positive anticardiolipin antibodies manifesting with a clotting disorders of vessels. It was also observed that it caused poor obstetrical outcomes like pre-eclampsia. Literature does not support preeclampsia as a major criterion for diagnosis of APS, however it can be used as a minor criterion for APS diagnosis in patients having other APS manifestations.[4]

Study rationale is to determine the association of APLA with PE in obstetric population presenting in a tertiary care hospital 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. We planned

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this study to find whether there is any impact of APLA in the development of PE. Data is not available at local level and limited studies have been conducted in our setup. 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.

Material and Methods

This Case Control study was conducted in Unit II, Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore. The data collection technique was based on Non-probability consecutive sampling. The study sample size was 200. Both arms of study had 100 patients each (case and control) 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. Patients between 20-35 years of any parity and singleton pregnancy of gestational age > 20 weeks of gestation on ultrasound were included. Cases were Females with PE (as per operational definition) and controls were females without pre-eclampsia. Females with chronic hypertension (Bp 140/90 mmHg) before pregnancy, chronic or gestational diabetes (BSR>200mg/dl), recurrent early pregnancy loss, history of autoimmune disease and deep vein thrombosis, depleted clotting factors, females using anticoagulants, females with infectious diseases (HIV inclusive) and malignancies (on medical record) and females on steroid therapy were excluded from the study. Hospital ethical committee approved the study. After informed consent 12 ml blood was taken from every patient of case (PE) and control group (without PE) presenting to OPD of Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore to assess presence or absence of APLA. All demographic data information (name, age, address, parity and gestational age) and study results were recorded on the proforma (attached). SPSS version 20 was used to analyze data. Mean ± SD was calculated for maternal age and gestational age. Frequency was measured for parity. Odds Ratio was calculated to measure relation between APLA and PE. OR>1 was taken statistically significant. Data was stratified for age and parity. Post stratification OR was calculated. OR>1 was considered significant.

Results

27.60±4.96 years was the mean maternal age of patients among case group, the minimum age was 20 years and maximum was 35 years whereas 27.94±4.13 was the mean maternal age of control group, 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.

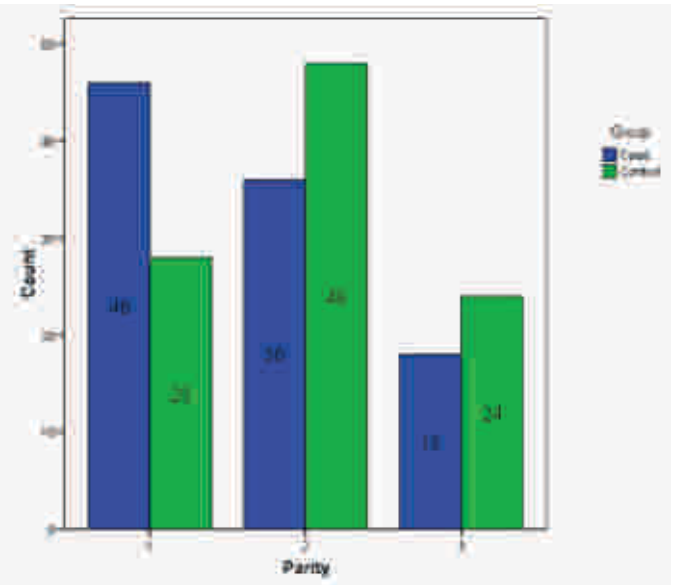

Fig-1: *Parity Status of Women*

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 whereas among 95 (95%) APLA was absent. There was significant association between pre-

eclampsia and Antiphospholipid antibodies (APLA)

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

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)

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

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	

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	

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.

There was no significant association between APLA and preeclampsia among the women whose parity was 1 but there were 4.08 times more odds of developing Preeclampsia among those women in which APLA was present whereas 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 pre-eclampsia if APLA was present.

Discussion

The results of our study indicate that patients presenting with preeclampsia tested positive for antiphospholipid antibodies more than those women without preeclampsia. Hypertensive disorders of pregnancy including preeclampsia are one of the major causes of maternal and perinatal morbidity and mortality. It is an estimation that preeclampsia complicates 2–8% of pregnancies[5,6] Patient manifests as having a high blood pressure, protein urea, lower limb edema and platelet aggregation.[5] It is a main cause of feto-maternal morbidity and mortality in developing countries.[7] Complication in pregnancies like recurrent early pregnancy losses are associated with the presence of APLA. Females with antiphospholipid syndrome have increased chance of developing preeclampsia, however the presence of APLA in preeclampsia is still not clear.[8] Devastating fetal and maternal complications like adverse fetal outcome, placental abruption, DIC and maternal mortality are linked to preeclampsia.[8] Above stated adverse events may not have APLA positivity. Literature associates APLA with miscarriages, intrauterine growth restriction, however there remains a controversy about their link with preeclampsia.[9-12] In a case control study in comparison to control that had 4.6% risk of complications in pregnancy, it increased to 59.1% in women with APLA particularly anti cardiolipin antibodies.[13,14] Benedict et al., found insignificant difference between preeclamptic and control females for presence of APLA i.e. 10% in preeclampsia group and 0% in control group.[15] Dreyfus reported no link between APLA 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.[16] However Roni Z, Mordechari D et al found that females with positive antiphospholipid antibodies were hospitalized earlier, had more complications including preeclampsia and gave birth at an earlier gestation.[17] The pathology of Pre-eclampsia and placental

insufficiency is multifactorial, but a proportion of cases are caused by antiphospholipid antibodies in maternal blood. Both case-control and cohort studies have reported associations between antiphospholipid antibodies and preeclampsia.[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 hence more chances of having APLA positive in them.

Conclusion

Results of this study showed a significant association and significant risk between APLA and preeclampsia. Women at high risk for preeclampsia should be stratified for APLA assay. However, women with early severe preeclampsia and other features of APS must be considered for APLA testing.

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Authors Contribution

SM: Conceptualization of Project
MJ: Data Collection
MJ: Literature Search
AI: Statistical Analysis
SP: Drafting, Revision
MH: Writing of Manuscript