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## Original Research Article

# A comparative study of the serum levels of antiphospholipid antibodies in hypertensive disorder of pregnancy and normotensive pregnancy

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### ABSTRACT

**Background:** Antiphospholipid antibodies have been associated with a number of obstetric complications however their role in the pathogenesis of preeclampsia has remained uncertain. Therefore, the utility of screening for antiphospholipid antibodies among women at risk for recurrent hypertensive disorder of pregnancy is still doubtful. This study is aimed to clarify relationship between hypertensive pregnancies and APLA.

**Methods:** A prospective, randomized was conducted and, 120 patients after 20 weeks of gestation were studied. 60 patients had hypertensive disorder in pregnancy and 60 were normotensive. Blood samples were obtained from them under all asepsis, serum was separated and tested for Antiphospholipid antibodies (Anticardiolipin, anti beta 2 glycoprotein I, phosphatidyl -serine, -inositol, -ethanolamin, -choline and sphingomyelin and lupus anticoagulant), apart from other routine investigations using Aeskulisa Phospholipid-Screen-GM.

**Results:** 4/60 and 3/60 hypertensive patients had raised IgM and IgG levels respectively. Their values came in equivocal range. 2 of the normotensive patients had equivocal range values of both IgM/IgG. Mean of IgM APLA in hypertensive and normotensive patients was 2.54 and 1.67 respectively and difference between these values was statistically non significant ( $p=0.081$ ). Mean of APTT is similarly statistically non significant in two groups ( $p=0.817$ ).

**Conclusions:** No significant correlation between the hypertensive state in pregnancy and antiphospholipid antibodies, hence this test should not be recommended as a screening test in pregnancies and there was no need to assess these antibodies in the hypertensive cases of pregnancy without the history of thrombosis or autoimmune diseases.

**Keywords:** Antiphospholipid antibodies, Aeskulisa phospholipid-screen-GM, Hypertensive disorder in pregnancy

### INTRODUCTION

Pregnancy is a hypercoagulability state. It is claimed that abnormality of natural coagulation inhibitor level, immunologic parameters and genetic parameters create a great tendency towards hypertensive disorder of pregnancy.<sup>1</sup>

Antiphospholipid antibodies (lupus anticoagulant, anticardiolipin antibodies, anti beta2 glycoprotein I antibodies, antiphosphatidylserine, -inositol, -ethanolamin, -choline and sphingomyelin antibodies) are heterogeneous antibodies directed against proteins that bind anionic phospholipids. Although they can be found

in normal individuals, a large body of evidence established clinical associations between antiphospholipid antibodies (APLAs) and venous and arterial thrombosis, thrombocytopenia, recurrent fetal loss, and many other conditions.<sup>2-5</sup>

During pregnancy, thrombosis and placental infarction have been implicated in some complications, such as recurrent fetal wastage, idiopathic fetal growth restriction (FGR), and hypertensive disorder of pregnancy. Considering the thrombotic predisposition that is apparently linked to antiphospholipid antibodies in women.<sup>6,7</sup> it was important to test for those antibodies during complicated pregnancies, in particular during

hypertensive disorder of pregnancy, to determine possible predictive or therapeutic effects.

Several mechanisms have been proposed to explain the action of APA: they can bind to and prevent antithrombin from functioning properly, enhance thromboxane release that can lead to platelet activation and aggregation, or they can prevent the activation of protein C, a cofactor necessary in the clotting cascade.<sup>5,8</sup> Pregnancies complicated by Antiphospholipid antibodies share several common features with preeclampsia; in both, the placenta may show infarctions and decidual, which suggest that the association between the two conditions is more than coincidental.<sup>9</sup>

Some studies have also detected elevated levels of APLA in women with hypertensive disorder of pregnancy.<sup>10,11</sup> However, others found no association between APLA and hypertensive disorder of pregnancy.<sup>12,13</sup> This situation shows that relationship between APLA and hypertensive disorder of pregnancy remains uncertain.

## METHODS

This prospective, randomized study was conducted after obtaining institutional ethics committee approval on 120 patients, including 60 patients with hypertensive disorder of pregnancy (Gestational Hypertension, Preeclampsia, Eclampsia, HELLP syndrome) with or without treatment and 60 normotensive pregnant patients without any disorder. All patients meeting the inclusion criteria were enrolled after taking the informed written consent from patients, a detailed history was taken including complaints during present pregnancy, past history, menstrual history, obstetrical history. Detailed general physical examination and obstetrical examination was done as per proforma. The following investigations were done: - Hb, BT, CT, Platelet count, Peripheral smear, Blood Group, Urine complete examination, VDRL, Liver function test, Renal function test, Activated Partial Thromboplastin Time and Antiphospholipid antibodies (APLA IgM and APLA IgG) were calculated using *AESKULISA* Phospholipid-Screen-GM. *AESKULISA* Phospholipid-Screen-GM is a solid phase enzyme immunoassay for the separate qualitative and quantitative detection of IgG and/or IgM antibodies against phospholipids in human serum. Each well is coated with highly purified bovine cardiolipin + beta 2 glycoprotein I, phosphatidyl-serine, -inositol, -ethanolamin, -choline and sphingomyelin. Data thus obtained was statistically analysed.

## RESULTS

APLA IgM (p 0.081) and IgG (p 0.091) levels have no statistical correlation with the blood pressure of a pregnant female. With very few patients having APLA IgM and APLA IgG levels in the equivocal range, we were not able to obtain any correlation of the blood pressure of the patients and the APLA levels (Table 1).

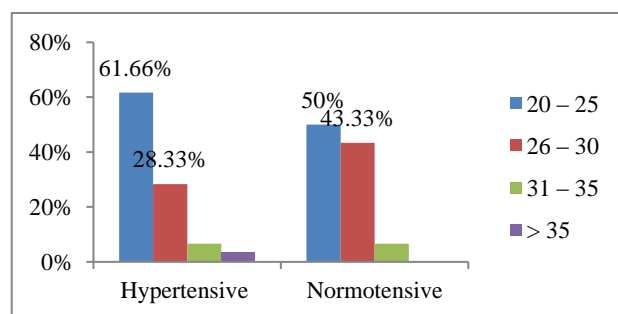
**Table 1: Comparison of APLA IgM and APLA IgG in two groups.**

Parameters	Hypertensive (N=60)		Normotensive (N=60)		P value
	Mean	SD	Mean	SD	
APLA IgM	2.54	2.95	1.67	2.40	0.081
APLA IgG	2.03	2.68	1.24	2.39	0.091

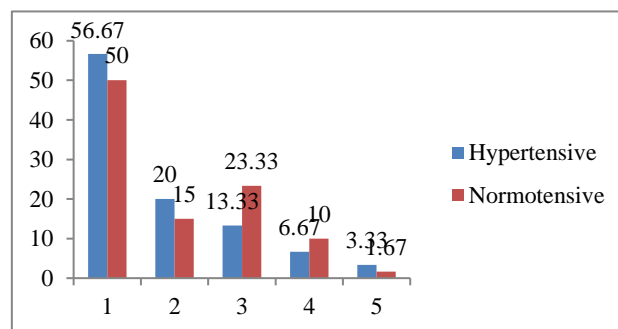
\*\*p value <0.01 highly significant; \*p<0.05 significant

The p value calculated from the mean of the APTT values was found to be non significant (p>0.05) suggesting that none of the patient in two groups is lupus anticoagulant positive, Hence this antibody has no correlation with hypertensive disorder in pregnancy. In spite of statistically non significant APLA values in two groups, we detected that incidence of APAs were nearly double in pre-eclamptic group (IgM: 6.67% in hypertensive group as compared to 3.33% in normotensive group; IgG: 5% in hypertensive patients as compared to 3.33% in normotensive patients).

The frequency of antiphospholipid antibodies detected in our hypertensive population of pregnant women (6.67%). The subjects included in the present study were comparable with respect to age. it was observed that the maximum number of patients in both the groups belonged to the age group between 20 to 25 i.e. 61.66% in hypertensive group and 50% in normotensive group. There was no patient above the age of 35 years in normotensive group and only 2 patients i.e. 3.33% in the hypertensive group (Figure 1).



**Figure 1: Distribution of patients according to age in both the groups.**



**Figure 2: Comparison of gravidity.**

Out of normal cases, 50.00% were primigravidae and 50.00% were multigravidae. Out of positive cases primigravidae were 56.67% and multigravidae were 43.33% (Figure 2).

The levels of blood urea, serum creatinine and liver function tests were significantly high in patients with hypertension as compared to the normal cases with all the values being well within the normal limits. Thrombocytopenia was common finding in patients with hypertensive disorder of pregnancy with a mean value of platelet count among the hypertensive cases being 1.80 lacs/cumm and the mean value of the normotensive cases being 2.53 lacs/cumm. The difference between the two groups was statistically highly significant (0.00) (Table 2).

**Table 2: Blood urea and serum creatinine in two groups.**

Parameters	Hypertensive (N=60)		Normotensive (N=60)		P value
	Mean	SD	Mean	SD	
Blood Urea	22.65	8.79	14.98	2.56	0.000**
S. creatinine	1.10	0.59	0.53	0.21	0.000**

\*\*p value <0.01 highly significant; \*p<0.05 significant

## DISCUSSION

Antiphospholipid antibodies are reported to be present in 7-10% of pregnant women, and it is believed that these antibodies may activate the coagulatory pathways and cause preeclampsia.<sup>14,15</sup> Therefore, we compared antiphospholipid antibody titers in normal pregnant women with hypertensive disorder of pregnancy. In the present study, 120 patients after 20 weeks of gestation were studied. 60 patients had hypertensive disorder in pregnancy and 60 were normotensive. All the patients were drawn from the same obstetrical population and were of same socioeconomic status. All the women included in this study had no clinically apparent nutritional deficiency or any manifestation of immunological diseases.

It is concluded in our study that APLA IgM (p 0.081) and IgG (p 0.091) levels have no statistical correlation with the blood pressure of a pregnant female. With very few patients having APLA IgM and APLA IgG levels in the equivocal range, we were not able to obtain any correlation of the blood pressure of the patients and the APLA levels.

The p value calculated from the mean of the APTT values was found to be non significant (p>0.05) suggesting that none of the patient in two groups is lupus anticoagulant positive, Hence this antibody has no correlation with hypertensive disorder in pregnancy. This is supported by Vahid et al in their study.<sup>16</sup> Previously, when women who developed hypertension during pregnancy were matched

with women who didn't, there were some conflicting results among authors. Many of the authors have described increased rates of APA, ranging between 10% and 20%, among women with preeclampsia, severe preeclampsia, or eclampsia.<sup>17-19</sup> On the other hand some of investigators have found no increased rate of APLA among women with preeclampsia.<sup>20</sup>

Branch et al in their study on association of recurrent preeclampsia with any of 5 antiphospholipid antibodies (anticardiolipin, antiphosphatidyl-serine, antiphosphatidyl-inositol, antiphosphatidyl-glycerol, and antiphosphatidyl-ethanolamine) concluded that testing for antibodies during pregnancy had little prognostic value in the assessment for recurrent preeclampsia of women with a history of preeclampsia.<sup>21</sup> Similarly in a study by Vahid et al for the serum level of antiphospholipid antibodies in normotensive pregnancies and women suffering from pre-eclampsia, they concluded that there was no significant differences in antiphospholipid antibody titers in normal pregnant women with those of pre-eclampsia cases.<sup>16</sup> Dreyfus et al in their study to assess the association between first incidents of pre-eclampsia and occurrence of antiphospholipid antibodies concluded that the antibody titres of women with pre-eclampsia were not very different than women with normotensive pregnancy in the same age and the same parity.<sup>22</sup>

In spite of statistically non significant APLA values in two groups, we detected that incidence of APAs were nearly double in pre-eclamptic group (IgM: 6.67% in hypertensive group as compared to 3.33% in normotensive group; IgG: 5% in hypertensive patients as compared to 3.33% in normotensive patients) Similarly, Acmaz et al detected that incidence of APAs were two times higher in preeclamptic group so this situation might be a result of excessive response in women with pregnancy associated hypertensive disorder.<sup>23</sup>

The frequency of antiphospholipid antibodies detected in our hypertensive population of pregnant women (6.67%) was not different from those of previous studies ranging from 1.8% to 7%.<sup>24</sup>

The subjects included in the present study were comparable with respect to age. it was observed that the maximum number of patients in both the groups belonged to the age group between 20 to 25 i.e. 61.66% in hypertensive group and 50% in normotensive group. There was no patient above the age of 35 years in normotensive group and only 2 patients i.e. 3.33% in the hypertensive group. These findings were comparable with those of Yucesoy et al who concluded that preeclampsia and eclampsia were apparently higher in younger women (less than 30 yrs).<sup>15</sup>

None of the patients included in the study were underweight i.e. body mass index <18.9. But majority of hypertensive patients (65%) were overweight with a body mass index of more than 25. It is in concordance with

Gudnadottir et al who concluded that overweight plays a crucial role in relation to hypertensive disorder during pregnancy.<sup>25</sup>

Out of normal cases, 50.00% were primigravidae and 50.00% were multigravidae. Out of positive cases primigravidae were 56.67% and multigravidae were 43.33%. So the incidence of hypertensive disorder was more among the primigravidae, than the multigravidae. These findings were in correlation with those of Rao et al.

The levels of blood urea, serum creatinine and liver function tests were significantly high in patients with hypertension as compared to the normal cases with all the values being well within the normal limits. This is supported by Hazari et al who concluded that serum GGT and LDH with AST and ALT are clinically beneficial for monitoring the liver function in the management of preeclampsia.<sup>26</sup> Wang et al found that women with hypertensive disorders during pregnancy were at higher of end stage renal disease than women without complicated pregnancies.<sup>27</sup>

Thrombocytopenia was common finding in patients with hypertensive disorder of pregnancy with a mean value of platelet count among the hypertensive cases being 1.80 lacs/cumm and the mean value of the normotensive cases being 2.53 lacs/cumm. The difference between the two groups was statistically highly significant. This is supported by Rahim R et al who stated that platelet count is an important investigation for antenatal mother having pregnancy induced hypertension as it is directly related to maternal and fetal outcome.<sup>28</sup>

## CONCLUSION

It can be inferred that there is no significant correlation between the hypertensive state in pregnancy and antiphospholipid antibodies, hence this test should not be recommended as a screening test in pregnancies and there was no need to assess these antibodies in the hypertensive cases of pregnancy without the history of thrombosis or autoimmune diseases and also anticoagulant therapy should not be recommended on this basis in routine practice. Our conclusion does not completely rule out the possibility of an association and only apply to women without any known risk of preeclampsia, who have no history of thrombosis and no known systemic autoimmune disease. The values were specifically raised to equivocal range in hypertensive patients complicated with HELLP syndrome and eclampsia and with a history of PIH/IUGR/BOH. Hence, in such patient this test can be recommended and should be done in all the fractions.

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