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Comparison of Anticardiolipin Antibodies Titer in Preeclampsia and Normal Pregnancy: A Case-Control Study

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Abstract--

Background and Aim: *Regarding the high prevalence of pre-eclampsia and its complications and also due to conflicting reports about the role of antiphospholipid antibodies, particularly anticardiolipin antibody, the aim of this study was to compare the anti-cardiolipin antibody titers in preeclampsia and normal pregnancy.*

Material and Methods: *In this cross-sectional study, 220 pregnant women in their third trimester were evaluated in Zahedan Ali ebn Abi Talib (AS) hospital in 2013. Participants were divided in two groups preeclapmtic pregnant and normal pregnant as the control group. Sampling method was simple and available method. Anticardiolipin IgG and IgM levels were measured in two groups. Samples were analysed by simple and available methods. Independent T- test was used for data analysis. P-value less than 0.05 was considered as significant.*

Results: *The mean age of pregnant women was 26.1±6.2 years. The gestational age was 37 ±2.1 and 38± 1.9 weeks in the Controls and Preeclampsia groups, respectively (P=0.14). The mean of IgM titer of anti-cardiolipin antibody in preeclampsia group was 1.85±0.84 Mg/L and in control group 2.21±1.61 Mg/L, which no significant difference was found between two groups (P=0.53). The mean of IgG titer of anti-cardiolipin antibody in preeclampsia group was 2.48±1.16 Mg/L and in control group 2.13±0.54 Mg/L and again no statistically significant difference was observed (P=0.34).*

Conclusions: *there was no correlation between anti-cardiolipin antibody titers in pregnant women with preeclampsia compared with normal pregnant women.*

Key words--*Preeclampsia, Anti-cardiolipin Antibodies, Normal Pregnancy.*

I. INTRODUCTION

The incidence of preeclampsia is 2-8% of all pregnancies (1, 2). Anti-phospholipid antibody syndrome is one of the main causes of recurrent abortion, fetal death, intrauterine growth restriction and preeclampsia.

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Antiphospholipid antibodies (APLA) can be found in low risk obstetrical population and ranges from 1-9% (3-6) . some studies have suggested an association between the presence of these antibodies and pregnancy complications like recurrent pregnancy loss (RPL) and utero-placental related complications such as late fetal losses, preeclampsia, placental abruption and intrauterine growth restriction (IUGR) (7, 8) . The association of clinical complications with APLA is related to the specificity of the antibodies, type of isotope, and probably to the time of the appearance of the antibodies (9,10). Women with high titers of antiphospholipid Ig G antibodies experience almost 28% of fetal death during pregnancy (11-13) . The incidence of anticardiolipin antibodies in patients with preeclampsia can reach up to 16%, according to a narrative review (14) . The role of anticardiolipin antibodies as a risk factor for preeclampsia in women with no evidence of autoimmune diseases has been the focus of many studies for the past decades, mainly in cohort and case-control studies (15, 16). A review study by do Prado and colleagues in 2010 showed that moderate to high levels of anti-cardiolipin antibodies are associated with preeclampsia, but there was no sufficient evidence to use anti-cardiolipin antibodies as a predictor of preeclampsia in clinical practice (17) .

In the 14th international congress in 2014 after reviewing all the related studies, it was concluded that high quality studies regarding Anti-phospholipid antibodies and its relationship to poor pregnancy outcome is quite missing (8).

However, concerning the relationship of anticardiolipin antibodies with preeclampsia and also regarding the high prevalence of preeclampsia in Iran, we performed this study to compare the anti-cardiolipin antibody titers in preeclampsia and normal pregnancy.

II. MATERIALS AND METHODS

This cross-sectional study was designed and conducted at Zahedan University of Medical Sciences in Ali ebn Abi Talib Hospital which is a Tertiary Center in the province. The hospital offers the services as research & educational center for undergraduate and postgraduate students and it is a major referral center.

220 pregnant women in the third trimester of pregnancy were enrolled to the study between may 2013 to august 2014. Sampling method was simple and available method.

110 women were referred to the hospital due to preeclampsia, and 110 women were selected as the control group from normal pregnant women without preeclampsia and any history of preeclampsia or hypertension who were hospitalized for delivery in the maternity ward of the hospital and were matched for age and parity with the preeclampsia group.

Inclusion criteria was detecting SBP equal to or more than 140 mmHg or DBP equal to or more than 90 mmHg, 6 hours apart after 20 weeks of pregnancy and the presence of proteinuria greater than 300 mg in a 24 hour collected urine. Exclusion criteria were women with autoimmune diseases such as lupus, thrombophilia, antiphospholipid syndrome, diabetes, chronic hypertension, and cardiac disease, history of repeated abortion, history of deep vein thrombosis, receiving Anticoagulants, any coagulopathies, positive HIV, malignancies, patients receiving corticosteroids.

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Women in the control group were followed up to delivery and were excluded if preeclampsia happened.At the beginning, the details were completely explained for the participants and a written informed consent was signed by them. This study was approved by the Ethics Committee of Zahedan University of Medical Sciences. Sampling was performed by Non-probable simple method. This means that from the beginning, all pregnant women referred to Ali ebn Abi Talib hospital were enrolled in the study after understanding the goals of the project and signed the consent and divided into two groups of preeclampsia (case group) and normal pregnancy (control group).

Preeclampsia was defined as blood pressure ≥ 140/90 mmHg, and proteinuria ≥ 300 mg in a 24-hour urine sample. Four milliliter of blood sample was taken from all women and sent to the one special laboratory under the standard conditions for laboratory analysis. Anticardiolipin IgG and IgM levels were determined by ELISA method (Immaco diagnostic, Buffalo, NY). The results were reported in unit /ML, GPL for IgG Isotype and MPL for IgM.

Statistical analysis

Demographic characteristics, history of underlying diseases, and women's current status of delivery were asked and were recorded in the questionnaire. Finally, the data were analyzed by SPSS software version 19. Descriptive analysis was used to calculate the mean and variance. Non parametric Mann-Whitney test was used to compare the mean of antibody titers in two groups.

III. RESULTS

The mean age of pregnant women in Preeclampsia group was 25.9±6.5 years and Controls groups was 27.06±8.69 years respectively (P = 0.32). The mean weight in the Controls and Preeclampsia groups was 72.03 ±17.25 kg and 75.12 ± 13.70 kg, respectively (P=0.09). The gestational age was 37 ±2.1 and 38± 1.9 weeks in the Controls and Preeclampsia groups, respectively (P=0.14). The number of previous pregnancies was evaluated in both groups. The Controls and Preeclampsia group had 2.9 ±1.7 births and 3.2 ±2.3 births, respectively. (p=0.25). Two groups were completely matched in terms of primary demographic information such as age and weight, gestational age and *pregnancy numbers* had no significant difference(Table1). The mean systolic and diastolic blood pressure in the Preeclampsia group were 149.73 and 92.01 mmHg, respectively, and these values were 129.71 and 81.64 in healthy pregnant mothers, respectively, indicating a higher blood pressure in pregnant mothers with preeclampsia (0.001).

Table 1. Demographic data in Controls and Preeclampsia group

Parameters	**Preeclampsia group (n=110)**	**Controls (n=110)**	**p-value**
Age (year)	25.9±6.5	27.06 ±8.69	0.32
Weight(kg)	72.03 ±17.25	75.12 ± 13.70	0.09
Gestational age (week)	38± 1.9	37 ±2.1	0.14
Gravida	3.2 ±2.3	2.9 ±1.7	0.25
Systolic blood pressure	149.73± 2.83	129.71 ± 2.84	<0.01

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(mmHg)			
Diastolic blood pressure (mmHg)	92.01 ± 2.69	81.64 ± 3.52	<0.01

In preeclampsia group, the mean titer of anticardiolipin IgM antibody was 1.85±0.84 MPL and mean titer of anticardiolipin IgG antibody was 2.48±1.16 GPL (P= 0.263). The correlation of these two variables were compared with the, (r = - 0.18) which showed a poor correlation coefficient between these two variables.

In control group, the mean titer of anticardiolipin IgM antibody was 2.21±1.61 MPL and the mean titer of anticardiolipin IgG antibody was 2.13±0.54 GPL (P= 0.338). The correlation of these two variables were compared with the, (r=0.05) which showed a poor c correlation coefficient between these two variables.

Independent T test showed that the mean titer of anti-cardiolipin IgM antibody had no statistically significant difference between two groups (P=0.531) (table 1). The mean titer of anti-cardiolipin IgG antibody had no statistically significant difference either (P=0.345).

Table 2: Comparison of anti-cardiolipin antibodies in preeclampsia and control groups

variables	**groups**	**N**	**Mean±SD**	**r**	**P-value**
IgM	preeclampsia	110	1.85±0.84	-0.18	0.531
	control	110	2.21±1.61		
IgG	preeclampsia	110	2.48±1.16	0.05	0.345
	control	110	2.13±0.54		

IV. DISCUSSION

Women with antiphospholipid syndrome are at higher risk for preeclampsia, but the role of antiphospholipids alone and without antiphospholipid syndrome is less known in predicting or developing preeclampsia. Antiphospholipids are seen in up to 5% of healthy people, and in 1-9% of the low-risk pregnant population (1) Managing and recognizing of anti-cardiolipin antibodies levels can be effective because of its important warning role (18).

Our study also did not show a clear correlation between the presence of anti-cardiolipin antibodies and preeclampsia. Cristina Gonzales and colleagues in 2015 showed that there was no relationship between Anti-phospholipid antibodies and severity of preeclampsia and also the incidence of Anti-phospholipid antibodies in preeclampsia was low but however it could be a predisposing factor for it (1).

In this regard, a review study by do Prado and colleagues showed that even though an association between anticardiolipin antibodies and preeclampsia has been found, implications for clinical practice are still unclear (17). The study of Hristoskova in Switzerland and the study of Lee in 2003 did not show any difference between anti-

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cardiolipin antibody levels in preeclampsia and normal individuals (19, 20) .The study of Benedict et al. although showed an increased level of antibodies in preeclampsia group(10%) but there was no significant relation between two groups of the study in odds ratio (21) .

On the other hand , Studies reported that anti-cardiolipin antibodies in patients with preeclampsia were significantly higher than the control group (22, 23). Moreover, Fialova and colleagues (2000) studied 410 patients. They found that 7.8 % of pregnant women had positive IgG and 9.8 % also had positive IgM. They reported that antiphospholipid antibody testing can even be used to identify women at risk for pregnancy complications (24) . Hradecky et al. performed a study in 2009 to investigate the occurence of autoantibodies to eight various phospholipids in time of urgent termination of the pregnancy in patients in reproductive age with severe preeclamptic symptoms and found an increase in various antiphospholipid antibodies (25). The different reports from different studies may be due to differences in research methodology, variations in measurement of anti-cardiolipin antibodies between different laboratories or the various underlying etiologies of preeclampsia which many factors probably play a role in its development. Studies of a systematic paper have shown that moderate to high levels of cardiolipin antibodies are associated to some extent, but this relationship has not been significant. But there is insufficient evidence to use anticardiolipin antibodies as predictors of preeclampsia in clinical practice (17).

However, we were faced with limitations in our study including the Cross-sectional nature of the study, sufficient for follow up of all patients up to 12 weeks after delivery especially in control group if preeclampsia happened and the small number of participants in the study groups. By the way, we couldn`t differentiates the patients in the preeclampsia group based on the severity which lead to failure to achieved significant results. That this undifferentiatiating is the methodological faults.

Therefore, we suggest to carry out a prospective cohort study with more participants and longer follow-up until delivery to assess the relationship between these antibodies and preeclampsia.

Regarding the prominent role of the Anti-phospholipid antibodies in prediction of the incidence of preeclampsia or its severity, it is worthwhile to perform a high quality and longer study to determine the prognostic role of the antiphospholipid antibodies.

V. CONCLUSION

We didn`t find any relationships between anticardiolipin antibody titers and preeclampsia. Concerning our goals in this study, we suggest to evaluate this hypothesis by stronger multi center studies with larger population and longer follow up.

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