Original Article

Clinical significance of nonspecificity of antiphospholipid antibodies in recurrent abortions and unexplained infertility

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Abstract

Background: Antiphospholipid antibodies (APLA) are acquired autoantibodies directed to phospholipids which are associated with slow progressive thrombosis and infarction of placenta. Infertility and recurrent pregnancy loss may occur because of impaired trophoblast function, placental infarction, and abnormal blood clotting. **Aim:** To evaluate APLA (IgG and IgM) in cases of infertility and recurrent abortions. **Materials and Methods:** A prospective study comprising 70 subjects was carried out. Fifty cases of unexplained infertility and recurrent abortions (25 each) constituted the study group. Twenty healthy multipara females of same reproductive age group constituted the control group. Venous blood samples were collected, and serum was analyzed for two types of APLA (IgG and IgM) by ELISA method. **Results:** The mean IgM and IgG levels in recurrent abortions group were 8.10 MPL-U/ml and 6.17 GPL-U/ml, respectively whereas in control group, the levels were 4.67 MPL-U/ml and 4.53 GPL-U/ml, respectively. The difference was statistically nonsignificant. The mean IgM and IgG levels in unexplained infertility group were 7.30 MPL-U/ml and 6.12 GPL-U/ml, respectively whereas in control group, the levels were 4.67 MPL-U/ml and 4.53 GPL-U/ml, respectively. Again the difference was statistically nonsignificant. **Conclusions:** The present study concludes that there is no significance of raised APLA in cases of infertility and recurrent abortions.

Key words: Antiphospholipid antibodies, ELISA method, placental infarction, thrombosis

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Introduction

Unexplained infertility, sometimes also called idiopathic infertility, refers to the failure to conceive in a couple for whom no definitive cause of infertility can be found. Generally, the duration of infertility is more than 2 years.[1,2] Approximately 10–20% of couples who are unable to conceive are determined to have unexplained infertility.[3]

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Recurrent abortions are historically defined as three consecutive pregnancy losses before 20 weeks from the last menstrual period. At present, there exist a small number of accepted etiologies for recurrent abortions [Figure 1].[4]

Antiphospholipid antibodies (ApLA) are acquired autoantibodies directed to phospholipids that are associated with slow progressive thrombosis and infarction of the placenta.[5] Substances in blood called phospholipids are required for the blood to clot. In some people, the body

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mistakenly identifies phospholipids as foreign substances and forms antibodies against them. This reaction can be viewed as a confusion of the immune system, called an autoimmune process.[6] APLA represent a family of autoantibodies of different specificities, most of which are directed toward different anionic phospholipids which include cardiolipin, phosphatidylcholine, phosphatidylserine, phosphatidic acid, and phosphatidylethanolamine.[7] Though APLA cause problems, surprisingly 2–15% of the healthy population actually have APLA in their blood. However, these people have very low levels of the antibodies and, therefore, they do not really cause a problem. It is only when they are at high levels that APLA begin to make trouble.[8] APLA are commonly found in people with unexplained infertility, lupus, migraine headache, deep vein thrombosis, and recurrent abortions. Complications caused by APLA include blood clotting, stroke, heart attack, miscarriage, and implantation failure.

Materials and Methods

The present study was conducted in the Department of Biochemistry on 70 cases reporting in the Department of Obstetrics and Gynaecology of a Tertiary Care Centre in North India. These cases were in three groups - study group (I) (n = 50): Group I (a) included 25 clinically confirmed cases of unexplained infertility of minimum 5 years duration and Group I (b) included 25 clinically confirmed cases of recurrent abortions; control group (II): Included 20 healthy multipara females of same reproductive age group.

Approval of Institutional Ethics Committee was procured. A written consent and a detailed history of each patient were taken. The cases of recurrent abortions and primary unexplained infertility were included. Females with the previous history of tuberculosis, diabetes mellitus, cardiovascular disorder, thyroid disorders, polycystic ovarian disease, abnormal hormonal assay, infections (TORCH, HIV), abnormal sonographic studies, cases of secondary infertility (those who have had a previous conception), and cases of male infertility were excluded.

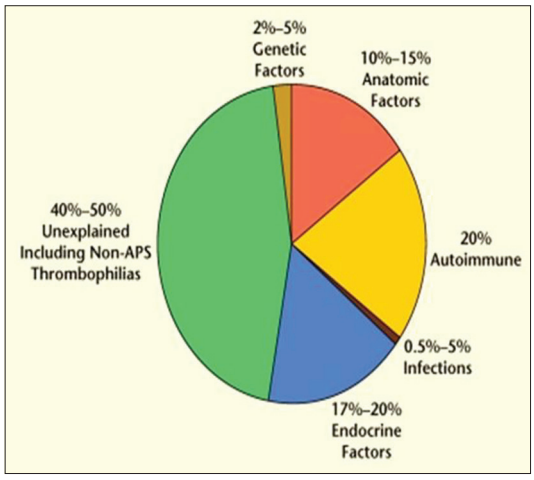

Figure 1: Etiology for recurrent abortions (adopted from Khamashta and Mackworth-Young)

APLA estimation (IgG and IgM) was done using ELISA kit method (Orgentec Diagnostika-Germany).[9] Antiphospholipid screen (IgG and IgM) is an ELISA test system to screen for the presence of IgG and IgM class autoantibodies against phospholipids in human serum. Blood samples were collected under all aseptic conditions and allowed to clot. The serum was then separated by centrifugation of the samples and was used for estimating APLA. Statistical analysis was performed using Pearson's correlation coefficients and results were analyzed accordingly.

Results

Though the mean IgM levels of APLA in cases of primary infertility were raised compared to controls, P = 0.598 which was found to be statistically nonsignificant. Similarly, the mean IgG levels of APLA in cases of primary infertility were raised compared to controls but P = 0.606 which was found to be statistically nonsignificant [Table 1].

In recurrent abortion cases, the mean IgM levels of APLA were raised compared to controls but P = 0.419 which was found to be statistically nonsignificant. Similarly, the mean IgG levels of APLA in cases of recurrent abortions were raised compared to controls. P =0.586 which was found to be statistically nonsignificant [Table 2].

Table 1: IgM and IgG levels of antiphospholipid in primary infertility cases and controls

Levels	Mean±SD	P	Significance
IgM (MPL-U/ml)			
Cases	7.30±10.48	0.598	NS
Controls	4.67±1.88		
IgG (GPL-U/ml)			
Cases	6.12±6.64	0.606	NS
Controls	4.53±1.12		

Normal levels: IgG <10 GPL-U/ml; IgM <10 MPL-U/ml. NS: Not significant; SD: Standard deviation

Table 2: IgM and IgG levels of antiphospholipid in recurrent abortion cases and controls

Levels	Mean±SD	P	Significance
IgM (MPL-U/ml)			
Cases	8.10±10.71	0.419	NS
Controls	4.67±1.88		
IgG (GPL-U/ml)			
Cases	6.17±6.33	0.586	NS
Controls	4.53±1.12		

Normal levels: IgG <10 GPL-U/ml; IgM <10 MPL-U/ml. NS: Not significant; SD: Standard deviation

Table 3: Comparison of antiphospholipid in the current study versus contemporary studies

Name of author	Study group	Control group	Number of positive cases (%)	Significance
Present study (2014)	25 (recurrent abortions) 25 (infertilty)	20	4 (16% infertility) 4 (16% abortions)	NS NS
Sauer *et al*.[12]	676 (recurrent implantation failure)	205	8% (infertility) 9% (recurrent abortions)	S S
Nekoo *et al*.[13]	200 (infertility)	-	23 (11.5)	NS
Parke *et al*.[14] (1991)	81 (recurrent abortions)	88	16%	HS
Chilcott *et al*.[15]	380 (recurrent abortions)	-	89 (23.4)	NS
Couto *et al*.[16]	52 (recurrent abortions) 104 (at least 1 live born child)	-	7.7%	NS
Simpson *et al*.[17]	93 (recurrent abortions)	190	4.2%	NS

NS: Not significant; S: Significant; HS: Highly significant

Discussion

Mechanisms of APLA-induced reproductive failure are not sufficiently well understood, but there is fetoplacental insufficiency, hypoxia and intrauterine fetal death.[10] *In vitro* studies suggest that APLA also act on trophoblasts at a very early stage by inhibiting syncytia formation.[11]

The role of APLA in infertility and recurrent pregnancy loss has been the focus of several clinical trials. In our study, the mean levels of APLA (both IgG and IgM) are raised in cases of infertility and recurrent abortions. Normal levels of APLA (IgG and IgM) were found in 84% of the patients of recurrent abortions and primary infertility. Only 4 patients in each group (16%) had levels higher than reference range.

Other authors have also studied the levels of APLA in infertility and/or recurrent abortions [Table 3].[10-15] The studies of Simpson *et al*., Couto *et al*., Chilcott *et al*., and Nekoo *et al*. corroborated our findings, i.e., APLA were raised but the results were statistically nonsignificant. In our study, APLA were raised in four cases of recurrent abortions (16%) and unexplained infertility (16%). However, the results were statistically nonsignificant. However, some studies (Sauer *et al*. and Parke *et al*.) found significant role of APLA in cases of infertility and recurrent abortions.

Conclusion

The mean levels of serum IgG and IgM were increased in both groups but were statistically nonsignificant, thus denying any role of raised APLA in infertility and recurrent abortion cases. Further studies with larger sample size are required to gather more evidence regarding the significance of APLA in such cases.

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Conflicts of interest

There are no conflicts of interest.

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