## Short communication

# Comparison of Anticardiolipin antibody and Antiphospholipid antibody in women with recurrent abortions

Seyed Mahmood Ghoraishian<sup>1</sup> Ph.D., Seyed Mehdi Klantar<sup>2</sup> Ph.D., Seyed Mohammd Seyed Hasani<sup>2</sup> M.D., Mohammad Ghafourzadeh <sup>2</sup> M.D.

- 1 Department of Immunology Medical School, Shahid Saduoghi University of Medical Sciences, Yazd, Iran.
- 2 Research & Clinical Centre for Infertility, Shahid Saduoghi University of Medical Sciences, Yazd, Iran.

Received: 1, May, 2006; accepted: 22, September, 2006

## **Abstract**

Recurrent abortion is a critical problem in which many factors play a crucial role such as anticordiolipin antibody and antiphospholipid antibody. This study was conducted to evaluate the frequency of anticardiolipin antibody and antiphospholipid antibody in pregnancy failures in women with the history of recurrent pregnancy loss. In 154 women with the history of two or more recurrent pregnancy losses, serum anticardiolipin and serum antiphospholipid were measured using ELISA method. The positive IgG anticardiolipin and IgG antiphospholipid were detected in 12. 34% (19 patients) and 6.5% (10 patients) of patients respectively. Although 16 out of 19 patients with positive IgG anticardiolipin were negative for IgG antiphospholipid and 7 out of 10 patients with positive IgG antiphospholipid were negative IgG anticardiolipin, but there was a significant correlation between IgG anticardiolipin and IgG antiphaspholipid ( r = 0.222 p=0.000). Our data concluded that anticardiolipin antibody is found to be more important than anti phospholipid antibody in recurrent abortion.

Key words: Anticardiolipin antibody, Antiphospholipid antibody, Recurrent abortion

## Introduction

Approximately 15% of all clinically recognized pregnancies are spontaneously aborted. Although the incidence of first trimester losses is high, spontaneous abortion material is often poorly described from a developmental perspective (1). Approximately 5% of couples trying to conceive have 2 consecutive miscarriages, and approximately 1% of couples have 3 or more consecutive losses (2). The etiology of early pregnancy loss is varied and often controversial. More than one etiologic factor is often present. The most common causes of recurrent miscarriages are genetic, endocrine, anatomic, immunologic, infectious and environmental factors (2).

The investigation of recurrent pragnancy loss is begining to deal increasingly with immunological factors and in particular, with the autoimmunity, regarding the presence of non-organ specific autoantibodies. Recurrent pregnancy loss has been associated with anitphospholipid antibodies (APA) and anticardialipin antibody (ACA)(3).

#### **Correspondence Author:**

Dr. Seyed Mahmood Ghoraishian, Department of Immunology, Medical School, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

 $\pmb{E\text{-mail}: smghoraishin@Hotmail.com}\\$ 

Anticardiolipin and antiphospholipid antibodies were detected in infertile women (3). APA directed to phospholipid is associated with slow progressive thrombosis and infarction of the placental which could lead to pregnancy loss (4). APA represent a family of antibodies of different specificities, most of which are directed towards different anionic phospholipids, which include cardiolipin and phosphotidylcholine (5).

ACA react with a plasma cofactor B-2 glycoprotein 1 (B-2 GP1) that stabilizes antigenic conformation of cardiolipin, so that ACA represent a mixture of autoantibodies to B2-GP1 and antibodies to phospholipid epitopes stabilized by interaction with B2-GP1 (3).

The low incidence of chrosomal abnormalities in the aborted fetuses supports pathogenetic significance of anitphospholipied (6). Mechanisms of Antiphospholipid—induced reproductive failure are not sufficiently well understood, but there is fetoplacental insufficiency, hypoxemia and intrauterine fetal death (5,7). In patients with recurrent spontaneous abortion, most frequent APA is ACA (5,8). "However, the significance of APA and ACA is unclear in patients with recurrent abortion. This study was conducted to

evaluate the frequency of ACA and APA in pregnancy failures in women with the history of recurrent pregnancy.

#### Materials and methods

This study was a case series of the 154 women who were diagnosed with history of two or more recurrent pregnancy losses. The patients didn't have lupus, other autoimmune disease or infections and were referred to the laboratory of Madar hospital or to the central laboratory of Shahid Saudoghi University of Medical science of Yazd by a Gynecologist between March 2004 to December 2005. From each patients, 5ml of peripheral blood was taken and its serum was separated. The serum was kept in the 80°C freezer until used. From each sample, IgM and IgG APA and IgM and IgG ACA were measured using ELISA method on the basis of the manufacturer's guide line (APA kit purchased from ORG. Co. Germany and ACA kit purchased from Trinity Co. Ireland).

The normal range of IgG for anticardiolipin and anti phospholipid was < 10 GPL/u/ml.

The normal ranges of IgM anticardiolipin and antiphospholipid was<10 MPL U/ml

The statistical data were analyzed using Pearson correlation. A p value of <0.05 was considered significant using SPSS statistical software, 11<sup>th</sup> version.

## **Results**

ACA and APA were measured in 154 women with recurrent pregnancy loss with the mean age of  $26\pm4.48$  years (range of 18-34). The frequency of distribution of ACA in patients with recurrent pregnany loss is shown in table I. Overall 12.34% (19 of 154) patients had abnormal IgG ACA but 2% had abnormal IgM ACA.

It is interesting that 16 out of 19 patients who had abnormal IgG ACA, had normal APA and 7 out of 10 patients who had abnormal IgG APA had normal IgG ACA but there was a significant correlation between levels of IgG ACA and IgG APA (r=0.212 p=0.000).

The frequency of distribution of APA in patients with recurrent pregnancy loss is also shown in table I. It can be seen that 6.5% patients had abnormal IgG APA but the rest (93.5%) had normal IgG APA and 2.6% of patients had IgM APA. There was no correlation between age and number of loss and abnormal APA or ACA.

**Table I.** The frequency distribution of anticardiolipin antibody and antiphospholipid antibody in patients.

Antibody Isotype	Total Number	Anticardiolipin		Antiphospholipid	
		Positive	%	Positive	%
IgM	154	3	2	4	2.6
IgG	154	19	12.34	10	6.5

#### Discussion

The present study showed that 12.34% of patients with recurrent abortion had positive results for ACA. The results are consistent with the previous reports that 8-24% of recurrent pregnancy loss is due to positive ACA (9).

Previous studies have subsequently confirmed the adverse effects of ACA on pregnancy with the experimental mouse model. The experimental induction of APA causes the increased resumption rate and at the same time decreases placental and embryo weight in pregnant mice (3). Our result shows that there is a significant relation between patients who had IgG ACA and those who had IgG APA and the frequency of IgM ACA and IgM APA were low. The researchers reported IgG ACA to be more strongly associated with clinical events than with IgM ACA (3). We reported that 9 out of 19 patients were positive IgG ACA but IgG APA was negative and 4 out of 10 patients with positive IgG APA were negative IgG ACA. The similar results were reported by Velayuthaprabhus et al (2005)(3). It is concluded from these studies that these two antibodies are not the same and many patients are positive but only one of these antibodies (3). We found that there is a significant correlation between IgG ACA and IgG APA. We have also observed that 10 out of 154 (6.5%) patients with recurrent pregnancy loss showed positive IgG APA. This result is in agreement with previous investigations (3). Ahlenius et al (1995) reported that APA is found in 10-15 % of women with fetal death (10). Although Sugi et al (2004) reported APA may be a risk factor for pregnancy losses (11) and Mitiracui et al (2005) reported association of APA with recurrent idiopathic pregnancy losses (12) but Haddow et al (1991) reported that fetal death is associated with APA (13) and our results showed that there is no relationship between patients who have positive APA to patients who have negative APA (P<0.1). In other prospective studies, investigators did not find any relation between APA and fetal growth restriction (14). Kdous et al (2005) reported that the exact mechanism of APA remains controversial (15).

#### Conclusion

Our data concluded that anticardiolipin antibody is more important than antiphospholipid antibody in recurrent abortion. There was a significant correlation between levels of IgG ACA and IgG APA.

## Acknowledgment

The authors wish to thank Mr Behravan, Mrs Modaresi and Miss Moeini from the Department of Immunology of Medical School in Shahid Sadoughi University of Medical Sciences in Yazd for their assistance.

### References

- 1. Tariverdian G, poul, M. Genetische diagnostic in Geburtshilf. Springer- verlag. *Heidelberg* 1999;191.
- 2. Klousek DK. Anatomical & chromosomal abnormalitic in specimens of early sportoneous aborthion. Seven years experience. *Birth defects* 1987; 23:153-168.
- 3. Velayuthaprabhu S, Archunan G. Evaluation of anticardiolipin antibodies and Antiphosphatidylserine antibodies in women with recurrent abortion. *IJMS* 2005;59:347-352.
- 4. Lockshin MD. Anitphospholipid antibody. *J Am Med Assoc* 1997; 277:1549-1551.
- 5. Kultech WH, Rote NS, Silver R. Antiphospholipid antibodies and Reproduction: the anti phospholipid antibodiy syndrome. *Am J Reprod Immunology* 1999;42:133-152.
- 6. Takokuwa k, Asano k, Arakawa M, Yasuda M, Hasegawa I, Tanaka K. Chromosome analysis of aborted conceptuses of

- recurrent aborters positive for anticardiolipin antibody. *Fertil Steril* 1997;68:54-58.
- 7. Arakawa M, Takakuwa K, Honda K, Tamura M, Kurabayashi T, Tanaka K. Suppressive effect of anticardiolipin antibody an the praliferation of human umbilical vein endothelial cells. *Fertil Steril* 1999;71:1103-1107.
- 8. Yetman DL, Kutteh WH. Antiphospholipid antibody panels and recurrent pregnancy loss. Prevalence of cardiolipin antibodies compared with other antiphospholipid antibodies. *Fertil Steril* 1996:66:540-546.
- 9. Rai RS. Antiphospholipid syndrome and recurrent miscarriage. *J Postgrad Med* 2002;48:3-4.
- 10. Ahlenius I, Floberg J, Thomassen P. Sixty-six cases of intrauterine fetal death: a prospective study with an extensive test pretocol. *Acta Obstet Gynecol Scand* 1995; 74:109-117.
- 11. Sugi T, Matsuboyashi H, Inmo A. Danl Makinat Anti phospholipid antibody in Recurrent early pregnancy loss and mild to late pregnany loss. *J Obstost Gynaecol Res* 2004;30:326-332.
- 12. Mitiracui N, Bergi L, Hizem S, Nsiri B, Finan RR, Gris JC, *et al.* Prevalence of antiphospholipid andibodies in early and lat recurrent pregmancy loss. *Eur J Obstest Gynecol Report Biol* 2005;119:164-70.
- 13. Haddow JE, Rote NS, Dostal–Johnson D, Palomaki GE, Pulkkinen AJ, Knight GJ. Lack of an association between late fetal death and antiphospholipid antidody measurements in the second trimester. *Am J Obstet Gynecol* 1991;165:1308-1312.
- 14. Lynch A, Marlar R, Murphy J, Davila G, Santos M, Rutledge, *et al.* Antiphospholipid antibodies in predicting adverse prepnancy. A prospective study. *Ann Intern Med* 1994; 120: 470-475.
- 15. Kdous M, Horchi Cho R, Gallard G. Antiphospholipid antibodies and pregnancy. *Tunis Med* 2005;87:1-5.