DOI: https://doi.org/10.53350/pjmhs2115123227

**ORIGINAL ARTICLE**

# Frequency of Anticardiolipin Antibodies in Women with Recurrent Fetal Loss

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## ABSTRACT

**Aim:** To find out the frequency of Anticardiolipin Antibodies in women with recurrent fetal loss
**Study design & duration:** One year descriptive study
**Methods:** Seventy five females were included in the study with ages ranging from 20-40 years with minimum two miscarriages. Diabetic females and females with history of bacterial or viral diseases were excluded from the study.
**Results:** In this group the mean age was 27.60±3.29 years. Mean number of fetal losses was 2.95±1.45 whereas mean duration of marriage was 5.79±4.11 years.
**Conclusion:** It is suggested that the patient with history of recurrent miscarriages must be screened for Anticardiolipin Antibodies to bring them out of psychological and physical trauma.
**Keywords:** Anticardiolipin Antibodies (aCL), Recurrent fetal loss (RFL), aPTT

## INTRODUCTION

Anticardiolipin antibodies (aCL) are the antiphospholipid antibody immunoglobulin's which bind to proteins and phospholipids of the cell membrane. This binding of anticardiolipin antibodies to the cell membrane proteins and phospholipids can lead to thrombosis and other complications of pregnancy leading to its termination (Joussen, 2007).

The prevalence of anticardiolipin antibodies in obstetric centers has been reported from 2.7 to 7.0% (Lynch et al, 1994).Their presence in the blood raises the risk of miscarriages from 3 to 9 time greater (Lock wood et al, 1989). This leads to the social dilemma of infertility. Anticardiolipin antibody cause retro placental thrombus with infarction, perivillus fibrin deposit and even chronic inflammatory lesions leading to placental insufficiency and resulting in fetal loss (Rand et al, 2010). There is in vitro evidence that these antibodies can inhibit trophoblastic proliferation resulting into impaired implantation of embryo in first trimester (Empson et al, 2012). These antibodies are mostly directed against beta-2–glycoprotein (a protein in the blood with unknown function) and Prothrombin (a protein in the blood which binds to phospholipids leading to its important role for blood clotting) (Sciascia et al, 2016). The placental dysfunction of second or third trimester can lead to placental abruption, preeclampsia, IUGR and intra uterine fetal death like complications (Hoffbrand,2006). These patients can present with arterial or venous clots like deep venous thrombosis of lower extremities and arterial infarcts in the form of strokes (Cervera et.al, 2014).They may have the presentation with headaches, migraine and oscillopsia (Toubi and Shoenfield, 2007).

## METHODOLOGY

Seventy five females were included in the study with ages ranging from 20-40 years with minimum two miscarriages after IRB permission. Diabetic females, females with renal and liver diseases, bleeding disorders, anticoagulant or antiplatelet therapy like NSAIDs, clopidogeral, aspirin, heparin, warfarin, oral contraceptive, steroid medication and females with history of bacterial or viral diseases were excluded from the study. Platelet count, aPTT, anticardiolipin antibodies were tested on blood samples.

Received on 24-06-2021
Accepted on 14-11-2021

## RESULTS

The study was conducted on 75 females with the mean age of 27.60±3.29 years whereas mean number of fetal losses was 2.95±1.45 and the mean duration of marriage was 5.79±4.11 years having history of at least two miscarriages. Out of 75 females, anticardiolipin antibodies were positive in 30(40%) females whereas in rest of 45(60%) females the antibodies were negative. A significant difference was seen in the duration of marriage which was higher in anticardiolipin positive females as compared to females with anticardiolipin antibodies negative which was not statistically significant. aPTT was prolonged in 15(20%) patients out of 75(100%) but the association between aPTT and anticardiolpin antibodies was significantly high, out of 30 anticardiolipin antibodies positive patients aPTT was raised in 10 patients (p-value =0.018),by fisher exact test.

## DISCUSSION

Anticardiolipin antibodies are auto antibodies in the blood, responsible for thrombophilic condition that recognize and attack phospholipid-binding proteins, rather than phospholipid itself (Hughes GR,1983). The clinical manifestations of anticardiolipin antibodies in pregnant women include vascular thrombosis and pregnancy complications (Hughes GRV,1993) especially recurrent spontaneous miscarriages and less frequently, maternal thrombosis (Roubey RAS, Hoffman M, 1997). These thrombotic events caused by anticardiolipin antibodies are either by binding and decreasing the function of Antithrombin III or by enhancing thromboxane release which leads to platelet aggregation or by decreasing the activation of protein C, needed to inactivate the clotting process (William H. Kutteh, 1996).

I conducted a study on 75 females who were selected for this descriptive study with ages ranging between 20-40 years by fulfilling the inclusion and exclusion criteria. The Females having history of at least 2 miscarriages were included in my study. I tried to find out the frequency of anticardiolipin antibodies in these women.

In my study for these 75(100%) females, I performed anticardiolipin antibodies blood test including platelet count, activated partial thromboplastin time (aPTT) and cardiolpin assay through ELISA. Out of these 75(100%) females, 30 females (40%) were positive for anticardiolipin antibodies, 22 had decreased platelet count and 15 had prolonged aPTT.

My study resulted into positive anticardiolipin antibodies in 30(40%) females out of 75(100%) having the positive history for recurrent fetal losses. A similar study was done by Deborah L. Yetman B.S and his colleague in 1996 on 866 females having recurrent fetal losses. His study reported 150 (17.3%) females positive for anticardiolipin antibodies in blood tests.
The scientist Olaniyi in 2011 told that the high frequency of 17.1% for anticardiolipin antibodies positive women with history of recurrent abortions necessitates regular screening in his research work. (Olaniyi, 2011; Creagh, 1991)

In 1995 Rai and his colleagues published the results of their cohort study on 100 females with ages ranged between 23-44 years with mean age of 33 years and number of recurrent miscarriages ranged from 3-10 with the mean of 4.

Similarly in 2005 Archunan and his colleagues reported 40% positive anticardiolipin antibodies cases in women with history of recurrent fetal losses. (Archunan, 2005). In another study done by Creagh et al (1999), sample size of 35 women with history of recurrent fetal losses showed 17.1% positive anticardiolipin antibodies (Creagh, 1999).

Meanwhile another study by Blumenfeld and his colleagues was done on 67 females for anticardiolipin antibodies with an enzyme-linked immunosorbent assay. High levels of anticardiolipin antibodies were detected in 34(50.7%) out of 67(100%) while it was not detected on 12 normal pregnant female (Blumenfeld, 1991).
Meanwhile an analysis was conducted on 25 different studies on association of anticardiolipin antibodies and recurrent miscarriages on articles published from 1975 to 2003 by Luice Opatrny and his colleagues in 2006. This metaanalysis showed a strong association between recurrent fetal losses and anticardioolipin antibodies positive tests.
**Platelet count:** Platelet count was performed on females with positive anticardiolipin antibodies. Out of these 30 females, only 12 (40%) had decreased platelet count. The association between platelet count and anticardiolipin antibodies was not significant p value=0.098.
Klara Gado and Gyula Domjan in 2017 published their observation that as anticardiolipin antibodies prone to thrombotic events but thrombocytopenia is one of the most common finding of the disease.
Similaraly Cervera and his colleagues in 2002 observed thrombocytopenia in their study with platelet count less than 100x $10^9$/L in females with recurrent fetal losses.

In another study done by Maria jose in 1997 for thrombocytopenic association by comaparing the two groups, one positive for anticardiolipin antibodies and another negative for it but no statistically significant difference was found between two groups regarding decreased platelet count which shows no significant association between thrombocytopenia and anticardiolpin antibodies.
**Activated partial thromboplastin time (aPTT):** An important association was found between aPTT and anticardiolipin antibodies during this study (p value is equal to 0.018).Out of 75 females, 30(40%) females were positive for anticardiolipin antibodies and 45(60%) females were negative for it. In ACA positive females, 10(33.3%) female patients showed prolonged aPTT and 20(66.7%) female patients showed normal aPTT whereas in aCL negative females only 5 showed prolonged aPTT and 40 showed normal aPTT.
A study done by Abu-Shakra et al in 1995 showed a strong association of patients having anticardiolipin antibodies with prolonged aPTT

Similarly in 2 studies carried out by Al-Mishari in 2004 and Olaniyi in 2011 showed prolongation of aPTT in 10.2% and 72.2% patients having positive anticardiolipin antibodies respectively.
**Anticardiolipin antibodies:** Blood samples were collected for all the 75 females. They were subjected to test for solid phase assay through ELISA to detect anticardiolipin antibodies. Out of 75 female patients, 30(40%) were positive for anticardiolipin antibodies, showing a significant association to females presented with history of recurrent miscarriages. Various studies have been conducted by different scientists and showed variable results.

A study done by Deborah et al in October 1996, conducted on 866 women with history of recurrent fetal losses ,out of 866,150(17.3%) had positive anticardiolipin antibodies,87(10.1%)were positive for other antiphospholipid antibodies. **A**nother study done by R .S Rai et al in 1995 on 500 women showed the prevalence of persistently positive tests for immunoglobulin G (IgG) and immunoglobulin M (IgM) aCL, was 3.3 and 2.2% respectively

## CONCLUSION

It was concluded that females with history of recurrent miscarriages should be investigated for anticardiolipin antibodies in their blood. These females should be screened in Obs Gyne centre so that to investigate them properly and to save them from the psychological and physical trauma.
**Conflict of interest:** Nil

## REFERENCES


1. Joussen A, Gardner T W, Kirchhof: Retinal Vascular Disease. ***Springer*** (2007).430. Retrieved 29 June, 2010.
2. Lynch A, Marlar R, Murphy J, Davila G, Santos M, Rutledge J, Emlen W: Antiphospholipid antibodies in predicting adverse pregnancy outcome. A prospective study***. Ann Intern Med****.* (1994).15;120(6):470–475[PubMed]
3. Lockwood CJ, Romero R, Feinberg RF, Clyne LP, Coster B, Hobbins JC: The prevalence and biologic significance of lupus anticoagulant and anticardiolipin antibodies in a general obstetric population. ***Am J Obstet Gynecol.*** (989).161(2):369–373. [PubMed]
4. Empson MB, Lassere M, Craig JC. & Scott JR: Prevention of recurrent miscarriage for women with antiphospholipid antibody or lupus anticoagulant. ***Cochrane Database of Systematic Reviews*** (2005). Issue2. Art. No**.:** CD002859.
5. Savino Sciascia, Simone Baldovino, Karen Schreiber, Laura Solfietti, Massimo Radin, Maria J Cuadrado, Elisa Menegatti and Doruk Erkan:Thrombotic risk assessment in antiphospholipid syndrome: the role of new antibody specificities and thrombin generation assay. *Clinical and Molecular Allergy.* (2016).14(6)
6. Hoffbrand AV, Catvsky D and Edward GD: Acquired coagulation disorders and vascular bleeding-Antiphospholipid(2005)
7. Cervera $R^1$, Serrano $R^1$, Pons-Estel $GJ^1$, Ceberio-Hualde $L^2$, Shoenfeld $Y^3$, de Ramón $E^4$, Buonaiuto $V^4$, Jacobsen $S^5$, Zeher $MM^6$, Tarr $T^6$, et al:Morbidity and mortality in the antiphospholipid syndrome during a 10-year period: a multicentre prospective study of 1000 patients. *Ann Rheum Dis.* (2015).74(6):1011-8.doi: 10.1136/annrheumdis-2013-204838. Epub 2014 Jan 24.
8. Toubi E, Shoenfeld Y**:**Livedo reticularis as a criterion for antiphospholipid syndrome. Clin Rev Allergy.***Immunol***.(2007). 32(2):138-44.
9. Hughes GR: Thrombosis, abortion, cerebral disease and the lupus anticoagulant. ***BMJ.***( 1983).287:1088–1089.
10. Hughes GR:The antiphospholipid syndrome: ten years ***on Lancet.***(1993).342:341–44.
11. Roubey RAS and Hoffman M: From antiphospholipid syndrome to antibody mediated thrombosis***. Lancet.***(1997)350:14913
12. William H kutteh: ***AJOG*** May (1996). 174( 5):1584–1589
13. Deborah L, Yetman BS, William H Kutteh **:** Antiphospholipid antibody panels and recurrent pregnancy loss: prevalence of anticardiolipin antibodies compared with other antiphospholipid antibodies. ***Fertility and Sterility*****.(**1996).66(4):540-546
14. Olaniyi JA, Olomu SA and Finomo SA:Lupus anticoagulant(LA) in pregnant women with history of recurrent fetal loss . ***J. Blood Med.***(2011).**2**:87-90
15. Creagh MD, Malia RG, Coper SM, Smith AR, Duncan SL, Greaves: Screening for lupus anticoagulant and anticardiolipin antibodies in women with fetal loss. ***J. Clin. Pathol***.(1999) 44(1): 45–47.
16. RS Rai, L Regan, K Clifford, W Pickering, M Dave, I Mackie, T McNally, H Cohen:Antiphospholipid antibodies and $\beta_2$-glycoprotein-I in 500 women with recurrent miscarriage: results of a comprehensive screening approach. ***Immunology:*** **Human Reproduction**.(1995).10(8) :2001–2005.

17. Archunan, G., Velayuthaprabhu, S., 2005. Evaluation of anticardiolipin antibodies and antiphosphatidylserine antibodies in women with recurrent abortion.Indian J Med Sci. **59**(8):347-52.,
18. Blumenfeld Z, Weiner Z, Lorber M ,Sujov P and Thaler:Anticardiolipin antibodies in patients with recurrent pregnancy wastage: treatment and uterine blood flow. ***Obstetrics and Gynecology***(1991).78(4):584-589
19. Lucie Opatrny, Michéle David, Susan R Kah, Ian Shrier and Evelyne Rey. Association between antiphospholipid antibodies and recurrent fetal loss in women without autoimmune disease: a meta analysis. ***The Journal of Rheumatology***.(2006) 33 (11) :2214-2221;
20. Klara Gado and Gyula Domjan: Antiphospholipid syndrome and thrombocytopenia.(2017):DOI:10.5772/intechopen.72509
21. Cervera R, Piette JC, Font J, Khamasht MA, Shoenfeld Y, Camps MT, Jacobsen S, Lakos, G et.al: Antiphospholipid syndrome: clinical and immunologic manifestations and patterns of disease expression in a cohort of 1,000 patients. ***Arthritis and Rheumatism***.(2002) 46: 1019–1027.Direct Link
22. Maria José Cuadrado, Fedza Mujic, Elisa Muñoz[c], Munther A Khamashta Graham R V Hughes: Thrombocytopenia in the antiphospholipid syndrome. ***Ann Rheum Dis*** **.**(1997) 56:194-196 doi:10.1136/ard.56.3.194
23. Abu-Shakra M, Gladman DD, Urowtiz MB, Farewell V: Anticardilipin antibodies in systemic lupus erythematosus: clinical and laboratory correlations. ***The American journal of Medicine.***(1995).99(6):624-628
24. Al-Mishari AA, Gader AG, Al-Jabbari AW, Al-Memon AK, El-Rab MO, Babay ZH & Mahmoud N: The prevalence of Lupus anticoagulant in normal pregnancy and in women with recurrent fetal loss-Recommendations for laboratory testing for lupus anticoagulant. ***Ann. Saudi Med***.(2004).24(6): 429–433.