

# Frequency of Lupus Anticoagulant Antibodies in women with Recurrent Fetal Loss

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## ABSTRACT

**Aim:** To determine the frequency of Lupus anticoagulant antibodies in women with recurrent fetal loss.

**Study Design:** Descriptive study

**Study Duration:** One year.

**Methods:** Seventy five females with the ages ranging between 20-39 years, who had at least two miscarriages were included in the study. Females with Diabetes Mellitus and Present history of bacterial/ viral disease were also excluded from the study.

**Results:** In this study group the mean age was  $27.60 \pm 3.29$  years. Mean number of fetal loss was  $2.95 \pm 1.45$  whereas mean duration of marriage was  $5.79 \pm 4.11$  years.

**Conclusion:** It is suggested that the patient with this history must be screened for lupus anticoagulant antibodies to bring them out of psychosocial and physical trauma.

**Keywords:** Lupus anticoagulant antibodies, recurrent fetal loss, aPTT.

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## INTRODUCTION

Lupus antibodies (LA) are immunoglobulins that bind to phospholipids and proteins associated with the cell membrane. They have been responsible for thrombosis and/or complications of pregnancy and failure<sup>1</sup>.

Lupus anticoagulant can be responsible either for the concentration of prothrombin on phospholipid surface in vivo resulting in enhanced thrombin generation or disrupting the interaction of beta2-glycoprotein 1 with anticoagulant factors such as protein C or increased tissue factor expression on monocyte and endothelial cells. (Hoffbrand, 2005)

The patients with Lupus anticoagulant have unusual antibodies in their blood that are targeted against their own body tissues. Lupus antibody causes an increase in partial thromboplastin time and is associated with arterial or venous thrombosis, fetal loss and thrombocytopenia (Mosby, 2009)

During antenatal period, placental vessels thrombosis can lead to placental insufficiency, which may result into fetal loss. There is also in vitro fact that such antibodies can reduce proliferation of trophoblasts resulting into impaired embryo implantation in first trimester of pregnancy (Empson et al., 2012). Complications like placental abruption, pre-eclampsia, intrauterine growth retardation and intra uterine death of fetus during the 2nd or 3rd trimester of pregnancy are the results of placental dysfunction (Hoffbrand, 2005). Current studies have shown the prevalence of decreased platelet count in patients having lupus anticoagulant antibodies (Viana et al., 1994).

## METHODOLOGY

Seventy five females with the ages ranging between 20-39 years, who had at least two miscarriages were included in the study. All females with other bleeding disorders, liver

disease, renal failure, history of drug intake e.g., NSAIDS, anti-platelet drugs, heparin, warfarin, oral contraceptives and steroids were not included in this study. Females with Diabetes Mellitus and Present history of bacterial/ viral disease were also excluded from the study. Blood samples were tested for Platelet count, aPTT and antibodies for lupus anticoagulant (LA).

## RESULTS

In this study group the mean age was  $27.60 \pm 3.29$  years. Mean number of fetal loss was  $2.95 \pm 1.45$  whereas mean duration of marriage was  $5.79 \pm 4.11$  years. Lupus anticoagulant (LA1) was present in 29 (38.7%) females whereas Lupus antibodies (LA) were confirmed to be present in only 11 (14.7%) females. A significant relationship was observed between family history and Lupus antibodies ( $p$ -value=0.717), between Aptt and lupus antibodies ( $p$ -value < 0.001) and between platelet count and lupus antibodies ( $p$ -value < 0.001), by Fisher's exact test.

## DISCUSSION

APS is one of the major causes of thrombosis and its complications in women. Arterial and venous thrombosis both are reported. APS is also associated with infertility and pregnancy complications such as spontaneous abortion, prematurity and stillbirths. Human APL antibodies mediate their biologic effects by;

1. Reacting with endothelial cell structures and disturb the production and balance of prostaglandinE2 and thromboxane
2. Interact with platelet PLs and promote platelet aggregation
3. Dysregulate complement activation
4. Interaction of aPL with phosphatidylserine exposed during trophoblast syncytium formation which may be the reason of a more direct effect of these auto antibodies on placental structures.

We performed a descriptive study on 75 female patients who ranged between the age of 20 to 39 years and

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fulfilled the inclusion criteria. They had a history of at least 2 miscarriages. Objective of the study was to determine the frequency of Lupus anticoagulant antibodies in women with recurrent fetal losses. A similar study has been conducted by Creagh et al., in 1999, on 50 women with an age range of 26 to 39 years with history of at least 2 lost pregnancies. 68% of these women reported in the first trimester. Later on, Rai and his colleagues (1995) published a study, which was conducted on 500 female patients with age range between 19 to 45 years with mean age of 33 years. Number of recurrent fetal losses ranged from 3 to 16 with the mean loss of 4.

**Platelet count:** Role of platelets has a primary importance in homeostasis. Platelet count was carried out on every patient. The present study showed a significant association between deranged platelet count and Lupus antibody positive results in women with recurrent fetal loss (P value less than 0.001).

Out of 11 patients who were positive for lupus antibodies 10 (90.9%) had decreased platelet count and only one patient (9.1%) had normal platelet count. Cervera and his colleagues in 2002 carried out a trial and observed thrombocytopenia with platelet count less than  $100 \times 10^9 / L$  in patients with recurrent fetal losses.

**Activated partial thromboplastin time (aPTT):** This study revealed an important association between aPTT and lupus antibodies (P value less than 0.001).

Prolonged aPTT has been noticed in patients with lupus anticoagulant positive patients. It was observed that in 11 patients (100%) who were positive for LA, 8 patients (72.7%) had prolonged aPTT where as 3 patients (27.3%) had normal values of aPTT. Only 7 patients (10.9%) had prolonged aPTT, whereas 57 (89.1%) had normal aPTT, simultaneously out of a group of 64 patients who were negative for lupus anticoagulant antibodies.

In a case reported by Indian consultant, prolonged aPTT has been reported in Lupus anticoagulant positive patients. Similarly, 2 studies were carried out by Al-mishari (2004) and Olaniya (2011), also showed prolongation of aPTT in 10.2 % and 72.2% patients having positive antiphospholipid antibodies respectively, in patients with recurrent fetal losses.

**Lupus Anticoagulant:** All the blood samples were tested and screened for lupus anticoagulant screening test. Out of a total of 75 samples, 29 (38.7%) samples were initially positive for LA 1. Confirmatory test was performed on these 29 cases of LA 1 screening positive patients. These confirmatory lupus antibodies were detected only in 11 (14.7%) cases. Out of a total of 29 females who had positive screening lupus anticoagulant (LA1) test, only 11 (39.7%) females were declared positive through confirmatory test, where as 18 (62.1%) were negative for LA confirmatory test. So, out of a total of 75 patients, both screening and confirmatory test were positive only in 11 (14.7%) patients.

Various studies have been carried out by different scientists and showed variable results. It was Archunan and his colleague (2005) who reported positive Lupus anticoagulant antibodies in 19% of women with history of recurrent fetal loss turning out positive for lupus anticoagulant antibodies, in their study. Similarly Creagh et al (1999) conducted a study and reported that out of 35

women with recurrent fetal loss, 20% (7) were positive for lupus anticoagulant, whereas out of 31 females having 1-2 episodes of fetal loss, only 3.2% (1) had lupus anticoagulant positive result. Rivard et al (1991), reported that in the blood of 17 patients (5.1 percent) and 38 controls patients (3.8 percent), it was found that the rough probability ratio for the correlation between lupus anticoagulants positive cases and fetal loss was 1.36 (95% confidence interval, 0.75 to 2.43); the probability ratio adjusted for confounders was 1.42 (95% confidence interval, 0.72 to 2.80). Olaniya et al (2011) published in his analysis that 24% positive tests for LA were detected in women with recurrent fetal losses. This necessitates regular screening for the females having recurrent miscarriages. At the same time Opatry et al (2006) reported that LA was associated with recurrent fetal loss (OR 7.79, 95% CI, 2.30-26.45). MacLean MA et al in 1994 conducted a study on 243 women, which showed 16 women (6.6%) positive for lupus anticoagulant. The most commonly used positive test for lupus anticoagulant was the dilute Russel viper venom time. It was observed that with increasing number of miscarriages, the number of females with positive lupus anticoagulant antibodies also increased. Women with a history of only two miscarriages, 15% had an issue of lupus anticoagulant compared with women having history of three or more miscarriages, 18.5% had an issue of lupus anticoagulant antibodies. Taylor in 1990 conducted a study on 189 couples with recurrent fetal losses; his analysis stated that the lupus anticoagulant was detected in only 3% of patients. Rai in 1995 conducted a study on 500 females who presented with recurrent miscarriages. He reported the occurrence of persistently positive cases for Lupus Anticoagulant as 9.6%.

## CONCLUSION

It is concluded that females with history of recurrent fetal loss have a high frequency of lupus anticoagulant antibodies in their blood. It is suggested that the patient with this history must be screened for lupus anticoagulant antibodies to bring them out of psychosocial and physical trauma.

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