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## Original Research Article

# Incidence of thrombophilia in patients with recurrent pregnancy loss

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### ABSTRACT

**Background:** Approximately 1-3% of women of reproductive age suffer from recurrent pregnancy loss. Objective of this study was to evaluate the association between recurrent pregnancy loss and thrombophilia.

**Methods:** This is a descriptive study, involving retrospective analysis of patients with recurrent pregnancy losses. Patients with recurrent pregnancy loss in whom associated morbidity factors were excluded underwent screening for both acquired and inherited thrombophilia.

**Results:** A total of 20 patients were screened for acquired and inherited thrombophilia with recurrent pregnancy loss. Thrombophilia was diagnosed in 70% cases. Out of which, anticardiolipin antibodies was found positive in 57% of patients, protein C 7% and protein S deficiency was observed in 35% cases.

**Conclusions:** Thrombophilias are associated with recurrent pregnancy loss. Patients in whom other associated morbid factors are excluded, should be offered screening for thrombophilia. Multidisciplinary management involving hematologist is vital for management.

**Keywords:** Abortion, Antithrombotic therapy in pregnancy, Antiphospholipid antibody syndrome and pregnancy, Protein C deficiency and pregnancy, Recurrent pregnancy loss, Thrombophilia

### INTRODUCTION

Approximately 1-3% of women of reproductive age suffer from recurrent pregnancy loss.<sup>1</sup> In one-third cases, there is no etiology identified, and the remaining have a persistent underlying cause for their pregnancy losses. The common causes of recurrent pregnancy loss are uterine anomalies, endocrine disorders, immunological factors and parental chromosomal abnormalities including those associated with antiphospholipid antibody syndrome and infections. Even after a thorough evaluation, however, the potential cause remains unexplained in about one third of cases.<sup>2,3</sup>

A number of studies have reported an increased risk of RPL in women with inherited thrombophilia.<sup>4-6</sup> In the European prospective cohort study on thrombophilia

(EPCOT), a significant association between thrombophilia and miscarriage was reported.<sup>7</sup> The term thrombophilia is generally used to describe a hematological abnormality which increases the tendency to venous thromboembolism in any site or pulmonary embolism.

Thrombophilia can be acquired or hereditary. Hereditary thrombophilia includes a number of conditions, such as antithrombin (AT) III deficiency, protein S (PS) and protein C (PC) deficiencies, factor V Leiden, prothrombin 20210A mutation, elevated factor VIII level, and mutation of gene encoding the enzyme methylenetetrahydrofolate reductase (MTHFR).

It is still not certain if heritable thrombophilia causes recurrent miscarriage, and routine testing in women with

recurrent miscarriage is preferable but not currently advocated.<sup>8</sup> The principal acquired thrombophilic states include APS and hyperhomocysteinemia.<sup>9</sup> Thrombophilia has been suggested to be a cause for microembolism in the placenta resulting in abortion or adverse outcome of pregnancy.

The objective of the study was to evaluate the association between thrombophilia and recurrent pregnancy loss which is so far not conclusively evaluated and may help in future to successfully treat cases of recurrent pregnancy loss with this condition.

## METHODS

This is a descriptive case series, incorporating a retrospective analysis of patients with recurrent pregnancy loss in whom other associated morbid factors are excluded. Screening for thrombophilia was carried out in patients with above obstetric complication.

### Inclusion criteria

- Cases with confirmed diagnosis of thrombophilia.

### Exclusion criteria

- Cases with cervical incompetence, uterine anomalies, thyroid disorder, diabetes mellitus, auto-immune disorders and chromosomal anomalies.

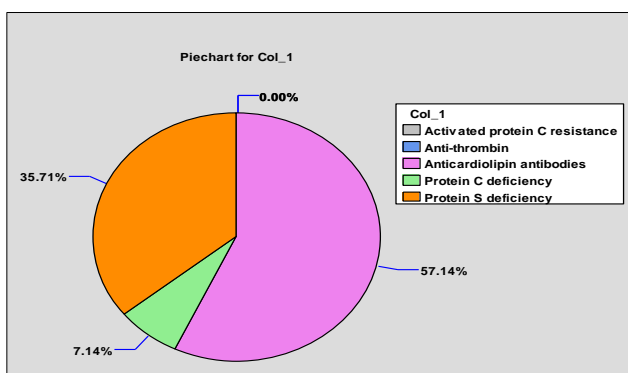
A total of 20 patients were screened in the above series, from January 2010 to January 2012, over a period of 25 months. Thrombophilia screening was carried out from a single laboratory providing test facilities for both acquired and inherited thrombophilia.

Screening was carried out six weeks after delivery. Recurrent pregnancy loss is defined as three consecutive first trimester or second trimester pregnancy losses. Women having bad obstetric history viz three first trimester losses, or two fetal losses during second trimester or one fetal loss during third trimester were included in the study.

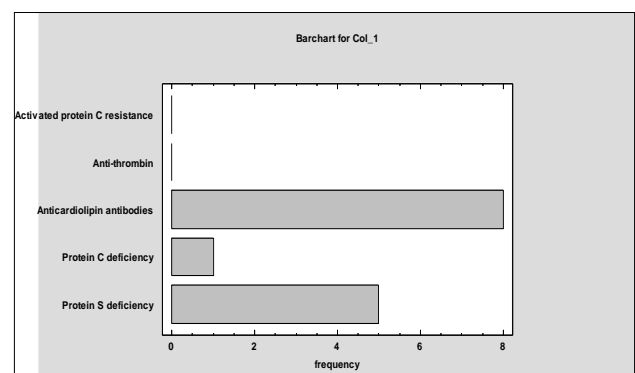
Mentioned below are Table 1 showing relative and cumulative frequencies of individual thrombophilic condition from given sample population.

**Table 1: Estimate of frequency of thrombophilia in given sample population.**

Class	Value	Frequency	Relative Frequency	Cumulative Frequency
1	Activated protein C resistance	0	0.0000	0
2	Anti-thrombin	0	0.0000	0
3	Anticardiolipin antibodies	8	0.5714	8
4	Protein C deficiency	1	0.0714	9
5	Protein S deficiency	5	0.3571	14
Cum. Rel.				
Class	Frequency			
1	0.0000			
2	0.0000			
3	0.5714			
4	0.6429			
5	1.0000			



**Figure 1: proportion of each Thrombophilic conditions.**



**Figure 2: Proportion of each Thrombophilic conditions.**

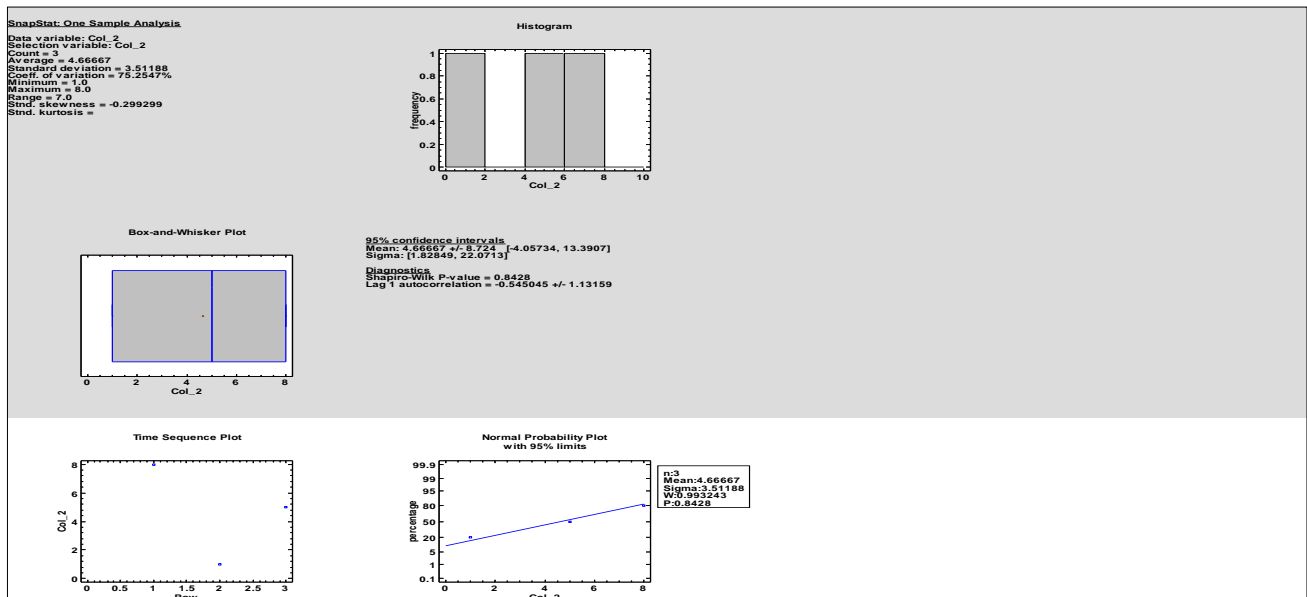


Figure 3: Statistical analysis.

Figure 1 shows percentage distribution of individual thrombophilic condition. Highest percentage is observed for anti-phospholipid antibodies. Figure 2 depicting graphic proportion of thrombophilic conditions.

Figure 3 shows statistical calculations.

## RESULTS

Thrombophilia was detected in 14 patients under evaluation for recurrent pregnancy loss. Table shows the results of screening. Anti-cardiolipin antibodies (57%), natural anticoagulants protein C (7%) and protein S (35%) were found deficient.

**Table 2: Estimate of thrombophilia screen positive in patients with recurrent pregnancy loss.**

Estimate of thrombophilia	
Anticardiolipin antibodies	08
Protein C deficiency	01
Protein S deficiency	05
Anti-thrombin	00
Activated protein C resistance	00

Out of 20 patients who were screened, 14 (70%) patients were found screen positive for thrombophilia.

## DISCUSSION

This was a descriptive study, which was done to see the association between recurrent pregnancy loss and thrombophilia.

The mechanism, leading to recurrent pregnancy loss involves impaired placental development and function.<sup>4</sup> The association between recurrent pregnancy losses and anticardiolipin antibodies is well established. Out of 20 women with recurrent loss, 08 screened positive for anticardiolipin antibodies, 1 had protein C deficiency and 5 had protein S deficiency. Positive Anticardiolipin antibodies are associated with pregnancy loss at all gestational ages.

Women deficient in natural anticoagulants like protein C and S and antithrombin III, have been found more prone to utero-placental microthrombosis, leading to recurrent pregnancy loss.<sup>4-6</sup> Recurrent pregnancy losses have also been attributed to factor V leiden mutation.

Though the incidence of thrombophilia is low in general population, there is a strong association with recurrent pregnancy loss.<sup>7</sup> These complications do recur in subsequent pregnancies; hence there is advantage of screening and offering prophylaxis in the subsequent pregnancy for healthy outcomes.

The major limitation of the study is that the screening done during the antenatal or immediate post-natal period within 4 weeks will yield false positive results. Hence the cases need to be evaluated in non-pregnant state and often patient fails to follow up for evaluation after pregnancy loss.

This will help in subsequent management of these patients in pregnancy by adequate antithrombotic therapy which can be initiated from very early days of pregnancy to prevent placental vasculopathy and coagulation

defects, and thereby improve maternal and perinatal outcomes of these pregnancies to a great extent.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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