
IMMUNE HABITUAL ABORTION: INCIDENCE AND MANAGEMENT

Mohamed El Samra, Mohamed El Abd, & Sherif Agag

Department of Obstetrics & Gynecology,
Alexandria University, Egypt

ABSTRACT

The objective of this study of patients with habitual abortion, was planned to determine their autoimmune profile and to try to prevent new abortions using low-dose aspirin (Rivo® 75mg) for 7 months with solupred® 20 mg in the first trimester only, or with low-dose aspirin alone. A total of 100 patients with three or more HA were investigated for antiphospholipid antibodies, antinuclear and anti thyroid antibodies. Among these patients, auto antibodies were present in 34% of the patients, in 82.4% of them anticardiolipin antibodies were found to be isolated alone or associated with lupus anticoagulant, anti thyroid, or, antinuclear antibodies. In auto antibodies-negative pregnant women treated by solupred and aspirin or aspirin alone, the success rate of live births was 90.9% (30 out of 33) and 75.7% (25 out of 33) respectively ($p < 0.01$) in auto antibodies - positive patients treated with solupred and aspirin the success rate was 85.2% (29 out of 34) (not significant) solupred and aspirin seemed to be as efficient in auto antibodies - negative or positive women but better than aspirin alone in autoantibody - negative women.

INTRODUCTION

Habitual abortion is defined as 3 or more consecutive spontaneous abortions, which is a frustrating problem for both the patient and the clinician. It affects about 1% of those women who are desiring pregnancy⁽¹⁾.

the causes of habitual abortion are diverse which may be due to anatomical, hormonal, genetic abnormalities, infections or autoimmune mechanisms.^(2,3) Immunologic causes for spontaneous abortion or failure of implantation are thought to be the result of abnormalities in antibody responses⁽⁴⁾. A fetus develops from genetic material from both mother and father. An abnormal immune response may therefore occur against the mother's genetic contribution (autoimmune) or the father's (alloimmune)⁽⁵⁾.

Eighty percent of the unexplained pregnancy failures are proposed to have an immunological background. The frequency of autoantibody association with habitual abortion differs greatly from one study to the other, depending upon the way patients are recruited, tests performed and their threshold values^(4,5).

Although many studies have focussed on the understanding of habitual abortion, about one third of them remains unexplained⁽⁶⁾.

There is no doubt that lupus anticoagulant is a major cause for recurrent pregnancy loss even in women who did not present with systemic lupus erythematosus⁽⁷⁾. On this basis, it was decided that glucocorticoids and aspirin treatment should be used to try to prevent abortion^(8,9).

Not only lupus Anticoagulant can cause habitual abortion but also recent studies have

Corresponding author : Mohamed El Samra, Department of obstetrics and Gynecology, Alexandria University
E-mail: Dr_elsamra@yahoo.com.

shown the presence of multiple autoantibodies in the body of habitual aborters⁽¹⁰⁻¹²⁾.

The objective of this study was to determine the autoimmune profile of Apparently healthy women with habitual abortion by searching for Anticardiolipin antibodies, lupus anticoagulant (LA) antinuclear antibodies (ANA) and Antithyroid antibodies (a Th) to assess the possible prevention of a new abortion, in autoantibody - positive or - negative (Rivo[®] 75 mg) until the end of the seventh month with or without glucocorticoids (Solupred[®] 20 mg) in the first trimester of pregnancy.

MATERIALS & METHODS

Hundred healthy patients with habitual abortion were included in this study aged between 20 to 30 years. All these cases were subjected to:

- (1) Full history taking.
- (2) Routine laboratory investigations which include:-
 - Complete blood count.
 - Fasting blood sugar
 - Renal function tests
 - Liver function tests
 - Coagulation profile
 - Complete urine analysis
- (3) Radiological & Imaging evaluation including
 - Hysterosalpingography.
 - Ultrasonography
- (4) Special tests:-
 - IgG and IgM anticardiolipin antibodies measured by ELISA.
 - Lupus anticoagulant (LA) measured by coagulation assay.
 - Antinuclear antibodies (ANA) measured by ELISA.
 - Antithyroid antibodies (a Th).
 - Thyroglobulin antibodies (TG-Ab)
 - Thyroperoxidase antibodies (TPO-Ab) measured by ELISA.

RESULTS

Auto antibodies were found to be positive in 34 patients out of 100 patients with habitual abortion while 66% of the patients were antibodies negative (Table I).

the most frequent Auto antibodies were aCL which were found in 82.4% of cases (28 out of 34). IgG aCL were present in almost three out of four cases and IgM aCL in about 35%.

LA were observed in only 1% out of all the patients and mostly associated with aCL. 79.4% of the auto antibodies were found alone and 20.6% were found to be associated with one or two other auto antibodies (Table II).

In auto antibodies-negative women, the rate of live birth in the group of women treated with solupred[®] in the first trimester and aspirin until the end of the seventh month was significantly increased compared with women treated with aspirin alone: 90.9% of women (30 out of 33) treated with prednisone and aspirin had live births compared with 75.7% of women (25 out of 33) treated with aspirin alone ($P < 0.01$). In auto antibodies positive women treated with solupred[®] and low dose aspirin the success rate was 85.2% (29 out of 34) the rate of live births was 85.2%; there was no significant difference in the rate of live births between auto antibodies - negative and auto antibodies - positive women ($P > 0.5$). (Table III).

DISCUSSION

The percentage of auto antibodies in our study of habitual abortion (HA) patients was 34%, in which aCL were present in the majority of these

Table I : Auto antibodies in 100 patients with habitual abortion.

	No.	(%)
Negative patients	66	
Positive patients	34	
Antinuclear antibodies	3	(3)
Anticardiolipin antibodies	28	(82.4)
IgG	18	(64.3)
IgM	6	(21.4)
IgG + IgM	4	(14.3)
Lupus anticoagulant	1	(1)
Antithyroid antibodies	2	(2)

Table II : Association of autoantibodies in women with habitual abortion.

	Antibody alone	Antibody Association
aCL	22	X X X X X
LA	1	X X X
ANA	3	X X
aTH	1	X X X X
No.		1 1 1 1 2 1
Total	27 (79.4)	7 (20.6)

ANA = antinuclear antibodies; aCL= anticardiolipin antibodies; LA= lupus anticoagulant; a Th= antithyroid antibodies

Table III : Treatment with solupred® in the first trimester and or low-dose aspirin until the end of the seventh month, in women with habitual abortion.

Group of patients	No. of patient	Successful births	Abortions
Antibody-negative solupred® + aspirin	33	30 (90.9)	3 (9.1)
Aspirin alone	33	25 (75.7)	8 (24.3)
Antibody – positive Solupred® + aspirin	34	29 (85.2)	5 (14.8)

cases (82.4%). This percentage is in accordance with findings previously published.^(6,8) IgG aCL were twice as frequent as IgM.

Antithyroid antibodies were observed in only 2% of the patients. LA were found in very few cases and generally associated with aCL. Elevated ANA was observed in 3% of patients. These Percentage are in accordance with previously published findings.

Solupred[®] and aspirin treatments were superior to aspirin treatment alone in auto antibodies - negative women: the success rate was 80.9% compared with 75.7% in patients given aspirin alone (P < 0.01).

Previously, the outcome of pregnancies was followed in a similar cohort of 102 HA patients without treatment ⁽⁵⁾ and 58% resulted in births. This observation would mean that low - dose aspirin could foster pregnancy in auto antibodies - negative patients. However, in a recent study ⁽⁹⁾ a difference was found in the success rate in HA women treated with either aspirin (70%) or placebo (70%).

Solupred[®] and aspirin treatments have the same success rate in both autoantibodies - negative and autoantibodies - positive women. The results presented here confirm those of a recent study ⁽⁸⁾.

This series of 34 treated patients established that solupred[®] and aspirin treatment is safe, in accordance with previous reports ⁽⁸⁾. This contrasts with other studies which described Adverse side - effects (e.g. hypertension, diabetes mellitus and prematurity) in the solupred[®] and aspirin - treated group. This contrast may be due to the difference in the duration of solupred treatment which was 2 months in the present study, and 3.5 months in Geva's study⁽⁸⁾.

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