# The association of anticardiolipin antibody IgM with first trimester recurrent abortions.

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## العلاقة بين الجسم المضاد للدهون من نوع آي جي آم والإسقاطات المتكررة خلال أول ثلاثة العلاقة بين الجسم المضاد الشهر من الحمل

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### الخلاصة

الخلفية: الجسم المضاد للدهون علاقة مثبتة مع الاسقاطات المتكررة في حالة وجود الامراض المناعية المكتسبة مع ذلك فان العلاقة غير مثبتة في حالة عدم وجود الامراض المناعية المكتسبة.

**الغرض**: معرفة وجود او عدم وجود علاقة بين الجسم المضاد للدهون من نوع آي جي ام والاسقاطات المتكررة خلال اول ثلاثة اشهر من الحمل.

المواد والطرق: تمت دراسة ٩٠ حالة (٥٤ من النساء الحوامل ممن لهم اكثر من حالتين من الاسقاطات اول ثلاثة اشهر من الحمل و ٥٥ من النساء ممن لهم اكثر من ولادة طبيعية وليس لديهم أي حالة اسقاط كمجموعة تتمتع بالصحة). تم جمع عينات الدم والادرار لاجراء التحليلات المرضية التالية: فصيلة الدم، نسبة السكر في الدم، يوريا الدم، صورة الدم الكاملة، نسبة ترسيب الكريات الحمراء، تحليل الادرار العام، اختبار تورج، اختبار السفلس، والجسم المضاد للدهون من نوع آي جي ام بطريقة اليزة وتم اعتبار المستوى الاعلى من ١٥ وحدة ايجابيا والمستوى الاقل او يساوي ٥٠ سلبيا.

النتائج: وجدت نسبة ٤٤٢ % (عدد ١١) ممن لديهم اسقاطات متكررة مفسرة (٩ منهم بسبب داء القطط و ٢ منهم بسبب السايتوميجالوفايروس) بينما نسبة ٦٥٠ % (عدد ٣٤) ممن ليس لديهم اسباب لتفسير الاسقاطات المتكررة. وجد ان مستويات الجسم المضاد للدهون من نوع آي جي ام بطريقة اليزة عالية احصائيا لدى ١١ من مجموع ٥٥ مريضة أي ٤٤٢ % (٨ مرضى ممن لديهم اسقاطات متكررة أي ٧٢.٨ و ٣ مرضى فقط ممن لديهم اسقاطات غير مفسرة الاسباب أي ٨.٨%)

#### **Abstract**

**Background:** Anticardiolipin antibody has a clearly documented association with recurrent abortions in patients with autoimmune diseases; however, the association of Anticardiolipin antibody with first trimester abortions is not clearly documented in patients with no evident autoimmune diseases.

<u>Aim:</u> To estimate the prevalence of Anticardiolipin antibody IgM in patients with first trimester recurrent abortions and to find if there is any association between them.

Materials and methods: A total number of 90 women were included, 45 had history of recurrent abortions(more than 2 abortions) and 45 were healthy control women with one or more than one delivery and no history of abortions. Blood samples from the 90 women were taken for investigations including blood group, blood sugar, blood urea, complete blood picture, ESR, general urine examination, TORCH test, VDRL test and Anticardiolipin antibody IgM by ELISA technique in which levels higher than 15 MCL unit are considered to be positive, while levels below 15 MCL unit are considered to be negative.

Results: Out of 45 patients, 24.4%(n=11) had history of explained recurrent abortions, 9 of them due to toxoplasmosis and 2 of them were due to cytomegaloviral infection. while 75.6%(n=34) had no explained causes. Significantly raised levels of anticardiolipin antibody IgM was present in 11 out of 45 patients i.e 24.4% of patients while IgM levels were normal in 34 out of 45 patients i.e 75.6%. The total number of explained recurrent abortions was 11 (8 out of 11 had significantly high IgM antibody i.e 72.7% while 3 out of 11 had normal IgM levels i.e 27.3%). The total number of unexplained recurrent abortions was 34 (3 out of 34 had significantly high anticardiolipin antibody IgM i.e 8.8% while 31 out of 34 patients had normal levels i.e 91.2%) while the antibody was negative (normal) in the control group. Patients with significantly high levels of anticardiolipin antibody who had history of explained recurrent abortions are eight. Seven of them i.e 87.5% had positive antitoxoplasma antibody IgM and one of them i.e 12.5% had positive anticytomegalovirus antibody IgM.

<u>Conclusion:</u> Anticardiolipin antibody IgM is not associated with first trimester recurrent abortions.

**Key words:** anticardiolipin antibody, recurrent abortions, first trimester.

#### Introduction

Spontaneous abortion is the fate of about 15% of all clinically recognized pregnancies<sup>1</sup>. The commonest causes of first trimester recurrent abortions are genetic, endocrine, anatomical, immunologic, infectious and environmental causes<sup>2</sup>. It was reported that certain Antiphospholipid antibodies interfere with fetal implantation which may be related to the pathological mechanism responsible for recurrent abortions<sup>3</sup>. Anticardiolipin antibodies (ACA) had clearly documented association with recurrent abortions in patients with autoimmune diseases<sup>4</sup>. Investigations of cases with recurrent abortions are increasingly dealing with immunologic factors, particularly autoimmunity, regarding the presence of non organ specific autoantibody. Recurrent abortions had been associated with antiphospholipid antibodies and anticardiolipin antibodies<sup>5</sup>. Anticardiolipin antibodies were detected in infertile women<sup>6</sup>. Anticardiolipin antibodies react with a plasma cofactor B<sub>2</sub>-glycoprotein1 (B<sub>2</sub>-GP1) that stabilizes antigenic conformation of cardiolipin. So that anticardiolipin antibody represented a mixture of autoantibody to B<sub>2</sub>-GP1 and autoantibodies to phospholipids epitopes stabilized by interaction with B<sub>2</sub>-GP1<sup>7</sup>. The low incidence of chromosomal abnormalities in the aborted fetuses supported the pathologic significance of antiphospholipid antibodies<sup>8</sup>. In patients with recurrent abortions, the most frequent antiphospholipid antibodies are anticardiolipin antibodies<sup>9</sup>; however, the significance of anticardiolipin antibodies and antiphospholipid antibodies is unclear in cases with recurrent abortions 10. First trimester recurrent abortions are the most common type of abortions in women with antiphospholipid antibodies<sup>11</sup>. This study was planned to detect if there is an association of ACA IgM with first trimester recurrent abortions.

#### **Materials and methods**

A total number of 90 women were included, 45 had history of recurrent abortions (more than 2 abortions) and 45 were healthy control women with one or more than one delivery and no history of abortions. All women were visitors of outpatient clinic and investigations were arranged in Karbala legal private laboratories for immunological and hematological investigations. After a full medical history and physical examination, blood samples from the 90 women were taken for investigations including blood group, blood sugar, blood urea, complete blood picture, ESR, general urine examination, TORCH test, VDRL test and Anticardiolipin antibody IgM by ELISA technique in which levels higher than 15 MPL unit were considered to be positive, while levels below 15 MPL unit were considered to be negative. Statistical data were analyzed using Pearson correlation, P value of < 0.05 was considered to be significant using SPSS statistical method.

#### **Results:**

Blood sugar and blood urea levels were normal in all study group

GUE revealed the presence of pus(4-10 cells) in two patients, while It was normal in the control group.

Complete blood picture revealed features of iron deficiency anemia with Hb levels ranging between 8.2 -10.7 g/dl in 6 patients, while it was normal in the control group. ESR was normal in all women.

TORCH test showed:

positive antitoxoplasma antibody IgM in nine patients, while it was negative in the control group.

negative antirubella antibody IgG and IgM in all women.

positive cytomegaloviral antibody IgM in two patients, while it was negatively in the control group.

negative antiherpes simplex antibody IgG and IgM in all women.

Negative VDRL in all women.

Out of 45 patients, 24.4% (n=11) had history of explained recurrent abortions, 9 of them due to toxoplasmosis and 2 of them were due to cytomegaloviral infection. while 75.6% (n=34) had no explained causes. Significantly raised levels of anticardiolipin antibody IgM was present in 11 out of 45 patients i.e 24.4% of patients while IgM levels were normal in 34 out of 45 patients i.e 75.6%. The total number of explained recurrent abortions was 11 (8 out of 11 had significantly high IgM antibody i.e 72.7% while 3 out of 11 had normal IgM levels i.e 27.3%). The total number of unexplained recurrent abortions was 34 (3 out of 34 had significantly high anticardiolipin antibody IgM i.e 8.8% while 31 out of 34 patients had normal levels i.e 91.2%) while the antibody was negative (normal) in the control group. Patients with significantly high levels of anticardiolipin antibody who had history of explained recurrent abortions are eight. Seven of them i.e 87.5% had positive antitoxoplasma antibody IgM and one of them i.e 12.5% had positive anticytomegalovirus antibody IgM.

Table 1: Significantly raised levels of anticardiolipin antibody IgM in women with recurrent first trimester abortions.

Patients' number	ACA IgM (MCL units)	Presence of infection
1	27	Not present
2	22	Toxoplasmosis
3	20	Toxoplasmosis
4	23	Toxoplasmosis
5	22	CMV infection
6	18	Toxoplasmosis
7	19	Toxoplasmosis
8	21	Toxoplasmosis
9	26	Toxoplasmosis
10	22	Not present
11	19	Not present

Table 2: Number of patients with significantly raised levels of ACA IgM according to the history of recurrent abortions

History of recurrent abortions	Number of patients with	Number of patients with
	high ACA IgM	normal ACA IgM
Group of explained abortions	8/11 i.e 72.7%	3/11 i.e 27.3%
(11/45), 24.4%		
Group of unexplained	3/34 i.e 8.8%	31/34 i.e 91.2%
abortions (34/45), 75.6%		

#### **Discussion**

The present study showed that ACA IgM is significantly raised in 8.8% in women with unexplained first trimester recurrent abortions which is consistent with previous report which showed that 8-24% of recurrent abortions are due to positive ACA<sup>12</sup>. A study on women with unexplained recurrent abortions reported that the prevalence of IgM was 9.8% <sup>13</sup>

which is in concordance with the present study. Non specific binding of IgM was reported in a study which suggests polyclonal IgM elevation in 82% of cases<sup>5</sup>. In the present study, 87.5% of cases of explained recurrent abortions had associated with infections, namely toxoplasmosis which suggested the polyclonal binding of IgM. A study showed the adverse effects of ACA on pregnancy using experimental mouse model. The experimental induction of ACA causes increased resumption rate and at the same time decrease placental and embryonal weight in pregnant mice<sup>3</sup>. A study on unexplained recurrent abortions showed that ACA IgM is significantly raised in 7% of cases<sup>14</sup>. The corresponding value in the present study was 8.8%. High levels of ACA IgM are found transiently in patients with certain infections like CMV and HIV infections as shown in a study<sup>15</sup>.

The present study showed that antitoxoplasma IgM antibody is positive in 7 out of 11 women with history of explained recurrent abortions, suggesting polyclonal binding of ACA IgM and showing that ACA IgM are not responsible for first trimester recurrent abortions.

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