

Relationship Between Increases Anticardiolipin Titer with CMV Infection In Pregnant Women

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Abstract

Background: Recurrent miscarriage is a severe medical problem occurs in women infected with cytomegalovirus and associated with anticardiolipin antibodies IgM.

Objective: To estimate the prevalence of anticardiolipin antibodies in pregnant women with cytomegalovirus infection and history of recurrent loss.

Patients and Methods: One hundred women (21-41) years old with recurrent pregnancy loss. Samples were taken from Al-yarmook and Baghdad hospital. This study group was subdivided into four subgroups depends on times of abortion. Anticardiolipin (IgM) and cytomegalovirus antibodies were estimated in the sera by the enzyme linked immunosorbent assay method and compared with 50 apparently healthy pregnant volunteers as a control group at the same age range.

Results: It was observed that there is a positive correlation coefficient between anticardiolipin and cytomegalovirus titer ($r=0.34729$). Also there is significantly difference (t-test, $P < 0.05$) between mean of anticardiolipin and cytomegalovirus titers of study and control groups.

Conclusion: Anticardiolipin antibodies IgM may be associated with first trimester recurrent abortions for women infected with cytomegalovirus.

Key words: Recurrent abortion, anticardiolipin, human cytomegalovirus antibodies.

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Introduction

The aetiology of early gestation loss is varied and often controversial. There are many etiological factors may be the cause, and the most common causes of recurrent miscarriages are genetic, hormonal, immunologic, infectious and environmental factors [1][2]. Cytomegalovirus (CMV) is one of the infectious agents. The species infect human is commonly known as human cytomegalovirus (HCMV).

Infectious HCMV may be shed in bodily fluid (saliva, blood, urine, semen, breast

milk, tears and cervical secretion) in human, intermittently with no detectable signs and symptoms of the infection [3]. A person is able to transmit the virus to others only when the virus is active in human system (not dormant), but the virus can rarely be transmitted by blood transfusion or organ transplantation [4].

Human cytomegalovirus is a ubiquitous virus and it infects human of all ages. Acquisition of the virus as a general in the population usually occurs early in life, mainly during the first two decades, and

often during the first year [5][6]. Human cytomegalovirus infection is typically unnoticed in healthy people, but can be life-threatening for the immunocompromised, such as HIV-infected persons, organ transplant recipients, or new born infant. After infection, HCMV has an ability to remain latent within the body over long periods [3]. Human cytomegalovirus is the virus most frequently transmitted to a developing fetus. A baby can be born with congenital CMV if their mother had a CMV infection during pregnancy, the infection is more widespread in developing countries and in communities had lower socioeconomic status and represent the most significant viral cause of birth defects in industrialized countries, the virus seems to have a large impact on immune system parameters in later life and may contribute to increased morbidity and eventual mortality. It can become active again at any point in time [7,8]. The virus remains latent lifelong within the host cell, and the immune defence is unable to clear the virus completely from the host. Various HCMV gene products may give the ability of the virus to evade the host immune system [9].

Anticardiolipin syndrome is a major reproductive complication in women, which is characterized by recurrent fetal loss in association with anticardiolipin antibodies [10]. The IgM antibody is the largest immunoglobulin and appears the first in an immune response [11].

The more sensitive and specific for fetal loss is anticardiolipin antibody assay in comparison to lupus anticoagulant [12]. The most common type of miscarriage in women with antiphospholipid antibodies is first trimester loss of pregnancies. This may be due to defective implantation and subsequently causing placental defects [11][13].

Recurrent spontaneous abortion (RSA) and also called recurrent miscarriage, is usually

defined as three or more consecutive pregnancies losses prior to 20-28 weeks of pregnancy. RSA affects up to 5% of fertile couples [14].

The immunological correlation between the mother and the fetus is a bi-directional determined on one hand by fetal antigen presentation and on the other hand by recognition to these antigens by the maternal immune system. Immunological recognition of gestation is important for the maintenance of conception [15]. Most abortions occur within 12 weeks of pregnancy. The cause of recurrent gestation loss is often very difficult to assess. The cause can be determined in only 50% of patients [16].

The aim of this study is to spot the light on possible relation between ACL IgM & CMV antibody titer in women with RSA in the first trimester of pregnancy.

Materials and Methods

A total of one hundred blood samples were collected from Al-yarmook and Baghdad hospital during the period September of 2014 till August 2015. Samples were collected from (21-41) years old pregnant Iraqi women with positive CMV antibody from were included in the investigations as a study patient group. This study group was subdivided into four subgroups according to numbers of abortions history (No previous abortion, one time abortion, two times and three times). The results of investigations were compared with those for 50 apparently healthy pregnant volunteers as a control group at the same age range.

According to the gestational period both of them (i.e. study and control groups) were at the 1st trimester.

Sera were used for estimation of antibody titer for CMV (Catalog number: BC-1091, Biocheck, Inc, CA94404) and ACL (IgM) (Orgentec diagnostika GmbH. 2004; 55129 Mainz, Germany) by ELISA technique for both patients' and control groups [17][18].

The research work was done in the college of Health and Medical Technology and private laboratories.

Statistical analysis

Statistically analyzed using one-way ANOVA analysis and application of SPSS program version 18. A P value <0.05 was considered statistically significant.

Result

Table [1] shows the relationship between age, ACL, and CMV titers. This table revealed that the mean of patients' age was (32.27±5.02 years). While the mean of ACL and CMV were (24.11±13.85 IU/ml), and

(14.95±5.60 IU/ml) for patients groups respectively, on the other hand, the mean of control group age was (32.96±4.89), whereas ACL and CMV titers were (5.09±2.41 IU/ml), and (3.73±1.70 IU/ml) respectively.

There was no significant difference in the mean age of studied groups (P>0.05), while ACL and CMV titers were significantly higher among study group compared with lower titers among control group (P< 0.01). There was a positive highly significant correlation between ACL and CMV titer (r=0.3472).

Table (1): Mean of age, ACL, and CMV titer of study and control groups.

	Range	study groups (n=100)	control group (n=50)	correlation coefficient (r)	t-student test (P value)
Age (years) (Mean±SD)	21-41	32.27±5.026	32.96±4.898		>0.05 (N.S.)
ACL titer (Mean±SD)	Cut-off (10 IU/ml)	24.11±13.850	5.09±2.410	0.34729	<0.01 (H.S.)
CMV titer (Mean±SD)	Cut-off (7 IU/ml)	14.95 ±5.609	3.73±1.702		<0.01 (H.S.)

Table [2] revealed ACL titer (19.0±7.85 IU/ml) and CMV titers (10.4±3.808 IU/ml) for 15 positive cases for CMV and ACL negative (depending on the cut-off values) among the studied groups in comparison with 50 negative cases (control group) for ACL (5.09±2.41 IU/ml) and CMV (3.73±1.7

IU/ml) and with no history of abortion for both groups (The 15 cases and control group). The table showed statistically significant (P<0.05).

Table (2): Mean of ACL and CMV titer of women without history of abortion from study and Control groups.

Antibody	Study group CMV+ve (n=15)	Control CMV-ve (n=50)	P value
ACL titer	19.0±7.653	5.09±2.41	< 0.05*
CMV titer	10.4±3.80	3.73±1.70	< 0.05*

*Differences between mean of ACL and CMV titers of women without history of abortion from studied group were statistically significant (p < 0.05).

Table [3] showed the relationship between ACL and CMV titer and number of abortions. It seems to be that there was a proportional relationship between

antibody titer and times of abortions. Hence there was a highly significant difference between those two variant (P<0.01).

Table (3): Distribution of patients afflicted with ACL and CMV titer according to abortion history groups.

	No abortion history (n=15)	one time abortion (n=70)	two times abortion (n=12)	three times abortion (n=3)	ANOVA *
ACL titer	19.0±7.850	22.94±13.213	34.91±18.203	33.66±12.583	P <0.01
CMV titer	10.4±3.808	15.42±5.648	18.5±4.40	12.66±1.527	P <0.01

* Differences between mean of ACL and CMV titer among abortion history groups were statistically highly significant (ANOVA, $p < 0.01$).

Discussion

Recurrent abortion is a difficult medical problem happening in about 1-2% of fertile women [19].

In this study distribution of studied groups according to age showed statistically non-significant difference, that is mean the age may did not influence in the titer of ACL and CMV ($P > 0.05$).

There is a positive relation between ACL titer and CMV titer by ELISA test among studied groups ($r=0.34729$). This result is consistent with that for researcher who reported that ACL antibodies in pregnant women were found to be the important factor for recurrent abortion especially in the first trimester of pregnancy [20]. The explanation for this finding is attributed to ACL which causes tiny blood clots in the blood vessels within the placenta that can lead to complications in pregnancy and the most common problem is recurrent miscarriage [21].

In the current study, there is a statistically significant difference noticed between mean of ACL and CMV titer for study and control groups ($P < 0.05$). This result was going well with that of a study done by Kalra *et al.* (2002) who denoted that high level of ACL antibodies IgM may be found transiently in patients with recurrent abortion (positive CMV) [15]. However, Risan *et al.* showed that IgG ACL were significantly elevated in

the sera of aborted pregnant women [20]. Furthermore, there were other studies which harmonized with the present evidence, which referred to higher prevalence of ACL antibodies in women with first trimester pregnancy loss [22][23]. These evidence confirmed the presence of a statistically significant higher prevalence of ACL antibodies in women with first trimester pregnancy loss which consistent with groups of researchers [15][20][24].

On other hand, results of other workers were compatible with current findings and demonstrated that HCMV are the main cause of RSA [24][25]. Also other notes in spontaneous abortions that in the majority of such cases the etiology remains unknown, but anticardiolipin antibodies are gaining recognition as potential causes of recurrent miscarriage [26]. However our results disagree with findings of workers who revealed that there is no role of HCMV infections in women with RSA during first trimester of pregnancy [27]. The report in 1998 showed the lack of association between ACL antibodies and spontaneous abortion [28, 29]. Moreover, some studies mentioned that CMV infection may cause RSA, in second trimester of pregnancy; whereas, while the role of infection in first trimester RSA is still controversial [30].

The present study revealed that there was a steadily proportional positive association

between level of ACL and times of recurrent miscarriage. The interpretation of these findings perhaps may be attributed to the action of CMV and its role on tissue destruction with micro thrombi formation in maternal circulation represented by ACL levels. These events result in recurrent abortion [28, 31, 32]. Though low concentration level of ACL and CMV titer may not effectively enough to cause fetal loss for pregnant women and presence of environmental agents, or physiological factor that enhance the recurrent miscarriage.

In conclusions, there is a significant positive correlation between each ACL IgM and CMV antibody with recurrent abortion of women in the first trimester of pregnancy. But ACL is more important than CMV infection.

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