

## STUDY OF INCREASED ANTIPHOSPHOLIPID ANTIBODIES WITH INCREASED ANTI RUBELLA ANTIBODIES IN PREGNANT WOMEN IN BAGHDAD CITY

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### ABSTRACT

**Back ground:** Many infections which founded with antiphospholipid antibodies (aPL), so a major cause of pregnancy complications and recurrent miscarriages if no found other causes, as well as rubella causing this complication and abortion. **Subjects and methods:** To investigate the relevance of Antiphospholipid antibodies with Anti Rubella antibodies in pregnant women in Baghdad city, by collected 176 sera from January to July -2015 from pregnant women with and without abortion in Baghdad hospital, and determine aPL and Rubella antibodies by enzyme linked immunosorbent assay (ELISA). **Results:** the results revealed high percentage 80.9% of aPL with abortion in pregnant women infected with Rubella viruse, while 13.8% aPL

negative (-ve) without abortion, 5.3% aPL (-ve) with abortion, so results represent a relation between aPL and abortion in Rubella infected pregnant women, as well as low percentage (13.3%) of aPL (+) with abortion in non-infected pregnant women with Rubella viruse, while high percentage (73.9) appeared with non-Rubella infected pregnancy with aPL (-ve), but (13.3%) abortion with aPL (+) in control. **Conclusion:** Antiphospholipid antibodies high correlated with increased Anti Rubella antibodies in pregnant women but low relation between of aPL with abortion in non-infected pregnant women with Rubella viruse in Baghdad city.

**KEYWORD:** aPL (Antiphospholipid antibodies), Rubella, Pregnancy, abortion.

### INTRODUCTION

Pregnancy loss has been attributed to several factors involved in human reproduction, anatomic features, genetic, diabetes, infections, systemic hypertension, hyperthyroidism

(endocrine), environmental pollutants, psychogenetic and Immunological factors which are remarkable causes of abortion. Still, elevation of the antiphospholipid antibody plasma level (aPL) was important one of these factors [Souza *et al.*, 2003], These antibodies include antiphosphatidylglycerol (aPG), anticardiolipin (aCL), anti-beta2-glycoprotein 1 (aB-2-GP-1), lupus anticoagulant (LA), antiphosphoserine (aPS), anti-phosphatidyl inositol and anti-phosphatidic acid [Levine *et al.*, 2002], but more critical and more important roles in spontaneous abortion are lupus anticoagulant and anticardiolipin [Vinatier *et al.*, 2001]. In addition, recurrent pregnancy wastage due to maternal infections transmissible in utero at various stage of gestation can be caused by a wide array of organisms which include the TORCH complex (*Toxoplasma gondii*, Rubella virus, Cytomegalovirus, Herpes simplex virus) [Monsalve, *et al.*, 2001]

Rubella (German measles) is a common childhood rash disease, most serious consequences of rubella result from infection during the first trimester of gestation including miscarriage, fetal death, and congenital anomalies [Banatvala *et al.*, 2004], In general population, the prevalence of Antiphospholipid antibodies were ranged between (1-5)% [Mehranian and Petri, 2009], during first weeks of gestation, up to 90% of infants born to mothers infected are develop congenital rubella syndrome (CRS) [brook *et al.*, 2007], Therefore it is essential to evaluate the susceptibility of women (anti-rubella IgG seronegative) in the reproductive age in order to set a strategy for prevention of CRS [Langford 2002].

Antiphospholipid antibodies are autoantibodies as a heterogeneous group directed act against negatively charges phospholipid and phosphides binding proteins, Also associated with thrombocytopenia, venous and atrial thrombosis, reproductive autoimmune failure and complications of pregnancy [Espinosa, *et al.*, 2003], So aPL promote activation of endothelial cells, monocytes and platelets, causing an overproduction of tissue factor and thromboxane A<sub>2</sub>, as well as complement activation might have a central pathogenetic role, these factors associated with the typical changes in the hemostatic system during normal pregnancy result in a hypercoagulable state, In pregnancy thrombophilia is a popular research topic in recurrent miscarriage, two type of thrombophilia (inherited and acquired) are associated with a risk of pregnancy failure, so Antiphospholipid syndrome is only thrombophilia known to have a direct adverse effect on pregnancy, Additionally, Anti-phospholipid syndrome is thought to be a major cause of early pregnancy loss, this condition is characterized by the presence of anti-phospholipid antibody [Godoy *et al.*, 2006].

But not all aPL are pathogenic, because only a certain group of aPL induced by certain bacterial or viral products are important in development of disease [Gharavi *et al.*, 2003].

## METHODS

### Measurement of Antiphospholipid antibodies and antirubella antibodies concentration

1. Prepared the microplate to accommodate controls and prediluted sample of patient.
2. Dispensed 100  $\mu$ l of standards, controls and prediluted patient samples into wells to determination autoantibodies standards, controls and samples was pipetted in two attempts.
3. Incubated samples for 30 minutes at room temperature (20 - 28 °C). discarded and the microwells and washed 3 times by using 300 $\mu$ l of wash solution.
4. Dispensed 100  $\mu$ l of enzyme conjugate into wells and incubated for 15 minutes at room temperature.
5. Discarded the microwells and washed 3 times with 300 $\mu$ l of wash solution, after then by 10  $\mu$ l of TMB substrate solution was dispensed into each well and incubated for 15 minutes at room temperature.
6. Added 100  $\mu$ l of stop solution to each well and incubated for 5 minutes at room temperature. Read the results of optical density at 450 nm. The developed color is stable for at least 30 minutes. Read optical densities during this time.

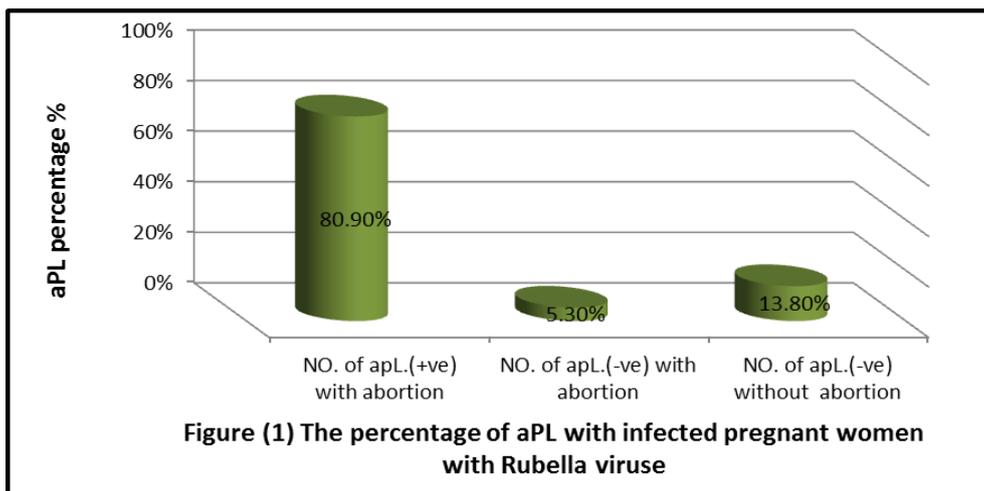
## STATICALLY ANALYSIS

Statistically analyzed of the Data by using SPSS, and P value of < 0.05 was considered significant.

## RESULTS

**Table (1): Number and percentage of apL with Rubella infected pregnant women.**

NO. of Rubella infected women	NO. of apL.(+ve) with abortion	NO. of apL.(-ve) with abortion	NO. of apL.(-ve) without abortion
131	106	7	18
Percentage 100%	80.9 %	5.3 %	13.8 %



The results revealed high percentage 80.9% of aPL with abortion in pregnant women infected with Rubella virus as shown in table (1) and figure (1), while 13.8% aPL negative (-ve) without abortion, 5.3% aPL (-ve) with abortion. This results represent a relation between aPL and abortion in Rubella infected pregnant women

**Table (2) Number and percentage of aPL with abortion in nonRubella infected pregnant women as control.**

NO.of nonRubella infected women	NO. of aPL.(-ve) without abortion	NO. of aPL.(+ve) with abortion	NO. of aPL.(+ve) without abortion
45	33	6	6
Percentage 100%	73.9 %	13.3 %	13.3 %

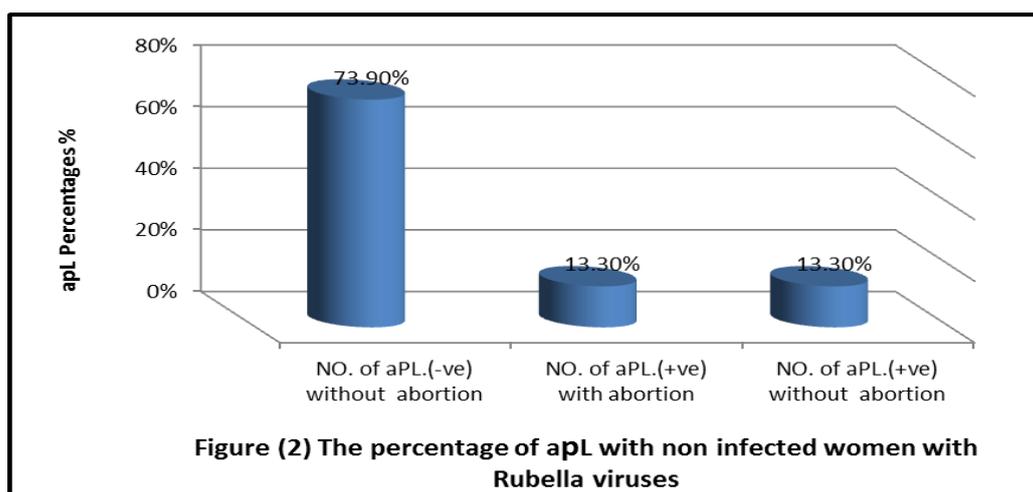
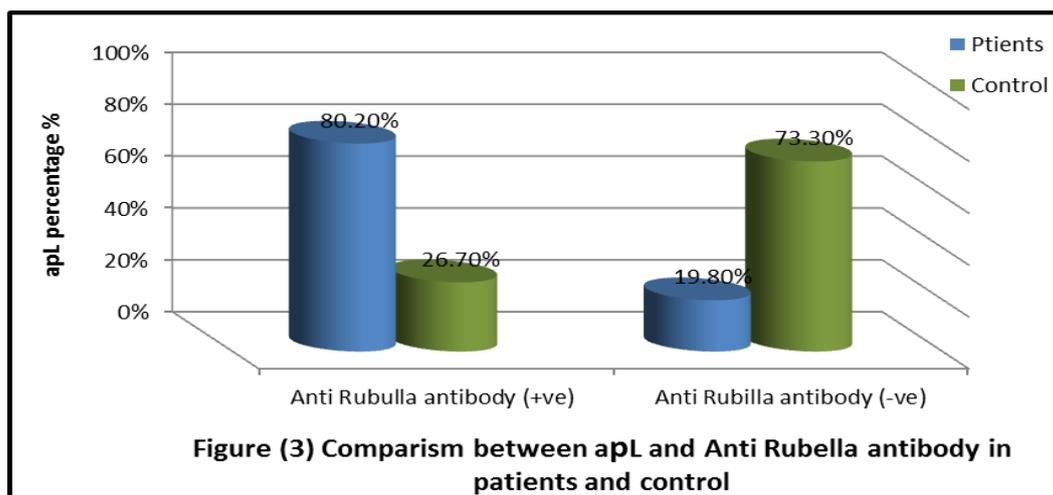


Table (2) and figure (2) represent low percentage (13.3%) of aPL (+) with abortion in non-infected pregnant women with Rubella virus, while the high percentage (73.9) appeared with non-Rubella infected pregnancy with aPL (-ve). Also the table (2) revealed (13.3%) abortion with aPL (+) in control.



The present study demonstrated a strong association between Anti rubella antibodies and Antiphospholipid antibodies in Iraqi women, 80% positive for both aPL and Antirubella antibodies compare to the control 26.70%.

## DISCUSSION

The results revealed high percentage (80.9%) of aPL with abortion in pregnant women infected with Rubella virus, while low percentage (13.8%) aPL negative (-ve) without abortion, 5.3% aPL (-ve) with abortion. This results represent a relation between aPL and abortion in Rubella infected pregnant women, around 15% of the women who have recurrent miscarriages have high levels of antiphospholipid antibodies. Data was agreed well with that reported by Abdul-karrim *et al.*, (2009) who found in seroprevalence of rubella virus in women with RSA was 34.2%, and in Palestine rubella was considered as an etiologic agent for abortion in pregnant women (Al-Hindi *et al.*, 2010) as well as aPL are responsible for clots in placenta's vessels and causing prevent growth fetal additionally may attack tissues of placental so block the growth and development, therefore this infection may lead to intra uterine death, spontaneous abortion, or preterm delivery as well as Infection with rubella virus is initially unapparent and asymptomatic and it is difficult to diagnose on clinical grounds, so infection with rubella virus can be disastrous in early gestation. The virus may affect all organs and cause a variety of congenital defects.

In another report from Russia, the seroprevalence of rubella virus in women with abortion and in healthy women were 77.5 and 59.8% respectively (Odland *et al.*, 2001), while in Nigeria, the seroprevalence of rubella virus in women with abortion and in healthy women were 86% and 77% respectively (Onyenekwe *et al.*, 2000). So, this study showed low

percentage (13.3%) of aPL (+) with abortion in non infected pregnant women with Rubella viruse, while the high percentage (73.9) appeared with non-Rubella infected pregnancy with aPL (-ve), as well as many factors as oral contraceptives, surgical procedures, prolonged immobilization, or a genetic prothrombotic state play important role in increase the likelihood of an aPL positive patient developing a vascular event so, women with pregnancy events alone have a high likelihood of developing thrombosis in later years [Erkan *et al.*, 2001].

As well as this study demonstrated a strong association between rubella infection and RSA (Recurrent spontaneous abortion) in Iraqi women, so it is evident that maternal infection like rubella play a critical role in pregnancy wastage and their occurrence in women with RSA is a significant factor but early detection and timely intervention can prevent morbidity and mortality of infants born to such mothers. All antenatal cases with RSA should be routinely screened for rubella, so that early diagnosis and appropriate intervention of these infections will help in proper management of fetal outcome. In addition to this, there is a need to modify vaccine strategies to immunize all adolescent girls and/or women of child bearing age before conception to reduce incidence of congenital rubella syndrome and bad obstetric outcome, maternal thrombophilia has been identified as a major cause of adverse pregnancy outcome, including recurrent spontaneous abortion, still-birth, severe preeclampsia, placental abruption, and intrauterine growth restriction (Greer, 2000).

The involvement of aPL in clinically important normal procoagulant and anticoagulant reactions and on certain cells altering the expression and secretion of various molecules may offer a basis for definitive investigations of possible mechanisms by which aPL may develop thrombotic events in patients with APS additionally APS is the most common cause of acquired thrombophilia (Girling and de Swiet, 1998). It is associated with complications spanning all trimesters of pregnancy (Rai, 1998 and Kupfermanc *et al.*, 1999), aPL are circulating antibodies are associated with thrombosis and/or pregnancy morbidity [Misita and Moll, 2005].

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