

Cytokines network in patients with obstetric complications and antiphospholipid syndrome (APS)

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INTRODUCTION

ANTIPHOSPHOLIPID SYNDROME IS AN AUTOIMMUNE DISORDER CHARACTERIZED BY

1. THE PRESENCE OF ANTIPHOSPHOLIPID ANTIBODIES (APLA):
 - anticardiolipin antibodies (ACA) and/or
 - lupus anticoagulant antibodies (LA)
2. CLINICAL COMPLICATIONS
 - venous and/or arterial thrombosis
 - pregnancy morbidity

THE SYNDROME IS CALLED

- **PRIMARY APS**

(when it occurs without underlying disorder)

- **SECONDARY APS**

(in patients with other diseases such as auto-immune diseases, particularly systemic lupus erythematosus, or malignant diseases)

**IN A POPULATION WITH
RECURRENT PREGNANCY LOSS
ANTIPHOSPHOLIPID ANTIBODIES
ARE DETECTED IN 10-20% OF
INDIVIDUALS**

WHY IS THE STUDY IMPORTANT?

Management of pregnant women with antiphospholipid syndrome (APS) has improved over the last 10 years.

The recurrent pregnancy loss that is associated with this disease is managed with prophylactic low dose aspirin and heparin therapy. This therapy leads to a 40% absolute risk reduction in pregnancy loss.

**However, many women (60%)
still fail to deliver a live infant
despite this therapy**

Understanding the type of cellular immunity in these patients is important in unraveling the pathogenic mechanisms of the disease, which may lead to the development of therapeutic strategies targeting the autoreactive T cell clones and to improve obstetric outcome

- **Communication between trophoblastic and decidual cells is mediated by cytokines**
- **The human T cells can be classified on the basis of their pattern of cytokine production**
- **Type 1 T cells (Th1)**
produce pro-inflammatory cytokines:
interleukin (IL)-2, tumor necrosis factor-alpha (TNF- α), interferon-gamma (IFN- γ)
- **Type 2 T cells (Th2)**
produce anti-inflammatory cytokines: IL-4, IL-8, IL-10, IL13.

**The balance of
pro-inflammatory (Th1) cytokines and
anti-inflammatory (Th2) cytokines is
critical to normal, successful
pregnancy**

METHODS

- Women admitted for pregnancy morbidity in Women's Reproductive Health Care Centre of "Erebouni' Medical Centre" and 'Nairi' Medical Centre
- Structure questionnaire applied by doctor

OBJECTIVES

1. To measure ACA of IgG and/or IgM isotypes in the sera.
2. To measure the concentration of interleukins (IL-6, IL-8, IL-10, IL-12), tumor necrosis factor-alpha (TNF- α), interferon-gamma (IFN- γ) in the sera.
3. To compare the changes in the levels of the T-Helper Cells Type 1 (pro-inflammatory cytokines) to T-Helpers Type 2 (anti-inflammatory cytokines) in patients with antiphospholipid syndrome and controls.

TYPE OF STUDY

Case-control retrospective study

The study will be conducted in “Erebouni” Medical Centre and “Nairi” Medical Centre - Obstetric and Rheumatology Departments.

Baseline characteristics of cases and controls

*Patients (n= 100) of childbearing ages, all
residents of Armenia with pregnancy
morbidity*

PREGNANCY MORBIDITY

- One or more unexplained deaths of a morphologically normal fetus at or beyond the 10th week of gestation, with normal fetal morphology documented by ultrasound or by direct examination of the fetus.
- One or more premature births of a morphologically normal neonate at or before 34th weeks of gestation because of severe preeclampsia or eclampsia, or severe placental insufficiency.
- Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, without maternal anatomic or hormonal, or paternal and maternal chromosomal abnormalities.

CASES - patients with laboratory criteria of APS:

- 1) ACA of IgG and/or IgM isotype in blood, present in medium or high titer, on 2 or more occasions, at least 6 weeks apart, measured by a standardized ELISA for β 2-GPI-dependent ACA.
- 2) LA present in plasma on 2 or more occasions at least 6 weeks apart.

CONTROLS - patients without laboratory criteria of APS

| | <u>Cases</u> (patients with pregnancy morbidity and APS) | <u>Controls</u> (patients with pregnancy morbidity without APS) |
|-----|---|--|
| Th1 | a | c |
| Th2 | b | d |
| All | | |

Exclusion criteria

- Patients positive for any other autoantibody, except antiphospholipid antibody.
- Patients with underlying collagen disease.
- Patients on immunosuppressive treatment.
- Patients on antiplatelet or anticoagulant treatment.
- Patients with current infectious disease.

ANALYSIS METHOD

To calculate:

- the prevalence of inflammatory cytokines in cases and controls;
- the odds ratio (OR) to measure association between disease and exposure.

- To assess the possible role of inflammatory cytokines and T- Cells activation in the pathogenesis of APS and pregnancy complications.
- In case the results show higher levels of pro-inflammatory cytokines and lower levels of anti-inflammatory cytokines among patients with APS and pregnancy morbidity we shall begin the next step of this research – the randomized clinical trial of intravenous immunoglobulin for the reduction of obstetric complications.

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