Interferon, complement and immune cell imbalances in pregnant women with systemic autoimmune diseases

Published: 21-12-2022
Last updated: 21-09-2024

Overall aimIdentify immunologic imbalances, with a focus on IFN, NETs, complement and lymphocyte subsets during pregnancy in women with systemic autoimmune diseases.HypothesisWe hypothesize that increased IFN activation and NET formation in patients...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational non invasive

Summary

ID

NL-OMON51715

Source
ToetsingOnline

Brief title
Immune dysregulation in pregnant women with systemic autoimmune diseases

Condition

- Autoimmune disorders
- Pregnancy, labour, delivery and postpartum conditions

Synonym
Systemic autoimmune diseases

Research involving
Human

Sponsors and support

Primary sponsor: Reumatologie en Klinische Immunologie

Source(s) of monetary or material Support: Abel Tasman Talent Program (ATTP) sandwich PhD collaboration between Universidad de Antioquia and UMCG

Intervention

Keyword: Antiphospholipid syndrome, Pregnancy, Primary Sjogren Syndrome, Systemic Lupus Erythematosus

Outcome measures

Primary outcome

The association between adverse pregnancy outcomes and immunologic imbalances

with a focus on the upregulation of interferon, as measured by expression of

the IFN type I signature, blood MxA levels and MxA expression in the placenta.

Secondary outcome

Induction of NETs by autoantibodies in serum

Presence of neutrophils and NETs in placental tissue

Distribution of immune cell subsets in blood and placental tissue, with a focus

on B cells, T cells, and myeloid cells

Complement levels in blood and placental tissue

Study description

Background summary

Systemic lupus erythematosus (SLE), primary Sjögren*s syndrome (pSS) and antiphospholipid syndrome (APS) are systemic autoimmune diseases with a strong female predominance and are associated with adverse pregnancy outcomes. SLE and pSS are characterized by chronic immune cell activation. Throughout pregnancy, the maternal immune system must tolerate a semi-allogenic fetus. Multiple and specific immune adaptations are known to be involved in this immune tolerance, and maternal immune activation is associated with pregnancy complications as preterm birth, preeclampsia, low birth weight, recurrent pregnancy losses, and fetal growth restriction (FGR) (1). The underlying causes of such placenta-related complications in SLE, pSS and APS patients have not been fully

elucidated.

Study objective

Overall aim
Identify immunologic imbalances, with a focus on IFN, NETs, complement and lymphocyte subsets during pregnancy in women with systemic autoimmune diseases.

Hypothesis
We hypothesize that increased IFN activation and NET formation in patients with SLE, pSS and APS result in a more inflammatory state of the maternal immune system resulting in complement activation and altered distribution of immune cell subsets in the placenta and maternal peripheral blood.

Objectives
- To assess IFN upregulation in maternal and cord blood and placental tissue during pregnancy in women with SLE, pSS and APS

- To establish the amount of (autoantibody-induced) NET formation using serum of pregnant patients with SLE, pSS and APS

- Describe alterations in blood and placental immune cell composition during pregnancy in women with SLE, pSS and APS

- Identify the association between IFN upregulation, NETs formation, levels of complement and lymphocyte subsets with adverse pregnancy outcomes in women with SLE, pSS and APS

Study design

This is a longitudinal follow-up study of pregnant SLE, pSS, and APS patients. Data, clinical as well as biological, will be collected prospectively. The data will be compared to pregnant patients with rheumatoid artritis (RA) as disease control and to healthy pregnant women. As part of standard care, these patients will be followed at the department of Gynaecology and Obstetrics and at the department of Rheumatology and Clinical Immunology during their pregnancy. Visits will take place before pregnancy, during each trimester and at delivery.

Study burden and risks

All patients will receive standard care and treatment during follow up. Procedures that will be solely done for research purposes are: extra blood withdrawal during each trimester and at delivery. Also cord blood will be taken and placental tissue will be collected at delivery. All study visits and all extra blood donations will be combined with regular care visits and regular withdrawal of blood for diagnostic purposes.

Furthermore the participants will be asked to fill in questionnaires online. The knowledge generated in this project will be useful to propose innovative and personalized interventions to achieve better pregnancy outcomes in the future in patients with systemic autoimmune diseases.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Pregnancy wish or pregnant
- Fulfilling disease specific criteria for SLE, Sjogren, APS or Reumatoid Artritis (RA)
- written informed consent
- > 18 years old and *wilsbekwaam*

Exclusion criteria

- Not able to give written informed consent
- Other auto-immune diseases
- Malignancies

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2023
Enrollment:	59
Type:	Actual

Ethics review

Approved WMO

Date:	21-12-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL79172.042.22