The identification of novel markers for premature birth based on the investigation of pregnant women with congenital heart disease.

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1. To obtain early diagnostic and prognostic markers for preterm premature rupture of membranes and premature labour, based on ultrasound examinations of mother, placenta and fetus and markers present in blood and urine of mother at 11-14 weeks and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Congenital cardiac disorders
Study type	Observational invasive

Summary

ID

NL-OMON36198

Source
ToetsingOnline

Brief title
ZAHARA3

Condition

- Congenital cardiac disorders
- Pregnancy, labour, delivery and postpartum conditions

Synonym
premature labour

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: 675000

Intervention

Keyword: congenital heart disease, pregnancy, premature birth

Outcome measures

Primary outcome

To relate ultrasound, clinical, biological and molecular markers to the

occurence of premature delivery resulting from preterm premature rupture of

membranes and/or premature labour.

Secondary outcome

none

Study description

Background summary

Delivery before the 37th week of pregnancy is premature and with a prevalence of 9.6% this yearly affects about 14 thousand neonates in the Netherlands. Prematurity is the leading cause of neonatal mortality and morbidity and is strongly associated with delayed neurological- and motor development during the first years of life.
Usually, premature delivery is the consequence of preterm premature rupture of membranes and/or premature labour. It is known that the growing fetus, the placenta and the myometrium contribute to the initiation of parturition but the molecular mechanism that initiates labour is not known and there are no prognostic markers available. Treatment can delay delivery for a short time, probably because the events initiating labour occured weeks before. If active labour has started, this process can not be reversed.
Detailed knowledge on the molecular events in placenta and myometrium and the interaction between these tissues that initiate parturition, is essential to develop prognostic tests and rational treatment.

The prevalence of idiopathic premature delivery is increased in women with

congenital heart disease. The overall prevalence is 16% with excesses to 30% in case of complete transposition of the great arteries or pulmonary atresia with ventricular septum defects. The undelying molecular hypothesis is that the cardiomyoctes and the uterine myocytes contain a number of similar pathways and mechanisms, that can be disregulated in pregnant women with congenital heart disease who deliver prematurely.

Because pregnant women with congenital heart disease
1. go to the clinic relatively early in pregnancy,
2. are closely counselled to diagnose and if possible treat additional cardiac complications of the mother or heart disease of the developing fetus,
3. have a relatively high chance of developing preterm premature rupture of membranes and/or premature labour,
non-invasive tests during pregancy and biobanking of tissue samples in this patient group offers the opportunity to develop prognostic tests and rational and effective therapeutics that are important to diagnose and treat prematurity in general.

Study objective

1. To obtain early diagnostic and prognostic markers for preterm premature rupture of membranes and premature labour, based on ultrasound examinations of mother, placenta and fetus and markers present in blood and urine of mother at 11-14 weeks and 20-24 weeks of gestation.

2. To obtain a durable biobank containing placenta, placenta-bed and myometrium, combined with a clinical database. The tissues will be used to detremine the differences tissue specific expression that relate to the abovementioned obstetrical complications.

Study design

The study is observational.
In case of informed consent
1. ultrasound examinations of mother, placenta and fetus will be done and at the same time blood and urine samples will be taken. All samples will be stored in the ZAHARA3 biobank.
2. placental biopsies will be taken after delivery as well as a myometrium and placenta-bed biopsies in case of delivery by caesarean section and all these samples will be stored in the ZAHARA3 biobank. Feasibility of biosampling will be decided on by the obstretrician perfoming the operation.
Ultrasound data, clinical data on mother, the course of pregnancy and the pregnancy outcome will be stored in a clinical database. The tissue samples will be used to investigate RNA and protein profiles.

Study burden and risks

Ultrasound testing during pregnancy is a normal routine in this patient population. Ultrasound examination of cervical length and utero-placental flow is usually not done at these gestational ages, but will be done in the current study. The Doppler-ultrasound evaluations will not infer additional risk or discomfort for the patient.
The venapuncture infers minimal burden. The risks are the risks for any venapuncture; sometimes a mildly sore spot or a hematoma.
The collection of a urine sample is without discomfort or risk.
The placenta sampling will be done postpartum and does not infer risk or discomfort for mother or baby.
The taking of the myometrium and placent-bed biopsies are considered a procedure with minimal risk. The duration of the operation will be extended a few minutes and the taking of the biopsies will not contribute to bloodloss or healing of the wound.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

Pregnant women with a congenital heart defect

Exclusion criteria

HIV positive

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	17-10-2011
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL36326.018.11