Cardiac- and vascular disease (-abnormalities) as underlying cause of premature birth.

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The PRELHUDE study investigates the reversal of the ZAHARA3 study; whether subclinical congenital heart disease occurs in women who deliver prematurely for unknown reason. The biosamples taken during and after delivery will be used to determine...

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

Summary

ID

NL-OMON39237

Source
ToetsingOnline

Brief title
PRELHUDE

Condition

- Congenital cardiac disorders
- Pregnancy, labour, delivery and postpartum conditions
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
premature birth

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ZonMW TOP subsidie

Intervention

Keyword: hart disease, premature labour, vascular disease

Outcome measures

Primary outcome

The determine if (subclinical) congenital heart disease (CHD) is present in women with idiopathic premature delivery.
As there is no data on the prevalence of this in the general population, if we find CHD in our study population we will additionally seek METC approval to study the prevalence in women who deliver at term after an uncomplicated pregnancy.

To estblish the presence, nature and molecular basis of vascular pathology in placenta and placenta-bed of women with idiopathic premature delivery.
Control samples are being collected from women who deliver by casearean section at term (PANDA-postnataal project, door de AMC METC positief beoordeeld op 24 augustus 2010 METC 10/128 # 10.17.1418corr).

The myometrium biopsies acquired after c section will be used as control samples for the molecular analysis on myometrium biopsies acquired from women with congenital heart disease who deliver prematurely (the ZAHARA3 study).

Maternal and umbilical cord blood will be used to determine levels of

biomarkers putatively relevant for premature delivery

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. Usually, premature delivery is the consequence of preterm rupture of membranes and/or premature labour. It is known that the growing fetus, the placenta and the uterus 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 only. Prematurity is an important cause of neonatal mortality and morbidity.

Recently it has become evident that maternal cardiovascular pathology is a risk factor for premature delivery. Investigation of the placenta after premature birth often shows vascular abberations of unknown cause. Additionally, pregnant women with a congenital heart disease have an increased risk to deliver prematurely.
This last finding is the basis of the ZAHARA3 project, where pregnant women with a congenital heart disease are asked early in pregnany to participate in this study where between 11 and 14 and again between 20 and 24 weeks of gestation, fetal growth, the placenta and the uterine vessels that feed the placenta are evaluated using Doppler ultrasound. In this study we investigate if there are clinical markers that can also be used to predict premature delivery in women without congenital heart disease. Additionally we collect blood and urine at these timepoints.
The molecular biology part of the study investigates the development of placenta and myometrium in mice with a congenital heart disease during pregnancy. The molecular leads for diagnostics and theraphy of premature delivery coming from these animal experiments will be validated on human biosamples taken with informed consent during delivery of pregnant women with congenital heart disease.

The PRELHUDE study investigates the reversed situation; whether subclinical congenital heart defects or vascular pathology of the placenta and/or placenta bed are present in women with idiopathic premature delivery.
It is important to investigate this. The detection of a subclinical hart defect and treatment of this condition may improve long term health. Additional

molecular data on the nature of the placental vascular pathology may lead to improved diagnostics and improved prognosis of a threatening premature delivery. The identification of the genes involved in this process will benefit the treatment of threatening premature delivery in future.

Study objective

The PRELHUDE study investigates the reversal of the ZAHARA3 study; whether subclinical congenital heart disease occurs in women who deliver prematurely for unknown reason. The biosamples taken during and after delivery will be used to determine vasular pathology in the placenta and the placenta-bed. Molecular biology investigations of these tissues and myometrium will be aimed at identifying the molecular basis of these aberrations and premature birth.

Study design

Pregnant women who present with threatening premature labour will be asked to participate in the PRELHUDE study. In case of informed consent, women will be included if they deliver prior to 37 weeks of gestation.

--> At the time of delivery, blood of mother will be drawn.
--> If the delivery is done by caesarean section, or if after delivery the placenta has to be removed under anaesthesia, biopsies of the placenta-bed and the myometrium will be taken.
--> After birth placenta biopsies and umbilical cord blood from the placenta will be taken.
--> Within 72 hours after deliver, the cardiac status of mother is evaluated by ECG and ultrasound.

Study burden and risks

The venapuncture infers minimal burden. The risks are the risks for any venapuncture; sometimes a mildly sore spot or a hematoma.

The taking of myometrium and placenta-bed biopsies are considered a procedure with minimal risk. The duration of the operation will be extended with a few minutes and the taking of the biopsies will not contribute to bloodloss or healing of the wound.

Placenta sampling and umbilical cord blood collection will be done postpartum and do not infer risk or discomfort for mother or baby.

Within 72 hours after delivery an ECG and maternal cardiac ultrasound will ne done. These procedures do not infer risk or burden for the patient.

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

Women who deliver prematurely for unknown reasons

Exclusion criteria

HIV positive, patients with congenital heart disease, multiple pregnancies, uterine anomalies, congenital/chromosomal anomalies.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2012
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO Date:	31-01-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-10-2013
Application type:	Amendment
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	NL38175.018.11