Non-interventional study to investigate the transfer of vaccination induced maternal antibodies in infants with fetal growth restriction.

Published: 07-03-2025
Last updated: 04-04-2025

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Ethical review	Approved WMO
Status	Pending
Health condition type	Bacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON57353

Source
ToetsingOnline

Brief title
FEtal Growth Restriction And Maternal Immunization; the FEGRAMI-study

Condition

- Bacterial infectious disorders

Synonym
pertussis, whooping cough

Research involving
Human

Sponsors and support

Primary sponsor: RIVM

Source(s) of monetary or material Support: ZonMW subsidie 10150022310029

Intervention

Keyword: antibody transfer, immunogenicity, intrauterine growth restriction, maternal vaccination

Outcome measures

Primary outcome

Comparing the antibody concentrations against pertussis, diphtheria, and

tetanus, measured in both mother and infant directly after birth and the infant

at the age of two months, as well as the transmission ratio from mother to

infant, across the following five groups:

1. FGR mother-child pairs, with late-developed FGR after 32 weeks of gestation.

2. FGR mother-child pairs, with early-developed FGR before 32 weeks of

gestation.

3. SGA mother-infant pairs

4. Term non-FGR and non-SGA mother-infant pairs

5. Preterm non-FGR and non-SGA mother-infant pairs

Secondary outcome

We compare the antibody concentrations against measles and the respiratory

syncytial virus (RSV) immediately after birth among four groups:

1. Mother-child pairs with late FGR, after 32 weeks of pregnancy.

2. Mother-child pairs with early FGR, before 32 weeks of pregnancy.

3. Mother-child pairs with SGA.

4. Mother-child pairs with term-born children without FGR or SGA.

Additionally, we investigate the composition of the placentas, focusing on the

ratio and expression of FC receptors and B cells, in vaccinated pregnant women:

1. Late FGR pregnancies (n=10).

2. Term pregnancies with a normally growing child (n=10).

Furthermore, we describe the medical and sociodemographic characteristics of the study population. We compare the growth, development, and occurrence of infections in FGR and SGA children during the first six months with those of term-born children of mothers who have not received maternal DKT vaccination (historical cohort).

Study description

Background summary

Maternal vaccinations offer infants protection against infectious diseases from the day of birth onwards till the start of their own vaccination schedule (NIP). In the Netherlands, term infants of mothers vaccinated against diphtheria, tetanus and pertussis (DTaP) receive a reduced and postponed vaccination schedule compared to preterm infants. In 5-10% of infants fetal growth restriction (FGR) occurs, mostly due to placental insufficiency. Currently, FGR infants of vaccinated mothers receive the immunization schedule according to their gestational age at birth. In case of a reduced and postponed schedule, this may be insufficient for optimal protection because in FGR the transplacental antibody transfer is probably negatively impacted. The transfer of antibodies may depend on the concentration of antibodies the mother has during pregnancy after vaccination. It is possible that the efficiency of this transfer is influenced by the composition of the placenta and the presence of FC receptors and possibly B cells.

Study objective

The aim of this study is to investigate whether the transfer of antibodies from mother to infant is less effective in infants with intrauterine growth restriction (FGR) compared to term-born infants without intrauterine growth restriction or who are small for gestational age (SGA), in relation to the duration of pregnancy.

Study design

We will conduct a prospective cohort study in collaboration with top-clinical hospitals and university medical centers. We will assess antibody concentrations against pertussis, diphtheria, tetanus and measles in blood of women who are pregnant of a FGR or SGA infant and in the FGR and SGA infants themselves. These antibody concentrations will be compared with two previous studies, coordinated by the RIVM. Infants within these studies were born term or preterm whilst none of them were FGR or SGA. Additionally, in a small group of pregnancies with late FGR (n=10), placental material will be examined. This will focus on the composition and the expression and ratio of FC receptors and B cells. These placentas will be compared with those from mothers with a normally growing child (n=10). We will relate the composition of the placentas to the antibody concentrations found in the blood of the pregnant women and their children.

Study burden and risks

In this study, we collect blood samples and placentas from pregnant women vaccinated with DKT and their children. We focus on women pregnant with a child experiencing intrauterine growth restriction, a child with low birth weight, or a normally growing child. At birth, we collect blood from the mother via a finger-stick and from the child via umbilical cord blood. When the child is two months old, we take another blood sample with a heel-stick. These three blood samples are used to examine the amount of antibodies present in the blood. The finger- and heel-sticks may be briefly painful but pose no risks. The collection of umbilical cord blood is painless for both the child and the mother.
We ask 20 pregnant women, recruited at Radboudumc, to donate their placenta. There are no risks associated with this. Additionally, we ask participants to complete three questionnaires: one before birth, one when the child is two months old, and one when the child is six months old. The questions cover the health and sociodemographic information of the mother and child, vaccinations, and previous pregnancies. A home visit also takes place when the child is two months old. Completing the questionnaires and the home visit together takes about one and a half to two hours, ensuring the mother is not overly burdened.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Newborns

Inclusion criteria

inclusion criteria for pregnant woman:
• at least 18 years of age
• Being pregnant
• Receiving a standard routine Tdap vaccination after at least 20 weeks of gestation in the routine NIP before study entry
• Receiving antenatal care in a secondary or tertiary care center because the fetus has signs of FGR or SGA
• Signed IC from the parents.
• Parents who are willing to adhere to the protocol, perform all planned visits, and sample collections for themselves and their newborn child (in The Netherlands)

Inclusion criteria for infants (in utero):
• Fulfills the case definition of (50 participants per definition)
o SGA and not FGR, or
o Early fetal growth restriction, or
o Late fetal growth restriction
• Alive during inclusion
• Considered to be viable for at least the study period.

Exclusion criteria

- All women with one or more missing inclusion criteria
- history of having pertussis disease in the year prior to study entry.
- Known or suspected serious underlying condition that can interfere with the results of the study such as but not limited to cancer, autoimmune disease, immunodeficiency, seizure disorder or significant psychiatric illness.
-Receipt of immune modulating medication, e.g. oral corticosteroids, biologicals.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2025
Enrollment:	150
Type:	Anticipated

Ethics review

Approved WMO

Date:	07-03-2025
Application type:	First submission
Review commission:	METC NedMec

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	NL87270.041.24