The impact of amniotic fluid on the development and microbial colonization of the preterm intestinal tract: the AMFIBIE study

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neonatal and perinatal conditions
Study type	Observational non invasive

Summary

ID

NL-OMON56939

Source
ToetsingOnline

Brief title
Amniotic fluid and preterm gut health: the AMFIBIE study

Condition

- Neonatal and perinatal conditions

Synonym
Prematurity, preterm birth

Research involving
Human

Sponsors and support

Primary sponsor: Máxima Medisch Centrum

Source(s) of monetary or material Support: Stichting Steun Emma

Intervention

Keyword: Amniotic fluid, gut microbiome, intestinal tract, preterm infants

Outcome measures

Primary outcome

The main outcome is the characterization of the bacterial and metabolic composition of AF derived from obstetric patients delivering their infants extremely preterm using advanced biomedical techniques.

Secondary outcome

The secondary outcome measures are:

1. Analysis of amniotic fluid profiles of extremely preterm infants exposed to inflammation in utero versus extremely preterm infants not exposed to inflammation in utero.

2. Analysis of amniotic fluid profiles of extremely preterm infants with fetal growth restriction versus extremely preterm infants without fetal growth restriction.

3. Assessment of course of key metabolites throughout gestation identified in objective 2 and 3.

4. Correlation of amniotic fluid profiles with neonatal diseases, such as necrotizing enterocolitis, sepsis, and bronchopulmonary dysplasia, and identification of potential biomarkers in amniotic fluid for identifying extremely preterm infants at increased risk of these diseases.

5. Correlation of bacterial and metabolic composition of amniotic fluid with

microbial colonization of the neonatal gut in the first month of life.

Study description

Background summary

Preterm birth remains a major global health issue. Extremely preterm infants, born with gestational age below 28 weeks, are especially vulnerable to adverse health outcomes. Necrotizing enterocolitis, an inflammatory disease of the neonatal intestines, and sepsis, a systemic response to microbial invasion of the bloodstream, are more common in this population. The pathogenesis of both conditions has been linked to the immaturity of the preterm intestines and preclinical alterations in the gut microbiome. It has been hypothesized that amniotic fluid impacts the intra-uterine development of the fetal gastro-intestinal tract as the intestines are exposed to amniotic fluid through swallowing in utero. Previous studies on the characterization of amniotic fluid have demonstrated that the constitution of amniotic fluid gradually changes over the course of pregnancy. However, current literature still lacks knowledge on the, potentially, critical changes, that occur in the content of amniotic fluid. between the 24th and 28th week of pregnancy, their effect on the development of the fetal gastro-intestinal tract and impact on the microbial colonization of the neonatal gut.

Study objective

The aim of this study is to characterize the composition of amniotic fluid, collected during preterm delivery, of extremely preterm infants (24-28 weeks), using novel molecular techniques. These approaches include microbial (e.g. IS-pro analysis) and metabolomic (e.g. (un)targeted metabolomics) techniques. The impact of amniotic fluid on the neonatal gut colonization will be assessed through analyses of neonatal stool samples, which are collected in line with the eMINDS study.

Study design

In this multicenter observational cohort study, amniotic fluid will be isolated from mothers delivering their infants extremely preterm. Two subgroups are of particular interest due to their association with morbidity and mortality in the neonatal phase: 1) preterm infants exposed to intra-uterine inflammation, and 2) preterm infants with fetal growth restriction. To assess the impact of the composition of amniotic fluid on the colonization of the neonatal gastro-intestinal tract, neonatal stool samples are collected daily for the first 28 days of life, according to the ongoing eMINDS study.

Study burden and risks

Collection of AF, which is generally discarded as biological waste, is noninvasive, posing no additional strain on the obstetric patient. AF can safely be isolated without interfering with practice of a C-section or a vaginal delivery.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

Amniotic fluid will be collected from the study population consisting of obstetric patients delivering their infants extremely preterm (pregnancy duration between 24 + 0 - 27 + 6/7 weeks) (n = 125) and from a reference cohort (respectively, early midtrimester (< 24 weeks), very preterm to moderate and late preterm (28 + 0 - 36 + 6/7 weeks), and full term pregnancies (37 + 0 - 41 + 6/7 weeks) (n = 150).

Inclusion criteria study population: If the obstetric patient is > 16 years of age and mentally competent, amniotic fluid can be collected at time of extremely preterm delivery between 24 and 27 + 6/7 weeks of gestation and informed consent is obtained from the obstetric patient, the participant can be included in the study.

Inclusion criteria reference cohort: If the obstetric patient is > 16 years of age and mentally competent and amniotic fluid can be collected during clinically indicated amniocentesis (during early midtrimester pregnancies) or at time of delivery, by means of vaginal delivery or cesarean section, in very to moderate and late preterm pregnancies or full term pregnancies, the participant can be included in the study.

Exclusion criteria

Exclusion criteria study population: Obstetric patients < 16 years of age and/or mentally incompetent or with pregnancies complicated with major fetal congenital or chromosomal comorbidities will be excluded from the study.

Exclusion criteria reference population: Obstetric patients < 16 years of age and/or mentally incompetent or with pregnancies complicated with major fetal congenital or chromosomal comorbidities will be excluded from the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	25-10-2024

Enrollment:	275
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	06-08-2024
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	NL86579.015.24