May 23, 2024

Fetal and neonatal outcomes in syphilis infected pregnant women in Reunion Island

DOI
dx.doi.org/10.17504/protocols.io.6qpvr83mblmk/v1

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DOI: https://dx.doi.org/10.17504/protocols.io.6qpvr83mblmk/v1

Protocol Citation: Camille CRAMEZ, Phuong Lien TRAN 2024. Fetal and neonatal outcomes in syphilis infected pregnant women in Reunion Island. **protocols.io https://dx.doi.org/10.17504/protocols.io.6qpvr83mblmk/v1**

Protocol status: Working
We use this protocol and it's working

Created: May 23, 2024

Last Modified: May 23, 2024

Protocol Integer ID: 100510

Keywords: neonatal outcomes in syphili, congenital syphilis rate, congenital syphili, optimal syphilis monitoring, syphili, syphilitic infection, treatment of syphili, proven syphilitic infection, pregnancy in reunion island, pregnant women in reunion island abstract objective, neonatal morbidity, pregnant patient, neonatal outcome, neonatal mortality rate, pregnant women, pregnancy, specific antenatal care, obstetric complication, mortality in pregnant women, newborn, given birth, fetal mortality rate, fetus, reunion island population, vulnerable group of patient, gestational age

Abstract

Abstract

Objectives **:**

To evaluate the fetal and neonatal morbidity and mortality in pregnant women with syphilis during their pregnancy in Reunion Island, population benefiting from early and well-conducted screening and treatment.

Methods :
This is a retrospective observational study conducted in the four Reunion hospital centers between 2017 and 2022. The included patients were all pregnant patients with a biologically proven syphilitic infection and having given birth in one of the four centers mentioned.

Results :
108 patients were included, with 113 fetuses and newborns. Fetal mortality rate was 2.7%, neonatal mortality rate was 1.8% and congenital syphilis rate was 7%. Despite 37% of patients with a vulnerable psycho-social context, 72% were screened early, 13% in the second trimester, 44% had received optimal treatment and 48% optimal syphilis monitoring. We found 43% of obstetric complications with 12% of IUGR and 4.6% of pre-eclampsia. 21% of newborns were preterm and 17% small for gestational age. There was a significant trend between psycho-social vulnerability and congenital syphilis.

Conclusions :
Fetal and neonatal morbidity and mortality is low in our Reunion Island population where screening and treatment of syphilis are early and well conducted, although a vulnerable group of patients remain who require specific antenatal care.

Troubleshooting

METHODS

1 We conducted a multicenter retrospective observational study in the four hospital centers of Reunion Island (Centre Hospitalier Universitaire Nord et Sud - CHU, Centre Hospitalier Ouest Réunion - CHOR, Groupe Hospitalier Est Réunion - GHER), between January 1, 2017 and December 31, 2022, on fetal and neonatal morbidity and mortality in women with syphilis during pregnancy. Data were accessed for research purposes on May, 1 2023.
During consultation, verbal consent was obtained from patients to transcript their history in their medical records. Then, for this retrospective study of medical records, all data were fully anonymized before we accessed them. Authors had not access to information that could identify individual
participants during or after data collection. This work was approved by the Research Ethics Committee of the University Hospital of Bordeaux, under the reference CER-BDX 2023 – 138.

Study population

2 We included any pregnant patient with biologically proven syphilis infection who had given birth at one of the four above-mentioned centers. Serology was considered positive when TPHA was positive as well as VDRL titer (≥ ½). Any pregnancy with missing neonatal data was excluded.
Patients were recruited via the files presented to the Multidisciplinary Center for Prenatal Diagnosis (CPDPN in France) and via a search by the Department of Medical Information (DIM) using the key words "pregnancy; syphilis". Under the regional protocol, all pregnant patients with syphilis are presented to the Indian Ocean CPDPN, guaranteeing exhaustive case registration.

Data collection

3 Data were collected retrospectively from paper or computerized medical records at each
hospital. In order to meet our primary objective, our composite primary endpoint included fetal mortality, defined as spontaneous cessation of cardiac activity in utero at 14 WG and
above, and neonatal mortality, defined as death of a newborn at less than 28 days of age. (1, 2)
Secondary objectives were multiple and consisted in assessing fetal and neonatal morbidity.
Antenatally, these were ultrasound signs of infectious fetopathy : oligo-anamnios, fetal anemia (hydramnios, ascites, pericardial effusion, hydrops, middle cerebral

artery systolic peak > 1.5
MoM), bone mineralization disorders, hepatosplenomegaly, intestinal hyperechogenicity, calcifications, cerebral malformations and IUGR. IUGR is defined as an estimated fetal weight below the 10th percentile (small for gestational age - SGA) associated with arguments in favor of a pathological
growth defect. (3)
For newborns, the secondary endpoints were :
- prematurity, defined as birth between 22 and 37 WG of a child weighing over 500g (4) ;
- hypotrophy, defined by a birth weight < 10th percentile according to the Reunion Island
perinatal network curve (5) ;
- microcephaly, defined by a cranial perimeter (CP) at birth < 3 standard deviations on the AUDIPOG
curves (6,7) ;
- the existence of congenital syphilis proven by biological and imaging examinations according to
the Center for Diseases Control and Prevention (CDC) classification (8).
The CDC scenario classification, updated by the French National Reference Center (CNR), is described as follows :
- CDC scenario 1 "congenital syphilis confirmed or highly probable" : newborn with clinical signs of congenital syphilis, positive PCR on biological sample (placenta or cord blood, nasal or oral secretions, skin lesion), positive IgM or VDRL four times higher than maternal VDRL.
- CDC scenario 2 "probable congenital syphilis" : asymptomatic newborn whose VDRL is less than four times the maternal VDRL, and whose mother has been inadequately treated (treatment other than that of reference, treatment carried out < 4 weeks before delivery, undocumented, no serological decline or no treatment).
- CDC scenario 3 "possible congenital syphilis" : asymptomatic newborn whose VDRL is less than four times the maternal VDRL and whose mother was correctly treated during pregnancy but after 16 months' gestation, with no argument for reinfection and no VDRL re-ascension.
- CDC scenario 4 "congenital syphilis unlikely": a newborn as described in scenario 3, but whose mother was properly treated before 16SA, with stable, low VDRL follow-up.
We collected maternal characteristics such as age, geographical origin, level of education, profession, marital status, psycho-social context, social security coverage, body mass index (BMI), gestity, parity, drug use, history of STI (gonorrhea, chlamydia, herpes, syphilis) and history of obstetric complications such as prematurity, IUGR, IUF or pre-eclampsia. Pre-eclampsia is defined as systolic (≥ 140 mmHg) and/or diastolic (≥ 90 mmHg) gravid hypertension associated with significant proteinuria (> 0.3g/24h) from 20 WG onwards. (9)
In addition, we collected data concerning the pregnancy such as dating, co-infections, obstetrical

complications as described above and the context of syphilis screening (place, reason, term, first VDRL, stage). Screening was considered successful if it was carried out in the first trimester and then
repeated in the second trimester of pregnancy. Treatment modalities were recorded (number and timing of injections, adverse effects, prevention of Herxeimer reaction according to recommendations). Treatment was considered optimal if the number of injections was adapted to the stage of syphilis, given before 16 WG and more than 30 days before delivery. Follow-up of syphilis during pregnancy was considered optimal if the patient was referred to infectious disease department (CEGGID) and Antenatal Diagnosis (DAN), if monthly ultrasound and VDRL tests were carried out, and if psychosocial care was provided in accordance with the regional protocol. (10) Partner screening and
treatment were specified. Treatment of the newborn was also recorded.

Statistical analysis

4 The data, anonymized by identification number and classified using Excel spreadsheet, were analyzed
using P-value and XLstat softwares.They are presented as numbers and proportions (%) for categorical variables, and as means and standard deviations for continuous variables for descriptive data analysis.

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