Clinical Characteristics and Predictors of Impaired Neonatal Outcomes in Chorioamnionitis at Term Gestation: A cross-sectional cohort study

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Abstract

Objective: To describe clinical and laboratory characteristics of term deliveries complicated by chorioamnionitis, and to assess their association with adverse neonatal outcomes. **Design:** Cross-sectional cohort study **Setting:** The study is based on data from the Swedish Pregnancy Register, enriched with clinical data extracted from medical charts. **Population and Sample:** A random sample of 500 term singleton deliveries in Stockholm County with registered diagnosis of chorioamnionitis in the Swedish Pregnancy Register between 2014 and 2020. **Methods:** Logistic regression was used to estimate odds ratios (OR) as a measurement of the association between clinical and laboratory characteristics and neonatal complications Main Outcome Measures: Neonatal infection and asphyxia-related complications. **Results:** Maternal fever, maternal and fetal tachycardia, and elevated inflammatory laboratory markers were frequent signs of chorioamnionitis. The prevalence of neonatal infection and asphyxia-related complications was 10 and 22%, respectively. First leukocyte count in the second tertile (OR 2.14 [95% CI 1.02-4.49]), maximum CRP level in the third tertile (OR 4.01 [95% Cl 1.66-9.68]), and positive cervical culture (OR 2.22 [95% Cl 1.10-4.48]) were associated with an increased risk of neonatal infection. Maximum level of CRP in the third tertile (OR 1.93 [95% Cl 1.09-3.41]), and fetal tachycardia (OR 1.63 [95% Cl 1.01-2.65]) were associated with increased risk of asphyxia-related complications. **Conclusions:** In addition to maternal intrapartum fever, maternal and fetal tachycardia, and elevated inflammatory laboratory markers were common signs of chorioamnionitis. Elevated inflammatory laboratory markers were associated with both neonatal infection and asphyxia-related complications, and fetal tachycardia was associated asphyxia-related complications.

INTRODUCTION

Intraamniotic infection, or chorioamnionitis, is an infection caused by microbial invasion of the amniotic cavity, triggering maternal inflammatory response and acute inflammation of any combination of the placenta, amniotic fluid, fetus, fetal membranes or decidua (1, 2).

Established risk factors for chorioamnionitis include nulliparity, urogenital infections during pregnancy, prolonged membrane rupture, and multiple cervical examinations during labor (1-4). Chorioamnionitis should be suspected in the presence of maternal intrapartum fever in combination with clinical signs of infection and/or fetal distress, such as maternal leukocytosis, fetal tachycardia (5), purulent cervical drainage (2), uterine tenderness, maternal tachycardia, maternal malaise, elevated C-reactive protein (CRP) and foul-smelling water or discharge (1, 3, 6, 7).

Between 1 and 5% of term deliveries are estimated to be complicated by chorioamnionitis, which is associated with a significantly increased risk of maternal, fetal and neonatal morbidity and mortality (2, 3). Neonates

exposed to chorioamnionitis are at increased risk of severe infections in the neonatal period (3, 8-10), and are likewise at an increased risk of impaired short- and long-term neurological outcomes, hypothesized to be a consequence of the fetal hyperinflammatory response to the infection (11, 12). Undoubtedly, early identification and timely treatment of chorioamnionitis in combination with close collaboration between obstetric and pediatric care is essential to improve neonatal outcomes (13), but precise clinical predictors of neonatal complications are lacking. A majority of studies have focused on chorioamnionitis complicating preterm deliveries, whereas only a few studies have investigated the potential impact of clinical and laboratory characteristics of term deliveries complicated by chorioamnionitis. Risk prediction models based on gestational age (14), duration of membrane rupture, highest maternal intrapartum temperature and timing of intrapartum antibiotic administration have been proposed (2, 3), but except for maternal intrapartum temperature, no study have investigated the association between clinical and laboratory characteristics of chorioamnionitis and risk of adverse neonatal outcomes at term gestation.

The aim of our study was therefore to describe clinical and laboratory characteristics of term deliveries complicated by chorioamnionitis. Moreover, we aimed at assessing the impact of these clinical and laboratory characteristics on the risk of adverse neonatal outcomes in term deliveries complicated by chorioamnionitis.

METHODS

Design

We performed a cross-sectional cohort study of term deliveries complicated by chorioamnionitis. The study was approved by the Swedish Ethical Review Authority.

Setting

Annually, approximately 115,000 women give birth in Sweden. The vast majority of all pregnant Swedish women attend the free of charge maternal health program, including between 9 and 11 antenatal visits in low-risk multiparous and nulliparous pregnancies, respectively. Assessment of the need of additional visits or health care resources, such as specialized maternity care, is determined at the first antenatal visit based on the patient medical history and current disease-status, or later by indication. Essentially all women give birth at hospital-based delivery wards. The Stockholm region has six delivery wards with approximately 28 000 deliveries annually, accounting for approximately one fourth of all deliveries in Sweden.

Data sources

The Swedish Pregnancy Register (www.graviditetsregistret.se) is a national quality register, established in 2013. It receives data from multiple sources. A majority of variables are directly transferred from the electronic medical records (EMR). The register contains detailed information of the pregnancies, prospectively entered prospectively into the EMR by midwives and physicians in a standardized manner, starting with the first antenatal visit, and thereafter subsequently at every subsequent visit, including ultrasound examinations, delivery and postnatal care visits. Additionally, the register includes diagnoses and procedure codes for both mothers and infants, coded using the International classifications of disease (ICD) system (with version 10 in use since 1997). Information on clinical characteristics (symptoms and clinical findings such as maternal and fetal heart rate pattern), and laboratory measurements (CRP, leukocyte count and cultures) were extracted manually from medical records by the main author (PB).

Study participants

All term deliveries in the Stockholm Region between January 1st 2014 and August 31st 2020 complicated by chorioamnionitis, defined as a registered diagnosis in the Swedish pregnancy register (*ICD-10* O41.4) were identified. From these, a random sample of 500 was identified and made up the study population. Recently, an expert panel of maternal and neonatal experts recommended dividing chorioamnionitis into the three separate categories 'Isolated maternal fever', 'Suspected chorioamnionitis', and 'Confirmed chorioamnionitis' (Supportive information, eTable 1)(2). Based on this categorization, and for the purpose of this study, 'Isolated maternal fever' is defined as at least 1 registered maternal temperature between 38.0°C and 38.9°C,

and no additional signs of infection. 'Suspected chorioamnionitis' is defined as i) [?] 1 registered maternal temperature [?] 39.0degC or ii) [?] 1 registered maternal temperature between 38.0degC and 38.9degC in combination with at least one clinical sign of infection of: fetal tachycardia (>160 beats per minutes [bpm] for 10 minutes or longer), maternal leukocytosis (leucocyte count >15,000 cells/mm^3), or purulent discharge from the cervical os. 'Confirmed chorioamnionitis' is defined as i) a positive culture from cervix or amniotic fluid, confirming the presence of bacteria or ii) placental histopathological changes typical for chorioamnionitis. The registered chorioamnionitis diagnosis in the Swedish Pregnancy Register has not previously been validated, wherefore we validated the chorioamnionitis diagnoses of the study cohort against medical chart information. In total, 49 (9.8%) fulfilled the criteria of isolated maternal fever, 397 (79.4%) of suspected chorioamnionitis and 151 (30.2%) of confirmed chorioamnionitis. The corresponding positive predictive value of chorioamnionitis overall was excellent (0.92 [95% CI 0.89-0.94]) (Supportive information eMethods 1 and eTable 2).

Exposure and covariates

Baseline characteristics were extracted from the Swedish Pregnancy Register. Maternal age was categorized into <25, 25-30, 31-35 and >35 years of age at delivery. Parity was categorized into nulliparous, primiparous or multiparous ([?]2 para). Early pregnancy BMI (based on early pregnancy weight and height measure) was categorized according to WHO's nutritional status categories into underweight (BMI <18.5), normal weight (BMI 18.5-24.9), overweight (BMI 25.0-29.9) and obesity (BMI [?]30). Information on educational level, smoking status in early pregnancy, and selected pre-pregnancy comorbidities was also obtained from the register (Supportive information eTable 3) according to self-reported information collected and transferred by the midwife at the first antenatal visit. Educational level was categorized into less than 9 years of schooling, at least elementary school (or equivalent) and up to high school (9-12 years of schooling), and higher level of education, i.e. university, college or equivalent (>12 years of schooling). Self-reported presence of pre-pregnancy diabetes mellitus, essential hypertension and recurrent urinary tract infection was reported as yes/no, as was smoking-status in early pregnancy.

Delivery characteristics were also obtained from the Swedish Pregnancy Register. Gestational age at delivery was further stratified into early term (between 37+0 and 38+6/7 gestational weeks), full term (between 39+0 and 40+6/7 gestational weeks), late term (between 41+0 and 41+6/7 gestational weeks) and post term deliveries ([?] 42+0 gestational weeks). The delivery onset was stratified into spontaneous, medically induced and cesarean delivery before onset of contractions. Mode of delivery was categorized into non-instrumental vaginal delivery, instrumental delivery (vacuum extraction) and cesarean delivery according to registration in the Swedish Pregnancy Register.

Specific clinical and laboratory characteristics used to diagnose chorioamnionitis were collected from medical charts. Information on maternal temperature during delivery was obtained and reported as: i) no reported temperature [?]38.0degC, ii) at least one reported temperature between 38.0degC and 38.9degC, iii) reported temperature between 38.0 and 38.9degC persisting for at least 30 minutes, and iv) at least one reported temperature of 39.0degC or above. First and highest leucocyte count and CRP level was extracted from medical charts and categorized into tertiles. First reported values were, in general, based on blood samples taken in conjunction with diagnosis (during labor, prior to or in conjunction with delivery), whereas highest laboratory values were based on follow-up laboratory values, including postpartum care. Fetal tachycardia was defined as a fetal heart rate above 160 beats per minute (bpm) (and a duration of >10 minutes) during a period of maternal fever, and was extracted from the cardiotocography (CTG) registration. Maternal tachycardia was defined as heart rate above 100 bpm in the presence of maternal fever, and was extracted from text, registered clinical parameters or if captured on CTG registration (by pulse oximetry). Clinical findings and symptoms of chorioamnionitis (purulent cervical drainage, uterine tenderness, maternal malaise and/or foul-smelling amniotic fluid or discharge) was registered as present if specified in the medical chart text. A positive culture, cervical or blood, was defined as the presence of bacteria confirming the diagnosis microbiologically. Positive pathological-anatomic diagnosis (PAD) was defined as the presence of acute inflammatory changes in the amnion or chorion in pathological analysis of the placenta.

Outcomes

Adverse neonatal outcomes were stratified into neonatal infection and asphyxia-related conditions, defined by registered ICD-10 diagnoses in the Swedish Pregnancy Register. Neonatal infection included necrotizing enterocolitis, congenital pneumonia, sepsis, urinary tract infection, skin infection, umbilical infection and unspecified infections during the neonatal period. Asphyxia-related conditions included meconium aspiration, hypoxic ischemic encephalopathy, convulsions/seizures, hypoglycemia, jaundice and respiratory distress syndrome (RDS). (ICD-codes are available in Supportive information eTable 4).

Statistical analyses

Descriptive statistics was compiled, tabulated and presented as absolute numbers with means or medians and corresponding standard deviation or interquartile range, depending on covariate distribution. To assess the impact of clinical and laboratory characteristics of deliveries complicated by chorioamnionitis the cohort was - for this specific question - treated as a case-control study, where the specific characteristics of chorioamnionitis was the exposure and composite adverse neonatal outcome was the outcome. Logistic regression models were used to estimate odds ratios (ORs) of the association between each exposure and risk of neonatal outcomes. Inflammatory laboratory measurements were categorized into tertiles, with the lowest tertile used as a reference. A multivariate model adjusted for maternal age at delivery, smoking status, BMI and parity. All analyses were performed using SAS(r) Software (Statistical Analysis Software version 9.4, SAS Institute Inc, Cary, North Carolina, USA).

RESULTS

Study population

Between January 1st 2014 and August 31st 2020, 133 382 term singleton deliveries in Stockholm region were registered in the Swedish Pregnancy Register, whereof 629 (0.47%) had a registered chorioamnionitis diagnosis. A random sample of 500 of these made up the study population (Figure 1).

Baseline characteristics

Baseline characteristics, including demographics, pregnancy and delivery characteristics of all study participants are presented in table 1. The mean maternal age at delivery was 31.5 +- 5.2 years. Approximately four of five study participants were nulliparous (79.2%). In total, 243 (48.6%) study participants had a normal BMI, and 221 (44.2%) were overweight (29.8%) or obese (14.4%). Half of the study participants (50.8%) reported an educational level >12 years of schooling, and 15 (3%) reported smoking in early pregnancy. Five (1%) study participants had diabetes mellitus prior to pregnancy, and 66 (13%) reported pre-pregnancy recurrent urinary tract infection. In total, 28 (5.6%) study participants developed gestational diabetes and 49 (9.8%) were diagnosed with pregnancy-induced hypertensive disorder.

In total, 72 (14.4%) of deliveries occurred at early term, 247 (49.4%) at full term, 136 (27.2%) at late term, and 45 (9%) at post term gestational age. For 310 (62%) study participants, the delivery onset was spontaneous, 186 (37.2%) were medically induced and 4 (0.8%) had a cesarean delivery before labor onset. The delivery mode was non-instrumental vaginal for 136 (27.2%), instrumental vaginal for 55 (11%) and cesarean for approximately two thirds (61.8%).

Clinical and laboratory characteristics of chorioamnionitis and neonatal outcomes

Information on clinical and laboratory characteristics of all study participants is presented in table 2, and data on neonatal and maternal outcomes in table 3. Approximately half of all women had a temperature [?] 38.0degC persisting for more than 30 minutes, and 23% had at least one measured temperature [?] 39.0degC. In two thirds of the deliveries, maternal and/or fetal tachycardia was present. Maternal malaise was specified as present in one of five patients. In close to 60% of patients, meconium-stained amniotic fluid was noted. The vast majority (96%) received intravenous antibiotics. In total, 348 (70%) cervical cultures were sent for analysis, whereof 133 (38%) were positive. The most frequently isolated bacteria were Group B Streptococci

(GBS), present in 60% of positive cervical cultures, followed by Escherichia Coli (12%) (All specific bacteria detected in the positive cervical cultures are presented in supportive information *eTable 5)* .

In total, 29 (6%) neonates had an Apgar score < 7 at 5 minutes, and 10% suffered from an infection in the neonatal period. In 58 (12%) of neonates, the umbilical artery blood gas indicated fetal acidemia, and 110 (22%) suffered from a complication, which could indicate asphyxia.

Clinical and laboratory characteristics of chorioamnionitis and risk of neonatal infection

The association between each clinical or laboratory characteristic and risk of composite neonatal infection is displayed in table 4. Maternal intrapartum persisting temperature between 38.0 and 38.9degC, or a single maternal temperature [?] 39degC was not associated with an increased risk of neonatal infection. A first leukocyte count in the second tertile was associated with an approximately doubled risk of neonatal infection (adjusted OR 2.14 [95% CI 1.02-4.49]), whereas there was no association between a first leukocyte count in the third tertile and risk of neonatal infection. There was no significant association between highest maximum leukocyte count, or first CRP level, with risk of neonatal infection. Highest CRP in the third tertile was associated with an ˜4-folded increased risk of neonatal infection (adjusted OR 4.01 [95% CI 1.66-9.68]). There was a borderline significant association between fetal tachycardia and neonatal infection (adjusted OR 1.99 [95% CI 0.99-4.00]). A positive cervical culture was associated with a doubled risk of neonatal infection (2.22 [95% CI 1.10-4.48]).

Clinical and laboratory characteristics of chorioamnionitis and risk of asphyxia related complications

The association between clinical and laboratory characteristics of chorioamnionitis and composite neonatal asphyxia related conditions is displayed in table 4. Neither maternal fever, first or highest leukocyte count were associated with an increased risk of asphyxia related complications. Likewise, there was no association between first measure of CRP and the outcome. A highest CRP in the third tertile was associated with an approximately doubled risk of composite asphyxia related complications (adjusted OR 1.93 [95% CI 1.09-3.41]). Fetal tachycardia was associated with an increased risk of asphyxia related complications (adjusted OR 1.63 [95% CI 1.01-2.65]).

DISCUSSION

Main findings

In this cross-sectional cohort study, we found that i) maternal fever, fetal and maternal tachycardia, elevated leukocyte count and CRP were common findings in term deliveries complicated with chorioamnionitis, ii) the prevalence of neonatal complications was high, iii) elevated inflammatory laboratory values, and positive cervical culture were associated with an increased risk of neonatal infection, and iv) elevated inflammatory laboratory values, and fetal tachycardia were associated with an increased risk of asphyxia-related complications. Our findings highlight the importance of acknowledging signs of chorioamnionitis, and stresses the need of research focusing on identifying better predictors and preventive measurements for perinatal complications in chorioamnionitis at term gestation.

The chorioamnionitis prevalence of 0.47% in our study is considerably lower compared to previously reported rates of between 1 and 5%. However, these previously reported rates are, in general, based on older studies of placental findings of primiparous women, and are consequently not readily comparable with our results (15). Maternal fever is the most important clinical sign of chorioamnionitis, and was present in approximately 90% of the study participants. Surprisingly, maternal fever was not noted in remaining 10%, which may be a consequence of inadequate medical chart documentation rather than absence of elevated maternal temperature. Maternal and fetal tachycardia was highly prevalent (65% and 67% respectively), which is consistent with previously reported rates between 50 and 80% (16, 17). Likewise, in line with previous reports, the presence of subjective clinical signs, such as uterine tenderness and foul-smelling amniotic fluid, were rare (17). Uterine tenderness was only noted in 2% of the women with chorioamnionitis, but can be difficult to determine during active labor and the presence was only recognized if explicitly stated

in the medical chart text. Hence, the prevalence of these highly subjective clinical signs is presumably underestimated.

Importantly, according to current guidelines chorioamnionitis diagnosis can only be confirmed postpartum by histopathological analysis of placenta and/or positive cervical culture (2). Therefore, we must rely on clinical signs and laboratory markers of infection when diagnosing and managing patients with suspected chorioamnionitis in clinical practice. Suspected chorioamnionitis should imply initiating treatment with broad-spectrum intravenous antibiotics, careful monitoring and labor progression should be ensured (2). Although standard obstetric indications for cesarean delivery apply in deliveries complicated by chorioamnionitis, the myometrial contractility can be affected by the inflammation, leading to an increased risk of labor dystocia, cesarean deliveries and postpartum hemorrhage (18, 19), which presumably explains the observed high cesarean delivery and postpartum hemorrhage rate in our study.

Chorioamnionitis is an established risk factor for early- and late-onset neonatal sepsis (10), and its presence motivates intensified monitoring, testing, and sometimes empiric antibiotic treatment of the neonate. Multiple attempts to develop prediction models of the risk of developing neonatal sepsis have been made, not the least in order to reduce the usage of empiric antibiotic treatment, which has been associated with an increased risk of negative childhood outcomes, including asthma (20). The impact of clinical and laboratory characteristics of chorioamnionitis on the risk of neonatal complications has not been addressed in detail previously. We found that a moderately elevated first leukocyte count, highest maximum CRP level, and positive cervical culture were associated with neonatal infection, and that high maximum CRP and fetal tachycardia were associated with asphyxia-related complications, which is partly a novel finding. Fetal tachycardia in the presence of maternal fever is a known predictor of adverse neonatal outcomes, and may be a sign of fetal inflammatory response, which has been proposed as a mechanism of impaired short- and long-term neurological outcomes (21, 22). A release of fetal pro-inflammatory cytokines, in response to inflammation, has been hypostasized to have a direct toxic effect on the brain leading to adverse neurological outcomes (12).

A culture was sent in only 70% of cases and of these, only 40% were positive. However, during the medical chart review it was noted that a majority of patients were treated with intravenous antibiotics prior to the culture being taken, which could distort bacterial growth and lead to false negative cultures. Additionally, there is emerging evidence of chorioamnionitis being a clinical syndrome with various etiologies, whereof intra-amniotic infection is one, and sterile intra-amniotic inflammation is another (23). In fact, similar with our result, previous studies report low rates of bacteria isolated from cervical or amniotic fluid cultures in patients with chorioamnionitis (24, 25).

Strengths and Limitations

This study has multiple strengths. Firstly, the population-based approach of identifying the study population naturally minimize the risk of selection bias. We could include the majority of cases with chorioamnionitis at term gestation in the region of Stockholm, accounting for 25% of all deliveries in Sweden, during the study period. Secondly, the Swedish Pregnancy Register contains prospectively collected detailed information from the pregnancy and postpartum period, which precludes the risk of recall bias. Specific clinical information was extracted retrospectively from medical charts, but the information on neonatal outcomes was added separately after the medical chart review, why we regard the risk of recall bias as minor. Thirdly, our validation of registered chorioamnionitis diagnosis against medical chart data revealed an excellent validity ensuring the internal study validity. Despite of these methodological advantages, our results should be interpreted in the light of some potential study limitations. The validity of neonatal diagnoses in the Swedish Pregnancy Register has not been assessed. There may be cases of delayed presentation of adverse neonatal outcomes, which might not be captured by the Swedish Pregnancy Register, potentially leading to an overall underestimation of adverse neonatal outcomes. It is possible that there were patients with chorioamnionitis who were misdiagnosed (false negative) during the study period, and consequently not included in the study. Finally, the regional cohort makes it difficult to fully extrapolate our results to other settings due to potential differences in demographic characteristics among pregnant women between

regions and countries, and different diagnostic traditions. We do however think that our main findings – an association between specific signs of chorioamnionitis and neonatal complications – may be generalizable to other populations.

Interpretation

Our results pin-point the difficulties in identifying clinical tools of timely prediction of adverse neonatal outcomes associated to chorioamnionitis. We observed a strong association between highest measured CRP and positive cervical culture with neonatal infection. Importantly, it reflects the dynamic nature of CRP, with a characteristic slow increase in response to inflammation. Thus, CRP has limited usefulness in predicting neonatal outcomes prior to delivery. Likewise, the result from a cervical culture will similarly take at least 24 hours to be analyzed. Nevertheless, our findings underline the importance of prioritizing a continuous collaboration between obstetric and neonatal care extending past the delivery time point to communicate emerging maternal symptoms which could affect neonatal care.

CONCLUSION

In conclusion, we found that in addition to maternal fever, fetal and maternal tachycardia, elevated leukocyte count and CRP were common findings in term deliveries complicated by chorioamnionitis. Elevated inflammatory markers were associated with both neonatal infection and asphyxia-related complications, and fetal tachycardia additionally predicted asphyxia-related complications. Our findings highlight the importance of a close collaboration between obstetric and neonatal care extending past delivery to detect maternal dynamic laboratory changes which could impact neonatal outcomes.

ADDITIONAL INFORMATION

Disclosure of Interests

None of the authors have any conflicts to declare

Contribution to Authorship

All authors contributed substantially to this study.

Details of Ethics Approval

This study was approved by the Swedish Ethical Review Authority.

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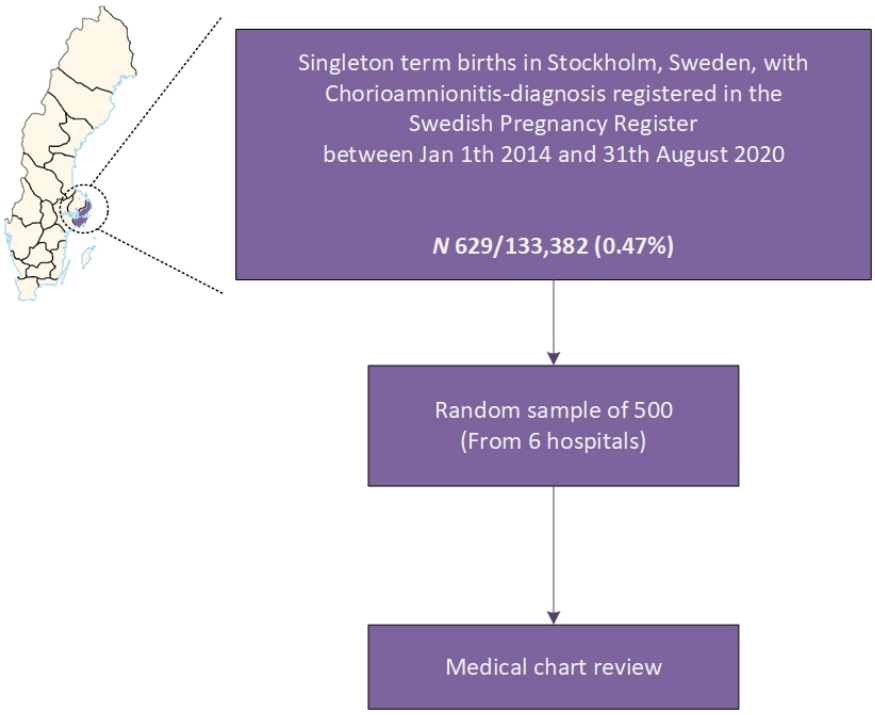
TABLES AND FIGURES

Figure 1 . Overview study-population and case-selection



Tables 1. Baseline information on study population consisting of 500 term deliveries complicated by chorioamnionitis

	Number (%)
Maternal age at delivery	
Mean ± SD	31.5 ± 5.2
< 25 years of age	56 (11.2)
– 30 years of age	138 (27.6)
31-35 years of age	177 (35.4)
> 35 years of age	129 (25.8)
Parity	
0	396 (79.2)
1	82 (16.4)

[?] 2	22 (4.4)
BMI, kg/m^2	
Underweight (<18.5)	9 (1.8)
Normal (18.5-24.9)	243 (48.6)
Overweight (25.0-29.9)	149 (29.8)
Obese ([?]30.0)	72 (14.4)
Missing	27 (5.4)
Educational level*	
< 9 years of schooling	7 (1.4)
9-12 years of schooling	156 (31.2)
>12 years of schooling	254 (50.8)
Missing or not specified	83 (16.6)
Smoking early pregnancy	
Yes	15 (3.0)
No	467 (93.4)
Missing	18 (3.6)
Pre-pregnancy comorbidities+	
Diabetes mellitus	5 (1.0)
Essential hypertension	1 (0.2)
Recurrent UTI	66 (13.2)
Pregnancy complications++	
Gestational diabetes	28 (5.6)
Pregnancy-induced hypertensive disorders	49 (9.8)
UTI	12 (2.4)
PROM	8 (1.6)
SD, Standard deviation; BMI, Body Mass Index; UTI, Urinary Tract Infection; C/D, Cesarean delivery; PROM, Premature rupture of membrane *Based on self-reported data from the Swedish Pregnancy Register +Based on self-reported information registered in the Swedish Pregnancy Register. Data on diabetes mellitus and recurrent UTI missing on 14 individuals and data on hypertension missing on 16 individuals. ++Based on registered ICD-10 diagnostic code in the Swedish Pregnancy Register	SD, Standard deviation; BMI, Body Mass Index; UTI, Urinary Tract Infection; C/D, Cesarean delivery; PROM, Premature rupture of membrane *Based on self-reported data from the Swedish Pregnancy Register +Based on self-reported information registered in the Swedish Pregnancy Register. Data on diabetes mellitus and recurrent UTI missing on 14 individuals and data on hypertension missing on 16 individuals. ++Based on registered ICD-10 diagnostic code in the Swedish Pregnancy Register

Table 1. Continued

Delivery characteristics
Gestational length
Early term (37+0-38+6/7)
Full term (39+9-40+6/7)
Late term (41+0-41+6/7)
Post term (42+0 and beyond)
Labor start
Spontaneous
Medically induced
Cesarean delivery before labor onset
Delivery Mode

Vaginal, non-instrumental
Vaginal, instrumental
Cesarean delivery
SD, Standard deviation; BMI, Body Mass Index; UTI, Urinary Tract Infection; C/D, Cesarean delivery; PROM, Premature

Table 2. Clinical characteristics of 500 term deliveries complicated by chorioamnionitis

Clinical parameters
Temperature
Mean ± SD
No temperature [?] 38.0degC
1 temperature between 38.0-38.9°C
Temperature 38.0-38.9°C [?]30 minutes
1 temperature [?] 39.0°C
Maternal tachycardia[a]
Fetal tachycardia[b]
Leukocyte count, first[c]
14.7
14.8-19.2
>19.2
Leukocyte count, highest[c]
17.0
17.1-21.5
>21.5
CRP, first[d]
33
34-109
>109
CRP, highest[d]
147
148-232
>232
Maternal malaise[e]
Uterine tenderness[e]
Cervical discharge[e]
Foul smelling amniotic fluid[e]
Meconium-stained amniotic fluid[e]
Microbiology and pathology
Positive cervical culture
Confirmed placental histopathology
Intravenous antibiotics

SD, standard deviation; CRP, C-reactive protein [a]Maternal tachycardia defined as maternal heart rate [?]100 bpm during e

Table 3. Neonatal and maternal outcomes among 500 study participants with term delivery complicated by chorioamnionitis

Neonatal
Apgar score < 7 at 5 minutes
Apgar score < 4 at 5 minutes

Neonatal infection[a]
Asphyxia-related comorbidities[b]
Meconium aspiration
Respiratory distress syndrome
Hypoxic ischemic encephalopathy
Seizures/convulsions
Jaundice
Hypoglycemia
Any of above
Fetal acidemia, umbilical artery[c]
Maternal
Postpartum hemorrhage[d]
[a]Including congenital pneumonia, sepsis, urinary tract infection, skin infection, umbilical infection and unspecified infections

Table 4. Clinical chorioamnionitis predictors of adverse neonatal outcomes in study participants with chorioamnionitis. Crude and adjusted Odds ratios with corresponding 95% confidence intervals.

	Chorioamnionitis = 500 No neonatal infection N 448	**Chorioamnionitis = 500 Neonatal infection[a] N 52**	**OR (95% CI) Crude**
No temp. [?]38.0°C	48 (10.7)	6 (11.5)	*Reference (1.0)*
1 temp 38.0-38.9°C	400 (89.3)	46 (88.5)	0.92 (0.37-2.27)
Temp 38.0-38.9°C [?]30 minutes	211 (47.1)	31 (59.6)	1.66 (0.92-2.97)
1 temp [?] 39.0°C	104 (23.2)	10 (19.2)	0.79 (0.38-1.62)
Leukocyte count first			
14.7	137/395 (34.7)	12/48 (25.0)	*Reference (1.0)*
14.8-19.2	121/395 (30.6)	24/48 (50.0)	**2.26 (1.09-4.72)**
>19.2	137/395 (34.7)	12/48 (25.0)	1.00 (0.43-2.30)
Leukocytes, highest			
17.0	131/395 (33.2)	15/48 (31.3)	*Reference (1.0)*
17.1-21.5	131/395 (33.2)	18/48 (37.5)	1.2 (0.58-2.48)
>21.5	133/395 (33.7)	15/48 (31.3)	0.98 (0.46-2.09)
CRP first			
33	128/384 (33.3)	15/47 (31.9)	*Reference (1.0)*
34-109	132/384 (34.4)	13/47 (27.7)	0.84 (0.39-1.84)
>109	124/384 (32.3)	19/47 (40.4)	1.31 (0.64-2.69)
CRP, highest			
147	136/384 (35.4)	7/47 (14.9)	*Reference (1.0)*
148-232	129/384 (33.6)	16/47 (34.1)	**2.41 (0.96-6.05)**
>232	119/384 (31.0)	24/47 (51.1)	**3.92 (1.63-9.42)**
Fetal tachycardia	291/441 (66.0)	41/52 (78.9)	1.91 (0.96-3.84)
Positive cervical culture	113/316 (35.7)	20/36 (55.6)	**2.25 (1.20-4.51)**

[a] Including congenital pneumonia, sepsis, urinary tract infection, skin infection, umbilical infection and unspecified infections during the neonatal period bade on registered ICD-10 codes in the Swedish Pregnancy Register.[b] Adjusted for maternal age at delivery, maternal early pregnancy BMI, maternal smoking and parity

Table 4. Continued

	Chorioamnionitis = 500	**Chorioamnionitis = 500**

	No neonatal asphyxia-related condition N 390	**Neonatal asphyxia-related co**
No temp. [?] 38.0°C	44/390 (11.3)	10/110 (9.1)
1 temp 38.0-38.9°C	346/390 (88.7)	100/110 (90.9)
Temp 38.0-38.9°C [?]30 minutes	184/390 (47.2)	58/110 (52.7)
1 temp [?] 39.0°C	89/390 (22.8)	25/110 (22.7)
Leukocyte count first		
14.7	114/343 (33.2)	35/100 (35.0)
14.8-19.2	107/343 (31.2)	38/100 (38.0)
>19.2	122/343 (35.6)	27/100 (27.0)
Leukocyte count, highest		
17.0	112/343 (32.7)	34/100 (34.0)
17.1-21.5	120/343 (35.0)	39/100 (29.0)
>21.5	111/32.4 (32.4)	37/100 (37.0)
CRP, first		
33	116/333 (34.8)	27/98 (27.6)
34-109	114/333 (34.2)	31/98 (31.6)
>109	103/333 (30.9)	40/98 (40.8)
CRP, highest		
147	119/333 (35.7)	24/98 (24.5)
148-232	111/333 (33.3)	34/98 (34.7)
>232	103/333 (30.9)	40/98 (40.8)
Fetal tachycardia	250/384 (65.1)	82/109 (75.2)
Positive cervical culture	102/277 (36.8)	31/75 (41.3)

[a] Including meconium aspiration, respiratory distress syndrome, hypoxic ischemic encephalopathy, seizures/convulsions, jaundice and hypoglycemia based on registered ICD-10 codes in the Swedish Pregnancy Register and fetal acidemia in the umbilical artery. [b] Adjusted for maternal age at delivery, maternal early pregnancy BMI, maternal smoking and parity