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The Influence of Asymptomatic Cervical Bacterial Colonisation in Third Trimester of Pregnancy

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Abstract

Objective: To determine the impact of cervical bacterial colonization during the third trimester of pregnancy on maternal and neonatal morbidity during the postpartum period.

Materials and methods: 1676 pregnant women were allotted to one of two study groups according to the gestational age at parturition (preterm labor - 195 patients vs. full-term labor - 1481 patients). Microbiological samples were collected from the cervices of mothers, as well as from the gastric and ear secretions of newborns. The following variables were cross-analyzed: the presence of cervical colonisation, type of birth, neonatal weight and the need for neonatal respiratory birth support.

Results: Cervical bacterial colonisation during the third trimester of pregnancy was detected in 16.4% of preterm labor patients and 18.7% of full-term labor patients. Premature neonates with mothers with positive cervical cultures were twice as likely as full-term neonates to be colonised with the same pathogens as their mothers (OR= 2.4). Premature neonates with positive cultures were also three times as likely to weigh under 2000 grams at birth (OR = 3.4). The weights of full-term newborns with positive gastric and ear secretions and those of full-term newborns with negative secretions were comparable.

Conclusions: No correlation exists between the microbial agents isolated from the maternal cervix and those isolated from full-term neonates. Maternal cervical colonization impacts neither birth weight, nor neonatal morbidity. In conclusion, pregnant women who are not at risk for premature birth do not seem to require routine third-trimester screening for pathogens other than Group B Streptococci.

Keywords: Cervical colonization; Prematurity; New borns; Morbidity

Introduction

Lower genital tract infections appear in 10 - 20% of all pregnant women and are frequently associated with a higher risk of premature birth [1]. Most lower genital tract infections are asymptomatic and go undiagnosed in the absence of screening tests. Normal cervico-vaginal flora plays a crucial role in the defense against the growth and ascension of pathogens. The production of lactic acid and hydrogen peroxide by lactobacilli is also a notable local defense mechanism [2]. During pregnancy, any imbalance in the vaginal flora favors the Colonisation of the uro-genital system by microorganisms, which in turn may lead to complications with the pregnancy itself [3].

Prematurity and low birth weight represents the most important causes of neonatal death. 40% of all premature births are statistically associated with an infectious cause [4]. Studies which analyze the types of bacterial infections most often associated with premature birth, as well as the optimal moment at which infection should be diagnosed, have reached a varied palette of conclusions. The meta-analyses of randomized trials which have been carried out so far have been negatively influenced by the heterogeneity of the groups of patients included in these trials. These meta-analyses have failed to demonstrate that local or oral treatment of genital infections may reduce of the risk of premature birth or influence perinatal morbidity [5]. Based on these findings, numerous prenatal care guides do not recommend routine screening for lower genital tract infections during pregnancy [6]. The Centers for Disease Control and Prevention (CDC) in the USA recommend local applications of clindamycine or metronidazole only in the case of symptomatic bacterial infections

of the lower genital tract in pregnancy [7]. However, it has been statistically demonstrated that the treatment of these infections in asymptomatic patients does not reduce the risk of premature birth, regardless of whether the patient is already at risk for this condition [8,9].

The objective of the present paper is to analyze the influence of bacterial Colonisation of the uterine cervix upon the pregnancy itself, as well as upon the development of the neonate. Thus, in order to demonstrate the necessity of third-trimester diagnosis for lower genital tract infections, we set out to determine the relationship between the presence of cervical bacterial Colonisation during the third trimester of pregnancy and maternal and neonatal morbidity during the postpartum period. The relationship between premature birth and bacterial Colonisation of the cervix was additionally analyzed in order to establish whether the latter acts as a risk factor for the former.

Materials and Methods

The present study involved 1676 pregnant women admitted to the high-risk maternity ward of Saint Pantelimon Clinical Hospital (affiliated with the *Carol Davila* University of Medicine and Pharmacy of Bucharest, Romania) between January 10th and December 30th 2011.

Two study groups were created: a preterm labor group consisting of 195 patients under 36.6 weeks gestation (according to the date of the patient's last menstrual period of and / or first trimester ultrasound) and a full-term labor group, which consisted of 1481 patients with a gestational age ranging between 37 and 42 weeks. All the patients were personally consulted by one of the researchers involved in this study and were included in the study only after signing the appropriate informed consent forms. Each patient underwent a gynecological examination and cervical samples were collected at the time of admission into the maternity ward for microbiological study. These cervical samples were inoculated on both soy agar with 5% Sheep Blood (for B group Streptococci) and on Bromthymol-Blue Lactose Agar (BBLA). Samples were prelevated at birth from the gastric and ear secretions of newborns and were subsequently inoculated on both soy agar with 5% Sheep Blood and on BBLA. Newborns with infected mothers were also screened for neonatal inflammatory syndrome via full blood count (FBC) and C-reactive protein levels (CRP).

Data were collected, introduced into a database and analyzed using the statistical program GraphPad Prism 6.0b. A analysis of the data was completed by constructing frequency tables for various socio-demographic factors. The following variables were cross-analyzed: the presence of cervical Colonisation in patients with full-term or preterm labor, type of birth, newborn weight and the need for neonatal respiratory birth support. Pearson's Chi-Square test and Yates' corrections were used to identify differences among the variables. A statistical significance level of $p<0.05$ was adopted for all tests.

Patients with cervical cultures which were positive for bacterial infection were evaluated for complications along with their newborns.

This study was approved by the ethics committee of the Faculty of Medicine of the *Carol Davila* University of Medicine and Pharmacy of Bucharest, Romania.

Results

The socio demographic analysis of the patients' data indicated that in the preterm delivery group consisting of 195 patients, 78.9% women were married, 22.5% were smokers and that the average age was 23. In the full-term delivery group consisting of 1481 patients, 85.14% patients were married, 29.3 % were smokers and the average age was 25. No statistically significant differences of the socio demographic variables were therefore observed between the two study groups (**Table 1**).

The rate of preterm labor was 11.6% in the study group. The incidence of cervical bacterial Colonisation during the third trimester of pregnancy was 16.4% in the preterm labor group and 18.7% in the full-term labor group.

A number of pathogenic agents were identified in the cervical secretions of both women with preterm and full-term labor, as well as in newborn gastric and aural secretions: Escherichia coli, Enterococcus sp. and Staphylococcus aureus. The pathogenic agent which was most frequently isolated from cervical secretions was Group B Streptococcus (37.9%). The procentual distribution of the various species of bacteria isolated from the cervical secretions of mothers and the gastric and aural secretions of newborns are presented in **Table 2**.

The correlation between maternal cervical and fetal infection

Table 1 Sociodemographic characteristics of the patients.

Sociodemographic variables	Preterm labor group (n=195)	Full-term labor group (n=1481)	p
Age n (SD)	23 (6.5)	25 (7.4)	1.000
Married n (%)	154 (78.9)	1261 (85.14)	
Smoker n (%)	43 (22.05)	435 (29.3)	
Number of prenatal consults n	4	7	

Table 2 Pathogenic agents identified by microbiological examination in pregnant women and neonates.

N	Preterm labor group (n=195)		Full-term labor group (n=1481)	
n% cultures positive for:	Neonates (28/14.3)	Mothers (32/16.4)	Neonates (259/18.7)	Mothers (277/18.7)
Enterococcus sp. (%)	10.7	25	5.4	17.3
Escherichia coli (%)	46.4	37.5	55.2	30.3
Staphylococcus aureus (%)	42.8	37.5	38.9	11.5
Klebsiella sp. (%)	-	-	-	2.8
Group B Streptococcus (%)	-	-	0.3	37.9

appeared in 21.8% cases from the preterm labor group and in 9% of cases from the full-term labor group. Premature neonates whose mothers have positive cervical cultures are twice as likely as full-term neonates to be colonized with the same agents as their mothers - OR=2.495; 95% CI (1.1-5.1). The risk of isolating the same pathogen from both the cervical secretions of the mother and the gastric and aural secretions of the neonate was insignificantly higher in vaginal birth compared to birth by Caesarean section - OR=1.6; 95% CI (0.7 – 3.7).

The identification of bacterial pathogens in the gastric and aural secretions of the neonates was inconstantly associated with clinical and Para clinical signs of inflammation. CRP was elevated in 50% of premature newborns and in 45% of full-term newborns with positive cultures. Clinical and Para clinical signs of infection were identified in 4.6% of full-term neonates. However, targeted antibiotic therapy was initiated in all cases of newborns with positive gastric and aural cultures.

Premature newborns with positive cultures required respiratory support in 25% of cases (7 patients), whereas 7.7% of full-term newborns (20 cases) needed respiratory support through continuous positive airway pressure (CPAP) or endotracheal intubation (ETI). 39.2% of neonates (102 patients) were treated with oxygen therapy. Premature newborns with positive gastric and aural cultures were more than three times as likely to require ventilator support compared to full-term newborns - OR=3.9; 95% CI (1.504 – 10.50), p=0.008.

No correlation could be made between maternal cervical bacterial Colonisation and low birth weight in full-term infants (under 3000 g) - OR=0.9; 95% CI (0.7-1.2). The presence of cervical bacterial Colonisation was not associated with a risk of low birth weight in preterm infants (under 2000 g). The analysis of the correlation between the presence of positive gastric and aural cultures in neonates and the risk of low birth weight shows that premature neonates with positive cultures are twice as likely to weigh under 2000 g at birth - OR=3.4; 95% CI (1.4 - 7.9). The weight of full-term newborns with positive gastric and aural secretions and that of full-term newborns with negative secretions were comparable (**Table 3**).

Maternal postpartum evolution was mainly free of complications, with the exception of one patient with an asymptomatic cervical E. coli infection who developed puerperal endometritis after Caesarean section. One premature newborn (born at 34 weeks and weighing 2100 g) developed sepsis with Escherichia coli. The neonate's mother had negative cervical cultures and her membranes had ruptured 6 hours before birth.

Discussion

Routine third-trimester diagnosis for cervical bacterial Colonisation is not recommended by routine prenatal care guides, as it has not been proven that the treatment of these infections can reduce the risk of premature birth [3]. The present study did not find any correlation between asymptomatic cervical bacterial Colonisation diagnosed in the third trimester of pregnancy and a higher risk of premature birth. Pregnant patients with positive cervical cultures in the third trimester of pregnancy did not have a higher risk of giving birth prematurely - OR=0.8; 95% CI (0.6 – 1.2).

Group B Streptococcus proved to be pathogen most frequently isolated pathogen from the cervical cultures of women with preterm, as well as full-term labor. However, routine screening for group B streptococcus is included in most prenatal care guides due to the high risk of fetal morbidity which it carries. This is not the case of most microbes which can colonize the lower genital tract during pregnancy. Cervical infections with Group B Streptococci were therefore taken into consideration only in the general tally of microbial agents isolated from the mother and newborn, but not in correlation to maternal and neonatal morbidity.

In the premature labor group, there was a significant correlation between the microbial agents which were isolated from maternal cervical cultures and those isolated from neonatal gastric and aural cultures, as both mother and newborn were twice as likely to be colonized with the same agent than those in the full-term group (p=0.03). This can be explained by the presence of a latent cervical infection during the second trimester of pregnancy, which can infect the fetus even through intact membranes [10].

The presence of gastric and aural bacterial Colonisation in neonates is more frequently associated with the development of neonatal infection in premature infants (25%). Premature neonates with positive microbiological gastric and aural cultures are three times as likely to require ventilator support in comparison with full-term neonates (p=0.008).

In the case of full-term neonates, there is an insignificant correlation between microbial agent prelevated from the mother's uterine cervix and the agent present in the gastric and aural cultures taken from the infant. 5% of the newborns with positive cultures have no altered Para clinical parameters.

Positive cervical cultures are not associated with low birth weight (under 3000 g in the case of full-term neonates and under 2000 g in the case of premature neonates). However, the presence of gastric and aural positive cultures is associated with low birth weight (under 2000 g) in premature infants (p=0.005). There is

Table 3 The correlation between birth weight and the results of the microscopic examination of maternal and neonatal cultures.

	Premature neonates				Full-term neonates			
Birth weight (n)	<2000 g (42)	2000-2500 g (153)		p	<3000 g (578)	>3000 g (903)		p
Positive cervical cultures (n/%)	4 (9.5 %)	28 (18.3%)	OR=0.46 95% CI (0.15 - 1.4)	0.2	86 (15.5 %)	191 (20.7%)	OR = 0.9 95% CI (0.7-1.2)	0.5
Positive gastic / aural cultures (n/%)	12 (28.5%)	16 (57.1%)	OR=3.4 95% CI (1.4 - 7.9)	0.005	51 (19.6 %)	208 (22.5%)	OR = 0.3 95% CI (0.23-0.44)	<0.001

no correlation between low birth weight and the presence of positive gastric and aural cultures in full-term infants ($p < 0.001$). These statistical results do not indicate a correlation between low birth weight and cervical bacterial Colonisation. Gastric and aural bacterial Colonisation of the neonate only affects the birth weight of premature newborns.

Depending on the modality of birth, the risk of isolating the same pathogen from the secretions of the mother and those of the newborn is significantly higher in vaginal birth than in the case of birth by Caesarean section. Delivery by Caesarean section does not exclude the risk of contamination of newborns with mothers with positive cervical cultures. Likewise, one cannot exclude the possibility of persistent cervical Colonisation present from the second trimester of pregnancy onwards and the subsequent antepartum Colonisation of the fetus through the ascension of the microbes through the mother's genital tract and their penetration through intact membranes [11]. Studies which have evaluated the vaginal micro flora of pregnant and non-pregnant women have demonstrated the episodic presence of Escherichia coli, Enterococcus sp., Staphylococcus aureus throughout pregnancy [12,13]. The microbial Colonisation of premature newborns influences their evolution by making the necessity for ventilator support and prolonged hospitalization in the neonatal intensive care unit more likely.

Given these data, one can only recommend the careful selection of patients at great risk for premature birth and their screening for cervical bacterial Colonisation beginning with the second trimester of pregnancy. Knowing that there is a frequent and significant correlation between the bacteria isolated from the cervix of the mother and those found in the gastric and aural secretions of her newborn, the collection of routine cervical samples upon admission to obstetrical wards is also recommended in this particular category of patients.

Pregnant women who are not at risk for premature birth do not require routine screening during the third trimester for the detection of cervical bacterial Colonisation. However, the detection of Group B Streptococcus in the lower genital tract of pregnant women is mandatory, as the significant impact of this pathogen on neonatal morbidity is very as already been proven. This study supports this conclusion by asserting that there is no correlation between the microbial agents isolated from the maternal cervix and those isolated from full-term neonates. There is also no impact of maternal cervical Colonisation on birth weight and the presence of neonatal morbidity. The detection of microbial cervical agents during the third trimester in patients who are not at risk for premature birth does not need to be followed by local or systemic treatment, because it has no impact upon neonatal morbidity.

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