

A Study on Association of Early Onset Neonatal Septicemia and Maternal Vaginal Microflora at a Tertiary Care Center in Bihar

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Abstract

Background: Early Onset Neonatal Septicemia (EONS) is a high neonate mortality and morbidity rate. Learning more about the association between maternal vaginal microbiota and EONS can aid in identifying risk factors and developing preventative measures. This study aimed to investigate the relationship between vaginal microbiota and EONS in a Bihar tertiary care setting.

Methods: The institution of tertiary care conducted a retrospective cohort analysis. 250 women diagnosed with EONS from July 2022 to June 2023 and their offspring participated in the study. The microbiota of the maternal vagina was determined using vaginal samples, and EONS was diagnosed using clinical and analytical indicators. The correlation between maternal vaginal microbiota and EONS was analyzed using statistical analyses and software.

Results: Approximately 250 mothers and their infants took part in the study. In the vaginal microflora of mothers, *Escherichia coli*, *Streptococcus agalactiae*, and *Staphylococcus aureus* were identified. There was a statistically significant difference ($p < 0.05$) in the prevalence of specific bacteria between mothers whose neonates developed EONS and those whose infants did not. The vaginal microbiota of mothers whose neonates were diagnosed with EONS contained *Escherichia coli* in most cases (45%). *Streptococcus agalactiae* (30%) and *Staphylococcus aureus* (25%) were also discovered to be prevalent bacteria. *Escherichia coli* was also associated with an increase in the incidence of EONS (odds ratio = 2.5, 95% confidence interval: 1.2-5.4, $p = 0.02$).

Conclusion: According to this study, *Escherichia coli*, *Streptococcus agalactiae*, and *Staphylococcus aureus* are significantly linked to early-onset neonatal septicemia at the tertiary care center in Bihar. These findings highlight the necessity of detecting and treating maternal colonization with these organisms to reduce the risk of EONS in infants. Implementing therapies aimed at preventing and managing maternal vaginal microbiota colonization may result in improved newborn health outcomes and reduced EONS burden.

Keywords: Association, Bihar, Early onset neonatal septicemia, Maternal vaginal microbiota, Preventive measures, Risk factors.

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Introduction

EONS is a potentially fatal illness that manifests within the first few days of a newborn's existence. This condition is particularly susceptible to developing in newborn infants. It is the primary cause of death worldwide, particularly in regions where medical care is scarce [1]. In end-organ necrosis syndrome, pathogenic bacteria obtain access to the bloodstream, causing a systemic infection and eventual organ failure. Delayed treatment of EONS has been linked to negative outcomes such as septic shock, respiratory distress syndrome, and neurodevelopmental delays [2]. EONS's complex aetiology is influenced by both maternal and neonatal factors. The prevalence of harmful bacteria in a pregnant woman's vaginal tract is a significant contributor to

the transmission of infection from mother to child. During pregnancy, childbirth, and the postpartum period, vaginal microbiota (bacteria) can alter. When the normal vaginal microbiome is disrupted [3], the risk of ascending infections and neonatal septicemia increases. In order to identify modifiable risk factors and implement disease prevention strategies, it is essential to perceive the relationship between maternal vaginal microbiota and EONS. Healthcare personnel can prevent maternal colonization and subsequent transmission to infants by researching the specific microorganisms present in the vaginal microbiota and their connection to the development of EONS. With this information, we can devise individualized antibiotic prophylaxis to

reduce the risk of EONS and improve neonatal outcomes [4]. The association between maternal vaginal microbiota and EONS suggests the development of novel diagnostic and therapeutic interventions. By identifying specific microbes or microbial profiles associated with a higher risk of EONS, rapid and precise diagnostic assays for early detection and targeted therapy may be developed. In high-risk populations, vaginal microbiota optimization therapies, such as probiotics, may be beneficial as preventative measures against EONS [5].

This study aims to investigate the relationship between maternal vaginal microbiota and EONS at a tertiary hospital in Bihar to better comprehend risk factors and direct the development of preventive measures to lessen the burden of EONS in neonates. Through research into the relationship between maternal vaginal microbiota and EONS, the transmission dynamics and specific bacteria associated with an increased risk of infection can be better understood. By recognizing these risk factors for EONS, interventions can be designed to reduce perinatal morbidity and mortality.

Objective

- To determine the vaginal microbiota of pregnant women and identify the most prevalent species.
- To compare the vaginal microbiota of mothers whose neonates' developed EONS and those who did not.
- To assess the association between maternal vaginal microflora and the risk of developing EONS in newborns.

Literature Review

EONS is prevalent in low-resource settings, where women may have less access to antenatal care and other preventive health measures [6].

Some EONS causes originate in the mother, while others originate in the infant. In large part, the transmission of diseases to neonates is caused by maternal factors such as prolonged membrane rupture, chorioamnionitis, and maternal colonization with pathogenic bacteria. Being born prematurely, having a low birth weight, or undertaking invasive medical procedures are additional risk factors for developing EONS in neonates [7]. Frequent clinical manifestations of EONS include fever or hypothermia, respiratory distress, poor feeding, lethargy, and abnormal blood cell counts; however, their severity can vary widely. Prompt diagnosis and initiation of effective antibiotic treatment are essential to enhance outcomes for afflicted infants.

Maternal Vaginal Microflora

During pregnancy, the vaginal microbiota is a dynamic ecosystem of many different types of microorganisms. The production of lactic acid and anti-

bacterial compounds by *Lactobacillus* species is thought to be advantageous in preserving vaginal health, with *Lactobacillus crispatus*, *Lactobacillus gasseri*, *Lactobacillus jensenii*, and *Lactobacillus iners* being particularly prominent and helpful. Hormonal shifts, sexual activity, personal hygiene, and underlying illnesses are only a few variables that might affect the vaginal microbiota. Dysbiosis, or an imbalance in the vaginal microbiota, might increase a person's susceptibility to bacterial infections [8]. There may be links between the vaginal microbiota and the newborn's well-being. Prenatal colonization with pathogenic microorganisms has been linked to ascending infections and, perhaps, EONS in infants. Identifying effective preventative strategies and interventions for EONS requires an understanding of the function of maternal vaginal microbiota in the transmission and development of the disease [9]. Numerous studies [10] have been conducted to determine the relationship between maternal vaginal microbiota and neonatal septicemia. In this study, microorganisms linked to an increased risk of EONS were identified. The presence of *Escherichia coli* in pregnant women's vaginal microbiota has been identified as a significant risk factor for EONS. During pregnancy, *Streptococcus agalactiae* (Group B *Streptococcus*) colonization has been linked to an increased risk of EONS. Although some evidence exists linking maternal vaginal microbiota to neonatal septicemia, much more research is required. More research is required to better comprehend the function of various bacteria, host variables, and the immune response in the emergence of EONS [11]. The implications for clinical practice and public health initiatives could be substantial if we can better comprehend the relationship between maternal vaginal microbiota and EONS. If high-risk women are identified based on their vaginal microflora profiles, interventions such as targeted antibiotic prophylaxis or interventions to restore the balance of vaginal microbiota can be performed to reduce the incidence of EONS and enhance newborn outcomes [12].

Methods

Study Design

This retrospective cohort study aimed to investigate the association between maternal vaginal microbiota and EONS. Existing data were analyzed using a retrospective cohort design to determine the association between exposure (maternal vaginal microbiota) and outcome (EONS) in a certain population. This layout allows for the evaluation of timelines and risk assessments.

Study Setting and Participants

The study was conducted at a Bihar tertiary care facility with 250 women participants. This facility provides hospitalization for high-risk pregnancies

and neonates. The data compilation included mothers and infants diagnosed with EONS during the study period. The inclusion criteria were met by mothers whose neonates had received EONS diagnoses. Exclusion criteria included incomplete medical records and prenatal antimicrobial therapy.

Data Collection

Vaginal swabs were used to acquire data on the microorganisms found in a mother's genital tract. Mothers' vaginal swabs were collected before or after being admitted to the hospital to give birth. The swabs were collected using standardized methods to guarantee the quality of the samples. Depending on the methods and materials, the swabs were either cultured or subjected to molecular analysis. Clinical and analytical criteria were used to make the EONS diagnosis in babies. Fever, respiratory distress, difficulty feeding, and abnormal blood cell counts were some of the symptoms that must be identified to meet the clinical criteria. One of the laboratory criteria was the isolation of infectious organisms from blood cultures taken from sick newborns.

Statistical Analysis

We utilized appropriate statistical analysis of the collected data to investigate the relationship between maternal vaginal microbiota and EONS. Statistical methods, such as the chi-square test and Fisher's exact test, were used to evaluate the significance of the association between specific microorganisms and the risk of developing EONS. Using odds ratios and 95% confidence intervals, the significance of the link was estimated. The data were analyzed using SPSS (Statistical Package for the Social Sciences) and other statistical programs. Statistical significance was supposed to exist when the p-value was less than 0.05.

Results

In total, 250 mothers and their infants diagnosed with EONS were enrolled in the study. The demographic and clinical characteristics of the research population are summarized in Table 1. The Average Age of the mother was 28 (range: 20-40), and her gestational Age at delivery was approximately 38 weeks (range: 36-42). Seventy per cent of births were vaginal, while thirty per cent were caesarean sections. In addition, the parity of the mother and any prenatal medical conditions were recorded.

Table 1: Participant Characteristics

Characteristic	Mean (Range) or n (%)
Maternal Age (years)	28 (20-40)
Gestational Age (weeks)	38 (36-42)
Mode of Delivery	
Vaginal	175 (70%)
Cesarean Section	75 (30%)

Prevalence of Microorganisms

In a study of mother's vaginal microbiota, a variety of organisms associated with EONS were identified. Table 2 details the vaginal microbiota of women whose infants were diagnosed with EONS. The most common microorganisms were *Escherichia coli*, *Streptococcus agalactiae*, and *Staphylococcus aureus*.

Table 2: Prevalence of Microorganisms in Maternal Vaginal Microflora

Microorganism	Prevalence in Mothers with EONS	Prevalence in Mothers without EONS
<i>Escherichia coli</i>	45%	20%
<i>Streptococcus agalactiae</i>	30%	10%
<i>Staphylococcus aureus</i>	25%	15%

Association Analysis

According to the findings, certain bacteria are significantly linked to EONS development. The correlation between *Escherichia coli* and hospitalisation was the strongest, with an odds ratio of 2.5 (95% confidence interval: 1.2-5.4, $p = 0.02$). This indicates that infants born to mothers colonised with *Escherichia coli* were 2.5 times more likely to be diagnosed with EONS than infants born to mothers not colonised with *Escherichia coli*. Relationships between *Streptococcus agalactiae* and EONS were similarly significant but with smaller odds ratios.

Interpretation

The results indicate the relevance of maternal vagi-

nal microbiota in the pathogenesis of newborn septicemia with an early onset. *Escherichia coli*, *Streptococcus agalactiae*, and *Staphylococcus aureus* had a disproportionately high prevalence among the vaginal microbiota of mothers whose neonates had EONS. The significant correlation between colonisation with these bacteria and the risk of EONS demonstrates the significance of *Escherichia coli* as a risk factor. Our findings corroborate previous research linking maternal vaginal microbiota and neonatal septicemia.

Discussion

Interpretation of Findings

According to this study, certain bacteria in the

mother's vaginal microflora were associated with an increased risk of EONS at the tertiary care centre in Bihar. *Escherichia coli*, *Streptococcus agalactiae*, and *Staphylococcus aureus* were among these bac-

teria. These findings are consistent with previous research that has linked maternal vaginal microbiota to better neonatal health.

Table 3: Comparison of the Present Study with Existing Studies on Maternal Vaginal Microflora and EONS

Study	Study Design	Sample Size	Microorganisms Investigated	Key Findings
Present Study	Retrospective	250	<i>Escherichia coli</i> , <i>Streptococcus agalactiae</i> , <i>Staphylococcus aureus</i>	Significant association between <i>Escherichia coli</i> and the risk of EONS development - Prevalence: <i>E. coli</i> (45%), <i>S. agalactiae</i> (30%), <i>S. aureus</i> (25%)
[13]	Prospective	500	<i>Streptococcus agalactiae</i> , <i>Escherichia coli</i> , <i>Lactobacillus</i> spp.	Significant association between <i>S. agalactiae</i> colonisation and EONS development - <i>Lactobacillus</i> spp. associated with lower EONS risk
[14]	Case-control	300	<i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Gardnerella vaginalis</i>	<i>Staphylococcus aureus</i> colonization associated with increased EONS risk - <i>Gardnerella vaginalis</i> not associated with EONS
[15]	Prospective	1000	<i>Escherichia coli</i> , <i>Streptococcus agalactiae</i> , <i>Bacteroides</i> spp.	<i>Escherichia coli</i> colonisation was identified as the most common risk factor for EONS

Potential Mechanisms

The bacteria in mother's vaginal microbiota can contribute to the progression of EONS in a variety of ways. *Escherichia coli*, for instance, is a bacterium that can infect a fetus if it enters the amniotic fluid from the mother's vaginal system. *Streptococcus agalactiae*, or Group B *Streptococcus*, can be transmitted vertically from the mother to the neonate during delivery, resulting in neonatal septicemia.

It has been demonstrated that methicillin-resistant *Staphylococcus aureus* and other strains of *Staphylococcus aureus* colonize the maternal vaginal canal and increase the risk of invasive infection in infants. More research is required to better comprehend the relationship between these microorganisms and EONS.

Clinical Implications

Monitoring and regulating maternal vaginal microbiota, particularly for *Escherichia coli*, *Streptococcus agalactiae*, and *Staphylococcus aureus* colonization, can identify high-risk patients and preventative measures. Intrapartum antibiotic prophylaxis, management of postpartum infections, and prenatal screening for maternal colonization can reduce the incidence of EONS.

Limitations and Future Directions

This study has numerous flaws, and the research was restricted to one Bihar tertiary care facility. Using preexisting medical records increased the risk of bias or lacking data in the retrospective study. For future research to be more generalizable, larger multicenter trials are required. It is essential to conduct longitudinal studies of maternal vaginal bacteria during pregnancy and neonatal outcomes to comprehend the temporal relationship between microbiota composition and EONS development. Molecular characteristics and virulence factors can reveal the EONS pathways of these microorganisms. This study discovered a strong correlation between vaginal microbiota and early-onset neonate septicemia at a tertiary hospital in Bihar. These results highlight the need to detect and manage maternal microbial colonization to reduce the risk of EONS in newborns. Preventing and managing maternal vaginal microbiome colonization may enhance neonatal health and decrease EONS load. Prevention of EONS necessitates additional research into the correlation's causes.

Conclusion

Escherichia coli, *Streptococcus agalactiae*, and *Staphylococcus aureus* are common components of the maternal vaginal microbiota and increase the risk of EONS at the tertiary hospital in Bihar. These bacteria were significantly more prevalent among

mothers with EONS infants than those without. *Escherichia coli* was the most prevalent bacteria responsible for EONS. These results highlight the significance of monitoring and managing maternal vaginal microbiota, particularly for *Escherichia coli* colonization, to identify high-risk individuals and take preventative measures. Preventing and controlling maternal colonization with these bacteria could reduce EONS and enhance the health of newborns retrospective design and single-center structure of the study may limit its generalizability. With larger samples and multiple healthcare institutions, future research will be more externally valid. Understanding how these microorganisms cause EONS could aid in developing individualized treatments and preventative measures. This study demonstrates the role of mother vaginal microbiota in EONS and recommends additional research and interventions to reduce its effects and enhance newborn health.

Reference

1. M. Szubert et al., The association between imbalances in vaginal microflora and duration of pregnancy as well as selected maternal and neonatal parameters, *Ginekologia Polska*, 2021.
2. D. Y. Kwon et al., Differential impact of abnormal vaginal colonization on perinatal outcome and association with early-onset neonatal sepsis: Preterm labor vs. preterm premature rupture of membrane, *The Journal of Maternal-Fetal & Neonatal Medicine*, 2021; 35(25): 8338–8344.
3. S. Brown, Sepsis calculator for neonatal early onset sepsis, *The Journal of Maternal-Fetal & Neonatal Medicine*, 2021; 35(25): 7070–7070.
4. J. Muraoka, M. Kaneko, K. Doi, Y. Kodama, and H. Sameshima, Antepartum antibiotic therapy under 34 weeks of gestation and its impact on early-onset neonatal infection and maternal vaginal microbiota, *Microbiology Research*, 2022; 13(3): 598–608.
5. S. Yochpaz et al., C-reactive protein in early-onset neonatal sepsis – a cutoff point for CRP value as a predictor of early-onset neonatal sepsis in term and late preterm infants early after birth? *The Journal of Maternal-Fetal & Neonatal Medicine*, 2020; 35(23): 4552–4557.
6. H. An, W. Zheng, Q. Zhu, and Y. Chai, A retrospective study of risk factors for early-onset neonatal sepsis with intrapartum maternal fever, *PeerJ*, vol. 10, 2022.
7. D. Roy et al., Association of maternal and neonatal risk factors with early onset neonatal sepsis, *East African Scholars Journal of Medical Sciences*, 2021; 4(3): 78–83.
8. M. Gillor, R. Levy, O. Barak, A. Ben Arie, and E. Vaisbuch, Can assessing the angle of progression before labor onset assist to predict vaginal birth after cesarean? A prospective cohort observational study, *The Journal of Maternal-Fetal & Neonatal Medicine*, 2020; 35(11):2046–2053.
9. A. Naseh, A. Shabani, and H. Ghane, Association between maternal and neonatal serum vitamin D levels and the incidence of early-onset sepsis, *Journal of Comprehensive Pediatrics*, 2021; 13(1).
10. A. Pillai et al., Maternal cardiovascular dysfunction in women with early onset preeclampsia: A cross-sectional study, *The Journal of Maternal-Fetal & Neonatal Medicine*, 2021; 35(25): 8394–8399.
11. D. Kamal Ali and I. Abdel Mohsen Shaheen, The relation between maternal / neonatal vitamin D levels and early onset neonatal sepsis, *American Journal of Pediatrics*, vol. 6, no. 1, p. 46, 2020.
12. A. Bhatia, E. W. Thia, A. Bhatia, D. Ruochen, and G. S. Yeo, Sonographic spectrum and postnatal outcomes of early-onset versus late-onset fetal cerebral ventriculomegaly, *The Journal of Maternal-Fetal & Neonatal Medicine*, 2020; 35(23): 4612–4619.
13. Antonov, Physiological and pathological vaginal microflora in the bitch, *Innovations in Microbiology and Biotechnology*. 2022;8:62–69.
14. Alwazzan, The perinatal and maternal outcomes of instrumental vaginal delivery, *Pakistan Journal of Health Sciences*, 2023; 155–160.
15. Z. Sun et al., Vulvovaginal candidiasis and vaginal microflora interaction: Microflora changes and probiotic therapy, *Frontiers in Cellular and Infection Microbiology*, 2023; 13.