

Maternal Infections During Pregnancy and Their Association with Neonatal Sepsis and Developmental Delay: A Longitudinal Observational Study.

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Abstract

Background:

Maternal infections during pregnancy may contribute to adverse neonatal outcomes, while neonatal sepsis may be associated with subsequent developmental impairment.

Objective:

To evaluate the association between maternal infections during pregnancy and neonatal sepsis and to assess the relationship between neonatal sepsis and developmental delay at 6 months.

Methods:

A prospective longitudinal cohort study was conducted at Community Health Centre, Fatehpur, Gaya, Bihar. A total of 150 mother–infant pairs were followed prospectively. Maternal infections diagnosed during pregnancy were documented based on clinical and laboratory findings. Neonatal sepsis was assessed using clinical and laboratory criteria, and infants were followed until 6 months of age for developmental assessment. Associations were evaluated using chi-square and Fisher's exact tests, as appropriate.

Results:

Maternal infection was documented in 42 mothers (28.0%). Urinary tract infection was the most frequent infection (14.0%), followed by respiratory infection (6.7%), genital infection (4.7%), and suspected intra-amniotic infection/chorioamnionitis (2.7%). Neonatal sepsis occurred in 18 infants (12.0%). Sepsis occurred in 21.4% of infants born to mothers with documented infection compared with 8.3% of those without maternal infection ($p = 0.026$). Developmental delay at 6 months was identified in 15 infants (10.0%) and occurred in 27.8% of infants with neonatal sepsis compared with 7.6% without sepsis ($p = 0.012$).

Conclusion:

Maternal infection during pregnancy was associated with neonatal sepsis, while neonatal sepsis was associated with developmental delay at 6 months.

Recommendation:

Early recognition and management of maternal infection, neonatal surveillance, and developmental screening may help identify infants requiring closer follow-up. Larger longitudinal studies are warranted.

Keywords: maternal infection; pregnancy; neonatal sepsis; developmental delay; longitudinal cohort; neonatal outcome; antenatal infection.

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Introduction

Maternal infection during pregnancy represents an important clinical and public-health concern because infection can adversely affect maternal health and may also influence fetal and neonatal outcomes. Maternal sepsis is defined by the World Health Organization as life-threatening organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or the postpartum period. Maternal infection and sepsis remain important contributors to maternal morbidity and mortality and may also increase the likelihood of neonatal infection and other adverse outcomes. [1,2]

Neonatal sepsis is a major cause of neonatal morbidity and mortality worldwide, with the burden being particularly substantial in low- and middle-income countries. Systematic reviews have demonstrated considerable variation in the incidence and burden of neonatal sepsis across populations, reflecting differences in diagnostic definitions, healthcare resources, surveillance systems, and underlying risk factors. [3]

Maternal infection is an established risk factor for early neonatal infection. Infection or colonization of the maternal genital tract may facilitate vertical transmission of microorganisms to the newborn during pregnancy or delivery. Evidence from global systematic reviews has demonstrated an association between maternal colonization and early-onset neonatal infection, particularly for group B streptococcal disease. [4,5]

Among maternal infectious conditions, chorioamnionitis is of particular importance because inflammation of the fetal membranes may expose the fetus to an inflammatory environment before birth. A systematic review and meta-analysis demonstrated that both clinical and histological chorioamnionitis were associated with increased odds of neonatal sepsis, including early-onset sepsis. [6]

Maternal infections may also influence pregnancy outcomes indirectly through preterm birth. Preterm infants have increased susceptibility to infection because of immature immune responses and other physiological vulnerabilities. A systematic review and meta-analysis reported increased risk of preterm birth among pregnancies affected by maternal influenza or SARS-CoV-2 infection. [7]

The possible relationship between maternal infection and later neurodevelopment is more complex. Intrauterine infection and inflammation have been investigated as potential contributors to neurological injury, particularly in relation to cerebral palsy. A systematic review and meta-analysis reported an association between maternal infection during pregnancy and increased risk of cerebral palsy,

although the strength of association varied according to infection type and clinical circumstances. [8]

Evidence also suggests that maternal infection during pregnancy may be associated with selected neurodevelopmental disorders in offspring. A systematic review and meta-analysis reported an association between maternal infection during pregnancy and autism spectrum disorders, although heterogeneity between studies and potential confounding factors should be considered when interpreting these findings. [9]

Neonatal sepsis itself may represent another pathway through which adverse perinatal exposures influence later developmental outcomes. In very preterm infants, a systematic review and meta-analysis found that neonatal sepsis was associated with increased risk of neurodevelopmental impairment. [10]

Despite these observations, evidence directly linking maternal infection during pregnancy with subsequent neonatal sepsis and early developmental delay within the same longitudinal cohort remains comparatively limited, particularly in primary and secondary healthcare settings.

The present study was therefore designed to assess the association between maternal infections during pregnancy and neonatal sepsis and to examine whether neonatal sepsis was associated with developmental delay at 6 months of age.

Materials and Methods

Study Design

A prospective longitudinal cohort study was conducted to evaluate the association between maternal infections during pregnancy and neonatal sepsis and to assess the relationship between neonatal sepsis and developmental delay during early infancy. Maternal infection status was assessed during pregnancy, neonatal outcomes were evaluated after delivery, and infants were followed prospectively until 6 months of age for developmental assessment.

Study Setting

The study was conducted at the Community Health Centre (CHC), Fatehpur, Gaya, Bihar, India. Pregnant women attending the centre for antenatal care were recruited and followed through delivery and subsequent infant follow-up.

Study Duration

The study period included antenatal recruitment, assessment of maternal infections, neonatal evaluation, and follow-up of infants until 6 months of age.

Study Population

The study population comprised pregnant women attending the study centre for antenatal care and their newborn infants.

A total of **150 mother–infant pairs** were included in the study.

Sample Size

The required sample size was calculated using the following single-proportion formula:

$$n = Z^2P(1-P)/d^2$$

where n represents the required sample size, Z is the standard normal deviate corresponding to the selected confidence level, P is the anticipated proportion, and d is the desired precision.

Inclusion Criteria

Pregnant women were eligible for inclusion if they: attended the study centre for antenatal care; had adequate clinical and antenatal information available for assessment; provided informed consent for participation and follow-up; and delivered an infant who could be followed after birth. These criteria are consistent with the current manuscript.

Exclusion Criteria

Participants were excluded if they had: incomplete antenatal or clinical records; inability to complete the required follow-up; or a major fetal congenital anomaly diagnosed before delivery. Infants with major congenital abnormalities independently likely to affect developmental assessment were excluded from the developmental-outcome analysis.

Assessment of Maternal Infection

Maternal infection during pregnancy was considered present when supported by documented clinical findings and/or relevant laboratory investigations recorded during antenatal care. Maternal infection was categorized according to the clinical diagnosis documented in the medical record.

The major infection categories assessed were:

- urinary tract infection;
- respiratory tract infection;
- genital/vaginal infection;
- suspected intra-amniotic infection/chorioamnionitis; and
- other clinically documented maternal infections.

For each participant, the presence or absence of maternal infection and the type of infection were recorded.

Assessment of Neonatal Sepsis

Following delivery, newborns were evaluated for evidence of neonatal sepsis based on the clinical and laboratory criteria used at the study centre. Relevant clinical findings, laboratory investigations, blood-culture results where

available, treatment received, and neonatal outcomes were recorded.

Neonatal sepsis status was categorized as **sepsis present or absent** according to the predefined clinical and laboratory assessment used for the study.

Developmental Assessment

The infants were followed prospectively until 6 months of age. Developmental status was assessed using a standardized developmental screening approach covering the major developmental domains, including:

- gross motor development;
- fine motor development;
- language/communication; and
- social/adaptive development.

Infants who failed the predefined developmental screening threshold were categorized as having **suspected developmental delay** and were considered eligible for further developmental evaluation.

Study Variables

The primary exposure variable was **maternal infection during pregnancy**. The principal neonatal outcome was **neonatal sepsis**, and the developmental outcome was **developmental delay at 6 months of age**.

Additional maternal and neonatal variables recorded included relevant demographic and clinical characteristics available in the study records, including maternal age, gestational characteristics, birth-related variables, and neonatal clinical factors.

Data Collection

Maternal and neonatal information was collected prospectively using a structured data-collection format. Maternal infection status was documented during antenatal care, while neonatal clinical findings and investigations were recorded following delivery. Infants were subsequently followed until 6 months of age for developmental assessment. Data were checked for completeness before statistical analysis.

Bias

Several measures were undertaken to minimize potential sources of bias. Participants were recruited prospectively using predefined eligibility criteria, and maternal infection status was documented using clinical and laboratory information recorded during antenatal care. Neonatal sepsis and developmental outcomes were assessed using predefined clinical and developmental criteria. Data were collected using a structured data-collection format and

checked for completeness before analysis. Prospective follow-up until 6 months was used to minimize recall bias. Potential confounding factors, including gestational age, birth weight, neonatal hypoxia, socioeconomic factors, nutritional status, and other perinatal characteristics, were recognized as potential influences on developmental outcomes. However, residual confounding cannot be excluded.

Statistical Analysis

Categorical variables were summarized using frequencies and percentages. Continuous variables, where applicable, were summarized using mean $\pm$ standard deviation or median with interquartile range, depending on the distribution of the data.

The association between maternal infection and neonatal sepsis was assessed using the **chi-square test and Fisher's exact test, as appropriate**. Similarly, the association between neonatal sepsis and developmental delay at 6

months was assessed using the **chi-square test and Fisher's exact test, as appropriate**.

Where appropriate, the strength of association was expressed using an appropriate effect estimate with a 95% confidence interval. A two-sided p -value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the ethical principles applicable to research involving human participants. Written informed consent was obtained from the participating mothers before enrolment and follow-up.

Result

Maternal Infection Status

A total of **150 mother–infant pairs** were included in the study. Maternal infection during pregnancy was documented in **42 women (28.0%)**, while 108 women (72.0%) had no documented infection. The distribution of maternal infection status is presented in **Table 1**.

Table 1. Maternal infection status

Maternal infection status	Number	Percentage
Infection present	42	28.0
No documented infection	108	72.0
Total	150	100.0

Among the 42 women with documented infection, **urinary tract infection was the most frequent infection**, followed by respiratory, genital/vaginal, and suspected intra-amniotic infection/chorioamnionitis. The pattern of maternal infections is shown in **Table 2**.

Table 2. Pattern of maternal infections

Type of maternal infection	Number	Percentage of total
Urinary tract infection	21	14.0
Respiratory infection	10	6.7
Genital/vaginal infection	7	4.7
Suspected intra-amniotic infection/chorioamnionitis	4	2.7
Total	42	28.0

Neonatal Sepsis

Neonatal sepsis occurred in **18 of 150 infants (12.0%)**. Among infants born to mothers with documented infection, **9 of 42 (21.4%)** developed neonatal sepsis, compared with **9 of 108 (8.3%)** among infants born to mothers without documented infection. This distribution is presented in **Table 3**.

Table 3. Association between maternal infection and neonatal sepsis

Maternal infection	Neonatal sepsis n (%)	No neonatal sepsis n (%)	Total
Present	9 (21.4)	33 (78.6)	42
Absent	9 (8.3)	99 (91.7)	108
Total	18 (12.0)	132 (88.0)	150

Maternal infection was significantly associated with neonatal sepsis ($\chi^2=4.95$, $p=0.026$).

Developmental Outcome at 6 Months

At 6 months of follow-up, **15 infants (10.0%)** were classified as having suspected developmental delay, whereas **135 infants (90.0%)** did not demonstrate developmental delay on screening. The overall developmental status at 6 months is summarized in Table 4.

Table 4. Developmental status at 6 months

Developmental status	Number	Percentage
No developmental delay	135	90.0
Suspected developmental delay	15	10.0
Total	150	100.0

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Association Between Neonatal Sepsis and Developmental Delay

Developmental delay was observed in **5 of 18 infants (27.8%)** who had neonatal sepsis compared with **10 of 132 infants (7.6%)** who did not have neonatal sepsis. The relationship between neonatal sepsis and developmental outcome is presented in Table 5.

Table 5. Association between neonatal sepsis and developmental delay at 6 months

Neonatal sepsis	Developmental delay n (%)	No developmental delay n (%)	Total
Present	5 (27.8)	13 (72.2)	18
Absent	10 (7.6)	122 (92.4)	132
Total	15 (10.0)	135 (90.0)	150

Neonatal sepsis was significantly associated with developmental delay at 6 months ($\chi^2=6.28$, $p=0.012$).

Discussion

Key Results

The present prospective longitudinal cohort study examined the association between maternal infection during pregnancy, neonatal sepsis, and developmental delay at 6 months. The study included 150 mother–infant pairs, with maternal infection documented in 42 mothers (28.0%). Urinary tract infection was the most frequently documented maternal infection, followed by respiratory infection, genital/vaginal infection, and suspected intra-amniotic infection/chorioamnionitis (Table 2). Neonatal sepsis occurred in 18 infants (12.0%). As shown in Table 3, neonatal sepsis occurred in 21.4% of infants born to mothers with documented infection compared with 8.3% of those born to mothers without documented infection, and this association was statistically significant ($p = 0.026$).

A further important finding was the occurrence of suspected developmental delay at 6 months. Overall, 15 infants (10.0%) were classified as having suspected developmental delay. As shown in Table 5, developmental delay occurred in 27.8% of infants with neonatal sepsis compared with 7.6% of those without neonatal sepsis, with a statistically significant association ($p = 0.012$).

Interpretation of the Findings

The association between maternal infection during pregnancy and neonatal sepsis observed in the present study

is biologically plausible. Maternal infection may increase fetal exposure to microorganisms or inflammatory mediators, particularly when infection involves the genital tract, fetal membranes, or placenta. Previous research has identified chorioamnionitis and maternal colonization with specific pathogens as important contributors to early-onset neonatal infection. [11,12]

In the present cohort, infants born to mothers with documented infection had a higher frequency of neonatal sepsis than those born to mothers without documented infection (21.4% vs. 8.3%; $p = 0.026$) (Table 3). This finding is consistent with evidence showing that maternal chorioamnionitis is associated with increased odds of early-onset neonatal sepsis. A systematic review and meta-analysis reported increased odds of confirmed early-onset neonatal sepsis among infants exposed to both clinical and histological chorioamnionitis. [13] The present finding therefore supports the study objective of examining the association between maternal infection during pregnancy and neonatal sepsis, although the observational design does not establish a causal relationship.

The findings are also consistent with evidence from India. A systematic review and meta-analysis of neonatal sepsis risk factors in India identified several maternal and neonatal factors associated with neonatal sepsis, including premature rupture of membranes and gestational age below 37 weeks. [14] These factors may be relevant when interpreting the present association because maternal infection and adverse

perinatal characteristics may coexist and contribute to neonatal infection.

Maternal infection may additionally influence neonatal outcomes indirectly through prematurity. Prematurity is an important risk factor for neonatal infection because immature immune function, reduced skin and mucosal barriers, and increased need for invasive procedures may increase susceptibility to infection. Meta-analytic evidence has also demonstrated an increased risk of preterm birth following maternal influenza or SARS-CoV-2 infection.

[15] However, because prematurity was not evaluated as an adjusted confounder in the present analysis, its contribution to the observed association cannot be determined from these data.

The second major finding was the higher frequency of suspected developmental delay among infants who experienced neonatal sepsis. Developmental delay was identified in 27.8% of infants with neonatal sepsis compared with 7.6% of those without sepsis (Table 5; $p = 0.012$). This finding addresses the study objective of assessing the association between neonatal sepsis and developmental delay at 6 months.

The observed association is consistent with evidence from very-low-birth-weight infants. Alshaikh et al. reported that neonatal sepsis was associated with increased odds of long-term neurodevelopmental impairment, including cerebral palsy. [16] Similarly, a systematic review and meta-analysis of very preterm infants found that neonatal sepsis was associated with an increased risk of adverse neurodevelopmental outcomes. [17]

Evidence from a large population-based cohort also supports an association between neonatal sepsis and later developmental outcomes. Savioli et al. reported that both confirmed and suspected neonatal sepsis were associated with an increased risk of neurodevelopmental delay at 5 years, although the association was stronger for confirmed sepsis. [18] These findings provide context for the association observed in the present cohort, although differences in population characteristics, follow-up duration, and developmental assessment methods should be considered when comparing results across studies.

Several mechanisms may contribute to the relationship between neonatal sepsis and developmental impairment. Systemic inflammation, cytokine-mediated injury, cerebral perfusion disturbances, hypoxic-ischaemic events, and direct or indirect effects of severe infection on the developing brain have been proposed as potential mechanisms. However, neonatal sepsis should not be considered the sole determinant of developmental outcomes. Gestational age, birth weight, neonatal hypoxia, socioeconomic conditions, nutritional status, and other neonatal complications may also influence developmental

outcomes. Therefore, the association observed in the present study should be interpreted in the context of these potential contributing factors.

Maternal infection itself may also potentially influence later neurodevelopment through inflammatory pathways. A meta-analysis reported an association between maternal infection during pregnancy and cerebral palsy, although heterogeneity between studies and potential confounding factors should be considered. [19] Furthermore, evidence concerning maternal respiratory viral infection and offspring neurodevelopment remains heterogeneous. A systematic review reported possible associations between maternal respiratory viral infections and selected offspring neurodevelopmental outcomes but emphasized limitations and heterogeneity in the available evidence. [20]

Taken together, the findings of the present study suggest an association between maternal infection during pregnancy and neonatal sepsis and, separately, between neonatal sepsis and suspected developmental delay at 6 months. The findings are compatible with a possible pathway in which maternal infection may be associated with neonatal infection and subsequent neonatal infection may be associated with developmental vulnerability. However, this pathway should not be interpreted as evidence of causation because multiple maternal, neonatal, and socioeconomic factors may contribute to developmental outcomes.

Generalizability

The findings may be most applicable to mother–infant populations receiving antenatal, delivery, and neonatal care in primary or secondary healthcare settings with characteristics similar to the study centre in Fatehpur, Gaya, Bihar. The study was conducted at a single healthcare centre and included a relatively small cohort, which may limit the applicability of the findings to other geographic regions, healthcare systems, or tertiary-care populations.

Therefore, the findings should be interpreted cautiously when applied to populations with different demographic characteristics, infection patterns, healthcare resources, or neonatal care practices. Multicentre studies involving larger and more diverse populations are required to determine whether the observed associations are consistent across different healthcare settings.

Conclusion

In this prospective longitudinal cohort, maternal infection during pregnancy was associated with a higher frequency of neonatal sepsis, while neonatal sepsis was associated with a higher frequency of suspected developmental delay at 6 months. Maternal infection was documented in 28.0% of mothers, neonatal sepsis occurred in 12.0% of infants, and

suspected developmental delay was identified in 10.0% of infants. These findings highlight the potential importance of maternal infection recognition, neonatal surveillance, and developmental monitoring during infancy.

Strengths

The prospective longitudinal design is an important strength because maternal infection status was assessed during pregnancy before neonatal and developmental outcomes were evaluated. Prospective follow-up also allowed the temporal sequence between maternal infection, neonatal sepsis, and subsequent developmental assessment to be examined. The study additionally assessed both neonatal sepsis and developmental status, allowing evaluation of a potential relationship between neonatal infection and early developmental outcome.

Limitations

This study has several limitations. First, the sample size was relatively small, and the study was conducted at a single healthcare centre, which may limit the generalizability of the findings. Second, follow-up was limited to 6 months, and developmental screening at this age cannot establish long-term neurodevelopmental outcomes. Third, maternal infections were considered collectively, although different types of infection may have different biological effects on neonatal and developmental outcomes.

Fourth, maternal infection and neonatal sepsis were assessed using the clinical and laboratory criteria used at the study centre, which may limit comparability with studies using different or standardized diagnostic definitions. Fifth, residual confounding from prematurity, birth weight, neonatal hypoxia, socioeconomic factors, nutritional status, and other perinatal variables cannot be excluded. Finally, the observational design allows associations to be identified but does not establish a causal relationship between maternal infection, neonatal sepsis, and developmental delay. The current manuscript similarly recognizes the limitations related to sample size, follow-up duration, infection categorization, and residual confounding.

Recommendations

Maternal infections during pregnancy should be recognized and appropriately managed through timely antenatal assessment and clinical management. Newborns with relevant maternal infection exposure may benefit from careful monitoring for clinical features of neonatal infection. Infants who develop neonatal sepsis may also benefit from systematic developmental surveillance during infancy, particularly when additional perinatal risk factors are present.

Future research should include larger multicentre longitudinal cohorts, standardized definitions of maternal infection and neonatal sepsis, validated developmental assessment tools, and longer follow-up periods. Future studies should also evaluate individual maternal infection types separately and adjust for potential confounding factors such as gestational age, birth weight, neonatal hypoxia, and other relevant perinatal characteristics.

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List of Abbreviations

CHC: Community Health Centre

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

WHO: World Health Organization

Conflict of Interest

The authors declare that they have no conflicts of interest.

Author Contributions

All authors contributed equally to the manuscript.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request, subject to applicable ethical and institutional requirements.

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