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MATERNAL GENITAL TRACT INFECTIONS AND THEIR ASSOCIATION WITH EARLY NEONATAL NEUROLOGICAL OUTCOMES

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ABSTRACT:

Background: Maternal genital tract infections (MGTIs) during pregnancy trigger localized and systemic maternal-fetal inflammatory responses. While MGTIs are established risk factors for preterm birth, their direct contribution to early neonatal neurological morbidities remains insufficiently quantified. This study evaluated the prevalence of MGTIs and systematically analyzed their association with early neonatal neurological outcomes within the first 28 days of life.

Methods: A prospective observational study was conducted at a tertiary care center from June 2025 to December 2025. A total of 320 pregnant women presenting for delivery were clinically and microbiologically evaluated for MGTIs, including bacterial vaginosis, Group B *Streptococcus* (GBS), *Chlamydia trachomatis*, *Trichomonas vaginalis*, and histologically or clinically confirmed chorioamnionitis. Neonates were systematically evaluated during the first 4 weeks of life. Neurological assessment included APGAR scoring, standardized neonatal reflex testing, Tone Assessment, and cranial ultrasound or video-EEG when clinically indicated. Primary adverse neurological outcomes included hypoxic-ischemic encephalopathy (HIE), neonatal seizures, hypertonia/hypotonia, and intraventricular hemorrhage (IVH). Multivariable logistic regression was used to calculate adjusted odds ratios while controlling for gestational age, birth weight, and delivery mode.

Results: Maternal genital tract infections were confirmed in 24.4% (n = 78/320) of mothers, with bacterial vaginosis (10.6%) and GBS colonization (8.1%) being the most prevalent. Neonates born to mothers with confirmed MGTIs demonstrated a significantly higher overall incidence of early neurological abnormalities compared to non-exposed controls (21.8% vs 6.6%, $p < 0.001$). After multivariable adjustment, maternal MGTI was identified as an independent predictor of adverse early neonatal neurological outcomes (aOR = 3.42, 95% CI: 1.68–6.96, $p = 0.001$). Specific observed neurological morbidities in the exposed group included abnormal muscle tone (12.8%), neonatal encephalopathy/HIE (7.7%), clinical/electrographic seizures (5.1%), and abnormal cranial ultrasound findings such as IVH or periventricular echogenicity (6.4%).

Conclusion: Maternal genital tract infections are strongly and independently associated with early neonatal neurological complications. Routine antenatal screening, timely pathogen identification, and prompt intrapartum microbial management are critical strategies to prevent fetal neuroinflammatory insults and improve early neonatal outcomes.

KEYWORDS: Maternal genital tract infections, Neonatal neurological outcomes, Chorioamnionitis, Hypoxic-ischemic encephalopathy, Neonatal seizures, Intraventricular hemorrhage.

INTRODUCTION

Maternal genital tract infections (MGTIs) during pregnancy remain a significant global health burden, contributing to adverse obstetric and perinatal outcomes worldwide [1]. Ranging from lower genital tract conditions—such as bacterial vaginosis (BV), Group B *Streptococcus* (GBS) colonization, *Chlamydia trachomatis*, and *Trichomonas vaginalis*—to ascending upper tract involvement leading to intra-amniotic infection (chorioamnionitis), MGTIs affect up to 25–30% of pregnant women globally [2, 3]. While the association between MGTIs and adverse pregnancy outcomes like preterm labor, premature rupture of membranes (PROM), and low birth weight is well recognized, their broader implications for fetal and early neonatal neurodevelopment are increasingly coming into focus [4].

The underlying pathophysiological mechanism linking MGTIs to neonatal brain injury centers on the fetal inflammatory response syndrome (FIRS) [5]. Ascending maternal pathogens trigger a localized immune response that can cross the placental barrier or enter the amniotic cavity, resulting in elevated fetal serum levels of pro-inflammatory cytokines, including Interleukin-6 (IL-6), Interleukin-1 beta (IL-1β), and Tumor Necrosis Factor-alpha (TNF-α) [6]. These circulatory inflammatory mediators cross the immature fetal blood-brain barrier, inducing neuroinflammation, microglial activation, and excitotoxic injury to vulnerable pre-oligodendrocytes and developing neurons [7]. Consequently, neonates exposed to maternal inflammatory environments face an elevated risk of developing structural brain injury, functional tone abnormalities, and clinical encephalopathy [8].

Despite advances in perinatal care, early neonatal neurological morbidities—such as hypoxic-ischemic encephalopathy (HIE), neonatal seizures, intraventricular hemorrhage (IVH), and abnormal muscle tone—continue to pose major clinical challenges [9]. Although severe chorioamnionitis is a recognized risk factor for cerebral palsy in long-term follow-up studies, the immediate impact of maternal lower and upper genital tract infections on early neonatal neurological status during the first 28 days of life remains under-investigated in routine clinical settings [10]. Most available literature focuses either on long-term neurodevelopmental outcomes or strictly on gestational age at birth, leaving a critical knowledge gap regarding the direct independent contribution of specific MGTIs to early neurological morbidities in both preterm and term infants [11].

Addressing this gap is vital for improving early diagnostic strategies and targeted intrapartum interventions. Therefore, this prospective observational study was conducted to evaluate the prevalence of various maternal genital tract infections among pregnant women presenting for delivery and to systematically assess their independent association with early neonatal neurological outcomes within the first 28 days of life.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of Obstetrics and Gynecology in collaboration with the Department of Neonatology and Pediatrics at a tertiary care center from June 2025 to December 2025. The protocol received formal ethical approval from the Institutional Review Board (IRB) or Ethics Committee prior to initiation. Written informed consent was obtained from all participating mothers or their legally authorized representatives before enrollment.

Study Population and Eligibility Criteria

All pregnant women presenting for labor and delivery at 28 weeks of gestation or greater during the study timeframe were consecutively screened for inclusion.

Inclusion Criteria:

- Pregnant women admitted for labor or delivery between June 2025 and December 2025.
- Availability of maternal microbiological and clinical screening data for genital tract infections.
- Live-born neonates delivered during the study period.
- Written informed consent provided by the parents or guardians.

Exclusion Criteria:

- Major congenital structural anomalies or chromosomal abnormalities in the neonate.
- Confirmed intra-uterine viral infections (TORCH panel: Toxoplasmosis, Rubella, Cytomegalovirus, Herpes Simplex Virus).
- Known maternal illicit drug abuse or severe chronic medical illnesses (such as poorly controlled diabetes or severe autoimmune disorders) that independently predispose to neurodevelopmental compromise.
- Neonates with incomplete clinical or 28-day follow-up data.

Data Collection and Maternal Assessment

Comprehensive demographic, clinical, and obstetric parameters were recorded upon maternal admission using a standardized data collection form. Maternal variables included maternal age, parity, gestational age (determined by last menstrual period and confirmed by early ultrasound), booking status, mode of delivery, duration of membrane rupture, and intrapartum fever greater than 38.0 degrees Celsius.

Diagnosis of Maternal Genital Tract Infections (MGTIs)

Maternal lower and upper genital tract evaluations were performed clinically and microbiologically upon admission or intrapartum:

1. **Microbiological Screening:** High vaginal swabs (HVS) and endocervical swabs were collected prior to the administration of intrapartum antibiotics. Samples were processed for:
2. **Bacterial Vaginosis (BV):** Diagnosed using Nugent's criteria (score of 7 or higher) or Amsel's clinical criteria.
3. **Group B Streptococcus (GBS):** Identified via selective enrichment broth (lim broth) followed by subculture on sheep blood agar.
4. **Other Pathogens:** Identification of Chlamydia trachomatis (via PCR or rapid antigen detection) and Trichomonas vaginalis (via wet mount microscopy or culture).

5. **Clinical Chorioamnionitis:** Diagnosed based on Gibbs criteria, including maternal pyrexia (38.0 degrees Celsius or higher) accompanied by at least two of the following signs: maternal tachycardia (greater than 100 beats per minute), fetal tachycardia (greater than 160 beats per minute), uterine tenderness, purulent cervical discharge, or maternal leukocytosis (greater than 15,000 cells per cubic millimeter).

Neonatal Neurological Evaluation

All live-born neonates were admitted for standardized neurological monitoring and followed up for the first 28 days of life (early neonatal period). Assessments were performed by experienced neonatologists blinded to the maternal infection status whenever possible.

1. Immediate Postnatal Assessment

- **APGAR Scores:** Recorded at 1 and 5 minutes post-delivery.
- **Cord Blood Gas Analysis:** Performed immediately after delivery where indicated to evaluate acid-base status (pH less than 7.00 or base deficit of 12 mmol/L or greater).

2. Clinical Neurological Examination

Serial clinical evaluations were conducted at 12 hours, 24 hours, 72 hours, and at 28 days (or prior to discharge).

- **Tone Assessment and Reflexes:** Evaluated using the Amiel-Tison Neurological Assessment or Sarnat and Sarnat staging for encephalopathy. Muscle tone was classified as normal, hypertonic, or hypotonic.
- **Neonatal Encephalopathy / HIE:** Staged according to modified Sarnat criteria into Mild, Moderate, or Severe categories.
- **Seizures:** Clinical seizure activity (clonic, tonic, or subtle) confirmed visually or via electrographic monitoring.

3. Neuroimaging and Electrophysiology

- **Cranial Ultrasound:** Performed on all symptomatic neonates and those with maternal MGTI exposure within the first 3 to 7 days of life using a real-time ultrasound machine with a high-frequency anterior fontanelle probe. cUS evaluated for Intraventricular Hemorrhage (IVH, graded I to IV according to Papile's classification), periventricular echogenicity, or cerebral edema.
- **Video-EEG / Amplitude-Integrated EEG:** Utilized in neonates presenting with encephalopathy or clinically suspected seizures to confirm electrographic seizure activity.

Outcome Definitions

- **Primary Outcome:** Overall incidence of adverse early neonatal neurological outcomes within the first 28 days of life, defined as the presence of one or more of the following: Moderate-to-Severe Neonatal Encephalopathy/HIE, clinical or electrographic seizures, persistent tone abnormalities (hypertonia or hypotonia), or abnormal cranial ultrasound findings (Grade II to IV IVH or periventricular leukomalacia).
- **Secondary Outcomes:** Need for neonatal intensive care unit (NICU) admission, length of NICU stay, and early neonatal mortality.

Statistical Analysis

Data were analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

- **Descriptive Statistics:** Categorical variables were summarized as frequencies and percentages. Continuous variables were assessed for normality using the Shapiro-Wilk test and presented as mean plus/minus standard deviation (SD) for normally distributed data or median with interquartile range (IQR) for non-normally distributed data.
- **Comparative Analysis:** Bivariate comparisons between the MGTI-exposed and non-exposed groups were conducted using the Pearson Chi-Square test or Fisher's Exact test for categorical outcomes, and the Student's t-test or Mann-Whitney U test for continuous parameters.
- **Multivariable Modeling:** Multivariable binary logistic regression was performed to determine the independent association between MGTIs and adverse early neonatal neurological outcomes. Adjusted Odds Ratios (aOR) and 95 percent Confidence Intervals (CI) were calculated after controlling for confounding variables, including gestational age, birth weight, mode of delivery, and maternal age.
- **Significance Level:** A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

Cohort Composition and Maternal Baseline Profile

Between June 2025 and December 2025, a total of 350 pregnant women presenting for labor and delivery were screened for participation. Following the application of predefined eligibility criteria, 30 individuals were excluded (12 due to major congenital fetal malformations, 8 owing to confirmed maternal TORCH infections, 6 because of incomplete 28-day follow-up data, and 4 due to severe chronic maternal systemic disease). Consequently, 320 maternal-neonatal dyads were included in the final analytical cohort.

Out of 320 participating mothers, confirmed Maternal Genital Tract Infections (MGTIs) were diagnosed in 78 cases, yielding an overall maternal infection frequency of 24.4%. The remaining 242 mothers (75.6%) constituted the

unexposed reference cohort. Baseline maternal age and parity distributions were comparable between the two study arms. However, mothers in the MGTI cohort demonstrated a significantly higher frequency of preterm labor (32.1% vs. 14.5%, $p = 0.001$) and membrane rupture exceeding 18 hours (28.2% vs. 9.9%, $p < 0.001$) relative to unexposed controls.

Table 1: Baseline Maternal Demographics and Obstetric Characteristics

Parameter	Total Cohort (N = 320)	MGTI Exposed (n = 78)	Non-Exposed (n = 242)	p-value
Maternal Age *(years, Mean ± SD)*	27.4 ± 4.8	26.9 ± 5.1	27.6 ± 4.7	0.274
Primiparous Status, *n (%)*	148 (46.3%)	39 (50.0%)	109 (45.0%)	0.443
Gestational Age *(weeks, Mean ± SD)*	37.2 ± 2.6	35.8 ± 3.1	37.7 ± 2.2	< 0.001
Preterm Delivery *(< 37 weeks), n (%)*	60 (18.8%)	25 (32.1%)	35 (14.5%)	0.001
Rupture of Membranes *(> 18 hrs), n (%)*	46 (14.4%)	22 (28.2%)	24 (9.9%)	< 0.001
Cesarean Delivery, *n (%)*	112 (35.0%)	34 (43.6%)	78 (32.2%)	0.071

Distribution and Etiology of Maternal Genital Pathogens

Microbiological and clinical evaluations identified Bacterial Vaginosis (BV) as the single most dominant infection type, present in 34 women (10.6% of the total cohort; 43.6% of infected mothers). Group B *Streptococcus* (GBS) colonization was detected in 26 cases (8.1% overall cohort), whereas clinical chorioamnionitis was established in 18 cases (5.6% overall cohort). Furthermore, 16 mothers (20.5% of the infected subset) presented with polymicrobial involvement or combined upper and lower genital tract inflammatory processes.

Table 2: Spectrum and Distribution of Maternal Genital Tract Pathogens

Diagnostic / Pathogen Category	Overall Cohort (N = 320)	MGTI Group Proportion (n = 78)
Bacterial Vaginosis (BV)	34 (10.6%)	43.6%
Group B *Streptococcus* (GBS)	26 (8.1%)	33.3%
Clinical / Histological Chorioamnionitis	18 (5.6%)	23.1%
Chlamydia trachomatis* / *Trichomonas vaginalis	12 (3.8%)	15.4%
Polymicrobial Infection Status	16 (5.0%)	20.5%

Early Neonatal Neurological Complications

Neurological assessments conducted across the initial 28 days of life revealed an overall adverse early neonatal neurological rate of 10.3% (n = 33/320) across the entire population. Infants delivered to mothers with confirmed

MGTIs displayed a significantly elevated rate of neurological complications compared to unexposed neonates (21.8%, n = 17/78 vs. 6.6%, n = 16/242; p < 0.001).
Specific neurological morbidity patterns within the MGTI-exposed group included:
1. **Motor Tone Disturbances:** Persistent motor tone abnormalities (hypotonia or hypertonia) occurred in 12.8% (n = 10) of MGTI-exposed infants compared with 3.3% (n = 8) of unexposed infants (p = 0.002).
2. **Neonatal Encephalopathy:** Moderate-to-severe hypoxic-ischemic or inflammatory encephalopathy was documented in 7.7% (n = 6) of exposed neonates versus 2.1% (n = 5) of controls (p = 0.018) (Tann et al., 2017).
3. **Electrographic Seizures:** Electroencephalographically confirmed seizures occurred in 5.1% (n = 4) of exposed infants vs. 1.2% (n = 3) of unexposed infants (p = 0.041).
4. **Cranial Ultrasonography Findings:** Abnormal neuroimaging findings, such as Grade II–IV intraventricular hemorrhage or periventricular echogenicity, were observed in 6.4% (n = 5) of exposed infants versus 1.7% (n = 4) of unexposed infants (p = 0.027).

Table 3: Comparison of Early Neonatal Neurological Outcomes (28 Days)

Neurological Outcome	MGTI Exposed (n = 78)	Non-Exposed (n = 242)	Total (N = 320)	p-value
Overall Adverse Neurological Outcomes	**17 (21.8%)**	**16 (6.6%)**	**33 (10.3%)**	**< 0.001**
Abnormal Muscle Tone *(Hypotonia / Hypertonia)*	10 (12.8%)	8 (3.3%)	18 (5.6%)	0.002
Moderate-to-Severe Encephalopathy / HIE	6 (7.7%)	5 (2.1%)	11 (3.4%)	0.018
Neonatal Seizures *(Clinical / Electrographic)*	4 (5.1%)	3 (1.2%)	7 (2.2%)	0.041
Abnormal Cranial Ultrasound *(IVH Grade II–IV)*	5 (6.4%)	4 (1.7%)	9 (2.8%)	0.027

Multivariable Logistic Regression Analysis
Multivariable binary logistic regression was executed to determine whether maternal genital tract infection serves as an independent predictor of adverse early neonatal neurological outcomes. After adjusting for potential clinical confounders—including gestational age at delivery, birth weight, delivery mode, and duration of membrane rupture—maternal MGTI remained independently associated with a more than three-fold increase in the odds of early neonatal neurological injury (Adjusted Odds Ratio [aOR] = 3.42, 95% Confidence Interval [CI]: 1.68–6.96, p = 0.001).
Subgroup risk estimation indicated that clinical chorioamnionitis carried the strongest predictive risk for neonatal neurological impairment (aOR = 5.12, 95% CI: 1.82–14.41, p = 0.002), followed by maternal Group B *Streptococcus* colonization (aOR = 3.18, 95% CI: 1.24–8.15, p = 0.016) (Tann et al., 2017) and Bacterial Vaginosis (aOR = 2.45, 95% CI: 1.05–5.72, p = 0.038) (Dingens et al., 2016).

Table 4: Multivariable Logistic Regression Analysis for Early Neurological Injury

Predictor Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)*	p-value
Maternal Genital Tract Infection (Overall)	**3.94 (1.89–8.21)**	**< 0.001**	**3.42 (1.68–6.96)**	**0.001**
Gestational Age *(< 37 weeks)*	2.85 (1.38–5.88)	0.004	2.11 (0.98–4.54)	0.056

Predictor Variable	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)*	p-value
Low Birth Weight *(< 2500g)*	2.41 (1.15–5.05)	0.019	1.84 (0.82–4.12)	0.138
Prolonged Rupture of Membranes *(> 18 hrs)*	2.15 (0.96–4.82)	0.063	1.62 (0.69–3.81)	0.267

Adjusted for maternal age, gestational age, birth weight, delivery mode, and duration of membrane rupture.

DISCUSSION

This prospective observational study provides compelling clinical evidence demonstrating that Maternal Genital Tract Infections (MGTIs) during pregnancy are strong, independent predictors of adverse early neonatal neurological outcomes within the first 28 days of life. Even after rigorous adjustment for key confounding variables—including premature birth, low birth weight, and delivery mode—infants exposed to intrauterine or lower genital tract infections demonstrated a more than three-fold increase in early neurological morbidities (aOR = 3.42, 95% CI: 1.68–6.96). These findings emphasize that intrauterine inflammatory exposure poses an independent neurodevelopmental hazard to the fetus, distinct from the mechanical risks associated with prematurity alone.

The high overall prevalence of MGTIs observed in our study cohort (24.4%) aligns with global epidemiological reports from lower- and middle-income countries, where antenatal lower genital tract screening is often underutilized [1, 2]. Bacterial vaginosis (BV) and Group B *Streptococcus* (GBS) emerged as the predominant pathogens in our cohort. Crucially, our subgroup analysis revealed that clinical chorioamnionitis conferred the highest risk for acute neonatal neurological injury (aOR = 5.12), followed by GBS colonization (aOR = 3.18) and BV (aOR = 2.45). These results reinforce previous observations by Tann et al. (2017), who demonstrated a profound association between maternal GBS exposure and acute neonatal encephalopathy across international cohorts [3]. Similarly, our findings regarding bacterial vaginosis corroborate the observations of Dingens et al. (2016), highlighting that even subclinical lower genital tract dysbiosis can trigger adverse inflammatory cascades affecting neonates [4].

The biological mechanisms linking maternal genital infections to early neonatal brain injury center on the activation of Fetal Inflammatory Response Syndrome (FIRS) [5]. Microorganisms or their molecular products (such as lipopolysaccharides) ascending from the vagina enter the amniotic cavity, triggering an intra-amniotic cytokine storm characterized by elevated levels of Interleukin-6 (IL-6), Interleukin-1 beta (IL-1β), and Tumor Necrosis Factor-alpha (TNF-α) [6]. These pro-inflammatory cytokines enter the fetal systemic circulation and breach the immature fetal blood-brain barrier [7]. Once inside the central nervous system, cytokines induce microglial activation, astrogliosis, and excitotoxic cellular damage specifically targeting pre-oligodendrocytes and developing cortical neurons [8]. This pathway leads directly to the white matter injury, cerebral edema, and electrographic disorganization observed as abnormal muscle tone, neonatal seizures, and intraventricular hemorrhage on cranial ultrasound in our exposed neonate group.

A key highlight of this study is the detailed breakdown of specific early neurological abnormalities within the 28-day postnatal window. Tone abnormalities (12.8%) and neonatal encephalopathy (7.7%) were the most prevalent clinical manifestations among infected mothers. While traditional clinical paradigms often attribute early neonatal encephalopathy exclusively to intrapartum hypoxic events, our data underscore that intrauterine infection and inflammatory cascades act as primary neurotoxic agents or significantly lower the threshold for hypoxic-ischemic damage [9, 10]. Furthermore, neuroimaging abnormalities, such as Grade II–IV intraventricular hemorrhage and periventricular echogenicity, were significantly higher in the exposed group (6.4% vs. 1.7%), supporting the concept that neuroinflammation destabilizes the delicate fetal germinal matrix vasculature [11].

Strengths and Limitations

The primary strength of this study lies in its prospective design, consecutive sampling, and comprehensive 28-day standardized neurological assessment incorporating both clinical scoring systems and objective neuroimaging (cranial ultrasound and video-EEG). However, certain limitations must be acknowledged. First, as a single-center study, the findings may reflect local demographic and microbial patterns, necessitating multi-center validation. Second, serum or amniotic fluid pro-inflammatory cytokine levels (such as IL-6 or TNF-α) were not routinely measured due to resource constraints; future studies incorporating biochemical inflammatory biomarkers alongside microbiological cultures would further clarify the precise dose-response relationship between FIRS severity and neurodevelopmental outcomes. Finally, while our study captures crucial 28-day early neonatal outcomes, long-term neurodevelopmental follow-up (at 18 to 24 months) is required to track persistent motor and cognitive deficits.

Clinical and Policy Implications

The clinical implications of our findings are direct and actionable. Antenatal care protocols must prioritize universal, routine screening for maternal lower genital tract infections—particularly GBS and bacterial vaginosis—during the late second and third trimesters. Timely identification and administration of targeted intrapartum antimicrobial prophylaxis can effectively disrupt ascending inflammatory pathways, reducing both maternal infectious morbidity and fetal neuroinflammatory exposure. Furthermore, neonates delivered to mothers with confirmed MGTIs or chorioamnionitis should undergo early, structured bedside neurological screening and neuroimaging prior to hospital discharge to facilitate prompt neuroprotective interventions.

Recommendations

Based on the empirical findings of this study, the following clinical and policy recommendations are proposed to mitigate the risk of infection-induced neonatal neurodevelopmental injury:

1. **Universal Antenatal Screening Protocols:** Health authorities and obstetrical units should implement routine screening for lower genital tract infections—specifically bacterial vaginosis and Group B *Streptococcus*—during late second and third-trimester prenatal visits, especially in low- and middle-income regions where screening is currently underutilized [3].
2. **Timely Intrapartum Antimicrobial Prophylaxis:** Standardized guidelines should be enforced for immediate targeted intrapartum antibiotic administration upon identifying maternal genital tract pathogens or clinical signs of chorioamnionitis to disrupt ascending infection pathways and limit fetal neuroinflammatory exposure [4].
3. **Targeted Postnatal Neurological Surveillance:** Neonates born to mothers with diagnosed MGTIs, prolonged rupture of membranes, or maternal intrapartum fever should undergo routine bedside clinical neurological assessments (using standardized tone and reflex scoring) prior to discharge [5].
4. **Early Neuroimaging and Monitoring:** Cranial ultrasonography and continuous amplitude-integrated EEG monitoring should be prioritized during the first week of life for all neonates exposed to maternal genital tract infections who exhibit subclinical or clinical neurological symptoms [6].
5. **Long-Term Neurodevelopmental Follow-Up:** Multi-center studies with extended follow-up cohorts up to 18 to 24 months of age should be established to assess the persistent cognitive, motor, and sensory impacts of intrauterine infection exposure beyond the early neonatal period [7].

REFERENCES

1. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008 Jan 5;371(9606):75-84.
2. Romero R, Dey SK, Fisher SJ. Preterm labor: one syndrome, many causes. *Science*. 2014 Aug 15;345(6198):760-5.
3. Tann CJ, Nkurunziza P, Nakakeeto M, Webb EL, Ssekyewa J, Kizza M, et al. Neonatal encephalopathy with group B streptococcal disease worldwide: systematic review, investigator group datasets, and meta-analysis. *Clin Infect Dis*. 2017 Nov 1;65(suppl_2):S173-89.
4. Dingens AS, Fairfortune TS, Reed S, Mitchell C. Bacterial vaginosis and adverse outcomes among full-term infants: a cohort study. *BMC Pregnancy Childbirth*. 2016 Sep 20;16(1):278.
5. Gomez R, Romero R, Ghezzi F, Yoon BH, Mazor M, Berry SM. The fetal inflammatory response syndrome. *Am J Obstet Gynecol*. 1998 Jul;179(1):194-202.
6. Hagberg H, Mallard C, Ferriero DM, Vannucci SJ, Levison SW, Fleiss B, et al. The role of inflammation in perinatal brain injury. *Nat Rev Neurol*. 2015 Apr;11(4):192-208.
7. Stolp HB, Dziegielewska KM, Ek CJ, Habgood MD, Lane MA, Koehn LM, et al. Breakdown of the blood-brain barrier to proteins in white matter of the developing brain during systemic inflammation. *Cell Mol Neurobiol*. 2005 Apr;25(3):409-26.
8. Volpe JJ. Brain injury in premature infants: a complex amalgam of destructive and developmental disturbances. *Lancet Neurol*. 2009 Jan;8(1):110-24.
9. Glass HC, Costarino AT, Stayer SA, Brett CM, Cladis F, Davis PJ. Outcomes for extremely premature infants. *Anesth Analg*. 2015 Jun;120(6):1337-51.
10. Wu YW, Colford JM Jr. Chorioamnionitis as a risk factor for cerebral palsy: a meta-analysis. *JAMA*. 2000 Sep 20;284(11):1417-24.
11. Dammann O, Leviton A. Inflammatory brain damage in preterm infants—the white matter damage hypothesis. *Dev Neurosci*. 2004;26(5-6):322-31.
12. Romero R, Miranda J, Chaiworapongsa T, Korzeniewski SJ, Chaemsaithong P, Gotsch F, et al. Prevalence and clinical implications of sterile intra-amniotic inflammation in preterm labor with intact membranes. *Am J Reprod Immunol*. 2014 Sep;72(3):262-74.

13. Leviton A, Allred EN, Kuban KC, Dammann O, O'Shea TM, Hirtz D, et al. Microbiologic and histologic characteristics of the placenta and risk of cerebral palsy in infants born before 28 weeks gestation. *J Pediatr*. 2016 Mar; 170:86-92.
14. Baud O, Aujard Y. Congenital and perinatal infections and brain damage. *Semin Fetal Neonatal Med*. 2013 Aug;18(4):191-5.
15. Yoon BH, Romero R, Park JS, Kim CJ, Kim SH, Choi JH, et al. Fetal exposure to an intra-amniotic inflammation and the development of cerebral palsy at the age of three years or older. *Am J Obstet Gynecol*. 2000 Mar;182(3):675-81.
16. Hitti J, Tarczy-Hornoch P, Murphy J, Hillier SL, Agnew K, Eschenbach DA, et al. Intrauterine infection, cytokines, and perinatal brain injury. *Obstet Gynecol*. 2001 Mar;97(3):421-8.
17. Malaeb SN, Dammann O. Fetal inflammatory response syndrome and post-natal brain injury. *Acta Paediatr*. 2009 Jan;98(1):21-9.
18. Schrag SJ, Verani JR. Intrapartum antibiotic prophylaxis for the prevention of perinatal group B streptococcal disease: experience and implications. *Vaccine*. 2013 Aug 28;31(Suppl 4):D20-6.
19. Verani JR, McGee L, Schrag SJ. Prevention of perinatal group B streptococcal disease--revised guidelines from CDC, 2010. *MMWR Recomm Rep*. 2010 Nov 19;59(RR-10):1-32.
20. Kurinczuk JJ, White-Koning M, Badawi N. Epidemiology of neonatal encephalopathy and hypoxic-ischemic encephalopathy. *Early Hum Dev*. 2010 Jun;86(6):329-38.