**Listeria monocytogenes infection during pregnancy**

Andreea Elena Dumitru¹, Nicolae Gica¹,², Radu Botezatu¹,², Corina Gica¹, Mihaela Demetrian¹, Anca Marina Ciobanu¹,², Brindusa Ana Cimpoca-Raptis¹,², Gheorghe Peltecu¹,², Anca Maria Panaitescu¹,²

¹Filantropia Clinical Hospital, Bucharest, Romania
²“Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

**ABSTRACT**

*Listeria monocytogenes* is an important pathogenic bacteria found in soil or water being the causative agent of listeriosis, a severe foodborne disease during pregnancy. The outcome can lead up to miscarriage, stillbirth, preterm birth and congenital neonatal infections, under occult or overt illness of the mother. We performed a literature review in the medical database PubMed, searching relevant information regarding listeriosis during pregnancy and neonatal outcome. Higher incidences were observed in ethnic minorities, as a reflection of specific dietary habits and where surveillance is not thoroughly implemented. Also, the infection was most commonly seen during the second or third trimester of pregnancy, with maternal presentation under the form of flu-like or pyelonephritis symptoms, or even asymptomatic. Regarding the neonatal infection, there are two types described according to the way of acquiring the bacteria. The obstetric outcome ranges from premature delivery to miscarriage and stillbirth. Treatment of choice is a combination of ampicillin and aminoglycoside. Despite the advances in the field of infectious diseases, challenges remain to completely understand the mechanism of placental invasion of *Listeria monocytogenes* and the severe consequences on fetal development.

**Keywords:** *Listeria monocytogenes*, listeriosis, pregnancy, early-onset, late-onset, rhombencephalitis

**INTRODUCTION**

Listeria monocytogenes is an important Gram-positive pathogenic bacterium for newborn, immunosuppressed patients, pregnant women and elderly, being the causative agent of listeriosis. It is the etiological agent of an important foodborne disease with a particular notoriety regarding development during gestational period due the increased incidence of listeriosis, 10 to 100 times higher compared to the non-pregnant population [1-4]. The outcome can lead up to miscarriage, stillbirth, preterm birth, and congenital neonatal infections, with all these complications possibly occurring in the absence of clinical illness of the mother, delaying the medical interventions [5].

There are two forms of neonatal infections: “the early onset” sepsis as a result of maternal chorioamnionitis and “the late onset” meningitis from perivaginal and perianal colonization of the mother with Listeria from the gastrointestinal tract, by transition through the birth canal. For infants with underdeveloped macrophage, the immunity system is impaired and invasive infection is more likely to occur if colonization of the liver, gastrointestinal tract or respiratory system appeared. Treatment of listeriosis involves use of ampicillin together with an aminoglycoside [6].
**Epidemiology**

The incidence of maternal-neonatal listeriosis is estimated around 4-10/100,000 pregnant women per year in Europe and North America, with higher incidence rates in countries where surveillance methods are not clearly defined [7-10]. Bearing in mind the foodborne character of this disease, more cases were reported and observed in ethnic minorities, as a reflection of specific dietary habits, for example Hispanic women in the US or African women in France [6,11-13].

Infection is most commonly seen in the first 30 days of life, with the two possibilities of acquiring the infection, as described before or in patients older than 60.

Clinical manifestation is as outbreaks of febrile gastroenteritis syndrome, with an average incubation period of approximately 24 h. As a foodborne pathogen, reported sources included sea food, rice salad, chocolate milk, corn salad, ready-to-eat meats, jellied pork and fresh cheese [6].

**Pathophysiology**

The mechanism of placental colonization and dissemination to the fetus of *Lysteria monocytogenes* involves the active cross of the epithelial barrier of the intestine after ingestion, translocation via lymph nodes and reach the primary target: organs as the liver and spleen where it can establish infectious foci that can be efficiently cleared by cell-mediated immunity in an immunocompetent human (the subclinical infection). Opposite, in immunocompromised adults, these primary inadequately resolved foci can lead to the dissemination of the bacteria into the bloodstream. It results in in febrile bacteraemia and, eventually, invasive infection of the brain [14].

In pregnant women, *L. monocytogenes* colonizes the uterus in addition to the liver and spleen. While the infection is controlled in the last two organs, the uterus in addition to the liver and spleen. While the infection is controlled in the last two organs, the placental immune tolerance mechanisms provides a permissive niche for the proliferation of *L. monocytogenes*. Bacteria from the placental reservoir may reinfect the mother’s liver and spleen, contributing to infection maintenance and amplification [15]. Transplacental dissemination to the fetus results in abortion, stillbirth, or neonatal sepsis [16].

**Clinical Features**

The mothers of these septic infants may be asymptomatic but commonly have flu-like or pyelonephritis symptoms before the early onset of labor, and their blood cultures are frequently positive for *L. monocytogenes*. Symptoms in the mother include fever, chills, and malaise, which resolve spontaneously following delivery of the infected infant and placenta [17]. Literature suggests that early treatment of the mother who has Listeria sepsis can prevent transplacental infection or treat the fetus in utero, with subsequent delivery of a normal uninfected infant [18]. Unfortunately, this only happens when the medical community is aware of this problem in a particular geographic region through public health reports. Only limited information regarding neurological involvement in pregnant women is mentioned, slight related to immunosuppressed mothers [19].

**Diagnosis**

Diagnosis of all forms of *L. monocytogenes* infection depends on germ’s isolation from a sterile site, usually blood or cerebrospinal fluid. Particular for pregnant women, stool or vaginal cultures may be positive when selective media for *L. monocytogenes* are used for culture.

In some forms of central nervous system infection, particularly rhombencephalitis, several samples may need to be obtained to isolate the bacteria. In case of focal neurologic findings, characteristic for rhombencephalitis, prompt computed tomography or magnetic resonance imaging scanning should be performed. The finding of multiple microabscesses in the hindbrain raises suspicion for Listeria rhombencephalitis and empiric treatment should be started.

**Fetal and Neonatal Infection**

Depending on the mode of acquiring the infection from the mother, current literature describes two types of neonatal infection: “the early-onset” and “the late onset” [20,21].

Due to the impaired cell-mediated immune response to *L. monocytogenes* in pregnant women along with the decreased gastrointestinal motility seen in pregnancy, it may be a predisposition to invasive listeriosis and subsequent transplacental infection of the infant. Occult or overt bacteraemia can result in chorioamnionitis producing early-onset neonatal listeriosis [22]. This is the mechanism for “early-onset” listeriosis characterized by the delivery of an often premature and severely ill infant. Spontaneous recovery of the mother from Listeria sepsis normally occurs after delivery, but neonates have severe affections. Clinical features include prematurity, sepsis at birth, fever, a diffuse maculopapular cutaneous eruption, and evidence of significant hepatic involvement with jaundice [17]. The mortality rate of early-onset listeriosis, even with treatment, is very high, and stillbirth is also
common in this setting. If recognized before giving birth, appropriate antibiotic therapy can save the infant.

The second type is the “late-onset” listeriosis, when the infant is infected during the transition through a colonized birth canal by maternal gastrointestinal carriage of *L. monocytogenes* without sepsis. In these cases, clinical disease in the infant develops 7 to 14 days later. Direct cutaneous invasion is unlikely, and it is believed that aspiration of the organism into the respiratory tract or swallowing of the organism by the infant may occur during the incubation period. A unique outbreak of neonatal listeriosis in Costa Rica has been described: the vehicle was *L. monocytogenes*-contaminated mineral oil used to clean infants after delivery from healthy mothers, with cross contaminations of shared mineral oil [5].

**OBSTETRICAL OUTCOME**

It ranges among the most severe maternal-neonatal infections. In only 5% of cases, the pregnancy course develops well, accomplishing with the delivery of a healthy baby [6]. Information from the MONALISA cohort study indicated several problems: a risk for fetal loss of approximately 25%, an increased risk for preterm birth before 32 weeks of gestation and enhanced changes of affected fetuses with early and late-onset listeriosis [6].

Clinical maternal signs include decreased fetal movements, perception of uterine contractions, or abdominal pain, vaginal bleeding or even premature rupture of membrane, that can lead to chorioamnionitis. Beside the meconium-like amniotic fluid, several abnormalities of the fetal digestive tract can be observed on the ultrasound. They include: fetal ascites, gallbladder enlargement and intestinal echo enhancement [23]. The gestational age correlated with the onset of infection has a fundamental influence on the prognosis of newborns. An infection diagnosed in early pregnancy leads to more than half of the pregnancies ending with abortion, while in infections occurring in the second or third trimester of pregnancy, only a quarter of cases can end up in stillbirths, uterine fetal loss or abortion [24]. Usually, the infection with *Listeria* occurs in the late pregnancy [25].

**REFERENCES**


**TREATMENT**

*L. monocytogenes* remains susceptible to most β-lactam antibiotics, except cephalosporins, to which the organism is usually resistant.

When listeriosis is a likely diagnosis, the use of ampicillin or, in penicillin-allergic patients, vancomycin provides empiric coverage for *L. monocytogenes* until the diagnosis is made by culture. A combination of ampicillin and gentamicin is the current therapy of choice for all forms of listeriosis. The duration of treatment for invasive listeriosis has not been studied. Relapses appear to be uncommon, and 2 to 3 weeks of therapy with ampicillin and gentamicin is sufficient for most forms of listeriosis. Rhombencephalitis with abscess formation in the central nervous system may require more prolonged therapy, but there is not available information to support the use of treatment beyond 4 weeks. Still, there is some data suggesting that this combination is not useful and could be harmful. Trimethoprim-sulfamethoxazole is an alternative treatment that has been recommended.

**CONCLUSIONS**

Antenatal care and pregnancy plan should inform pregnant women of the potential risks of foodborne diseases including *Listeria monocytogenes*, with particular attention to ethnic minorities, but without any form of discrimination. If suspicion for listeriosis in a pregnant woman with fever, flu-like or gastrointestinal symptoms, blood cultures should be considered rapidly due to the severe consequences on fetal development, even fetal loss. Listeriosis during pregnancy carries a poorer prognosis for fetuses affected during the first trimester compared to second and third one, with more than half of the pregnancies ending with abortion.

Several measures can help reduce the risk of infection: use of fresh food and follow strict rules of storage, cooking food, especially meat thoroughly, washing very good fruits and legumes under running water and keeping good hygiene of the instruments for food preparing.

All in all, despite the advances in science, the mechanism of placental invasion and the severe complications on the fetal development of this pathogenic bacteria cannot be fully explained or understood.