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LISTERIOSIS: OBSTETRIC AND PERINATAL ASPECTS

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Abstracts. *The article summarises the current data on listeriosis in pregnant women, taking into account the fact that the infection rate in this population is several times higher than in general population. Listeriosis in pregnant women is characterised by miscarriage, stillbirth, fever and flu-like symptoms. Therefore, listeriosis should be considered as a cause of fever in pregnancy in order to initiate appropriate treatment early. Prevention remains the best way to control listeriosis and should be reinforced, especially among patients and healthcare workers.*

According to the World Health Organisation (WHO), listeriosis is found in all countries of the world, especially in economically developed ones. Several thousand confirmed cases and even outbreaks are registered every year. The incidence is 2-3 cases per 1 million people. For example, in the United States, up to 1,600 cases are registered per year with a mortality rate of 27%. The peculiarities of listeria life determine their ability to contaminate food and multiply in it, which led to numerous cases of foodborne listeriosis in the 1980s [8]. Recently, there has been an increase in the number of listeriosis cases in industrialised countries, which requires careful consideration of the revision of existing regulations and strengthening of epidemiological surveillance of listeriosis in the context of an increasing number of susceptible people, including the elderly [6].

Listeriosis is a serious infection usually caused by eating food contaminated with the bacterium Listeria monocytogenes (LM). These bacteria are widespread in nature and can be found in soil, sand and water. The reservoir of infection is cattle, rabbits, pigs, chickens, etc., as well as wild animals and rodents. In addition, environmental objects such as silage, soil, hay, grain, water can be a reservoir of infection, where the pathogen can remain at low temperatures for years [1, 4, 5, 6]. Listeriosis is associated with the consumption of contaminated and/or improperly cooked food, especially dairy products, leafy vegetables, fish, and meat. It can be transmitted by consuming contaminated ready-to-eat food, foods with a long shelf life, deli meats and soft cheeses. The LM strain is characterised by high virulence and in some cases the disease can occur even with a low level of contamination. The routes of transmission include dietary, contact, aerogenic, and vertical (transplacental and perinatal). [7, 2, 3]. Given the increase in people with reduced immunity population (due to cancer and haematological diseases, HIV infection, after organ transplantation, due to taking glucocorticosteroids and cytostatics), it should be noted that this category of patients often suffers from listeriosis [1, 4].

Patients with listeriosis usually report symptoms that begin 1-4 weeks after eating food contaminated with LM, and it is also known that symptoms can appear 70 days after exposure or on the same day of exposure [1, 8].

The risk of infection in pregnant women is several times higher than in the general population due to the specific immune suppression associated with pregnancy and placental tropism of LM. The causative agent is a gram-negative rod-shaped bacterium LM, which belongs to the genus Listeria. It is a facultative anaerobe that can grow at low temperatures. The strains belonging to clonal complexes 1, 4 and 6 are hypervirulent surface proteins found on Listeria and are associated with maternal and neonatal infections. Maternal listeriosis occurs as a direct consequence of LM-specific placental tropism mediated by the conjugated action of internalin A and internalin B at the placental barrier. Listeria can rapidly change from saprophytic to parasitic forms and are also capable of reproducing intracellularly. Under unfavourable conditions, they can transform into L-forms, which leads to the presence of latent, prolonged and chronic forms and insufficient effectiveness of antibiotics. There are 16 serological variants of the pathogen, but 90% of all listeriosis cases worldwide are caused by serotypes 1a, 1b and 4b. It has pathogenicity factors (listeriolysin O, internalins A and B, etc.) [2].

Depending on the route of infection, the mucous membranes of the digestive tract, respiratory system, eyes, genitals, and affected skin can be the entry gate for the infection, and the pathogen can also pass through the placenta from mother to fetus. Penetration into the human body occurs due to pathogenicity factors of listeria. The pathogen may persist without clinical signs in immunocompetent individuals. In other cases, listeria enter the lymphatic system, then the bloodstream and penetrate cells of the mononuclear phagocyte system of the liver, spleen, kidneys, lymph nodes, and central nervous system, where they multiply and form specific listerial granulomas. They are greyish-white nodules that contain altered polymorphonuclear leukocytes, reticular leukocytes, monocytic cells and cellular detritus. Subsequently, they undergo necrosis with possible scarring or healing [5, 4, 8]. In transplacental infection, a generalised process, which is interpreted as granulomatous sepsis develops. Specific granulomas are formed in the internal organs, primarily in the liver, and on the skin of newborns. Despite considerable knowledge of the pathogenesis of LM, key aspects of listeriosis during pregnancy and the perinatal period remain unknown [3]. Experimental models of listeriosis were created in animals. In all experiments, a high level of embryo/fetal mortality was observed, but no congenital malformations associated with this infection were found. In addition, studies have demonstrated a dose-dependent association between the infectious dose and adverse pregnancy outcome, mainly pregnancy loss. Another study in mice found bradycardia in infected fetuses [3, 5].

Although LM infection is relatively rare, it always infects the mother-placenta-fetus system, which in turn can lead to adverse fetal outcomes such as chorioamnionitis, preterm birth, neonatal sepsis, meningitis and neonatal death.

Listeriosis associated with pregnancy increases the risk of intrauterine and neonatal mortality by approximately 21% and can present with a wide variety of non-specific symptoms, such as fever, flu-like or gastrointestinal symptoms, threatened abortion and preterm labour [3, 5, 7, 8, 11]. Animal models have been developed for the treatment of listeriosis associated with pregnancy and have shown similar sensitivities and clinical outcomes to those in humans. Primate and guinea pig animal models have similar LD50 values to the estimated human LD50. The WHO estimates the 50% human lethal dose (LD50) for intrauterine/neonatal loss to be 1.9×10^6 colony forming units (CFU) LM. More animal studies are needed to understand the pathways of fetal and neonatal listeriosis in humans, and more information is needed to understand the dose response, model the risk of listeriosis at lower concentrations, and determine why some pregnant women may be more susceptible than others.Bbiomarkers for early diagnosis of listeriosis are also needed to better treat listeriosis in pregnancy [9, 10]. The milder disease manifests as gastroenteritis with fever, diarrhoea, nausea and vomiting, which are common within 7 days of exposure. Invasive infection, characterised by bacteremia and encephalitis, can develop in high-risk patients. Fetal loss is the main complication of listeriosis during pregnancy [11]. Listeriosis in pregnancy is characterised by miscarriage clynical symptomes, as well as stillbirth, fever and flu-like symptoms. Other forms of listeriosis are defined by at least one of four symptoms: fever, meningitis or meningoencephalitis, septicaemia, and localised foci such as arthritis, endocarditis and abscesses.

There is no single clinical classification of listeriosis. Listeriosis of pregnant women and newborns is often distinguished. Acute, subacute and chronic listeriosis are distinguished Depending on the duration of the clinical course. Despite considerable knowledge about the pathogenesis of LM, key points about listeriosis during pregnancy and the perinatal period remain unknown. Literature reviews have summarised data on listeriosis in humans and domestic animals during pregnancy, as well as animal models used to study the pathogenesis and immune response to LM infection during these periods [9, 10].

The main method of diagnosis is bacteriological examination, and the material for testing can be blood, cerebrospinal fluid, tonsil swabs, eye discharge, vaginal swabs, meconium, amniotic fluid. Histological examination of the placenta or tissue of a dead fetus reveals specific granulomas macroscopically and/or microscopically. PCR detects Listeria DNA in blood, amniotic or cerebrospinal fluid, vaginal discharge, and placenta [6, 3].

In case of transplacental infection, a child with congenital listeriosis is usually born with low birth weight and may appear healthy immediately after delivery, and clinical manifestations of listeriosis in the form of sepsis or meningitis appear 1-2

weeks after birth. From the first few hours/days of life, the background temperature rises, the child's condition deteriorates sharply - shortness of breath, cyanosis, papular or papular haemorrhagic rash, jaundice, enlarged liver and spleen appear. Intrauterine sepsis, pneumonia, purulent pleurisy, hepatitis, and meningoencephalitis develop. Fetal listeriosis is characterised by a high mortality rate of up to 35%, depending on the gestational age at the time of infection [1]. Aspiration of infected amniotic fluid leads to severe lung damage. Most of these children die. The consequences of this disease in survivors can include hydrocephalus and mental retardation.

Listeriosis sepsis begins acutely, with typical hectic fever, chills and severe sweating. There may be a spotted and erythematous rash that accumulates around large joints and on the face in the form of a 'butterfly'. Secondary purulent foci appear in various organs, resulting in the development of hepatitis, which is manifested by jaundice, meningitis, carditis, polyserositis, pneumonia, pyelitis, and the development of haemorrhagic syndrome. The mortality rate reaches 60%. It is not yet fully understood why some pregnant women are susceptible to some outbreaks of listeriosis, and this accounts for a large percentage of cases, while others have a mild course of the disease. This may be due to differences in LM strains, or other factors may be involved [9]. Pregnant women are generally advised to avoid unpasteurised dairy products during pregnancy, but many are unaware that soft cheeses and other foods can pose a risk of infection. LM remains a cause of foodborne outbreaks and maternal and neonatal sepsis worldwide, so healthcare providers should ensure that expectant mothers are thoroughly counselled about potential sources of [7].

The EU and Ukraine have approved a list of criteria for determining cases of infectious and parasitic diseases to be registered in their legislation [12]. It defines the clinical, laboratory and epidemiological criteria for listeriosis and the definitions of possible, probable and confirmed cases of this disease. Adequate treatment of maternal listeriosis prevents and treats fetal disease, and it is essential for the treatment of newborns. Amoxicillin or ampicillin is the first line of treatment alone or in combination with gentamicin, followed by trimethoprim/sulfamethoxazole [1]. For invasive infection, penicillin-based therapy (high-dose penicillin or amoxicillin) in combination with gentamicin is recommended, and co-trimoxazole may be considered for patients with penicillin intolerance [11].

Conclusion

Therefore, listeriosis should be considered as a cause of fever during pregnancy in order to initiate appropriate treatment in advance. Given that there is no specific prevention of listeriosis and currently no vaccination, women should be informed about the list of foods that are dangerous from the point of view of

possible infection and about personal hygiene, storage, heat treatment and cooking, including at home. Prevention remains the best way to fight listeriosis and should be strengthened, especially among patients and healthcare workers.

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