## Listeria outbreaks cause maternal and perinatal mortality and morbidity: we must do better



Reports of the global threat of listeriosis to public health are increasing in number, despite the availability of effective antibiotic treatments. Listeria monocytogenes has an intracellular lifecycle and multiplies rapidly, infecting adjacent cells, undetected by antibodies in the extracellular fluid.1 Found in animal and human faeces, it can contaminate raw meat, and processed and prepared foods. The US Centers for Disease Control and Prevention recently reported a listeria outbreak in six states.2 As of Nov 9, 2022, 16 people were infected, although true numbers might be higher; of those with information available, 13 people were hospitalised, including one pregnancy loss and one adult death.<sup>2</sup> In the UK, 14 linked cases of listeriosis have been identified since 2020, including eight since January, 2022, one of whom was pregnant.3

According to WHO, listeriosis has an annual incidence of 0·1 to 10 cases per million.<sup>4</sup> Most have mild gastroenteritis that resolves within a few days. In the recent US outbreak, cases were linked to delicatessen meat; in the UK, most people who had listeriosis reported eating ready-to-eat smoked fish. Food-borne listeria outbreaks occur frequently, highlighting the need for constant vigilance.<sup>56</sup>

Clinically vulnerable individuals infected with listeriosis are at risk of severe illness, including meningitis and sepsis. This group includes adults older than 65 years; those with comorbidities, such as cancer, liver failure, or kidney failure; and immunosuppressed individuals.<sup>2</sup> As pregnancy reduces cell-mediated immunity, maternal listeriosis can be asymptomatic; if undetected and untreated, infection could lead to miscarriage, stillbirth, preterm birth, or life-threatening neonatal infection presenting with sepsis or meningitis.<sup>2,4,7</sup>

Listeriosis is reported to be 12–20 times more prevalent in pregnancy than in the general population,<sup>8</sup> although some of this prevalence might be due to increased identification during pregnancy. A recent systematic review including around 500 pregnant women infected with listeriosis found that diagnosis was primarily by bacterial culture; infection was most common in the third trimester (66%); symptoms were similar to influenza, including fever and fatigue; and

patients were treated with intravenous amoxicillin or ampicillin.<sup>6</sup> Neonatal listeriosis is categorised as early onset (ie, ≤2 weeks after birth, probably caused by intrauterine exposure) or late-onset (ie, >2 weeks after birth; could also be due to early postnatal exposure).

During a large outbreak in Spain in 2019, 207 cases were confirmed; the median age of those affected was 44 years (range 0–94), and 114 (55%) were women. Most (n=154) had mild gastroenteritis, 141 (68%) required hospitalisation and three died; five of 34 pregnant women had a miscarriage.<sup>9</sup>

In a 2017 outbreak in South Africa, 10 465 (50%) of 937 cases were associated with pregnancy, 406 (87%) of which occurred in neonates. 77 (38%) of the pregnancyassociated cases and 97 (46%) of the remaining patients were HIV positive. Concerningly, 193 (27%) of 728 patients with known outcomes died, including 28% of neonates and 8% of pregnant women, highlighting the disproportionate outcomes in different countries.<sup>10</sup> Severe adverse outcomes have also been observed outside outbreak settings. A retrospective US cohort<sup>11</sup> study of 134 pregnant women hospitalised with listeriosis during 2007-18 reported higher rates of severe maternal morbidity than in those without listeriosis (30.9% vs 1.6%, respectively; p<0.001; 21.2-fold higher adjusted risk; 95% CI 14·0-31·9) including acute respiratory distress syndrome (2.8% vs 0.1%, respectively; p<0.001), mechanical ventilation (1.4% vs 0.0%, respectively; p<0.001), sepsis (28.1% vs 0.1%, respectively; p<0.001), and shock (1.4% vs 0.0%, respectively; p<0.001). Pregnant women with listeria also had higher rates of caesarean delivery, as compared with those who did not (57.9% vs 32.9%, respectively; p<0.001), preterm birth (61.3% vs 7.7%, respectively; p<0.001), and stillbirth (13.5% vs 0.7%, respectively; p<0.001).11

The US Food and Drug Administration warns that symptoms can develop within a few hours or as late as 2–3 days after eating contaminated food, although intervals of up to 3 months have been reported. Real-time PCR from bacterial isolates should be used for rapid and accurate diagnosis. Pregnancy-related listeriosis can result in fetal death in 20–30% of cases,<sup>8</sup> although this percentage might be biased by under-reporting

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Published Online January 6, 2023 https://doi.org/10.1016/ S2666-5247(22)00388-3 of milder cases. Thus, in pregnant women, adequate antibiotic treatment and, depending on disease severity and gestation, immediate delivery might improve outcomes for the baby.

This recent listeria outbreak, like the COVID-19 pandemic and 2022 mpox (formerly known as monkeypox) outbreak, highlights the need to continually review and update guidelines for infectious diseases in pregnancy. Only 26% of pregnant women with listeria infection present with fever, and current recommendations might lead to many going undiagnosed, potentially placing fetuses at risk.8 We continue to advocate for investment in guidance, surveillance, and research in countries with high incidence, so that both local and international communities can benefit from evidence-based management of rare infectious diseases. High-risk populations, and in particular pregnant women and young infants, should not be excluded from treatment and prevention trials.

We declare no competing interests.

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