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Listeriosis and Its Public Health Implications: A Review

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Abstract

Nowadays, Listeriosis, often known as silage disease, circling sickness, or meningo encephalitis, is a foodborne disease caused by the *Listeria* genus. *Listeria* species have been isolated from the soil, water, plants, feces, rotten fruits and vegetables, meat, seafood, dairy products, and asymptomatic human and animal carriers. Almost all human infections are caused by *Listeria monocytogenes*, while exist a few occurrences of infection caused by *Listeria ivanovii*. Humans are infected simply by eating food products of diseased animals. The older, pregnant women, newborns and adults with immune compromised systems are highly susceptible to the disease. The majority of infections in animals are caused by *Listeria monocytogenes*; however infections could also be caused by *Listeria ivanovii* and *Listeria seeligeri*. In animals, three types of listeriosis such as septicaemic, encephalitic and abortion have been documented. Clinical symptoms and the presence of the bacteria in a smear are used to make the first diagnosis of listeriosis. Antibiotics should be used to treat listeriosis for a long time. Production losses owing to abortion, treatment costs, reduced animal welfare, and trade of animal and by-products are all economic importance of the disease. Controlling *Listeria* in foods is mostly based on a hazard analysis and critical control point strategy in food-processing sectors. Useful conclusions are presented for public health protection and food security.

Keywords: Bacterium, Foods, *Listeria monocytogenes*, Listeriosis, Public Health Importance, Zoonosis, food security

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1. INTRODUCTION

Listeriosis is an important foodborne disease that primarily affects the pregnant women, newborns, elders and adults with a weakened immune system [1]. It is often asymptomatic or presents with mild gastrointestinal symptoms in otherwise healthy people. It is caused by *Listeria* and is also known as silage disease, circling disease, and meningo encephalitis. It is also a problem in veterinary medicine, causing epidemic abortion and encephalitis in ruminants [2]. It is an infectious and fatal disease of mammals, birds and others [3].

Listeria species are classified as "*Listeria sensu lato*" or "*Listeria sensu strictu*" based on morphological and genotypic similarities and differences [4]. *Listeria* species are found in a wide range of settings due to their capacity to adapt to a variety of adverse conditions [5]. It's a widespread bacterium that's been isolated from soil, plants, silage, and water, especially in food processing environments and especially in refrigerated facilities, despite their being cleaned and disinfected on a regular basis [6].

Several types of foods, particularly ready-to-eat foods, such as meat, fish, dairy products, fruits, and vegetables, are the most common source of sporadic listeriosis cases and outbreaks [7]. *Listeria monocytogene* is pathogenic to humans and a variety of animal species, whereas *Listeria ivanovii* is primarily pathogenic to ruminants but can also infect humans. However, clinical cases caused by *Listeria seeligeri*, *Listeria grayi* (which includes the former *L. murrayi*), and *Listeria innocua* have been reported infrequently [8,9]. *Listeria monocytogene* is commonly found in food processing environment and can persist for lengthy periods of time in foods, processing plants, households, or the environment, especially when kept refrigerated or frozen [10].

Listeriosis is an infectious bacterial disease that affects a wide variety of animals throughout the world [8]. *Listeria* can be consumed if the silage has not been adequately fermented and is not acidic enough to destroy the bacteria. It can be eaten through soil on grass roots, as well as the placenta and feces of infected animals [11]. It is important to mention that meningoencephalitis, septicaemia, pneumonia, and abortion are described in animals [8].

The presence of organisms in the smears prepared from meconium is useful in the early diagnosis of neonatal infection. Florescent antibody staining technique can be employed to demonstrate the bacteria in the clinical specimens [8]. The CAMP (Christie-Atkins-Munch-Petersen) test has long been considered a definitive test. In order to prevent this disease in a food facility, proper cleaning and sanitation practices are required [12]. The economic impact of the disease includes production losses owing to abortion, treatment costs, reduced animal welfare, and trade of animal and by products [13]. The main objective of this book chapter is to review listeriosis and its public health significance.

2. ETIOLOGY

Listeriosis is caused by members of the genus *Listeria*, which has now 17 species [14]. *Listeria* is a small (0.5-2 µm x 0.5 µm), Gram-positive bacillus that grows in short chains [15]. Except for rare strains, it is facultative aerobic, catalase-positive, oxidase negative, and hydrolyzes esculin [16]. Many carbohydrates are fermented by Listeria without producing gas. *Listeria monocytogenes* strains are always D-xylose negative and produce lecithinase. They are generally β-haemolytic and L-rhamnose positive. *Listeria* species can also withstand a 20 percent (weight/volume) increase in salt concentration (NaCl) [17].

Listeria monocytogenes has peritrichous flagella, which give it a distinctive tumbling motility. When the organism is cultivated between 20°C and 25°C, flagellin is both generated and assembled at the cell surface, but when the temperature is raised to 37°C, flagellin production is drastically reduced [18]. At low temperatures, enzymes such RNA helicase are activated, which promotes *Listeria monocytogenes'* activity and replication. This technique allows the bacteria to propel itself and latch on to enterocytes early in infection. *Listeria monocytogenes'* ability to create biofilms improves its ability to survive in severe environment. It can grow in a pH that varies between 4.5–9.6, with an optimal pH of around 7 [19]. On the basis of somatic and flagellar antigens, *Listeria monocytogenes* has been categorized into 13 serotypes (1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4a, 4ab, 4b, 4c, 4d, 4e, 7) [20]. Human serotypes 1/2a, 1/2b, and 4b, also serotypes 1/2a and 4b in animals, are regularly documented [21].

3. EPIDEMIOLOGY OF LISTERIOSIS

Listeria are distributed worldwide affects a list of species in the Kingdom Animalia, including sheep, goat, cattle, buffalo, horse, pig, camel, canine, rodent, wild animals, birds and also humans [8]. Small ruminants, particularly sheep, are the most affected [3]. *Listeria* has been found in goat, sheep, cattle, horse, pig, rabbit, mink, gerbil, chinchilla, chicken, quail, turkey, partridge, duck, ostrich, canary, and sheep meat, buffalo meat and milk [7,22,23,24], fish and fishery, ice creams, vegetables, and other ready-to-eat foods [25,26], seafood [27].

Listeria primary reservoirs are soil and decaying vegetation, where they thrive as saprophytes, although they can also be found in plants, animal feces, and water [28]. The evidence indicates that, animal listeriosis is typically linked to stored forages and the environment as the primary source of contamination [9]. Raw meats from market and slaughter houses are a source of *Listeria monocytogenes*. Furthermore, the presence of this bacterium may be attributed to the unclean working environment, poor sanitary conditions of persons who are contacting with the meat and the equipments [24].

Transmission of *Listeria* species mostly occurs through the ingestion of the infected foods and water (fecal-oral route), but they can also enter the body through other routes, such as inhalation or inoculation into damaged skin or the eye. Nosocomial infection has been observed in hospital and institution. Neonatal infections are recorded in newborn children [8]. With or without clinical signs, animals and humans can shed *Listeria* in milk and/or vaginal secretions, and sick individuals can excrete the pathogen in other secretions and excretions such as nasal discharges and urine. Although person-to-person transmission appears to be absent or minimal, listeriosis has been transferred between human newborns in the hospital via direct contact or on fomites [11].

4. LISTERIOSIS IN HUMANS AND ANIMALS

4.1. Listeriosis in Humans

The most common route of infection of humans is consumption of foods contaminated by *Listeria monocytogenes* [29]. Listeriosis causes wide range of diseases that can be divided into two types: severe invasive listeriosis and non-invasive febrile gastroenteritis [30]. Septicemia, meningitis or meningoencephalitis, infection of the uterus in pregnant women, and encephalitis are all invasive types of listeriosis in humans [31]. The infection in pregnant women can lead to abortion, stillbirth, or premature birth, and can be preceded by flu-like symptoms, such as fever [8,32].

Non-invasive gastroenteritis can manifest in immune competent adults and can induce atypical meningitis, septicemia and febrile gastroenteritis, with symptoms fever and watery diarrhea that lasts 2–3 days and is frequently accompanied by headache and backache [33]. These symptoms are frequently self-limiting and can be resolved in a short period of time without the need for medical intervention, subsequently leading to undiagnosed and under reporting of cases [34]. The expression of both forms of listeriosis is determined by the individual's age, immunological condition, infectious dose and mode of infection, virulence of the ingested strain, and physiological stage [35]. Clinical signs of this disease usually appear after a long incubation time (1 day – 70 days), making epidemiological source tracing extremely challenging [30].

Listeria monocytogenes is the main *Listeria* species that can infect all human populations. It has a proclivity for causing severe problems in pregnant women, newborns, the elderly and immune-compromised individuals [36]. In healthy hosts, *Listeria monocytogenes* has an infective dosage of 10–100 million colony forming units (CFU), but only 0.1–10 million CFU in those at high risk of infection [37].

4.2. Listeriosis in Animals

Listeriosis is a seasonal disease that affects animals, with the maximum prevalence in the winter and early spring. It appears to be closely linked to the consumption of spoiled silage [38]. Rhombencephalitis (in rare cases more diffuse encephalitic alterations), septicaemia, and abortion are all clinical symptoms of listeriosis in animals, especially in sheep, goats, and cattle. The rhombencephalitic form, which is the most prevalent presentation of the disease in ruminants, is known as "circling disease" because of its tendency to revolve in one direction. The clinical signs include depression, anorexia, head pressing or turning of the head to one side and unilateral cranial nerve paralysis [39].

Monogastric animals, such as pigs, dogs, cats, domestic and wild rabbits, and many other small mammals, are most susceptible to septicemic or visceral listeriosis [3]. The septicaemic form is rather uncommon, and it usually, but not always, affects neonates. Depression, inappetence, fever, and death are among symptoms. Mastitis in ruminants has been linked to *Listeria monocytogenes* infection on rare occasions. Gastrointestinal infections can arise in sheep on occasion. Although birds are mainly asymptomatic carriers, occasional cases of listeriosis have been observed, with septicaemia and meningo encephalitis being the most prevalent complications [19]. *Listeria monocytogenes* can infect the uterus of all domestic animals, especially ruminants, at any stage of pregnancy, resulting in placentitis, fetal illness and death, abortion, stillbirths, neonatal mortality, metritis, and possibly viable carriers. Abortion is frequently performed in the late stages of pregnancy (after 7 months in cattle and 12 weeks in sheep) [3].

5. PATHOGENESIS

Internalins, haemolysin, listeriolysin O, fibronectin-binding protein, ActA protein, two phospholipases, metalloprotease, Vip protein, a bile exclusion system, and a bile salt hydrolase are all important virulence factors that are primarily regulated by PrfA protein and are required for adhesion, intracellular multiplication, and pathogenicity [15,40].

The virulence determinants of *Listeria monocytogenes* in their majority are clustered along the chromosome in genomic islands or *Listeria* pathogenicity island-1 (LIPI-1) [16]. Also, the LIPI-3 and LIPI-4 have been identified in whole genome sequencings to carry semantic virulence factors of *Listeria monocytogenes*. The LIPI-1 contains six virulence factors, which include internalin, phosphatidylinositol specific phospholipase, metalloprotease and actin polymerisation protein [41,42].

The ability of *Listeria monocytogenes* to generate infection is due to its ability to stimulate its own internalization via host cells. This pathogen has the ability to pass across three major human barriers: the intestinal epithelium, the blood–brain barrier, and the placenta, and then spread to other organs [43]. *Listeria monocytogenes* infected host cells through various stages, including adhesion and invasion of host cells, internalization by host cells, lysis of vacuole, intracellular multiplication, and intercellular spread to the adjacent cell [44].

Listeria monocytogenes is a versatile organism that survives high acidity, bile salts, non-specific inflammatory attacks, and proteolytic enzymes from the host system after being consumed through contaminated food [42]. *Listeria monocytogenes* survives this stage by adhering to and entering both phagocytic and non-phagocytic cells of the host with the help of surface proteins termed internalin [43]. Because phagocyte cells have mechanisms for destroying ingested bacteria, *Listeria monocytogenes'* capacity to survive within these cells contributes to its pathogenicity [45]. *Listeria monocytogenes* is contained in a double-membrane vacuole after being internalized by neighbouring cells, from which it escapes with the help of LLO and plcB to repeat its life cycle [46].

6. DIAGNOSTIC TECHNIQUES

Clinical symptoms and detection of the bacteria in a smear from blood, cerebrospinal fluid, brain tissue, spleen liver, abomasal fluid meconium of newborns, the fetus in abortion cases, as well as faeces, vomitus, foods (milk, meat, and their products), or animal feed are used to make the initial diagnosis of listeriosis [26]. Blood and placenta cultures are the most reliable ways to determine if symptoms are caused by listeriosis during pregnancy. In case of abortion, it is advisable to collect cotyledons, fetal abomasal contents, and uterine secretions for the diagnosis of disease [26,47].

The CAMP test can be used to distinguish between *Listeria monocytogenes, Listeria ivanovii,* and *Listeria seeligeri*, all of which are haemolytic *Listeria* species [48]. Molecular tools such as PCR, multiplex PCR, and real-time PCR using virulence-associated genes like Internalin A (inlA), inlB, and inlC for specific detection of *Listeria monocytogenes*, and Internalin D (inlD) for specific detection of *Listeria ivanovii*, have been found to be fast, specific, repeatable, and reliable [49]. PCR is now widely accepted as a valid and repeatable method for identifying *Listeria* species and, more crucially, distinguishing Listeria monocytogenes from other *Listeria* species [48].

The quick identification kit could be used to distinguish between species of the genus *Listeria*. In the regular microbiology food laboratory, the API Listeria system has been identified as one of the preferred quick methods for biochemical identification of *Listeria* species. Based on 10 sugar fermentation reactions and enzymatic reactions in microtubes, this approach takes 24 hours to identify *Listeria* species, usually without the need for additional testing [50]. *Listeria monocytogenes* can be quickly identified via immunofluorescence in smears from animals that have died or been aborted due to listeriosis, as well as milk, meat and other sources [51].

7. LISTERIOSIS AND PUBLIC HEALTH IMPORTANCE

Listeriosis is foodborne bacterial disease that can cause life threatening infections in susceptible individuals [1]. Direct transmission from animals to humans is possible, particularly among veterinarians who perform gynaecological treatments on aborted animals, and indirect transmission can occur simply by eating infected the food of animal origin [52].

Listeria is frequently present in raw foods of both plant and animal origin around the world and it can also be found in cooked meals owing to post-processing contamination. Raw and pasteurized fluid milk, cheeses (especially soft-ripened kinds), ice cream, raw vegetables, fermented raw meat and cooked sausages, raw and cooked chicken, raw meats, and raw and smoked fish have all been found to contain them [37].

Possible explanations for the emergence of human food-borne listeriosis as a major public health concern include major challenges in food production, processing and distribution, increased use of refrigeration as a primary preservation means for foods, changes in the eating habits of people, particularly towards convenience and ready-to-eat foods [53] and an increase in the number of people considered to be at high risk for the disease (elderly, pregnant women, newborns, immune compromised) [54].

8. POPULATION AT RISK

8.1 Pregnant Women

Pregnant women are 20 times more likely than healthy people to contract listeriosis. Around 20% of listeriosis-affected pregnancies terminate in spontaneous miscarriage or stillbirth, and two-thirds of surviving children develop clinical neonatal listeriosis, which includes pneumonia, sepsis, and accounting for 20% of all neonatal meningitis cases [55]. Meningitis; rare but distinguished from other bacterial meningitis by its special preference for brain parenchyma, bacteraemia, bloody vaginal discharge, endocarditis; occurs in 10% of pregnant women with listeriosis and mostly affects the left side of the valve, mortality can reach 50%, gastroenteritis, and focal infections such as cellulitis, conjunctivitis are the main clinical symptoms [56].

8.2 Immune Compromised Individuals

Individuals with impaired cell-mediated immunity are more vulnerable to disease infection. The risk of listeriosis is increased during medical conditions and drugs that reduce T-cell mediated immunity. Transplants and blood-related cancers pose the highest danger. People with AIDS are more likely to become ill than people who have a healthy immune system [57]. HIV/AIDS seems to rarely lead to listeriosis since the advent of highly active anti-retroviral therapy and trimethoprim-sulfamethoxazole. Disease like cancers, liver disease and diabetes all confer a moderate risk of infection [54].

8.3 Age related

Newborns and the elderly over the age of 65 are the two groups most at risk. The immune systems of those young are very immature, and older people's immune systems are weak in response to infection, making them especially vulnerable to these infection. *Listeria* can cause life-threatening infections in newborns, such as bacteraemia and pneumonia, and neonatal bacterial meningitis is a typical complication [58].

8.4 Complications

The majority of *listeria* infections are so mild that they go unnoticed. On the other hand, it can cause life-threatening problems in people who have generalized blood infection and inflammation of the membranes and fluid surrounding the brain (meningitis) [59]. In the pathophysiology of listeriosis, diabetes mellitus, cardiovascular illness, neoplastic disease, or hemodialysis failure are all important contributors. A patient without concomitant condition has a mortality rate of about 10.7%, whereas a patient with much morbidity, such as diabetes and heart disease, has a mortality rate of over 24% [4].

9. TREATMENT

Treatment of listeriosis can be difficult task because *Listeria* can invade virtually all cell types. Time period of treatment depends on the severity of the infection. Antibiotics have been used to treat listeriosis in animals and humans for a long time. Early and aggressive antibiotic treatment is critical for recovery. If the symptoms of encephalitis are severe, death is almost always the result, regardless of therapy [31].

Penicillin (the antibiotic of choice), ceftiofur, erythromycin, and trimethoprim/sulphonamide are all effective against *Listeria monocytogenes* [31]. Because achieving minimum bactericidal concentrations in the brain is difficult, high doses are required. Penicillin G should be administered IM every day for 1–2 weeks at a dose of 44,000 U/kg body weight; the first injection should be followed by an IV treatment of the same dose.

Trimethoprim-sulfamethoxazole or erythromycins are appropriate alternatives for penicillin-allergic patients. It is suggested that tetracycline should not be given to children less than 7-year-old. Ampicillin is preferred for maternal foetal listeriosis [8].

10. PREVENTION AND CONTROL

Presently, no effective vaccine is available to immunize the humans for prevention and control of listeriosis [1]. Early discovery of a listeriosis outbreak and prompt response are critical to halting the spread of the disease. To avoid the creation of bacteria in animals, feed high-quality silage with early grass cutting, little contamination with dirt or faeces, and optimal anaerobic fermentation, which will keep the pH below 5.0, which inhibits the growth of *Listeria* species [31].

In order to prevent listeriosis, the HACCP approach and the implementation of effective critical control points in the process are necessary [60]. Listeriosis is most dangerous when foods (refrigerated ready-to-eat foods) are consumed without being cooked further. As a result, proper food hygiene is critical, especially for those who are at risk. Soft cheeses, refrigerated ready-to-eat foods, unless heated to an internal temperature of 73.9° C (165° F) or until scorching hot immediately before serving. Refrigerated smoked fish, unless cooked, and raw (unpasteurized) milk should be avoided by those individuals who are at risk [61].

Proper monitoring schemes should exist in food security, production food process, functional food plans and food quality technologies, utilities within good hygiene practices [62,65,67,69,70,72,73,74]. Therefore, particular efficient designs, hazard analysis and critical control point studies, environmental impact assessment quality assurance and food security should exist properly for public health protection [62,63,64, 66,67,69,71].

11. CONCLUSION AND RECOMMENDATIONS

Listeriosis, principally caused by *L.monocytogenes* is an important food-borne bacterial disease that causes septicaemia, abortion, and latent infection in a wide range of animals, including humans and birds. Animal-to-animal transmission is via the faecal-oral route. Humans can acquire the disease from contaminated food and by contact with infected animals. Diseases range from flu-like symptoms to severe infections such as meningitis, which can be fatal if not treated promptly.

Based on the above conclusion the following recommendations are forwarded:

- ✓ Good hygienic practices (GHP) and good manufacturing practices (GMP) should be implemented based on the principles of hazard analysis and critical control point (HACCP).
- ✓ Attempts should be made to identify the virulence factors, major risks, environmental impacts and survival strategies of organism in the environment.
- ✓ Correct early diagnosis and prompt treatment is necessary to mitigate the suffering of the patient.

In this way taking into account all the above are necessary datasets in epedimiological studies, statistical analysis in relation to useful monitoring schemes, environmental impact assessments, risk assessment utilities and quality assurance. Therefore, are necessary useful efficient proper designs for all, including sanitation measures, safe facilities and associated project management actions for food security and public health protection.

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CONTRIBUTION OF AUTHORS

All the authors contributed equally. They read the final version, and approved it for the publication.

CONFLICT OF INTEREST

The authors declare that they do not have conflict of interest.

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