

Human Listeriosis: An Update

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Abstract Listeriosis in human is clinically characterized as perinatal listeriosis, neonatal listeriosis and adult listeriosis. *Listeria spp* are an established pathogen in animals, and human infections are usually seen following ingestion of contaminated food (processed food). Human infections of *Listeria spp* initially present with gastrointestinal symptoms. Meningitis, septicaemia, brain abscess and probably intrauterine and neonatal infections are considered as frequent complications of infection with *Listeria spp*. Of the six species of *Listeria* identified thus far, *L monocytogenes* and *L ivanovii* are considered as pathogenic strains to humans and animals respectively. *Listeria monocytogenes* are facultative intracellular bacterial pathogens, which pose a potential public health problem related to consumption of contaminated food that is facilitated by their ability to tolerate high concentrations of salt and able to survive and multiply in refrigeration temperatures. From being a saprophyte, pathogen responsible for abortion in cattle, *Listeria spp* have evolved in to potential human pathogens with ever increasing reports of human listeriosis.

Keywords: human listeriosis, pathogenecity, diagnosis

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1. Introduction

Human Listeriosis, the infection caused by *Listeria spp* has been traditionally known as a food-borne illness. *Listeria spp* are a group of saprophytic gram positive bacilli present in the environment (soil, water, effluents etc..) as well as colonized in alimentary tract of human and animals [1]. Infection with *Listeria spp* was first discovered as a cause of septicemia in laboratory animals (rabbits and guinea pigs) and later isolated from a patient suffering from meningitis [2,3,4]. Human listeriosis is normally acquired by the consumption of food (milk, milk products, meat, fish and vegetables etc..) and close contact with animals is considered as a predisposing factor [5]. Gastrointestinal infections, mastitis and abortions are usually associated with listeriosis in animals. Currently there are six species of *Listeria* identified among which *L monocytogenes* and *L ivanovii* are considered as pathogenic strains to humans and animals respectively [6]. Human infections of *Listeria spp* normally occur following ingestion of contaminated food as evidenced from most of the previous outbreaks world wide [7]. Recent reports have also confirmed the association of human listeriosis with geriatric age population [8,9]. Human listeriosis was confined to a select group of population including the pregnant women, neonates, individuals with weakened immune system [10,11,12]. Reports of *Listeria spp* infection among the pediatric age children who are immunologically competent, invasive infections in adult population with and without underlying

causes, the occurrence of nosocomial listeriosis and community acquired *Listeria* meningitis should be considered as a cause of serious concern [13,14,15,16].

2. Epidemiology of Human Listeriosis

Incidence of human listeriosis varies with geographical region [17]. It has been estimated that 0.24 per one lakh people suffer from infection with *Listeria* in America annually. A recent report from center for disease control and prevention (CDC) has noted that among the 147 infected during an outbreak after consumption of cantaloupe 33 (22.5%) had died and a pregnant women suffered miscarriage [18]. Report from Rio d Janeiro (Brazil) by Martins et al., revealed that there was an outbreak of human listeriosis affecting six elderly hospitalized patients [19]. A study by Brouwer MC et al among the human listeriosis cases that included 30 immunocompromised patients has revealed a mortality rate of 17% [20]. An Israeli study by Seigman-Igra Y et al which reviewed 161 cases and 1808 reported cases showed that 74% of the infected patients were immunosuppressed with a mortality rate of 30% [21]. Consumption of fresh cheese contaminated with *Listeria monocytogenes* was attributed to an outbreak in Spain [22]. A recent study from north India by Soni DK et al have characterized *Listeria spp* based on the serotype, antimicrobial susceptibility patterns and presence of virulence determinant genes. This study which included *Listeria spp* isolated from various sources (human clinical samples, milk and ganges river water) has revealed

occurrence of different serogroups that included 1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4b, 4d and 4e. The same report also demonstrated that the *Listeria spp* isolated from human source and other sources (milk and water) belonged to two different clones [23]. Another study by Orsi RH et al have revealed that serotypes of *Listeria spp* belong to 4 lineages (lineage I, II, III, IV) where in *Listeria monocytogenes*, the most common human pathogen belonged to lineages I and II (serotypes 1/2a, 1/2b and 4b) [24].

3. Clinical Presentation

Listeriosis in human is mainly characterized as perinatal listeriosis, neonatal listeriosis and adult listeriosis. Most cases of human listeriosis present as brain abscess or meningitis confirming the dissemination hematogenously from a local area (gastrointestinal tract) to central nervous system (CNS). Skin infections caused by *Listeria spp* have been noted among the farmers, agricultural workers and veterinarians presenting as pyogranulomatous rash [25]. Atypical clinical presentation of human listeriosis includes endocarditis, myocarditis, arteritis, pneumonia, pleuritis, cholecystitis, peritonitis, arthritis, osteomyelitis, sinusitis, otitis, conjunctivitis, ophthalmitis. Clinical presentation of human listeriosis is influenced by the physiological, pathological and immunological (T cell immunity) status of the host. Predisposing factors for human infections with *Listeria spp* include pregnant women, neonates, old age (>50 years), immunocompromised and debilitated individuals. Other predisposing factors for human listeriosis are malignancy, patients on cancer chemotherapy, immunosuppressive therapy, chronic kidney disease (CKD), and chronic liver disease. Metabolic disorders like diabetes mellitus and autoimmune diseases may also predispose to *Listeria spp* infections [11,26,27].

4. Pathogenicity and Virulence Determinants

Listeria monocytogenes are facultative intracellular bacterial pathogens, which pose a potential public health problem related to consumption of contaminated food that is facilitated by their ability to tolerate high concentrations of salt and able to survive and multiply in refrigeration temperatures [25]. It was only in the early 1980's *Listeria spp* have been recognized as a threat to food industry that later led to further studies on its virulence factors and potential to cause serious human infections. Previous studies have elaborated on the probable mode of entry and the nature of dissemination of *Listeria spp* using murine model experiments and have confirmed that acute infection of *Listeria spp* usually starts after ingestion of contaminated food [28,29]. *Listeria spp*, then get colonized intracellularly in the intestinal epithelial cells before invading to the nearest lymph nodes and then disseminating through blood first to liver and then to other organs [30]. Immunologically competent host is sufficient to eliminate *Listeria spp* before it establishes and that could be the main reason for less number reports of human listeriosis [31]. Other significant factor attributed to under reporting and missed diagnosis of human listeriosis is the

long incubation periods ranging from few days to months as noted by a recent study [32]. The profile of human listeriosis has shown a significant change from a bacterium that is responsible for gastrointestinal infections and meningitis, to a pathogen that has capability to cause invasive infections not only confined to immunosuppressed and debilitated patients but also in immunocompetent individuals [33]. The virulence factors associated with invasive *Listeria* infections include hemolysin (Hly), similar to the streptolysin O produced by *Streptococcus pyogenes* and is called as listeriolysin O (LLO), phospholipase (PLC) (PlcA and PlcB) similar to the one secreted by *Staphylococcus aureus*, Cholesterol dependent pore-forming toxin (CDTX), lecithinase, ActA (Actin-based intracellular motility) and internalins (InlA and InlB) that facilitate invasion [1,34].

5. Laboratory Identification Methods

Listeria spp are a group of non-sporing gram positive bacilli that have been recognized as established pathogens in animals including the cattle, sheep, wild animals, birds and other mammals [1]. Isolation rates of *Listeria spp* in traditional clinical microbiological laboratories are negligible when compared to other pathogenic bacteria. Studies have impressed on the importance of use of *Listeria* enrichment broth for increased chances of isolation from various samples [35,36]. Food processing industry has been identified as the most susceptible and possible source of *Listeria spp* contaminating food and food products [37]. Reports from studies including the *Listeria spp* isolated from such industries have identified that biofilm formation and resistance to the chemical preservative benzalkonium chloride is attributed to *Listeria spp* food contamination [38,39]. Studies have also stressed on the significance of molecular methods in the tracking of *Listeria spp* in food industry [40,41]. Human listeriosis is under reported and only few studies are available in literature, mostly from developed nations [42,43]. Use of rapid, advanced and molecular laboratory testing methods including the polymerase chain reaction (PCR) have been instrumental in the diagnosis as well as epidemiological characterization of human listeriosis. Novel techniques facilitating the study on serotypes, virulence determinants, colonization and invasive characters, clone identification and surveillance include optimized Multilocus variable-number tandem-repeat analysis assay (MLVA) (VNTR), pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST) and Fluorescence amplified fragment length polymorphism (fAFLP). Only few studies in the existing literature are available that report the predominant serotype prevalent and their association with a particular type of clinical illness [44,45,46].

6. Antimicrobial Chemotherapy

A evidenced from the available literature it is clear that most listerial infections in human are subclinical and clinical infections are usually associated with immunosuppressed and debilitated conditions. Ampicillin, amoxicillin and gentamicin were successfully tried among

pregnant women and the management of severe invasive infections in immunocompromised patients require long term antimicrobial therapy. *Listeria spp* are known to show resistance to cephalosporins and erythromycin and co-trimoxazole are other antimicrobial agents effective against human listerial infections [47,48,49].

7. Discussion including Preventive and Control Measures

Clinical presentation of human listeriosis is complex and is believed to be influenced by the physiological, clinical and immunological status of an individual. Mode of entry of the bacilli, its virulence factors also play an important role in the outcome of the disease. Gastrointestinal symptoms following food contamination is the most common presentation followed by neurological complications when *Listeria spp* invade the central nervous system (CNS). Existing literature also indicate that *Listeria spp* may be excreted through feces of immunocompetent host without contributing to any clinical symptoms, thus acting as transmission vehicles for further food contamination and spread to susceptible population (pregnancy, old age) and may contribute to community acquired human listeriosis. Previous studies have also noted that it is very difficult to analyze on the probable source and entry of *Listeria spp* in human. Adults aged > 65 years and pregnant women who are considered as high risk groups have to be carefully evaluated and they should be advised to pay attention to the various food sources of *Listeria* (milk and milk products: both raw and pasteurized, meat and processed meat products) to prevent infection. Thorough cleaning of vegetables, implementation of effective hand washing technique, avoiding consumption of soft cheese and consuming thoroughly cooked and steamed food may be helpful in control of human listeriosis.

8. Conclusion

The inclusion of human listeriosis in the notifiable infectious agent list would allow determination of the distribution and characteristics of this infection and molecular epidemiological studies concentrating on the clonal group identification associated with colonization and invasive infections will help in evolving effective prevention and control measures. Clinical microbiology laboratories and health care professionals should play a pro-active role in suspecting and diagnosing human listeriosis. Conventional microbiological methods, improved selective culture methods for *Listeria* when assisted with rapid, advanced and molecular techniques would facilitate increased identification of *Listeria spp* and help in understanding the epidemiology, demographic and clinical characteristics of human listeriosis. Sporadic reports of human infection with *Listeria spp* should not undermine its public health impact.

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Competing Interest

None.

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