

Listeriosis: Clinical Perspectives

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ABSTRACT

Listeriosis, caused by the bacterium *Listeria monocytogenes*, is a rare but severe food-borne illness primarily affecting individuals with compromised immune systems, pregnant women, and the elderly. The clinical manifestations of *Listeria* infection include chronic and asymptomatic bacteremia, meningitis, encephalitis, and adverse outcomes in pregnancy. This bacterium, a facultatively anaerobic, gram-positive organism, thrives at 37°C and is found in various agricultural and natural habitats, contaminating raw materials that enter food processing facilities. The epidemiology of listeriosis reveals its significant impact on mortality rates, with an increasing number of cases reported in the United States, particularly affecting the elderly. *Listeria* persists in diverse environments, from soil to meat products, water, and decaying vegetation, raising concerns about its transmission and potential sources.

Clinical predisposing factors for listeriosis include involvement of the central nervous system, initial bacteremia, age over 60, and various comorbidities. *Listeria*'s pathogenicity is multifactorial, involving factors such as hemolysin, phospholipases, internalin, ActA, p60 (iap), and mechanisms for metal ion uptake. The bacterium's ability to grow within cells and its virulence factors contribute to the severity of listeriosis. Recent developments in *Listeria* detection encompass various methods, including culture-based, immuno-based, and molecular approaches such as PCR and biosensor-based techniques. The detection of *L. monocytogenes* remains a significant challenge due to the bacterium's persistence in different environments. Molecular methods, particularly DNA microarrays, PCR, and biosensors, are considered reliable for sensitive and specific detection. In conclusion, Listeriosis poses a substantial health risk, especially to vulnerable populations. Preventive measures involve decontamination of livestock and food products. Ongoing research focuses on understanding the complex pathogenicity of *L. monocytogenes*, and molecular methods play a crucial role in its detection and control.

Keywords: Listeriosis, *Listeria monocytogenes*, food-borne pathogens, Polymerase chain reaction, immune system, molecular methods

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1. INTRODUCTION

1.1. INTRODUCTION TO LISTERIOSIS

Listeriosis is an uncommon but deadly food-borne illness that can be brought on by *Listeria monocytogenes*. The illness normally only affects people with low immune systems, such as babies, older adults (Suominen et al. 2023), pregnant women and their fetuses, new mothers, and those with impaired immune systems. On occasion, adults and children who are otherwise healthy are also affected (Donovan 2015).

1.2. CLINICAL MANIFESTATIONS

L. monocytogenes infects people when they eat food that is contaminated. It is believed to move from the mesenteric lymph nodes to the spleen and liver after being able to breach the intestinal barrier (Fig. 1). It is still unclear how much intraluminal multiplication occurs and exactly where it breaches the intestinal barrier. Infection of *L. monocytogenes* may result in chronic and asymptomatic bacteremia if the immune system cannot regulate it, particularly at the level of liver and spleen. Meningitis or encephalitis may develop because of it getting into the brain or placenta (Yousif et al. 1984) Pregnancy-related abortions, generalized infections in infected neonates (granulomatosis in antiseptic), and immunocompromised patients are the most common cases (Lecuit 2007).

(C). *L. monocytogenes* can lead to acute hepatitis. This condition typically presents as a sudden onset of fever and jaundice, with positive blood cultures for *L. monocytogenes*.

(D) In order to move into the blood stream and cause potentially fatal systemic infections, *L. monocytogenes* can easily get through this lymph node barrier.

(E) *Listeria* may grow unchecked in the liver, leading to increased low-level bacteremia and spread of preferred secondary target organs (tumour necrosis factor alpha).

(F) and (G) *Listeria* goes through an internal life cycle which involves early phagocytic compartment escaping, a speedy intra cytoplasmic process of replication via actin-based motility, and a speedy spread to adjacent cells, where they reactivate the cycle. *Listeria* was prevented from infecting the humoral portion of the immune system by this technique of spreading via human tissues. Several virulence factors have been discovered over the past 15 years at significant stages of this intracellular life cycle.

Pathogenic *Listeria* enters the body through the intestine. After intestinal translocation, the liver is believed to be the first organ to be targeted. Until a cell-mediated immune response removes the infection, *Listeria* actively grow in the liver (Werbrouck et al. 2006). In healthy individuals, exposure to listerial antigens over time likely contributes to the maintenance of memory T cells that are anti-*Listeria*. However, in immuno-compromised and weakened patients, *Listeria* may grow unchecked in the liver, leading to increased low-level bacteremia and spread of preferred secondary target organs (tumour necrosis factor alpha) (Longhi et al. 2004). Both *L. monocytogenes* and *L. ivanovii* are facultative intracellular parasites that can infect a range of typically non-phagocytic cells, including endothelial,

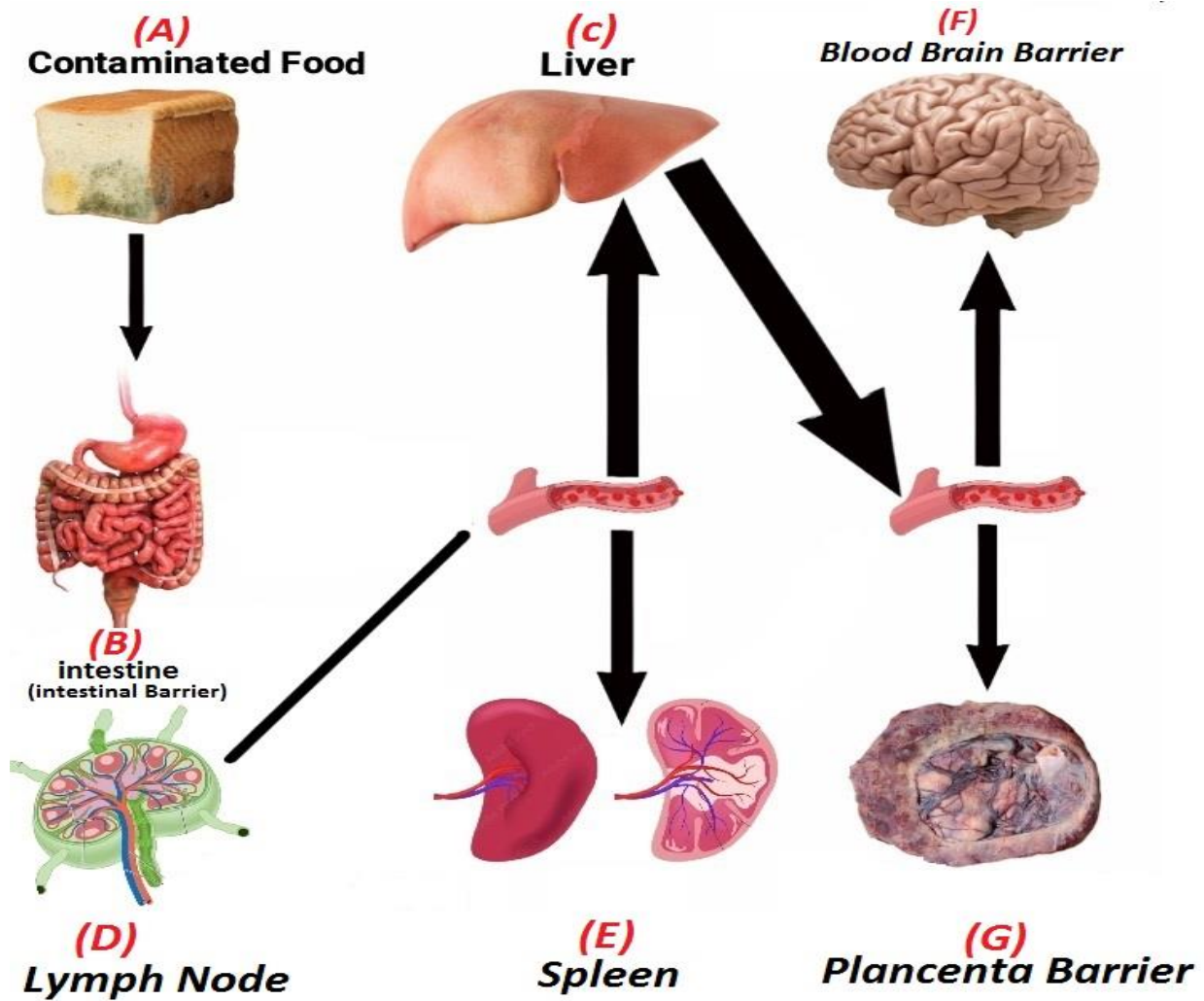


Fig 1: Clinical manifestations of *L. monocytogenes*: (A) main route of transmission is through contaminated food. (B) It causes Listeria gastroenteritis, a typical foodborne illness, a large proportion of people exposed to the contaminated food can become infected, with attack rates reaching up to 72%. The high infection rate is likely due to the presence of a substantial number of Listeria organisms in the contaminated food.

epithelial, and hepatocyte cells. They can also live in macrophages. In all the aforementioned cell types, pathogenic Listeria goes through an internal life cycle which involves early phagocytic compartment escaping, a speedy intra cytoplasmic process of replication via actin-based motility, and a speedy spread to adjacent cells, where they reactivate the cycle. Listeria was prevented from infecting the humoral portion of the immune system by this technique of spreading via human tissues. Several virulence factors have been discovered over the past 15 years at significant stages of this intracellular life cycle (Glaser et al. 2001).

Clinical symptoms might range from mild, invasive conditions like febrile gastroenteritis to more serious ones like sepsis, meningitis, rhombencephalitis, prenatal infections, and abortions. Numerous European nations have seen an increase in listeriosis cases in recent years. These increases are not related to socioeconomic status, gender, geography, ethnicity, or infectious serotypes and are mostly due to the greater risk of bacteremia in listeriosis in those under 65 years old (Allerberger and Wagner 2010).

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Consuming contaminated foods including raw meat, unpasteurized dairy products, frozen foods, already wrapped foods, factors influencing the environment, sporadic cases of listeriosis, and illness outbreaks are the primary manifestations of *L. monocytogenes* infection (Weis and Seeliger 1975; Wilson 1995; Beumer and Hazeleger 2003; Thevenot et al. 2006; Ramaswamy et al. 2007).

2. INTRODUCTION TO BACTERIUM

L. monocytogenes is a facultatively anaerobic, gram-positive bacteria that thrives at a temperature of 37°C. Between 22-28°C, it is movable, but around 30°C, it becomes immobile (Allerberger 2003).

L. monocytogenes can be found in agricultural and natural habitats, contaminating raw materials that are then brought into food processing facilities. If allowed, the bacterium can even grow at temperatures below freezing and pose a risk to human health when swallowed (Todd and Notermans 2011).

2.1. EPIDEMIOLOGY OF LISTERIOSIS

Bacteria account for 40% of yearly mortality rates (Kumar and Neelam 2016; Pourakbari et al. 2019). Bacteria and their toxins have been found to pollute water and food supplies (Tauxe, 2002). According to estimates, almost 48 million people in the United States of America are diagnosed with various foodborne illnesses every year, resulting in 128,000 hospital admissions and a 3000 case mortality rate (Mehranian et al. 2023). The combined information from the nationwide listeriosis surveillance in Finland, patient replies to patient interviews, lab results from patient samples, and comparison with listeria findings from food and food manufacturing facilities gathered as part of studies into the outbreak between 2011 and 2021. In Finland, invasive listeriosis occurs more frequently than the norm for the EU (1.3/100000 in 2021), and the majority of cases are seen in elderly people with a inclining condition. Numerous cases mentioned eating high-risk foods and storing food improperly (Suominen et al. 2023). Intrusive listeriosis cases totaling 253 were documented from 2011 to 2016 in 19 provinces, with a case-fatality rate of 25.7% overall and no deaths among minors or expecting women (Li et al. 2018).

According to CDC, since 2000, listeriosis has been a notifiable illness in United states (Donovan 2015).

3. OCCURRENCE OF LISTERIOSIS

Listeria occurs in our environment and many food products. The organism was isolated from the soil (Welshimer 1960), meat products (Gomez et al. 2015) water (Gartley et al. 2022), and decaying vegetation (Welshimer, 1968). *L. monocytogenes* was recovered using cold enrichment techniques from samples of manure, river water, and sewage mud, providing quantifiable evidence of the organism's capacity to persist in the environment. They discovered that *L. monocytogenes* quantitative counts from sewage sludge sprayed on farmland remained stable for at least 8 weeks. When this technique was suspected of being a factor in a significant epidemic of listeriosis in humans in Nova Scotia, the ramifications of utilizing fecal material as fertilizer for agriculture became clear.

3.1. HUMAN LISTERIOSIS

Bojsen-Moller investigated fecal transport in several population groups using cold enrichment. In hospitalized adult patients (1.2%), patients having diarrhea (1%), healthy abattoir employees (4.8%) and household contacts of listeriosis patients (26%). Up to eight samples were obtained from each patient's household contact. Because up to eight samples were taken from each patient's household contact, the prevalence of listeria isolates in this group cannot be directly compared to data from other populations.

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At least one member of five out of 14 households had *L. monocytogenes* positive in their stools. Only two of the families, though, had a family member who was infected with the same serotype as the patient. All the cultures were processed by cold enrichment, but comparisons across groups were made more difficult by the non-hospitalized patients' delayed delivery of specimens to a central laboratory and their increased use of antibiotics before culture (Schuchat et al. 1991).

Animal Listeriosis: It's important to keep in mind that *L. monocytogenes* only unintentionally contributes to the clinically visible human infection, even though this is what gives the organism popularity in the media. Therefore, it is doubtful that it would have created its pathogenic collection with a focus on humans. *L. monocytogenes* is largely an animal illness, and it can produce both solitary instances and outbreaks in both domestic and wild animals (Lecuit 2007).

3.2. CLINICAL LISTERIOSIS PREDISPOSING FACTORS

The meta-analysis supported the following set of listeriosis-related mortality risk factors: 1. involvement of the central nervous system, initial bacteremia, and Age 60 years were clinical predisposing factors; 2. non-hematological malignancies, alcoholism, chronic renal disease, cardiovascular disease, and pulmonary illness were the predisposing comorbidities (Huang et al. 2023).

3.3. PATHOGENICITY OF LISTERIA MONOCYTOGENES

Even though *L. monocytogenes* is frequently present in the atmosphere and human exposure to it is likely prevalent based on carriage studies, invasive listeriosis is a rare complication. Three factors can influence whether an invasive disease will manifest: the host's susceptibility, the virulence of the infecting organism, and the quantity of the inoculum.

The software "Find Target" is used to compare these genome sequences in order to find probable virulence genes and, more generally, to comprehend the pathogenicity of *L. monocytogenes* and its capacity to contaminate food. Additionally, a comparative genomics technique based on DNA arrays is being used to characterize clinical and environmental isolates of Listeria (Ramaswamy et al. 2007). A comparative genomics method using microarrays for the assessment of the biodiversity of Listeria, and that of the species *L. monocytogenes*, has shown amazing accomplishments in gene expression investigations (Jacquet et al. 2004).

3.4. CLINICAL FEATURES OF LISTERIA INFECTIONS

In all vulnerable hosts, *L. monocytogenes* infection manifests clinically in a fairly similar way. Perinatal listeriosis and listeriosis in mature patients are the two main ways in which these infections manifest. The CNS is affected by either a localized infection or a widespread illness in both cases. Even with early antibiotic therapy, listeriosis has an average fatality rate in humans of 20 percent to 30 percent or more, making it one of the deadliest bacterial illnesses presently known (Allerberger 2003; Mclauchlin 1990; Schuchat et al. 1991).

4. VIRULANCE DETERMINANTS

4.1. HEMOLYSIN (HLY)

This gene (*hly*) was the foremost virulence determinant factor recognized and sequenced in the Listeria species. Further investigation of the *hly* locus led to the finding of a chromosomal virulent gene group,

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which comprises the majority of the genetic elements compulsory for the intracellular developmental process of this pathogenic *Listeria* species (Fig. 2). The Hly product was also the pioneer pathogenic factor to play a specific role in the *Listeria* infection illness process. Hly is critical virulence factor required for the infection and participates in some different processes that occur when *Listeria* interact with their vertebrate host, including intracellular parasitism (Goebel et al. 2013).

4.2. PHOSPHOLIPASES

Pathogenic *Listeria* spp. produces three different phospholipase C (PLC) enzymes with virulence properties. PlcA and PlcB are present in both *L. ivanovii* plus *L. monocytogenes*, but SmcL is exclusive to the *L. ivanovii*. The first description of *L. monocytogenes* producing phospholipase activity was made in 1962 (Fuzi and Pillis 1962), this study showed that the strength of the opacity reactions in egg yolk agar associated with the tested strains' hemolytic ability.

4.3. INTERNALIN

Pathogenic *Listeria* spp. include a novel family of virulence-related genes, which generates the protein internalins. By examining a collection of mutants that are transposon-induced for reduced intrusiveness in Caco-2 cell monolayers, researchers revealed the first two members of this family to be characterised, InIA and InIB, encoded by the inlAB operon. Internalin was administered to InIA when it was shown that it behaved as an invasin, promoting bacterial internalisation by these typically nonphagocytic epithelial cells (Gaillard et al. 1991). Since then, many internalin homologs in *L. ivanovii* and *L. monocytogenes* have been discovered (Dramsı et al. 1997; Engelbrecht et al. 1998b, 1998a; Raffelsbauer et al. 1998).

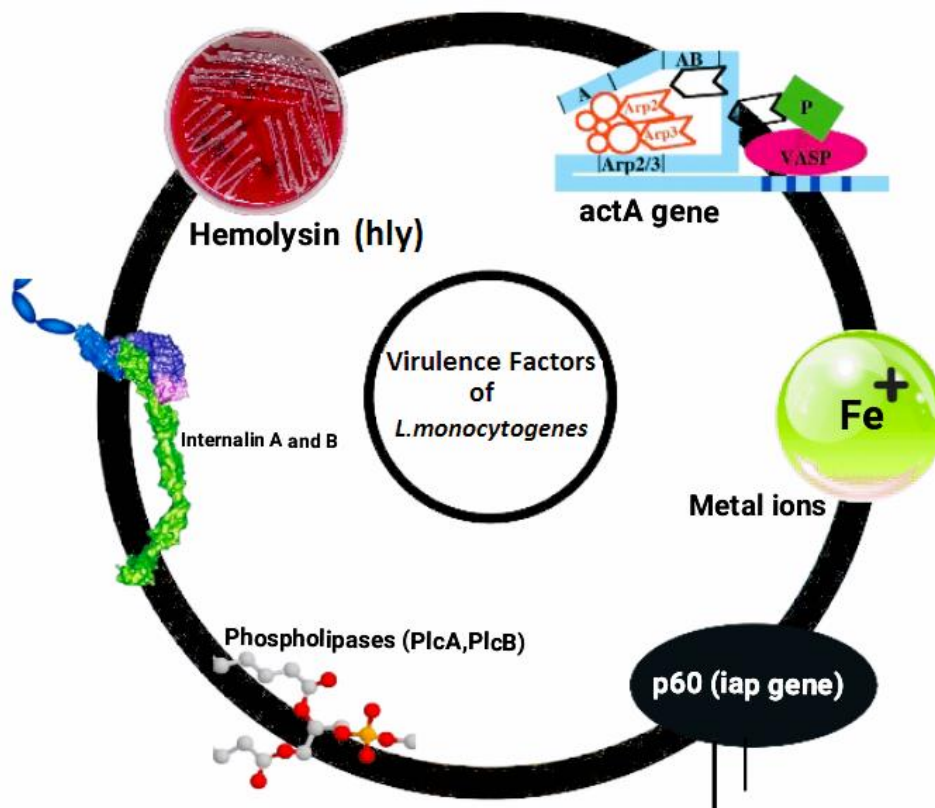


Fig. 2: Different Virulence Determinants present in *L. monocytogenes*

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A component known as a leucine-rich repeat (LRR) domain, that is a tandem repeat pattern of a sequence of amino acids with leucine repeats at specific places, is a feature shared by all internalins (Kajava 1998). Leucine or isoleucine residues are found at locations 3, 6, 9, 11, 16, 19, and 22 in the typical LRR unit of internalins (— —L— —L— —L—L— —N—I— —I/L— —L). This sequence produces a new, right-handed helix known as a parallel b-helix with a turn next to each LRR unit. It was initially found in the pectate lyase of *Erwinia chrysanthemi* (Heffron et al. 1998; Yoder et al. 1993).

4.4. ACTA

The crucial role of ActA in listerial intracellular mobility and virulence was first discovered through a mutation of *L. monocytogenes*-infected cultured tissue cells (Kocks et al. 1992). After entering the host cell, these bacteria were able to exit into the cytoplasm, but they gathered as micro-colonies in perinuclear region of the cell because they were unable to migrate about the cell. Phalloidin, a fungus toxin that is attached with F-actin and paralyzes actin cytoskeleton, was used to dye the mutant to demonstrate that it was unable to recruit actin. Additionally, a significant diminution of the actA mutant was seen in the research of mouse contamination example (Domann et al. 1992; Kocks et al. 1992).

4.5. p60 (iap)

L. monocytogenes suddenly produces colonies with a modified, stable, rough phenotype on plates of agar. These bacteria grow in the form of lengthy filaments made of chains of individual cells. Impaired invasiveness is correlated with this lack of virulence, especially in fibroblasts (Kuhn and Goebel 1989). The synthesis of the important 60-kDa extracellular protein p60, which is present in both the culture supernatant and the invasion deficit, is defective (Kuhn and Goebel 1989) and connected with the cell wall (Ruhland et al. 1993) and when exogenously introduced, breaks apart the bacterial networks and recovers invasiveness (Kuhn and Goebel, 1989). The *iap* gene, which codes for a 484-residue of polypeptide with core repeat regions of Thr-Asn units in *L. monocytogenes*, is responsible for producing the p60 protein (Kohler et al. 1990).

4.6. METAL ION UPTAKE

Every living thing, even prokaryotic cells, must have iron because it serves as the cofactor for huge collection of enzymes as well as necessary proteins that are associated in electron transport process. Because ferric transferrin and heme molecules in cells' interiors and ferritin in serum bind iron, it is not easily available in the tissues of animal hosts. Because of this, bacterial pathogens have created distinct methods for obtaining iron for development in host tissues. These procedures are essential for pathogenicity (Payne 1993).

4.7. RECENT DEVELOPMENTS IN LISTERIA DETECTION

One hypothesis states that food needs contain 100 CFU/mL/g of *Listeria* to be infectious. Because of overdue and ambiguous signs, it is problematic to detect at the very initial stage. According to Australian study, listeriosis can be brought on by 10 colony forming units in 25 g of fast food and can be reactivated by 100 CFU/mL. So, Scientists had settled a number of methods to address the requirement for a dependable, delicate, and repeatable method to discover *L. monocytogenes*. Below is a discussion of the most useful and accessible detection methods that have been created to yet.

4.8. CULTURE-BASED TECHNIQUES

The difficult yet exact cold enrichment technique was developed in the 1990s, (Lorber, 2002). The separation of the chromogenic substrate by the enzyme known as α -D-glucosidase and the hydrolysis of lecithin appeared to be because of the blue or green colonies. Their cities resembled hazy haloes. After the bacteria's existence was confirmed, it was re-dissolved in non-selective media to get ready for the 4-5 days biochemical test. Additionally, there used to be a significant risk of results that were false positives and a requirement for numerous chemicals, media, and reagents, and also the effort and time investment (Jadhav et al. 2012). A researcher got comparable outcomes using the ISO 11290-1 technique, which was created in 2004 and used a LOD of 1 CFU/g. They later learned that the LOD was 1 CFU/g utilising the 2013 USDAFSIS methodology (Valimaa et al. 2015). The most probable number technique (Dwivedi and Jaykus, 2011) was more sensitive than a chromogenic medium. *Listeria* was identified too rapidly, indicating that MPN-PCR was a more promising technology than earlier methods (Law et al. 2015).

4.9. IMMUNO-BASED TECHNIQUES

The use of antigen-antibody biochemistry in illness screening and diagnosis seems to have promise. To light this, (Gasnov et al. 2005) stated that an immunological procedure have sensitivity more than a conservative method, that is 105 cells per mL.

4.10. ELISA

ELISA was used for examining food models in 2010 (Ueda and Kuwabara, 2010). Another scientist used an indirect ELISA to test blood samples at a dilution of 1:200 for listeriosis; positive P/N ratios were set to greater than 2. Synthetic LLO-2 peptide (0.40 g/well) and rLLO (0.50 g/well) were used as antigens during this method. A LOD of 105-106 CFU/mL was found to be reliable based on the pH and basicity of the food specimen (Malla et al. 2021).

4.11. IMMUNO-MAGNETIC SEPARATION

In order to improve the sensitivity of the detection approach, a researcher first demonstrated a methodology in 2006 that required connecting a magnetic field with a substantial number of cells of bacteria (Amagliani et al. 2006). In order to identify the *hlyA* gene in milk samples, a researcher created a prototype in 2006 that combined real-time PCR with an immune-based technique employing rabbit anti-*Listeria* and beads coated with immuno-magnetic nanoparticle. The Limit of detection observed was $>10^2$ CFU/0.5 mL (Yang et al. 2007). Similar to this, a study from 2010 employed paramagnetic beads covered with the *Listeria* endolysin-derived cell wall domain from contaminated uncooked milk. This LOD ranges from 102 to 103 CFU/mL (Walcher et al. 2010).

5. MOLECULAR METHODS DETECTIONS

5.1. DNA MICROARRAYS

DNA microarray was used to recognize the *Listeria* virulence genes *plcB*, *inlB*, *plcA* and *clpE* in 2002. Using this technique, he claimed that the *Listeria* test was positive (Volokhov et al. 2002). By joining 585 mixed genomic DNA probes, a researcher explored serotype-specific probe differentiation and discovered that 29 probes were successful (Borucki and Call, 2003). As a follow-

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up, it was employed as a confirmatory approach to evaluate the sensitivity of PCR amplification and polymorphism. with an 8 log CFU/mL limit for detection, Another study found that 9/16 of the microarrays that were used to analyse the purposely contaminated milk returned positive results. He emphasised the accuracy and dependability of this strategy. Although encouraged, it requires persistence and has a chance to cross-hybridize, which could produce an inaccurate test result (Bang et al. 2013).

5.2. PCR BASED METHODS

In molecular diagnostics, PCR is frequently employed as a promising method for the identification of small samples. A specific set of specialised primers were needed for specific target amplification during a heat cycle in PCR. Gel electrophoresis is then utilised to analyse the outcomes. Below is a discussion of the adjustments that were made to allow for the detection of *Listeria* utilising PCR:

5.3. CONVENTIONAL PCR

Since PCR employs primers to identify pathogens in a sample, it is a promising technique. Aznar and Alacron (2003) claim that whereas only 17 cases were discovered to be positive during culture, 56 out of 217 instances in naturally infected testers obtained positive PCR results with an edge of detection of 1 CFU/g. They used primers to check for the presence of hypersensitivity protein and the proteins phospholipase C and fibronectin-binding protein, as well as the genes *hlyA*, *iap*, *inlB*, *inlA*, *16S*, and *23S* rRNA (Aznar and Alarcon 2003).

5.4. MULTIPLEX PCR

The immediate detection of numerous species in contaminated samples using multiplex PCR has been characterised as a reliable, efficient, and time-saving method (Alarcon et al. 2004). Samples with different LODs, including 260 CFU/ml of *S. aureus*, 79 CFU/ml of *L. monocytogenes*, and 57 CFU/ml of *Salmonella* species (Bang et al. 2013). Using LODs of 1-100 CFU/ml, this method was used to find six prevalent food-borne pathogens in RTE meals (Lei et al. 2008). The *hly* gene of *L. monocytogenes*, the *nuc* gene of *S. aureus*, the *invA* gene of *S. enterica*, the *stx* gene of *E. coli*, and the *intimin* gene of *E. coli* are targets of the MPCR method, which was developed and has a detection limit of 1 CFU/mL (Zhang et al. 2009). Another study from 2006 claimed that MPCR was not specific for amplicons of similar size and optimization (Liu 2009).

5.5. REAL-TIME PCR (RT-PCR)

With a detection limit of 10CFU per 25 g of food, a 3-day PCR-based test was created that is equal to the EN ISO 11290-1 or ISO 10560 protocols for *Listeria* discovery. The LOD was 1104 CFU/mL (Kačlikova et al. 2002). According to another study, the total viable count found in the salad was 1.35, 2 and 1.8 CFU/g and in the broccoli it was 0.35, 1.9 and 1.8 CFU/g. In which *L. monocytogenes* had a limit of detection of 1.74, 1.1, and 1.6 CFU/mL in salad and 6.37, 1.2 and 1.3CFU/mL in broccoli, with a total of less than 1000 cells/m (Bhagwat 2003). In 2005, a *hly*-IAC Q-PCR assay for the detection of *Listeria* was developed, the detection limit of 8 was established by using varied amounts to spike the sample (Rodriguez-Lazaro et al. 2005). A researcher created quantitative real time-PCR to determine the fluorescence released by the spiked sample in order to broaden the reach of the procedure (Berrada et al. 2006). The obtained LOD

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was 10–105 CFU/mL (Berrada et al. 2006). Targeting the *ssrA* gene in naturally and intentionally contaminated foods (dairy foodstuffs, vegetables and meat) led to a detection limit of 1–5 CFU/25 g/mL, according to another researcher (O' Grady et al. 2008). He therefore concluded that it was a wise scheme for the specific sample. The results of a qRT-PCR analysis on both naturally and intentionally infected ground beef, chicken, turkey, and pork with a detection limit of 18 CFU/10 g were published in a study in 2010 (Suo et al. 2010).

5.6. BIOSENSOR BASED TECHNIQUES

The biological specimen analyzer known as a biosensor uses an analyte as the object and an electrochemical setup as the transducer to provide legible data. He passed the antibody through a biosensor chip immobilised on polyclonal goat anti-rabbit Fab antibodies in 2004 to detect *L. monocytogenes* (Leonard et al. 2004). The procedure of surface plasmon resonance to identify *L. monocytogenes* was found to be promising, with a detection limit of 102 CFU/mL, according to another study that advanced the sensor platform (Poltronieri et al. 2009). Au-labeled secondary antibodies were applied on this platform. A study reported using collagen matrix-merged mammalian B-lymphocyte Ped-2E9 cells as a sensing tool to detect listeriolysin O from the contamination of a food section with an acceptable detection limit of 102-104 CFU/g in a subsequent study (Banerjee and Bhunia 2010).

6. CONCLUSION

Even though listeriosis is not a serious medical issue, the high death rate of apparent listeriosis in younger, older, and immune-compromised patients poses a difficulty for veterinary professionals, food microbiologists as well medical microbiologists, and doctors. Decontaminating domestic livestock and food products has been a crucial preventive measure since food has been identified as the primary source of illness.

Its ability to grow inside cells, iron compounds, catalase and superoxide dismutase, surface components, and hemolysins are just a few of the factors that have been suggested over time to affect *L. monocytogenes*' pathogenicity, which This suggests that it is their virulence is multifactorial.

Additionally, since meningitis and encephalitis are the most common symptoms of disease, it is important to choose medications that are easy to pass the blood-CSF barrier and the blood-brain barrier. It will be necessary to use unconventional techniques in the future to lessen the health danger that listeria poses. *Listeria monocytogenes* can be detected using a variety of approaches, but molecular methods such as DNA microarrays, PCR-based methods, and biosensor-based methods are thought to be the most reliable.

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