Review Article

Risk factors and Outcomes of Emerging Listeria Monocytogenes Infection in Pakistan: Insights from a Tertiary Care Hospital

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Abstract

Listeria monocytogenes is a Gram-positive rod responsible for listeriosis. This systemic infection often presents with bacteremia and may progress to severe manifestations such as meningoencephalitis, particularly in immunocompromised individuals and the elderly. In pregnant women, it is associated with fetal and placental involvement, frequently resulting in adverse outcomes. Over the past few decades, L. monocytogenes has emerged as a significant foodborne pathogen, implicated in numerous outbreaks worldwide. The objective of this study is to assess the risk factors, clinical features, and outcomes of patients admitted with Listeria monocytogenes infection at a tertiary care Centre in Karachi, Pakistan.

Keywords: infectious diseases; molecular diagnostics; next-generation sequencing (ngs); polymerase chain reaction (pcr)

Introduction

Listeria monocytogenes is a gram-positive rod, known to be an opportunistic food-borne pathogen worldwide [1].Its most common route of transmission in the community is consumption of contaminated food[2]. Listeria causes food-borne illness, can survive even in low-moisture, low temperatures usually found in refrigerators, high salt foods making it challenging to control in food environment[3].Due to its prolonged incubation period , prompt diagnosis is difficult. Numerous reports of listeriosis outbreaks have been linked to dairy products, meat products, as well as fresh produce [4]. Apart from causing non-invasive, non-fatal infections, it was discovered as a major human pathogen causing fatal illnesses, including severe meningoencephalitis and maternal-fetal infections [5].

The annual incidence rate of listeriosis varies from 0.1 to 10 cases per million people per year, depending on the countries and regions of the world [6]. Ready-to-eat dairy, seafood, and immunocompromised individuals, including pregnant women and geriatric populations, seem to be most affected by this pathogen [7-9]. Despite the low prevalence, it has a high mortality rate, particularly in high-risk populations such as neonates, pregnant females, age ≥ 60 years, primary bacteremia, CNS involvement and prior comorbidities such as malignancies, chronic kidney diseases[10]. Maternal infections with Listeria monocytogenes have been reported to be rare before 20 weeks of gestations. The incidence of listeriosis is higher among pregnant women than in the general population and is associated with adverse fetal outcomes, including miscarriage and stillbirth[9, 11].

Treatment recommendations for listeriosis rely on knowledge gained from animal models, in vitro experiments, and clinical studies, as listeriosis is not a common disease and there aren't many effective randomized controlled trials. Ampicillin is the recommended treatment, and trimethoprim/sulphamethoxazole, meropenem can be an alternative agent in case of penicillin allergy [12]. Although penicillin and ampicillin are the recommended treatments for listeriosis, most experts advise combining gentamicin with ampicillin due to its delayed bactericidal activity against Listeria[13]. While some retrospective studies have failed to show a survival benefit— and even suggested potential harm in neurolisteriosis—other data indicate a possible survival advantage when gentamicin is administered for more than three days[14].

We aimed to identify the risk factors, clinical characteristics, and outcomes of listeriosis at a tertiary care centre, Pakistan. with the goal of understanding various clinical manifestations and predisposing conditions in our population to facilitate early recognition and management of this potentially treatable condition

Methods: A retrospective study was conducted over 7 years and included all patients with culture-proven listeriosis. Comorbid conditions, clinical presentation, treatment, and outcomes were recorded and analyzed.

Results:

A total of 63 patients diagnosed with Listeria monocytogenes infection were included in the study. There was female predominance (n = 44, 70.9%), with

a mean age of 50.2 years. Diabetes mellitus was the most common comorbidity (43.5%). Among high-risk groups, 14 (22.6%) patients were pregnant, 10 (15.9%) were on immunosuppressive therapy, and another 10 (15.9%) were classified as elderly. The predominant presenting symptoms included fever (74.6%) and central nervous system involvement (52.0%), mainly meningoencephalitis. All patients received antibiotic therapy with either ampicillin or meropenem for a mean duration of 16.7 ± 8.4 days. The overall mortality rate was 11.1%.

Conclusion: Listeriosis was observed not only in the elderly but also in middle-aged individuals with underlying risk factors, as well as in pregnant women. Enhanced environmental hygiene, early diagnosis, and timely treatment are essential to improving outcomes, particularly in pregnancy-related cases. Public education, healthcare provider training, and community-level preventive strategies are critical for effective management and control of listeriosis

Methodology

This retrospective, observational study was conducted from January 2017 to December 2023 at the Aga Khan University Hospital (AKUH), Karachi, Pakistan. AKUH is a Joint Commission International (JCI) accredited state-of-the-art tertiary care centre that provides care to patients from all over the country. All patients admitted with culture-proven L. monocytogenes were evaluated for possible inclusion in the study. Patients with co-infections with other bacterial infections were excluded. An extensive review of electronic and paper-based medical records, together with radiology and laboratory databases of the selected patients, was undertaken.

Pertinent information—including demographics, comorbid conditions, predisposing factors, immune status, imaging findings, management strategies, complications, and clinical outcomes—was documented on a structured proforma.

Ethical consideration

The study was reviewed and approved by the Ethics Review Committee, Aga Khan University (ERC # 2023-9294-26813). Due to the retrospective chart reviews and lack of direct involvement of patients or other human participants, a waiver of informed consent was given by the Ethics Review Committee, Aga Khan University.

Data analysis was performed using RStudio (version 4.1.2; Boston, USA). The Shapiro-Wilk test was used to assess the normality of quantitative variables, including age, premature birth, and gestational age. As all variables were found to be non-normally distributed, they were summarized using median and interquartile range (IQR). Categorical variables, such as

gender, comorbidities, clinical manifestations, and patient outcomes, were summarized as frequencies and percentages. Stratified analysis was conducted based on the diagnosis Neurolisteriosis vs. Non-neurolisteriossis to explore potential statistical associations. The Mann-Whitney U test was used for continuous variables, while the Chi-square or Fisher's exact test was applied for categorical variables, as appropriate.

Results:

A total of 63 patients met the inclusion criteria and were included in the study. The mean age of participants was 50.2 (Median 53, [Q1, Q3] [32.0, 67.0]) years, and the majority were female (n=44, 69.8%). Diabetes Mellitus (n=27, 43.5%) was the most frequent co-morbid illness, followed by hypertension (n= 25, 40.3%) and CLD (n=12, 19.0%) (Table 1). Among the high- risk group,14 (22.6%) patients were pregnant, and 10 (15.9%) patients were on immunosuppressive therapy, and a similar percentage was classified as elderly.

The most common clinical features were fever (n=47, 74.6%), followed by drowsiness (n=20, 31.7%), abdominal pain and vomiting (n=10, 15.9%). Nearly half (n=27, 52.0%) of the study patients presented with CNS listeriosis, predominantly meningoencephalitis, one patient had brain abscess, and 16 (25.39%) patients had concomitant bacteremia as well (Table 3).

Overall, antimicrobial susceptibility data were available for 59 cases. In three cases where Listeria monocytogenes was detected by a commercial multiplex PCR (Filmarray meningitis encephalitis panel, Biomerieux) the organism did not grow on culture. The susceptibility rates for ampicillin, meropenem and trimethoprim/sulphamethoxazole were 96.6%, 100% and 86.4% respectively.

All patients were treated with ampicillin or meropenem, depending upon the availability of drugs for 4 – 6 weeks (mean 16.7±8.4) days. The overall mortality was 11.1% and most of the patients who died were older than 60 years of age. In subgroup analysis between CNS and non-CNS listeriosis (table 4), there was no major difference found, i.e age, comorbid illness and gender distribution and mortality. Most pregnant patients had non-CNS listeriosis (p value 0.014).

Mortality was observed in 5 patients (15.2%) in CNS listeriosis and 2 patients (6.7%) in the non- CNS group. Pregnancy-related mortality was significantly higher in non-CNS involvement, with 5 patients (16.7%) compared to 2 patients (6.1%) in CNS listeriosis (p = 0.024).

Hypertension	N	Percentage
No	38	(59.7%)
Yes	25	(40.3%)
Diabetes		
No	36	(56.5%)
Yes	27	(43.5%)
HIV-Status		
No	62	(98.4%)
Yes	1	(1.6%)
Autoimmune disease		
No	56	(88.9%)
Yes	7	(11.1%)
Malignancy		
No	57	(90.5%)
Yes	6	(9.5%)
Chronic Kidney Disease		
No	58	(92.1%)
Yes	6	(7.9%)
Chronic Liver Disease		
No	51	(81.0%)
Yes	12	(19.0%)
Others/ Description of known disease		
No	33	(52.4%)

Yes	30	(47.6%)
Immuno-compromised		
No	46	(73.0%)
Yes	17	(27.0%)
On Immunosuppressive therapy		
No	53	(84.1%)
Yes	10	(15.9%)
Pregnancy Status		
No	30	(77.8%)
Yes	14	(22.2%)
Extreme of Age		
No	53	(84.1%)
Yes	10	(15.9%)
Other		
Alcoholic	2	(3.2%)
Hypothyroidism, hemolytic anemia	1	(1.6%)
Multiple myeloma	1	(1.6%)

Table 1: Listeriosis and Comorbid Conditions

Clinical Manifestation	Number of Patients (n)	Percentage (%)
Diagnosis		
CNS Listeria	33	52.0
Non-CNS listeria	30	48..0
Break down of CNS Listeria		
Meningo-encpehalitis	26	41
Brain Abscess	1	1.58
Breakdown of Non-CNS Listeria		
Bacteremia	16	25.39
Colitis	2	3.17
Placental Infection	3	4.76
Non-specific diagnosis	4	6.34
Presenting Symptoms		
Fever	47	74.60
Drowsiness	20	31.74
Headache	8	12.69
Seizure	7	11.11
Abdominal Pain	10	15.87
Vomiting	10	15.87
Diarrhea	4	6.34
Other nonspecific symptoms- flu, jaundice, Per rectal bleeding, dysphagia	12	19.047
PATIENTS OUTCOME		
Discharged	44	69.8
Lost to follow up	11	17.5
Expired	7	11.1

Table 2: Clinical Manifestation of patients with Listeria Monocytogenes infection

Variable	CNS Listeria (N=33)	Non-CNS listeria (N=30)	P- value
Age (Years)			0.110
Median [Q1, Q3Max]	61.0 [35.0,68.0]	48.5 [29.5, 61.5]	
Gender			
F	23 (69.7%)	21 (70.0%)	1.00
M	10 (30.3%)	9 (30.0%)	
Hypertension			
No	17 (51.5%)	21 (70.0%)	0.198
Yes	16 (48.5%)	9 (30.0%)	
Diabetes			
No	20 (60.6%)	16 (53.3%)	0.616

Yes	13 (39.4%)	14 (46.7%)	
HIV Status- Affected			
No	32 (97.0%)	30 (100%)	1.00
Yes	1 (3.0%)	0 (0%)	
Autoimmune Disease			
No	30 (90.9%)	26 (86.7%)	0.700
Yes	3 (9.1%)	4 (13.3%)	
Malignancy			
No	30 (90.9%)	27 (90.0%)	1.00
Yes	3 (9.1%)	3 (10.0%)	
Chronic Kidney Disease			
No	31 (93.9%)	27 (90.0%)	0.662
Yes	2 (6.1%)	3 (10.0%)	
CLD			
No	25 (75.8%)	26 (86.7%)	0.344
Yes	8 (24.2%)	4 (13.3%)	
Others/ Description of known disease			
No	17 (51.5%)	16 (53.3%)	1.00
Yes	16 (48.5%)	14 (46.7%)	
Immuno-compromised			
No	25 (75.8%)	21 (70.0%)	0.777
Yes	8 (24.2%)	9 (30.0%)	
On Immunosuppressive			
No	28 (84.8%)	25 (83.3%)	1.00
Yes	5 (15.2%)	5 (16.7%)	
Pregnancy			
No	13 (92.9%)	7 (35.0%)	0.001
Yes	1 (7.1%)	13 (65.0%)	
Extreme of Age			
No	26 (78.8%)	27 (90.0%)	0.308
Yes	7 (21.2%)	3 (10.0%)	
Food Source			
No	26 (78.8%)	22 (73.3%)	0.877
NOT MENTIONED	6 (18.2%)	7 (23.3%)	
Yes	1 (3.0%)	1 (3.3%)	
No Food Source			
No	33 (100%)	29 (96.7%)	0.476
Yes	0 (0%)	1 (3.3%)	
Socioeconomic status			
High	11 (33.3%)	11 (36.7%)	0.639
Low	2 (6.1%)	0 (0%)	
Middle	20 (60.6%)	18 (60.0%)	
Missing	0 (0%)	1 (3.3%)	
Other- Comorbid Conditions			
Alcoholic	1 (3.0%)	1 (3.3%)	0.255
Multiple myeloma	1 (3.0%)	0 (0%)	
NA	3 (9.1%)	0 (0%)	
No	28 (84.8%)	28 (93.3%)	
Hypothyroidism, hemolytic anaemia	0 (0%)	1 (3.3%)	
If abortion/ premature birth, week of pregnancy			
Median [Q1, Q3]	30.0 [25.0, 33.5]	27.0 [24.0, 37.0]	0.970
PATIENTS OUTCOME			
Discharged	22 (66.7%)	22 (73.3%)	0.610
Expired	5 (15.2%)	2 (6.7%)	
Lost to follow up	6 (18.2%)	5 (16.7%)	
PREGNANCY OUTCOME			
EXPIRED	2 (6.1%)	5 (16.7%)	0.024
Premature delivery	1 (3.0%)	6 (20.0%)	

Discussion

Our study showed that although listeriosis is common at extremes of age, it also significantly impacts the middle-aged population, especially those with diabetes and also pregnant females. Central nervous system (CNS) listeriosis was found to be as frequent as non-CNS cases.

Although elderly patients were not the most frequently affected group, they accounted for the majority of the deaths, with an overall mortality rate of 11%.

Listeriosis is more common among patients with prior risk factors like pregnancy, immunosuppressive state or advanced age. A higher incidence of L. monocytogenes infection has been reported among individuals over 65 years of age, likely attributed to a weakened immune response and reduced ability to combat infectious agents.[15, 16]. The median age of our study population was 53 years, with only 15.9% patients being more than 65 years of age. Yan Liu et al. also found a median age of 56 years, but with 40.7% patients aged ≥60 years.[17] . In developing countries like Pakistan, increased cases of listeriosis among patients under 65 years of age may be secondary to poor food safety, inadequate sanitation, limited public awareness, weak health infrastructure and challenges in disease surveillance, diagnosis and prevention.[18, 19]

Pakistan faces a growing burden of diabetes mellitus (DM), increasingly affecting younger individuals. [20, 21] DM impairs immune responses, predisposing patients to infections. In our study, most patients had DM, which likely explains the lower median age (<65 years) of listeriosis cases compared to global patterns involving older adults.

Pregnant women are at increased risk of developing listeriosis than the general population, increased risk of severe disease, complications and adverse obstetric outcomes [22]. This is consistent with our study, in which 50% of pregnancies resulted in adverse outcomes, including IUD, miscarriages or neonatal death. A recent review on listeriosis during pregnancy also highlighted the significant adverse impact of Listeria infection on pregnancy outcomes, including stillbirth, intrauterine fetal demise, spontaneous abortion, neonatal listeriosis, and preterm birth [23]. This underscores the importance of educating pregnant women about preventive measures, raising awareness among healthcare professionals, including obstetricians, regarding early diagnosis and management of listeriosis during pregnancy to improve maternal and fetal outcomes.

Neurolisteriosis was also common in our study, with most patients experiencing meningitis or meningoencephalitis, and only one patient presenting with a brain abscess. The MONALISA group also reported that, among patients with neurolisteriosis, meningoencephalitis was the predominant presentation (84%), and brainstem involvement was observed in only 17%. In the subgroup analysis, no statistically significant difference was found between patients with and without CNS involvement regarding demographic characteristics, comorbidities, clinical presentations, and outcomes. CNS involvement appears to be less common among pregnant females. The incidence of neurolisteriosis reported in the literature is 30% but the occurrence of cerebral abscess secondary to monocytogenes is only 3%.[24].Our patient with listeria brain abscess was an elderly female with a history of diabetes mellitus, hypertension, non-B non-C chronic liver disease and showed complete recovery after 6 weeks of antibiotics . There is limited evidence available, primarily derived from case reports, about the management of listeria brain abscess. Prolonged antibiotic therapy (5-6 weeks) appears reasonable, with variable results of adjunctive surgical drainage. [25-27]

A recent meta-analysis reported a listeriosis-related mortality rate of approximately 23%, with most deaths occurring in individuals over 60 years of age and found that gender has no impact on mortality risk.[10]. The risk factors of mortality associated with listeriosis are neurolisteriosis, prior comorbidities like non-haematological malignancies, pulmonary diseases, chronic kidney diseases, cardiovascular diseases, malignancies, immunosuppression and multi-organ failure. [5, 10, 28].We also found high mortality among the elderly population, with no significant difference between males and females. All except one had existing comorbid illness or immunosuppressive state, but neurolisteriosis was not identified as a risk factor of mortality in the current study. This might be due to small sample size and timely management of patients presenting with neurological involvement, i.e. prompt diagnostic evaluation and early initiation of antibiotics in this high-risk group.

Our study has several limitations. It is a single-centre, retrospective study with a small sample size, and large-scale multicenter studies are required to validate our findings. It was a hospital- based study; many patients with less severe infections may have been managed in primary health centres and might not have presented to tertiary care hospitals, potentially leading to underrepresentation of milder cases. Additionally, retrospective design may have resulted in incomplete documentation with missing information on predisposing factors such as dietary history and environmental exposures.

Conclusion

Listeriosis significantly affects not only the elderly but also middle-aged individuals, particularly those with underlying risk factors and during pregnancy. Environmental hygiene, early diagnosis, and prompt treatment are crucial to reducing adverse outcomes, especially in pregnancy-related cases. Raising public awareness, educating healthcare workers for early diagnosis and management, and implementing preventive measures at the community level can greatly improve listeriosis outcomes.

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