AN 11-YEAR RETROSPECTIVE STUDY ON LISTERIOSIS IN LOS ANGELES COUNTY, 1992–2002

BACKGROUND

Listeria monocytogenes is a ubiquitous bacterium in the environment but rarely causes human disease. However, in addition to flu-like symptoms (e.g., fever, muscle aches, headache, nausea, diarrhea, and neck stiffness), human cases can experience septicemia, meningoencephalitis, and sometimes death. When sporadic and epidemic cases occur, transmission is by the fecal-oral route and cases are usually characterized by advanced age, compromised immune systems, and pregnancy. As *L. monocytogenes* is a cold-loving bacterium that can proliferate in refrigerators, foods that have been associated with listeriosis outbreaks include raw milk, raw milk products, Mexican style fresh cheese and other soft cheeses, raw vegetables, deli salads, bagged salads, raw or undercooked seafood, and ready-to-eat meats like pâtés and deli meats [1–8].

CDC estimates that *L. monocytogenes* causes 2,500 illnesses, 2,300 hospitalizations, and 500 deaths per year in US [9]. Relative to other foodborne disease agents, *L. monocytogenes* has a case-fatality rate of 20%, second only to *Vibrio vulnificus* (39%), and causes 27.6% of all foodborne disease related deaths, second only to nontyphoidal *Salmonella* (30.6%) [9]. A multi-site study conducted by CDC between 1989 and 1993 found that Los Angeles County (LAC) had the highest incidence of perinatal listeriosis[10]. With other selected California counties, LAC had the highest incidence rate of listeriosis among nine surveillance sites in 2001 [11]. Since 1985, *L. monocytogenes* has been a reportable disease in LAC. To describe the epidemiology of listeriosis in LAC, we performed a retrospective study using surveillance data from 1992 to 2002. The following results from this study were presented at the 2003 Infectious Disease Society of America Conference in San Diego, California.

METHODS

A listeriosis case was defined by culturing *L. monocytogenes* from a normally sterile body site. A single perinatal case was defined as a mother-fetus pair with at least one positive specimen between the two. A non-pregnant person over 42 days of age with a positive specimen defined a nonperinatal case. Consistent with traditional ACDC criteria for listeriosis case investigation, study cases were residents of LAC (excluding the cities of Long Beach and Pasadena), were confirmed by the LAC Public Health Laboratory, and had disease onsets between 1992 and 2002.

Data were collected as hospitals and laboratories reported cases. Infection control practitioners (ICP), public health nurses (PHN), and ACDC staff investigated risk factors for listeriosis including predisposing medical conditions, and ACDC epidemiologists reviewed case documents for consistency to enter case data into the ACDC surveillance database and report to the California State Department of Health Services. During case interviews or review of documents such as medical charts and death certificates, ICPs, PHNs, and ACDC epidemiologists defined presence of kidney disease, steroid use, and other risk factors. The authors reviewed surveillance data since 1985 and because of data consistency issues made the first study year 1992. Missing data and data discrepancies in the surveillance database were cross-referenced to archived case documents and corrected. Otherwise missing responses to risk factor questions were regarded as “no” answers.

Univariate and stratified analyses were performed using SAS and Microsoft Excel. These programs were employed to calculate frequencies, risk ratios, 95% confidence intervals (95% CI), and p-values as well as to described disease trends. Incidence rates were calculated from population data obtained from LAC Vital Records.

RESULTS

Of 367 cases, 114 (31%) were perinatal and 253 (69%) nonperinatal (NP). Among the NPs, 175 (69%) had *L. monocytogenes* cultured from blood only, 29 (11%) from cerebrospinal fluid (CSF) only, 23 (9%) from both blood and CSF, and 26 (10%) from focal sites (Table 1). Among the perinatal cases, 75% (n=85) had positive cultures from the mother and of these positive cultures 20% (n=17) of fetal/infant cultures were negative (Table 1).

Table 1. Summary of Listeriosis Cases LAC, 1992–2002

	Number	Percent
Case Type		
Nonperinatal	253	69%
Perinatal	114	31%
Culture Site		
Blood only	175	69%
CSF only	29	11%
Blood and CSF	23	9%
Focal site	26	10%
Results of Mother		
Positive	85	75%
Missing	29	25%
Results of Child from Positive Mother		
Positive	25	22%
Negative	17	15%
Missing	38	33%
Unborn	5	4%
Results of Child from Negative Mother		
Positive	28	25%
Negative	1*	<1%

* Twin was positive.

During 1992–2002, the number of annual cases generally decreased from 43 cases to 21 cases (Figure 1), and incidence rates declined from 2.7 to 1.5 NP cases per million LAC residents and 11 to 5 perinatal cases per 100,000 live births (Figure 2).

Figure 1. Listeriosis Cases (N=367)
LAC, 1992-2002

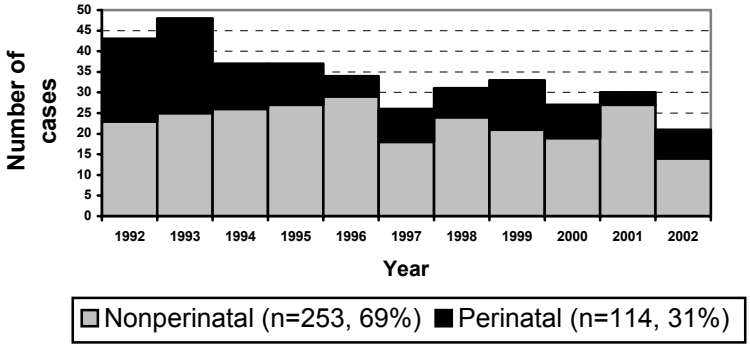
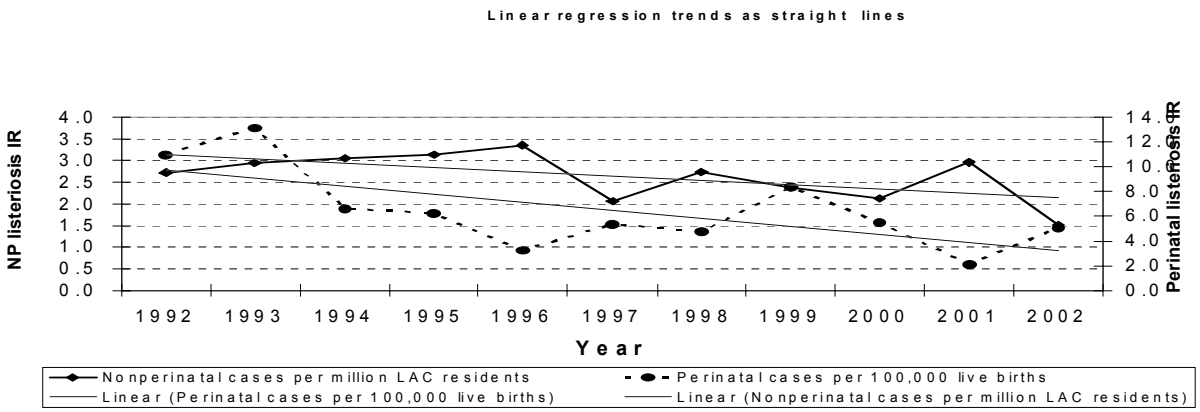


Figure 2. Listeriosis Incidence Rates (IR), LAC, 1992-2002



The average annual incidence rates were 2.6 NPs per million residents and 6.5 perinatal cases per 100,000 live births (Tables 2 and 3). Among NPs, case-fatality was 19.0% (47 died, 200 alive, 6 unknown outcome) and 138 (55%) of NPs were ≥65 years old (mean age=60.7 years). In addition, incidence rate increased with age, case-fatality was greatest at age ≥ 65years and 45-54 years, and males (n=139, 55%) had greater risk of disease (2.93 cases per million residents) and fatality (20%) than females. Among perinatal cases, case-fatality was 30% (birth outcomes: 27 stillborn, 7 died, 7 alive-sick, 67 alive-healthy, 6 unknown) and decreased with higher gestational age. Furthermore, mean maternal age was 28 years, and female infants (n=49, 53%) had greater risk of disease (5.7 cases per 100,000 live births) and death (33%).

Table 2. Nonperinatal Listeriosis Cases (n=253)
LAC, 1992–2002

Characteristics	No.	Percent	IR*	Deaths No.	Deaths CF†
Gender					
Male	139	54.9	2.93	27	20.0
Female	114	45.1	2.35	20	17.9
Age					
1-4	2	0.8	0.32	0	0.0
5-14	6	2.3	0.40	0	0.0
15-34	26	10.3	0.83	3	11.5
35-44	20	7.9	1.34	1	5.0
45-54	39	11.5	2.72	5	17.2
55-64	32	12.7	4.46	5	15.6
≥ 65	138	54.5	14.82	33	25.0

* Average incidence rate per one million LAC residents.
† Case fatality.

Table 3. Perinatal Listeriosis Cases (n=114)
LAC, 1992–2002

Characteristics	No.	Percent	IR*	Deaths No.	Deaths CF**
Gender†					
Male	46	48.4	5.1	5	11.1
Female	49	52.6	5.7	6	33.3
Gestation at Admission±					
Very immature (≤ 27 weeks)	39	39.8	–	25	69.4
Preterm (28–36 weeks)	47	48.0	–	7	15.9
Full-term (37–40 weeks)	12	12.2	–	1	8.3

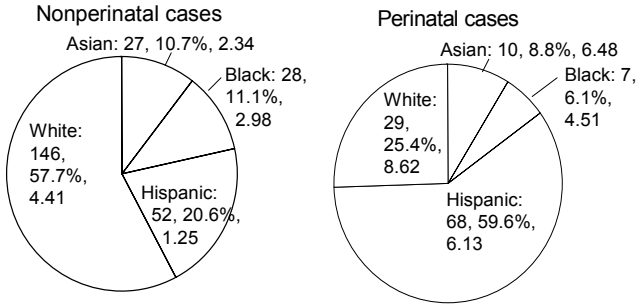
* Average incidence rate per one million LAC residents.
** Case fatality.
† Child's gender unknown for 19 cases.
± Gestational age unknown for 16 infant cases.

By race/ethnicity, among NPs, Whites had the most cases (146, 58%) and the highest average annual incidence rate (4.4 NPs per million LAC residents); among perinatal cases, Hispanics had the most cases (68, 60%) but Whites had the highest average annual incidence rate (8.6 perinatal cases per 100,000 live births, Figure 3).

Most of the NP and perinatal cases occurred in the spring and summer months (Figure 4). NP incidence increased in March, peaked in June and continued with higher numbers through October. Incidence of perinatal disease peaked in January, June, and September, and was higher from April to October.

Compared to NPs, perinatal cases were more likely to report consumption of Mexican cheese (RR=4.8, 95% CI: 2.9–7.9) and soft cheeses (RR=1.7, 95% CI: 1.1–2.6, Table 4). The most commonly reported risk food for NPs and perinatal cases were raw fruits and raw vegetables.

Figure 3. Number, Percent, and Average Annual Incidence* of Listeriosis by Race/Ethnicity
LAC, 1992-2002



*Nonperinatal incidence per million LAC residents, perinatal incidence per 100,000 live births

Figure 4. Listeriosis by Month of Onset,
LAC, 1992-2002

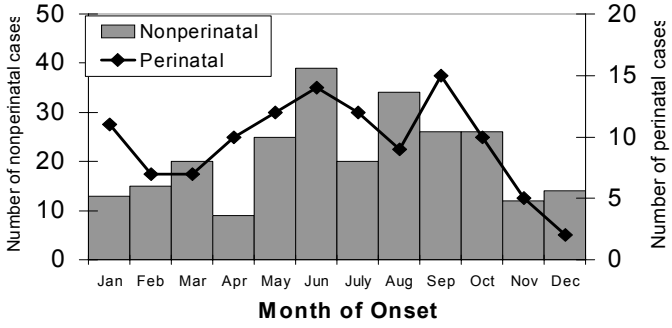


Table 4. Reported Consumption of Risk Foods Among Listeriosis Cases (n=253) LAC, 1992–2002

	Perinatal (n=114)		Nonperinatal (n=253)	
Risk Food	**No.**	**Percent**	**No.**	**Percent**
Raw milk	2	1.8	3	1.2
Other raw milk product	2	1.8	2	0.8
Mexican-style cheese	41	36.0	19	7.5
Soft cheese	31	27.2	40	15.8
Other cheese	33	29.0	69	27.3
Raw beef	2	1.8	8	3.2
Raw pork	0	0.0	2	0.8
Raw poultry	0	0.0	1	0.4
Raw eggs	3	2.6	5	2.0
Raw fish	5	4.4	14	5.5
Cold cuts	6	5.3	18	7.1
Raw fruits	69	60.5	124	49.0
Raw vegetables	63	55.3	118	46.6

Univariate analysis of risk factors found that among NPs risk of death increased with kidney disease (RR=2.1, 95% CI: 1.3–3.), being ≥65 years (RR=2.1, 95% CI: 1.2–3.6), and having cancer (RR=1.8, 95% CI: 1.1–2.9, Table 5). Risk factors of higher prevalence among NPs included age ≥65 years (55%), male gender (55%), steroid medication (33%), cancer (32%), antibiotic medication (28%), diabetes (23%), and kidney disease (19%).

Stratified analyses on NP data revealed evidence of confounding (Table 6). Stratification by steroid use found increased risk of death among non-steroid users with kidney disease (RR=2.7, 95% CI: 1.4–5.3) or with cancer (RR=2.4, 95% CI: 1.3–4.7), and among steroid users ≥ 65 years (4.1, 95% CI: 1.5–11.4) or with diabetes (RR=2.4, 95% CI: 1.1–5.1).

Table 5. Risk Factors for Death Among Nonperinatal Cases LAC, 1992–2002

Risk Factor	No.	Percent	Risk Ratio*	95% CI**
Kidney disease	47	18.6	2.10	1.25 – 3.54
≥ 65 years	138	54.5	2.05	1.16 – 3.64
Radiation	14	5.5	1.98	0.93 – 4.21
Liver disease	30	11.9	1.78	0.96 – 3.29
Cancer	82	32.4	1.75	1.05 – 2.91
Lung disease	5	2.0	1.72	0.79 – 3.74
Alcohol abuse	23	9.1	1.70	0.86 – 3.36
Diabetes	57	22.5	1.52	0.88 – 2.62
Steroids	83	32.8	1.37	0.81 – 2.29
Antibiotics	70	27.7	1.33	0.78 – 2.27
Asthma	8	3.2	1.33	0.39 – 4.54
Chemotherapy	39	15.4	1.30	0.69 – 2.47
Chemo-radiation	9	3.6	1.18	0.34 – 4.10
Male gender	139	54.9	1.12	0.67 – 1.89

* Risk of death: case deaths vs. case survivors, N=247, outcome missing for 6 cases.
** 95% confidence interval.

Table 6. Risk Factors Among Nonperinatal Cases by Steroid Use LAC, 1992–2002

	Steroid Use		No Steroid Use	
Risk Factor	**RR**	**95% CI**	**RR**	**95% CI**
Kidney disease	1.37	0.57–3.26	2.71	1.41–5.25
Cancer	1.01	0.45–2.29	2.44	1.26–4.72
Alcohol abuse	0.86*	0.14–5.17	2.23	1.04–4.76
∃65 years	4.13**	1.50–11.40	1.39	0.69–2.83
Diabetes	2.14	1.13–5.12	1.11	0.51–2.42
Male gender	1.80	0.79–4.11	0.85	0.43–1.67
Antibiotics	1.49	0.68–3.28	1.05	0.46–2.39
Radiation	1.92**	0.79–4.64	1.49*	0.26–8.42
Chemotherapy	1.02**	0.39–2.68	1.49	0.64–349
Asthma	3.10*	1.25–7.65	— †	— †

* One cell size <5 cases.
** Two cells have size <5 cases.
† No deaths.

DISCUSSION

Limitations of this study include possible misclassification of exposure data, small numbers for extensive mathematical modeling to more accurately measure risk of fatality among NPs, and possible reporting bias. Even though all available case documents were reviewed by ACDC epidemiologists conducting listeriosis surveillance, because different ICPs and PHNs over time helped define presence of exposures there is a small possibility of exposure misclassification that can affect risk estimates when prevalence exposures are very small. While the decline of listeriosis is a sign of improving health in the population, the smaller numbers impede accurate estimation of risks per exposure classification. Thus, with this study data building a mathematical model that includes several risk factors and possible confounders would result in low power as some strata may have counts of two or less. To limit reporting bias and be conservative, the authors considered blank responses and unknowns as “No” answers to presence of risk factors; otherwise, many risk ratios would be higher and significant at the p≤ 0.05 level.

The results of this study show that in general listeriosis is declining and that public health can target certain risk groups and effect interventions to prevent disease and fatality in LAC. For instance, public health education in early spring that targets adults who are ≥ 65 years of age, have kidney disease, or have cancer might reduce NP incidence. Health care providers should teach food safety to their elderly patients who use steroid medication or have chronic illness. Also, through consultation by pharmacists or warning labels, individuals at risk of listeriosis who need prescriptions for steroid medication or medication for a predisposing medical condition can be made aware of high-risk foods or situations. Furthermore, food safety education campaigns targeting pregnant women, especially recently pregnant women of Hispanic or White race/ethnicity might further reduce perinatal listeriosis. The results from this study show that 15% of perinatal cases would not be reported if only the infant is cultured for *L. monocytogenes*. Hence, public health should encourage obstetricians to culture febrile pregnant women to improve case detection. While the reported incidence of listeriosis is small compared to other foodborne diseases, the risk of hospitalization and death is relatively large and preventive efforts should be developed and initiated with this in mind.

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