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Invasive Group B Streptococcal Disease Among Nonpregnant Adults: Alaska, 2004–2023

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Abstract

We describe the epidemiology of invasive group B streptococcal (GBS) disease among nonpregnant Alaska adults using statewide surveillance data. During 2004–2023, 880 cases of invasive GBS disease were reported for an age-adjusted annual incidence of 9.1 (95% confidence interval [CI], 8.5–9.7) cases per 100 000 adults. Incidence increased 1.9-fold (95% CI, 1.6–2.2) between 2004–2013 and 2014–2023. Adults aged ≥65 years had a 4.4-fold higher risk of invasive disease compared to younger adults, and 47% of adults with invasive GBS had diabetes. Health care providers should be aware of populations at increased risk, potentially allowing for more prompt treatment.

Keywords

Streptococcus agalactiae; Alaska; adult; surveillance; public health; incidence

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Invasive group B streptococcal (GBS) disease occurs when *Streptococcus agalactiae* infects a normally sterile body site, such as blood, cerebrospinal fluid, or joint fluid [1]. The most common clinical manifestations among adults include sepsis, pneumonia, and soft tissue, bone, and joint infections [2]. Neonates, pregnant women, older adults, and people with certain underlying medical conditions are at increased risk for invasive GBS [1]. There are no licensed vaccines to prevent invasive GBS but at least 2 are being evaluated in clinical trials [3, 4].

Neonates born to women colonized with GBS are at risk for acquiring an invasive infection during the perinatal period [1]. Since the implementation of national screening and intrapartum antibiotic prophylaxis guidelines in the United States in 1996, the incidence of early-onset invasive GBS in neonates has decreased by approximately 88% [5, 6]. However, the invasive GBS incidence tripled among nonpregnant adults during 1990–2016, as reported to the Centers for Disease Control and Prevention (CDC) Active Bacterial Core surveillance (ABCs) system, which does not include Alaska [2, 7, 8]. The burden of invasive GBS disease among nonpregnant adults in Alaska has not been previously assessed. To address this knowledge gap, we used statewide surveillance data to describe the epidemiology of invasive GBS among nonpregnant Alaska adults during 2004–2023, including evaluating trends in incidence and selected demographic and clinical characteristics.

METHODS

Surveillance Population

In 2023, the State of Alaska had an estimated population of 736 812 people, including 560 111 (76%) adults aged ≥ 18 years [9]. Of the total population, 150 374 (20%) identified as Alaska Native or American Indian alone or in combination with another race [9].

Case Definition and Identification

A case of invasive GBS was defined as an Alaska resident aged ≥ 18 years with *S. agalactiae* detected in a normally sterile body site (eg, blood, cerebrospinal fluid, joint fluid) by bacterial culture or nucleic acid amplification test. Cases were excluded if the positive sterile site sample was collected while the patient was pregnant, or postpartum after birth or termination of a pregnancy.

Invasive GBS disease is a reportable condition in Alaska. All hospital-based laboratories report cases to the Alaska Division of Public Health and the CDC Arctic Investigations Program. Annual audits are performed to detect missing cases. This activity was reviewed by CDC and deemed not research.

Laboratory Testing

Invasive GBS isolates were confirmed by the CDC Arctic Investigations Program laboratory using standard microbiological methods, including colony morphology, β -hemolysis presence, catalase testing, and latex agglutination testing. Antimicrobial susceptibility testing was performed using microbroth dilution to determine the minimum

inhibitory concentration to 6 antibiotics, but the specific drugs tested varied by year. Clinical and Laboratory Standards Institute criteria were used to classify isolates as susceptible, intermediate, or resistant [10]. Isolates that were susceptible to clindamycin but nonsusceptible to erythromycin were assessed for inducible clindamycin resistance using the D-test. Isolates with either constitutive or inducible clindamycin resistance are reported as nonsusceptible. Beginning in 2022, whole-genome sequencing was used for isolate confirmation and to predict antimicrobial susceptibility [11].

Data Collection

Clinical and demographic data were obtained during routine surveillance by medical chart review performed by CDC staff using a standardized form. Cases were classified as Alaska Native if Alaska Native race was reported alone or in combination with other races. Urban residents were defined as those living in the Anchorage Municipality, Fairbanks North Star Borough, Juneau City/Borough, or Matanuska-Susitna Borough; residents of all other regions were considered rural. We defined an underlying medical condition or risk factor as those listed in Table 1.

Statistical Analysis

Analyses of surveillance data were conducted using SAS version 9.4. Population estimates were obtained from the Alaska Department of Labor and Workforce Development [9]. We calculated age-adjusted and age-specific invasive GBS incidence per 100 000 adults. Age-adjusted rates were calculated using direct standardization with the 2010 US population as the reference population. Confidence intervals (CIs) for rates were calculated using the Poisson distribution. We used Poisson regression to calculate incidence rate ratios (IRR) and 95% CI. To minimize the effect of expected year-to-year variation, we compared rates during the second 10-year period (2014–2023) to the first 10-year period (2004–2013). Categorical variables were compared with the Pearson χ^2 test or Fisher exact test and continuous variables were compared with the Wilcoxon rank-sum test.

RESULTS

Demographic and Clinical Characteristics

Of the 1023 invasive GBS disease cases reported in Alaska during 2004–2023, 102 (10%) were among infants aged <3 months, 14 (1%) were children aged 3 months to 17 years, 27 (3%) were pregnant or postpartum women, and 880 (86%) were nonpregnant adults aged ≥ 18 years. The proportion of all invasive GBS cases that occurred among nonpregnant adults increased from 77% (266/344) during 2004–2013 to 90% (614/679) during 2014–2023 ($P < .01$).

Of the 880 cases among nonpregnant adults, 788 (90%) were aged ≥ 40 years, 522 (59%) occurred in men, 225 (26%) were Alaska Native adults, and 648 (74%) were residents of an urban area (Table 1). Overall, 731 (83%) adults with invasive GBS disease had ≥ 1 underlying medical condition, including diabetes ($n = 416$, 47%), congestive heart failure ($n = 177$, 20%), and chronic respiratory disease ($n = 153$, 17%). Other risk factors included smoking ($n = 166$, 19%) and alcohol abuse ($n = 91$, 10%). The most common

clinical syndromes associated with invasive GBS infection were cellulitis ($n = 320$, 36%), bacteremia without focus ($n = 240$, 27%), bone or joint infection ($n = 209$, 24%), and pneumonia ($n = 95$, 11%). Of the 880 nonpregnant adults with invasive GBS, 798 (91%) were hospitalized and 66 (8%) died.

Cases among Alaska Native adults had a median age of 57 years (interquartile range [IQR], 47–68) compared to 62 years (IQR, 51–74) for non-Alaska Native adults ($P < .01$). The proportion of cases with ≥ 1 underlying medical condition was the same among Alaska Native (186/225, 83%) and non-Native adults (545/657, 83%) ($P = .85$). However, other risk factors were more common among Alaska Native adults (88/224, 39%) compared to non-Native adults (135/655, 21%) ($P < .01$).

There were no significant differences in the sex, age, or race of nonpregnant adults with invasive GBS disease during 2004–2013 compared to 2014–2023 (Table 1). However, the proportion of adults with ≥ 1 underlying medical condition increased from 79% (210/266) during 2004–2013 to 85% (521/614) during 2014–2023 ($P = .03$). Adults with invasive GBS during 2014–2023 were more likely to have diabetes, congestive heart failure, chronic renal failure, and preceding trauma compared to 2004–2013. The proportion of cases with ≥ 1 other risk factor did not differ between 2004–2013 (64/266, 24%) and 2014–2023 (159/614, 26%) ($P = .57$), but intravenous drug use increased from 1% (2/266) to 4% (23/614) ($P = .01$). The proportion of invasive GBS cases requiring hospitalization increased from 86% (230/266) during 2004–2013 to 93% (568/614) during 2014–2023 ($P = .02$). However, the case fatality ratio did not differ significantly between the time periods.

Incidence Rates

During 2004–2023, the age-adjusted average annual incidence of invasive GBS disease among nonpregnant adults in Alaska was 9.1 cases per 100 000 (95% CI, 8.5–9.7) (Table 2). Average annual incidence among adults aged ≥ 65 years was 25.1 (95% CI, 22.5–27.7) compared to 5.7 (95% CI, 5.2–6.2) among adults aged 18–64 years (IRR, 4.4; 95% CI, 3.9–5.0). Rates also were higher among men versus women (IRR, 1.4; 95% CI, 1.2–1.6), Alaska Native versus non-Native adults (IRR, 1.9; 95% CI, 1.6–2.2), and residents of urban versus rural areas (IRR, 1.2; 95% CI, 1.0–1.4).

Incidence increased 1.9-fold (95% CI, 1.6–2.2) from 6.6 (95% CI, 5.7–7.4) cases per 100 000 during 2004–2013 to 11.4 (95% CI, 10.5–12.3) during 2014–2023 (Table 2). Between 2004–2013 and 2014–2023, age-adjusted invasive GBS incidence increased among adults of all ages, men and women, Alaska Native and non-Alaska Native adults, and urban and rural residents. The magnitudes of the increases were similar (ie, 1.5–2.5-fold) across all demographic characteristics.

Antimicrobial Susceptibility

Among invasive GBS cases with an available isolate tested, all were susceptible to cefotaxime (532/532) and penicillin (770/770), and 99% (764/771) were susceptible to levofloxacin. In contrast, only 60% (423/706) were susceptible to clindamycin, 46% (356/771) were susceptible to erythromycin, and 22% (118/532) were susceptible to tetracycline.

DISCUSSION

The incidence of invasive GBS disease among nonpregnant Alaska adults nearly doubled during 2004–2023; rates increased among every demographic characteristic measured. Adults aged ≥ 65 years were at higher risk of invasive GBS compared to younger adults. Alaska's population is aging rapidly, which could contribute to a continued increase in the burden of invasive GBS disease [12]. The prevalence of underlying medical conditions among adults with invasive GBS also increased over the surveillance period, with half of patients having diabetes, a condition known to increase risk for invasive GBS [13]. The increased incidence of invasive GBS among Alaska adults may be associated with the increasing prevalence of chronic diseases found in the larger US population [8].

The incidence of invasive GBS disease among nonpregnant adults in Alaska was similar to rates reported from the 10 ABCs sites, which represented 12% of the US population in 2016 [2, 8]. Similarly, invasive GBS incidence at ABCs sites also was highest among older adults, with most cases requiring hospitalization and occurring in persons having ≥ 1 underlying medical condition [8]. During 1993–1998, 65% (5118/7867) of invasive GBS cases in the ABCs sites occurred among nonpregnant adults [14]. Recent comparable data have not been published for the ABCs sites and surveillance data are not available for Alaska from the 1990s. However, we found that nearly 90% of invasive GBS disease in Alaska during 2004–2023 occurred among nonpregnant adults.

We observed a nearly 2-fold higher risk of invasive GBS among Alaska Native adults compared with non-Alaska Native adults during 2004–2023. Alaska Native adults with invasive GBS had a similar prevalence of underlying medical conditions compared to non-Native adults. However, inequities in social determinants of health experienced by some Alaska Native communities (eg, crowded housing, indoor air pollution, and lack of in-home piped water) might have contributed to the disparity we observed in invasive GBS disease [15]. Similarly, the increased prevalence of other risk factors among Alaska Native adults with invasive GBS also is likely driven by long-standing socioeconomic inequities.

Antimicrobial susceptibility varied among the invasive GBS isolates tested. Importantly, all isolates tested were susceptible to penicillin and cefotaxime; these and other β -lactam antibiotics remain the first-line treatments for invasive GBS [7]. The majority of samples tested were nonsusceptible to tetracycline and erythromycin, consistent with other reports showing increased resistance to those antibiotics [7]. For those with allergies to β -lactam antibiotics, clindamycin can be used as an alternative treatment; however, resistance to clindamycin is a concern, with only 60% of isolates susceptible during 2004–2023. Whole-genome sequencing, which began for invasive GBS surveillance isolates in 2022, will help further characterize GBS resistance patterns in Alaska.

Currently, there are no licensed vaccines for the prevention of invasive GBS disease but at least 2 are in clinical trials [3, 4, 8]. If a GBS vaccine becomes available for use in adults, targeted public health messaging and outreach should be performed to maximize uptake and reduce disease burden among vulnerable groups, such as older adults and those with diabetes. In the absence of a vaccine, health care providers should be aware of the

populations at increased risk for invasive GBS disease, which may allow for more prompt diagnosis and treatment.

There are several limitations to this study. First, we were unable to estimate the invasive GBS disease risk associated with underlying medical conditions and risk factors because population prevalence data for those conditions were unavailable. Second, we were unable to evaluate if certain social determinants of health, such as crowded housing or reduced access to in-home piped water, impacted invasive GBS disease rates in Alaska.

We found an increase in invasive GBS disease in Alaska adults over the past 2 decades. Fortunately, invasive GBS isolates from Alaska adults remain susceptible to first-line antibiotics. Additionally, GBS vaccines currently in development could potentially decrease the burden of invasive GBS in Alaska, especially among adults aged ≥ 65 years and those with certain underlying medical conditions. Our findings highlight the importance of continued surveillance to monitor and evaluate the increase in invasive GBS disease among Alaska adults.

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Table 1.
Invasive Group B Streptococcal Disease Case Characteristics Among Nonpregnant Adults Aged ≥18 Years, Alaska, 2004–2023 (n = 880)

Characteristic	2004–2013, No. of Cases (%) (n = 266)	2014–2023, No. of Cases (%) (n = 614)	P Value
Age group, y			.36
18–39	22 (8)	70 (11)	
40–64	132 (50)	300 (49)	
≥65	112 (42)	244 (40)	
Sex			.14
Male	148 (56)	374 (61)	
Female	118 (44)	240 (39)	
Race			.74
Alaska Native	70 (26)	155 (25)	
Non-Alaska Native	196 (74)	459 (75)	
Location of residence			.04
Urban	208 (78)	440 (72)	
Rural	58 (22)	174 (28)	
Underlying medical conditions			
Diabetes	101 (38)	315 (51)	<.01
Congestive heart failure	42 (16)	135 (22)	.04
Chronic respiratory disease	45 (17)	108 (18)	.81
Cancer	41 (15)	78 (13)	.28
Chronic renal failure	15 (6)	81 (13)	<.01
Preceding trauma	15 (6)	65 (11)	.01
Surgery/surgical wound	17 (6)	59 (10)	.12
Cirrhosis/liver failure	29 (11)	35 (6)	.01
Stroke/cerebrovascular accident	16 (6)	42 (7)	.65
Immunosuppression	17 (6)	35 (6)	.69
Rheumatoid arthritis	8 (3)	6 (1)	.03
Cerebrospinal fluid leak	1 (<1)	1 (<1)	.54
Other risk factors			
Smoker within past year	49 (18)	117 (19)	.83

Characteristic	2004–2013, No. of Cases (%) (n = 266)	2014–2023, No. of Cases (%) (n = 614)	P Value
Alcohol abuse	33 (12)	58 (9)	.19
Intravenous drug use	2 (1)	23 (4)	.01
Homelessness	6 (2)	14 (2)	.98
Clinical syndrome ^a			
Cellulitis	70 (26)	250 (41)	<.01
Bacteremia without focus	92 (35)	148 (24)	<.01
Bone or joint infection	49 (18)	160 (26)	.01
Pneumonia	32 (12)	63 (10)	.44
Endocarditis	19 (7)	26 (4)	.07
Peritonitis	8 (3)	15 (2)	.63
Meningitis	4 (2)	3 (<1)	.12
Other ^b	6 (2)	21 (3)	.30
Hospitalized	230 (86)	568 (93)	.02
Died	26 (10)	40 (7)	.21

^aIn total, 477 cases (54%) had > 1 clinical syndrome.

^bOther clinical syndromes include necrotizing fasciitis (n = 11, 1%), empyema (n = 8, 1%), pericarditis (n = 5, 1%), toxic shock syndrome (n = 2, < 1%), and endometritis (n = 1, < 1%).

Table 2.
Invasive Group B Streptococcal Disease Annual Incidence Rates Among Nonpregnant Adults Aged ≥18 Years, Alaska, 2004–2023 (n = 880)

Characteristic	2004–2023, Rate ^a (95% CI)	2004–2013, Rate ^a (95% CI)	2014–2023, Rate ^a (95% CI)	2014–2023 Versus 2004–2013, IRR ^b (95% CI)
Overall	9.1 (8.5–9.7)	6.6 (5.7–7.4)	11.4 (10.5–12.3)	1.9 (1.6–2.1)
Age group, y				
18–39	2.1 (1.6–2.5)	1.0 (0.6–1.4)	3.0 (2.3–3.7)	3.0 (1.9–4.8)
40–64	9.2 (8.3–10.1)	5.5 (4.6–6.5)	13.0 (11.5–14.5)	2.4 (1.9–2.9)
≥65	25.1 (22.5–27.7)	21.5 (17.5–25.5)	27.2 (23.8–30.6)	1.3 (1.0–1.6)
Sex				
Male	10.6 (9.7–11.6)	7.5 (6.2–8.7)	13.6 (12.2–15.0)	2.0 (1.7–2.5)
Female	7.5 (6.7–8.3)	5.7 (4.6–6.8)	9.1 (7.9–10.2)	1.6 (1.3–2.0)
Race				
Alaska Native	14.6 (12.7–16.6)	10.4 (7.8–12.9)	18.4 (15.5–21.3)	1.9 (1.4–2.5)
Non-Alaska Native	8.1 (7.4–8.7)	5.8 (5.0–6.7)	10.1 (9.1–11.0)	1.8 (1.6–2.2)
Location of residence				
Urban	9.6 (8.8–10.3)	7.5 (6.4–8.5)	11.6 (10.5–12.7)	1.7 (1.4–2.0)
Rural	8.1 (7.0–9.1)	4.7 (3.4–5.9)	10.9 (9.3–12.6)	2.4 (1.8–3.2)

Abbreviations: CI, confidence interval; IRR, incidence rate ratio.

^aRates per 100 000 adults per year. Rates for sex, race, and residence were age adjusted.

^bIncidence rate ratio for the last 10 years (2014–2023) compared to the first 10 years (2004–2013).