J Microbiol Immunol Infect
2006;39:396-401

Original Article

Clinical characteristics of group B streptococcus bacteremia in non-pregnant adults

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Received: June 10, 2005 Revised: August 24, 2005 Accepted: September 2, 2005

Background and Purpose: Group B streptococcus (GBS) [*Streptococcus agalactiae*] is an emerging cause of disease in non-pregnant adults with underlying diseases. This retrospective study analyzed 90 episodes of GBS bacteremia in adults occurring over a 4-year period.

Methods: Basic and clinical data were collected by reviewing medical charts of patients. Blood cultures were performed on admission of patients suspected of bacteremia. Presence of underlying diseases, such as liver disease, heart disease, urinary tract disorders, and female-specific cancers, as well as possible portals of entry of infection was analyzed.

Results: In 56 episodes (62.2%), patients were aged 60 years or older and 40 (44.4%) episodes occurred in males. Skin and soft tissue were the most common sources of GBS bacteremia (22/90, 24.4%). GBS bacteremia was classified as primary in 50% of the episodes (45 patients). Liver diseases were more common in males, while malignancy was more common in females. Portals of entry with a significant gender predominance included skin and soft tissue in women (p=0.018), bone and joint in women (p=0.016), and urinary tract in men (p=0.042). The overall mortality rate was 18.9% and the attributable mortality rate was 7.8%.

Conclusions: Elderly people and those with underlying diseases are particularly susceptible to GBS infections. Preventive strategies, including GBS vaccine and skin care, are likely to be particularly important in these high-risk groups.

Key words: Adult, bacteremia, mortality risk factors, *Streptococcus agalactiae*

Introduction

Group B streptococcus (GBS) [*Streptococcus agalactiae*], a Gram-positive, catalase-negative, β-hemolytic bacterium, is one of the most clinically important pathogens in newborns, pregnant women, and non-pregnant adults with underlying medical conditions [1-11]. Patients with chronic underlying medical conditions such as diabetes mellitus (DM), malignancies, and liver diseases are at increased risk of invasive GBS infection [1-4]. Reported clinical manifestations of GBS infection included primary bacteremia, pneumonia, urosepsis, peritonitis, meningitis, endocarditis, catheter-related infections as well as soft tissue, bone, and joint infections [1-4].

However, limited data are available regarding GBS bacteremia in adults in Taiwan. This retrospective study analyzed the clinical characteristics and risk factors of GBS bacteremia in non-pregnant adults.

Methods

Patients

This study included patients 18 years or older with an episode of GBS bacteremia who were identified on the basis of microbiology laboratory records between 2001 and 2004. Bacteremia was defined as at least one set of positive blood cultures in a patient with compatible

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clinical infection symptoms and signs (such as fever >38°C and chills), or two or more sets of positive blood cultures. Basic and clinical data were collected by reviewing medical charts. A positive result of blood culture performed at admission or within 48 h after admission was considered to indicate community-acquired infection, while positive results obtained more than 48 h after admission were considered to indicate hospital-acquired infection. The following underlying diseases were analyzed: liver disease including liver cirrhosis, chronic viral or alcoholic hepatitis, hepatocellular carcinoma, and primary biliary cirrhosis; heart disease including congestive heart failure and coronary artery disease; urinary tract disorder including urinary tract stones and benign prostate hypertrophy; and female-specific cancers including cervical, endometrial, vaginal, vulvar, or breast cancers. The possible portals of entry included skin and soft tissue (including central venous catheter infection), bones and joints, urinary tract, respiratory tract, gastrointestinal (GI) tract (including peritonitis, postendoscopic bacteremia, and biliary tract infection) and central nervous system. When no obvious site of active infection was found, the episode was classified as primary bacteremia. If the patient died within 7 days after the onset of bacteremia, death was regarded to be attributable to GBS infection, as defined in a previous study [3].

Laboratory methods

Each blood specimen was obtained and incubated in media at 35°C and processed using the Bactec 9000 System (Becton Dickinson, Sparks, MD, USA). Isolates were identified as GBS based on the following criteria: a narrow zone of beta-hemolytic colonies on 5% sheep blood agar plate, Gram-positive cocci in pairs or short chains on Gram staining, a negative-catalase reaction, a positive reaction with Christie, Atkins, Munch-Peterson (CAMP) test, and Lancefield grouping with type B antiserum.

Statistical analyses

Differences between groups were analyzed by chi-squared test or Fisher's exact test (when 20% of the expected count was less than 5) using the Statistical Package for the Social Sciences (SPSS) for Windows (Version 10.0; SPSS Chicago, IL, USA) software. A *p* value of 0.05 or less was considered statistically significant and all tests of significance were two-tailed.

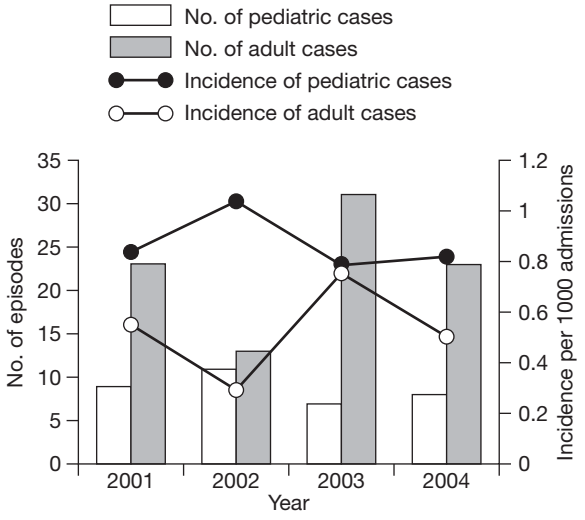

Fig. 1. Number of episodes and incidence of group B streptococcus bacteremia in adults and children, 2001-2004.

Results

A total of 125 episodes met the criteria of significant GBS bacteremia in our hospital during the study period. The annual incidences and episode numbers of GBS bacteremia are shown in Fig. 1. Although a greater number of episodes of GBS bacteremia were found in non-pregnant adults, the annual incidence of GBS bacteremia was higher in children. As shown in Fig. 2, 35 (28%) episodes occurred in children 1-year-old or younger but none in those aged between 1 and 18 years; 90 (72%) episodes occurred in non-pregnant adults aged 18 years or older; 7 episodes occurred in 3 patients, and the intervals between the first episode and the recurrent episodes were more than 6 months. Each of the 2 patients with single recurrent episode had chronic respiratory failure with tracheotomy and received long-term ventilator support in the respiratory care ward. One had type 2 DM and the other had cervical cancer and liver cirrhosis. The remaining patient with two recurrent episodes of GBS bacteremia had cervical cancer and presented with cellulitis over the inguinal and lower abdominal wall areas in all 3 episodes.

The basic and clinical characteristics, underlying diseases, portals of entry, and associated complications of 90 episodes of GBS bacteremia are summarized in Table 1. The mean age of the patients was 63 years (range, 20-90 years). There were 56 (62.2%) episodes in patients 60 years or older and 22 (26.7%) episodes were hospital-acquired. Forty (44.4%) episodes occurred in males. The number of females ≥60 years old was

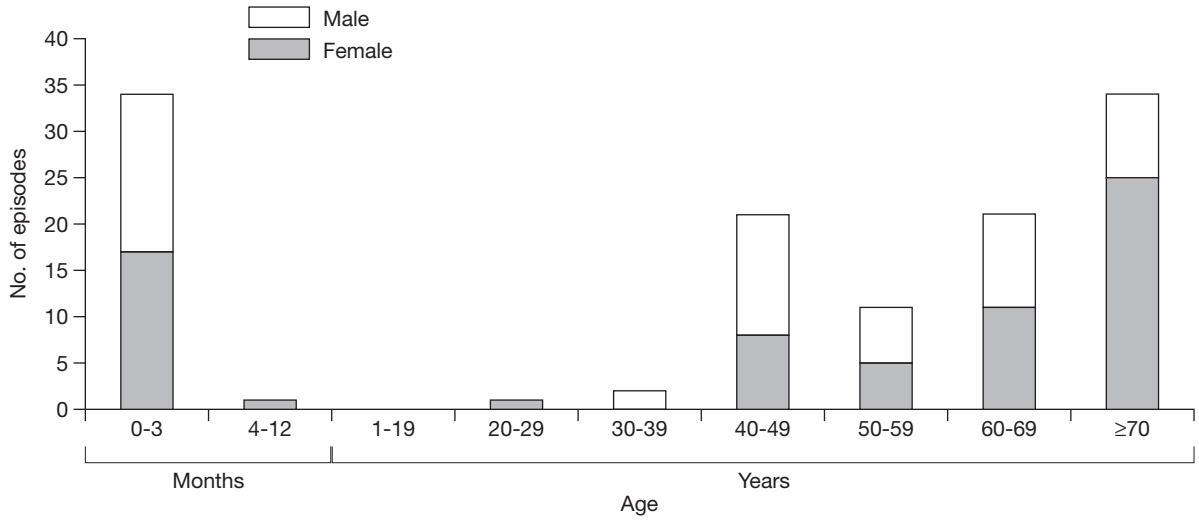

Fig. 2. Number of episodes of group B streptococcus bacteremia in different age groups and genders.

Table 1. Basic and clinical data of 90 episodes of group B streptococcus bacteremia in non-pregnant adults

Characteristic	Males (%)	Females (%)	Total (%)	*p*
Number of episodes	40 (44.4)	50 (55.6)	90 (100)	
Mean age (years) [range]	57.7 (34-79)	67.2 (20-90)	63.0 (20-90)	
Number of episodes in adults ≥60 years	20 (50)	36 (72.0)	56 (62.2)	0.032[a]
Acquisition				
Community	26 (65)	40 (80.0)	66 (73.3)	NS
Nosocomial	14 (35)	10 (20.0)	24 (26.7)	NS
Underlying diseases				
Liver diseases	15 (37.5)	8 (16.0)	23 (25.6)	0.020[a]
Malignancies	11 (27.5)	24 (48.0)	35 (38.9)	0.047[a]
Diabetes mellitus	16 (40)	17 (34.0)	33 (36.7)	NS
Heart diseases	8 (20)	7 (14.0)	15 (16.7)	NS
Chronic renal failure	2 (5)	0 (0)	2 (2.2)	NS
Urinary tract disorders	3 (7.5)	1 (40)	4 (4.4)	NS
Stroke	5 (12.5)	5 (10)	10 (11.1)	NS
COPD	1 (2.5)	2 (4.0)	3 (3.3)	NS
Portals of entry				
Primary bacteremia	22 (55)	23 (46.0)	45 (50.0)	NS
Skin and soft tissue	5 (12.5)	17 (34.0)	22 (24.4)	0.018[a]
Bone and joint	0 (0)	7 (14.0)	7 (7.8)	0.016[b]
Urinary tract	6 (15)	1 (2.0)	7 (7.8)	0.042[b]
Respiratory tract	2 (5)	0 (0)	2 (2.2)	NS
Gastrointestinal tract	4 (10)	2 (4.0)	6 (6.7)	NS
Central nervous system	1 (2.5)	0 (0)	1 (1.1)	NS
Complications				
Shock	8 (20)	6 (12.0)	14 (15.6)	NS
Acute renal failure	7 (17.5)	4 (8.0)	11 (12.2)	NS
ICU admission	8 (20)	4 (8.0)	12 (13.3)	NS
DIC	6 (15)	4 (8.0)	10 (11.1)	NS
Death	9 (22.5)	8 (16.0)	17 (18.9)	NS

Abbreviations: COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; DIC = disseminated intravascular coagulopathy; NS = not significant

[a] $p<0.05$ by chi-squared test.

[b] $p<0.05$ by Fisher's exact test.

Table 2. Basic and clinical data of group B streptococcus bacteremia in non-pregnant females

Characteristic	Cases with female-specific cancers (%)	Cases without female-specific cancers (%)	Total cases (%)	*p*
Number of episodes	22 (44)	28 (56)	50 (100)	
Mean age (years) [range]	63 (20-88)	70.5 (44-90)	67.2 (20-90)	
Number of episodes in adults ≥60 years	12 (54.5)	24 (85.7)	36 (72)	0.015[a]
Acquisition				
Community	19 (86.4)	21 (75)	40 (80)	NS
Nosocomial	3 (13.6)	7 (25)	10 (20)	NS
Underlying diseases				
Liver diseases	2 (9.1)	6 (21.4)	8 (16)	NS
Malignancies	22 (100)	2 (7.1)	24 (48)	<0.001[a]
Diabetes mellitus	1 (4.5)	16 (57.1)	17 (34)	<0.001[a]
Heart diseases	1 (4.5)	6 (21.4)	7 (14)	NS
Urinary tract disorders	0 (0)	1 (3.6)	1 (2)	NS
Stroke	1 (4.5)	4 (14.3)	5 (10)	NS
COPD	1 (4.5)	1 (3.6)	2 (4)	NS
Portals of entry				
Primary bacteremia	8 (36.4)	15 (53.6)	23 (46)	NS
Skin and soft tissue	12 (54.5)	5 (17.9)	17 (34)	0.007[a]
Bone and joint	2 (9.1)	5 (17.9)	7 (14)	NS
Urinary tract	0 (0)	1 (3.6)	1 (2)	NS
Gastrointestinal tract	0 (0)	2 (7.1)	2 (4)	NS
Complications				
Shock	0 (0)	6 (21.4)	6 (12)	0.028[b]
Acute renal failure	0 (0)	4 (14.3)	4 (8)	NS
ICU admission	0 (0)	4 (14.3)	4 (8)	NS
DIC	0 (0)	4 (14.3)	4 (8)	NS
Death	2 (9.1)	6 (21.4)	8 (16)	NS

Abbreviations: COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; DIC = disseminated intravascular coagulopathy; NS = not significant

[a] $p<0.05$ by chi-squared test.

[b] $p<0.05$ by Fisher's exact test.

greater than the number of males in that age group (p=0.032). Females without female-specific cancers were significantly older (≥60 years old) than those with gender-specific cancers (p=0.015, Table 2).

Only 1 patient had no obvious underlying medical condition. This 77-year-old man visited the emergency department because of fever and his symptoms resolved without any antibiotic treatment. Thus, transient GBS bacteremia was suspected. The most common underlying diseases were as follows: malignancy (38.9%), DM (36.7%), and liver diseases (25.6%) [Table 1]. None of the patients had human immunodeficiency virus (HIV) infection.

Females had a higher percentage of malignancy (48%, p=0.047), and males had a higher percentage of liver disease (37.5%, p=0.02). One female patient had nasopharyngeal cancer and another female patient had rectal cancer; all females with malignancies and GBS bacteremia had female-specific cancers. In females, DM was more common in those without gender-specific cancers (p<0.001, Table 2).

The portals of entry of GBS bacteremia were as follows: skin and soft tissue including 2 central venous catheter infections (24.4%); bone and joint (7.8%); urinary tract (7.8%); and GI tract, including 3 patients with bacteremia related to endoscopic procedures (6.7%). GBS bacteremia was classified as primary bacteremia in half of the cases. Postendoscopic bacteremia was found in 3 males with liver cirrhosis and esophageal varices bleeding, after upper GI endoscopy for varices ligation or sclerotherapy. In females, skin and soft tissue (female vs male, p=0.018) and bone and joint (female vs male, p=0.016) were more common portals of entry, while in males, the urinary tract (male vs female, p=0.042) was more common as a portal of entry. Among females, skin and soft tissue infections were more common in those with female-specific cancers (54.5% [12/22] vs 17.9% [5/28]; p=0.007). If those with female-specific cancers

were excluded, there was no gender difference in frequency of skin and soft tissue as a portal of entry (data not shown).

Polymicrobial bacteremia was found in 8 episodes (8.9%). The concomitant bacteria included oxacillin-susceptible *Staphylococcus aureus* (4 cases), *Streptococcus mitis* (1 case), *Proteus vulgaris* (1 case), *Streptococcus oralis* (1 case), *Klebsiella pneumoniae* (1 case), *Haemophilus influenzae* (1 case), and *Fusobacterium* sp. (1 case).

The overall mortality rate was 18.9% (17 patients), and that of patients aged 60 years or older was 21.4% (12 patients). Attributable mortality occurred in 7 (7.8%) patients. The clinical course was fulminant in these 7 cases and all died within 3 days of onset of illness despite antibiotic therapy.

Ten patients did not receive any antibiotics after onset of symptoms of GBS bacteremia. The common clinical features in these patients were several episodes of spiking fever that subsided quickly, suggesting a transient bacteremia. The portal of entry was unknown in 9 of these patients, who were classified as having primary bacteremia. Only 1 of the 10 patients who had vulvar cancer had mild focal skin infection. Only 1 of 2 sets of blood cultures was positive among 8 of the 10 patients, and 2 of 2 sets of blood cultures were positive among the other 2 patients.

Discussion

Over the past 2 decades, the incidence of invasive GBS disease in Atlanta, Georgia, United States, increased 2- to 4-fold, with 4.1 to 7.2 cases per 100,000 non-pregnant adults [1-3,12]. The incidence was higher in older patients, especially those residing in nursing homes [13]. In this study of non-pregnant adults, GBS bacteremia was usually noted in elderly patients or those with chronic underlying diseases, especially those with malignancy, DM, and liver disease. These findings are similar to previous reports [1-4,7-10,14] and might be attributable to the longer survival of patients with underlying conditions predisposing to this infection [2]. Three recurrent cases had more than one underlying disease, as reported in a previous study [15].

Our hospital is classified as an HIV-infected patient care center and had about 273 patients who were regularly followed-up at the outpatient department during the study period; however, no episode of GBS bacteremia was noted in this patient population, which has been described as a susceptible population [1,7]. Among underlying medical conditions, females had a significantly higher prevalence of malignancy (p=0.047) and males had a significantly higher prevalence of liver disease (p=0.02). The predominance of liver diseases in males with GBS bacteremia is likely explained by a higher incidence of liver diseases in males in Taiwan [16,17]. The predominance of malignancy in females might be due to cervical and breast cancers that rendered them more susceptible to GBS soft tissue infection. The pathogenesis could be attributed to predisposing local or regional conditions such as lymphatic or vascular insufficiency or radiation therapy. Vascular or lymphatic insufficiency may alter local host defenses and allow colonizing flora from adjacent skin to penetrate the subcutaneous tissues [2,18,19]. Multiple factors are likely involved in the initiation of the soft tissue infection, including focal trauma, hematoma or fluid retention, ischemia, venous or lymphatic outflow obstruction, or the presence of a foreign body [2].

According to 2 recent studies in healthy young subjects [20,21], the GBS colonization rate in men was 20%, and that in women was 34%. Isolates were most commonly found in specimens collected from the anal orifice, followed by the vagina, urinary tract, and throat. Sexually experienced subjects had twice the colonization rates of sexually inexperienced persons, but without site-specific colonization; other predictors of colonization varied with colonization site. These findings indicate that GBS is likely transmitted by intimate contact, but the transmission modes might vary depending on colonization sites. The colonization rate of GBS in older adults was similar to that in younger patients, except for a higher rate of colonization with invasive strains [22]. The findings of greater colonization rates in females and in sexually experienced patients suggest that patients with cervical cancers may have a high GBS colonization rate. This might also provide a reasonable explanation for the many cervical cancer patients in this study (12/50).

In contrast to a previous study on group B streptococcal osteomyelitis in adults in which males were found to outnumber females (1.79:1) [23], in this study, these infections were found exclusively in females (5 cases), excluding those with female-specific cancers. A higher GBS colonization rate and more soft tissue infections that could contiguously spread to surrounding bones or joints may be plausible explanations for the predominance of bone and joint infections in females [2].

In conclusion, elderly people and those with underlying diseases are particularly susceptible to invasive GBS infections. Due to the resulting morbidity and mortality, preventive measures such as the development of GBS vaccine and meticulous skin care in the susceptible population should be encouraged [2].

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