

Risk Factors for Mortality in Non-pregnant Adults with Group B Streptococcus Bacteremia

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Abstract

This study analyzed the prognostic factors of Group B streptococcus (GBS) bacteremia in non-pregnant adult patients in Central Taiwan. An observational study was conducted between January 1, 2001 and December 31, 2009 at the study hospital. The overall incidence rate of GBS bacteremia was 24.3 cases per 100,000 admissions during the study period. Among the 63 patients, 26 patients were male with a mean age of 57.1 years. The most common source of infection was skin and soft tissue infection (27, 42.9%). The C-reactive protein (CRP) and sepsis sign were markedly different between the expired and survival groups (8.8 ± 8.9 mg/dL vs. 18.7 ± 6.8 mg/dL, $p=0.013$ and 32.6% v.s. 64.1% , $p<0.001$), respectively. The diastolic blood pressure on the day of diagnosis had a statistically significant difference between the two groups (81.3 ± 11.8 mmHg vs. 63.1 ± 16.5 mmHg, $p=0.033$). The overall case fatality rate was 36.9% (17 cases). Elevated CRP level, low diastolic blood pressure and sepsis sign were most significant difference at the initial presentation, and were poor prognostic factors for mortality. (J Intern Med Taiwan 2013; 24: 131-136)

Key Words: Clinical presentations, Group B Streptococcus, Bacteremia, Mortality, Prognostic factor

Introduction

Streptococcus agalactiae (*S. agalactiae*), group B streptococcus (GBS), has been recognized as a major cause of sepsis and meningitis in non-pregnant adults¹, and GBS infection in non-pregnant adults has been increasingly reported worldwide^{2,3}. Common cases of GBS disease in adults include skin and/or soft-tissue infection, pneumonia and osteomyelitis. Serious clinical syndromes such as meningitis, streptococcal toxic shock syndrome and endocarditis are rare, but often associated with considerable morbidity and mortality^{4,5}. Majority of patients had underlying medical conditions including diabetes,

malignancy, genitourinary abnormalities, neurologic deficits, liver cirrhosis, renal dysfunction, steroid uses and acquired immunodeficiency syndrome (AIDS)^{6,7}. GBS bacteremia is a common disease in non-pregnant adults^{2,3,5,10,11}, with a mortality rate that ranges from 3% to 35.1%^{4,8}. This study aimed to analyze the prognostic factors of GBS bacteremia in non-pregnant adult patients admitted to study hospital, a medical center in central Taiwan, with a focus on the risk factors for mortality.

Material and Methods

Surveillance

Medical records were reviewed for GBS

bacteremic cases and a cross-sectional retrospective study of GBS infection done from January 1, 2001 through December 31, 2009, at the study hospital, which is an 1800 bed teaching hospital. All the patients documented with GBS bacteremia were enrolled during the study period. The exclusion criteria included age <18 years, pregnant women, inadequate clinical data and mis-interpretation of microbiological examinations, including wrong identification, contaminations and unknown clinical significance.

Definitions

An episode of GBS bacteremia was defined as the first set of positive blood cultures. A case of bacteremia was defined as isolation of GBS from blood. We divided source of infection among those patients with GBS bacteremia into two types. Primary infection with GBS typically occurs at the skin, the respiratory tract, or the genitourinary tract. Deep infections, for example, at heart valves, bone, and brain, represent secondary seeding from an earlier infection and bacteremia, although that event may have been subclinical and not appreciated or detected. In patients presenting with multiple anatomically separate foci of deep infection, we decided which focus was seeded first according to the severity. Sepsis is the systemic response to infection, and defined according to the Bone's criteria⁹.

Testing

The blood agar subcultures from clinical specimen after a 24-hour incubation at 35 to 37°C in 5% CO₂ atmosphere were analyzed for group B streptococci (*i.e.*, *S. agalactiae*). Agar plates with visible microorganism growth were observed for large, gray, translucent colonies with a narrow or absent zone of β -hemolysis, Gram-positive cocci in pairs and chains. The biochemical method was used to identify the species of group B streptococci¹⁰. Susceptibility was determined according to the

standards by the Clinical and Laboratory Standards Institute¹¹.

Statistical Analysis

Clinical data were presented in numbers, n (%), mean and standard deviation (SD) and median as appropriate. Comparisons of demographic data and clinical characteristics between groups of patients who survived vs. those who died were performed using Chi-square test or Fisher's exact test as appropriate. A two-sided test at a p-value of < 0.05 was used to indicate statistical significance.

Results

A total of 68 cases of GBS bacteremia were recorded in study hospital during 2001 through 2009. Five cases were excluded because of mis-matched information and the remaining 63 cases of GBS bacteremia were analyzed. The overall incidence rate was 24.3 cases per 100,000 admissions during the study period. Among 63 patients, 26 patients were male (41.2%) with the mean age of 57.1±28.7 years (range 18-83). A total of 44 patients (69.8%) had underlying medical conditions; 20 (31.7%), 17 (26.9%) and 7 (11.1%) and 1(1.6) having malignancy, diabetes, liver cirrhosis, and HIV infection, respectively. The most common source of primary infection was skin and soft tissue infection (27, 42.9%). The most common source of deep infection was septic arthritis (4, 6.3%).

We focused on the analysis of mortality in this study. The 17 expired cases (case-fatality rate was 26.9%) were analyzed. We compared the demographic and clinical characteristics between patients with GBS bacteremia of expired and survival groups, as shown in Table 1. The incidence of elderly and cancer was significantly different between those two groups. The diastolic blood pressure at the diagnosis day had statistical significance between those two groups (81.3±11.8 vs. 63.1±16.5, p=0.033). The C-reactive protein (CRP, normal range <0.748 mg/

dL) was markedly different between those two groups (8.8 ± 8.9 vs. 18.7 ± 6.8 , $p=0.013$). The sepsis sign at diagnosis day was markedly different between those two groups (32.6% vs. 94.1%, $p<0.001$). At the initial presentation, elevated CRP level and low diastolic blood pressure and sepsis sign were most significant in the expired group. The source of infection among expired group included three

patients with skin and soft tissue infection, one with septic arthritis and one with meningitis. Antimicrobial drug susceptibility data were obtained for all 63 cases. All 63 isolates were susceptible to penicillin and vancomycin. The non-susceptibility rate to erythromycin and clindamycin was 44.1% (30/63) and 48.5% (33/63) respectively. Some cases of mortality could result from the inadequate antibiotic

Table 1. Demographic and clinical characteristics of 63 patients with Group B Streptococcal Bacteremia between survival group and expired group Patients, n (%), mean \pm S.D.

	Survival group	Expired group	Overall	<i>p</i>
Patients number	46	17	63	
Age (years)	46.5 \pm 30.7	65.6 \pm 15.6	51.7 \pm 28.7	0.045
>=65 y/o	19(41.3)	12(70.5)	31(49.2)	<0.001
Gender (male)	17(37.0)	9(53.0)	26(41.2)	0.335
Length of stay, ward (days)	10.7 \pm 3.0	16.2 \pm 17.1	17.7 \pm 17.5	0.750
Length of stay, ICU (days)	5.2 \pm 14.0	9.9 \pm 22.2	3.6 \pm 14.3	0.038
Cancer	11(23.9)	9(52.9)	20 (31.7)	0.043
DBP at Diagnosis Day	81.3 \pm 11.8	63.1 \pm 16.5	73.5 \pm 16.3	0.033
GBS bacteremia without significant focus	11(23.9)	12(70.5)	23(36.5)	0.001
GBS bacteremia with significant focus	35(72.9)	5(27.8)	40(60.6)	0.903
Primary infection				
Skin and soft tissue infection	23(6.5)	3(17.6)	27(42.9)	
Pneumonia	1 (2.2)	0	1 (1.6)	
Urinary tract infection	4(8.7)	0	4(6.3)	
Deep infection				
Meningitis	2 (4.3)	1 (5.8)	2 (3.1)	
Septic arthritis	3(6.5)	1 (5.8)	4(6.3)	
Intra-abdominal infection	2 (4.3)	0	2 (3.1)	
Diagnosis Day _CRP (mg/dL)	8.8 \pm 8.9	18.7 \pm 6.8	10.5 \pm 9.3	0.013
Diagnosis Day _sepsis sign	15(32.6)	16(94.1)	31(49.2)	<0.001
Initial effective antibiotics usage	44(85.6)	15 (88.2)	59(93.6)	0.070

Notes:

1. *p*-value by Chi-square test or Fisher's exact test when appropriate.
2. CRP-C-reactive protein, DBP-Diastolic blood pressure, ICU-intensive care unit, GBS- Group B Streptococcus.
3. The source focus of infection was defined by the presenting symptoms in the medical records, related signs identified from physical examinations, positive findings from image studies or bacterial cultures from body sites.

usage on the day of diagnosis, but there were no significant differences between survival group and expired group (85.6% vs. 88.2%, $p=0.070$).

Discussion

The number of cases of invasive infection caused by *S. agalactiae* in non-pregnant adults is increasing⁴. Occurrence of GBS bacteremia was found to be apparent among the adults in our study. The incidence of invasive group B streptococcal diseases in the United States significantly increased from 3.4/100,000 population in 1999 to 5.0/100,000 population in 2005³. A similar trend was observed in Asia². In Chaiwarith's study, the number of cases increased significantly from 2006 to 2007, and there were five times more cases within four years⁴. In this study, the overall incidence rate was 24.3 cases per 100,000 admissions. Our study also supports the evidence of increasing number of patients who were not pregnant (from cumulative annual data of study hospital, and data not shown). In addition, infections in non-pregnant adults occurred in similar proportion (41.2%, vs. 58.8%, $p=0.335$) in male and female that corresponded to the previous studies^{2,12}.

Concurrent conditions of known risk factors for GBS bacteremia, with exception of age, included diabetes mellitus, malignancy and cirrhosis of the liver⁷. In this study, concurrent conditions were common in both groups. Although higher rates of malignancy in the expired group may be caused in

part by differences in underlying concurrent malignancy conditions, small case numbers, or other factors not collected as part of this study may also play a role. Those uncollected factors included colonization of GBS bacteria in women and the possible role of person-to-person transmission of GBS bacteria in the community.

In this study, the mortality rate of GBS bacteremia was 26.9%. The mortality rate in Chaiwarith's study was 15%, while the rate in other reports varied from 3% to over 30%^{1,3}. Other reports demonstrated that mortality was associated with bloodstream infection, hypotension, thrombocytopenia, other concurrent bacterial infections, infection with serotype Ia, and old age^{2,3,4,13}. Wang's study showed that the mortality rate of the invasive GBS diseases was 35.1%⁸. A literature review for mortality factors of GBS bacteraemia is summarized in Table 2¹⁴⁻¹⁶. Case-mortality rates in this study were lower than those reported in other studies. In this study, the CRP levels were significantly different between those two groups (8.87 ± 8.95 vs. 18.78 ± 6.89 , $p=0.013$), and the level of CRP was usually greater than 18 mg/dL initially. The diastolic blood pressure on the day of diagnosis had statistical significance between those two groups (81.38 ± 11.83 vs. 63.17 ± 16.53 , $p=0.033$). In addition, we presume that it resulted from relative low diastolic blood pressure in the expired patients.

Our conclusion is that GBS infection is a growing problem in non-pregnant patients,

Table 2. Evidence-based review for mortality factors of Group B streptococcal bacteraemia

Year	Country	Author	Mortality factor	Reference
1985-1994	Spain	Muñoz P	Central nervous system diseases, alcoholism, shock, renal failure, and consciousness impairment	13
2001-2003	Taiwan	Huang PY	Polymicrobial bacteremia, thrombocytopenia, and shock	14
2005	Texas ,U.S	Edwards MS	Delayed clinical recognition of GBS infection	15
1998	France	Trivalle C	Being bedridden amongst older patients	16
2001-2009	Taiwan	Chen CH	Elevated CRP level ,low diastolic blood pressure and sepsis sign	This study

particularly in patients who had underlying medical conditions. Physicians should include infection with GBS in the differential diagnosis of patients with septicemia. Additionally, the CRP level in particular, is elevated in the expired patients, usually exceeding 18 mg/dL at the outset. Sepsis signs are poor prognostic factors for the outcome. Also, diastolic blood pressure is low in expired group, usually less than 80 mmHg at initial stage.

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非懷孕成人B型鏈球菌感染的死亡因素分析

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摘 要

本研究分析台灣中部地區的非懷孕成年患者罹患B型鏈球菌菌血症的預後因素。2001年1月1日至2009年12月31日在研究醫院進行本研究。在研究期間，B型鏈球菌菌血症的發病率分別為每十萬住院病患有24.3例。在63例B型鏈球菌菌血症患者中，26例患者均為男性，平均年齡為57.1歲。最常見的感染源是皮膚和軟組織感染(27, 42.9%)。存活組與死亡組在C-反應蛋白、敗血症的現象有明顯不同(8.8 ± 8.9 mg/dL v.s 18.7 ± 6.8 mg/dL, $P=0.013$; 32.6% v.s. 64.1%, $P < 0.001$)。診斷日當天舒張壓在兩組之間差異有統計學差異(81.3 ± 11.8 mmHg vs. 63.1 ± 16.5 mmHg, $P = 0.033$)。總病死率為36.9% (17例)。C-反應蛋白升高和低舒張壓和敗血症的現象是B型鏈球菌菌血症的三項重要死亡因子。