Perinatal Infection of Group B Streptococcus in Taiwan

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Abstract

In this study we investigate perinatal vaginal infection of group B streptococcus among women in Taiwan. We gathered histories, vaginal and rectal swabs from 10 hospitals in northern, central, and southern part of Taiwan from 2,193 women pregnant between 35 to 37 weeks, and histories from 709 women, with a total of 2,702 women. Vaginal and rectal swabs were cultured and tested biochemically for group B streptococcus, and then serotyped and tested for drug sensitivity. Perinatal carrier rate among women in Taiwan was 17.2% (central Taiwan 18.3%, northern 16.1%, and southern 16.6%). Follow-up of 360 cases

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of group B streptococcus positive patients (GBSPP) by questionnaires showed that 10.3% of the doctors did not prescribe antibiotics, 23.6% prescribed oral antibiotics immediately, and 66.1% prescribed IV medication during labor. Among the 376 bacteria strains isolated, 57 (15.2%) were sensitive to nine antibiotics (penicillin, clindamycin, erythomycin, ampicillin, cefepime, vacomycin, chloramphenicol, cefotaxime, and ofloxacin). Resistance to clindamycin and erythromycin was 34.6% and 28.5%, respectively. There was no resistance to vancomycina or penicillin. Drug resistance was most severe in central Taiwan, followed by northern, then southern. Our results also showed that GBS in Taiwan were mainly serotypes V (27.1%) and III (19.7%). In the histories of GBSPP, 13.6% had GBS urinary tract infection, 10.3% had premature contraction, and 9.4% had premature rupture of membrane. Because the identification of GBS resulted in treatment, no GBS positive babies were born.

Keywords: Perinatal, Group B Streptococcus, serotype

Introduction

Group B streptococcus (GBS) is one of the main causes which threaten the lives of neonates, characterized by high morbidity and mortality. In the United States, Sweden, and the United Kingdom, GBS accounts for 22~60% of neonatal infections. It is also the main cause of neonatal mortality [1-5]. In 2001, the US CDC gathered multiple authorities to re-assess the GBS policy in 1996 [1]. The key conclusions include: 1. screening vaginal and rectal culture for GBS for women 35 to 37 weeks pregnant; 2. recommended antibiotics treatment during labor for perinatal GBS infection; 3. recommendation of treatment for pregnant women who are likely to have pre-term labor before 37 weeks. Currently GBS screening is not covered by the National Health Insurance, and most hospitals do

not routinely screen for GBS. The goal of this study is to establish GBS screening for women pregnant between 35-37 weeks and baseline information of GBS infection in Taiwan.

Materials and methods

1. Questionnaire for medical history

Samples were collected from 10 hospitals (three regional hospitals in northern Taiwan, one medical center, two regional hospital, and one local hospital in central Taiwan, and three local hospitals in southern Taiwan). Questionnaires were given to pregnant women, and their newborns were followed up for three months to monitor for GBS infections. A total of 2,193 cases were recruited from the 10 hospitals. An additional 509 persons only had surveys conducted, resulting in a total of 2,702 questionnaires. All recruits gave informed consents.

2. GBS specimens collection and culture

Vaginal and rectal swabs were collected from women pregnant between 35 and 37 weeks. Samples were inoculated into nonnutritive transport media, streaked onto selective media plates, incubated at 37℃ and 5%CO_2 for 18-24 hours, and transferred to sheep blood agar plates. Suspected streptococcal colonies were tested using grouping latex agglutination test or cAMP test.

3. Serotyping of GBS

Serotyping was conducted using modified Lancefield's method by a latex agglutination kit (Statens Serum Institut, KO). Pure culture of GBS was suspended and mixed with equal amount of latex reagent to generate visible clumps for serotyping.

4. Drug sensitivity test

Isolated GBS strains were tested for drug sensitivity using the National

Committee for Clinical Laboratory Standards (NCCLS) method. Drugs tested included penicillin (10 g), clindamycin (2 g), erythomycin (15 g), ampicillin (10 g), cefepime (30 g), vancomycin (30 g), chloramphenicol (30 g), cefotaxime (30 g), and ofloxacin (5 g). Strains were cultured in 5% CO_2 at 35-37 ^{0}C for 20-24hr.

Results

In this study, medical histories of 2,702 and vaginal and rectal swabs of 2,193 women pregnant between 35 and 37 weeks were collected from 10 hospitals across Taiwan. Among the 2,193 swabs, 376 (17.2%) were positive. There were 614 cases were collected from northern Taiwan, with 99 positive cases (16.1%), 854 from mid Taiwan with 156 positive cases (18.3%), and 725 from south Taiwan with 121 positive cases (16.7%). Of these, 94.2% of the cases were pregnant more than 35 weeks. It was the first pregnancy for 60.4% of the women. There were, 93.3% Taiwanese, and 2.6% from China and Vietnam. Highest educational level was 33.5% and 33.3% for high school and vocational school, respectively. Over all, 44.7% were aged 26–30 years, and 29.7% were aged 31–35 years. Past medical histories of cases are shown in Table 1. Chi-square analysis showed that smoking, alcohol consumption, diabetes, hypertension, previous low-birth-weight baby, premature contraction/rupture of membrane, prolonged rupture of membrane (>18 hours), fever during labor, previously delivered GBSP (Group B streptococcus patient), stillbirth, and premature birth were not associated with neonatal deaths. Table 1 showed that Chi-square test of all parameters in the histories have p >0.05, indicating no difference between the histories of GPSPP, GBSNP, and cases without samples collected. This demonstrates that we cannot use histories to infer whether the cases would be GPSPP or GBSNP.

Table 2 shows the histories of the current pregnancies. Among GBSPP, 13.6% had GBS urinary tract infection; 10.3% had premature contraction requiring antibiotics treatment; and 9.4% had premature rupture of membrane requiring antibiotics treatment. Because GBS drug sensitivity was performed, obstetricians were able to give appropriate treatment, and hence no GBSP babies were born by GBSPP. Treatment of GBSPP included no antibiotics treatment (10.3%), immediate oral antibiotics (23.6%), and intravenous medicine during labor (66.1%). Chi-square analysis showed no significant difference ($p > 0.05$) between GBSPP and cases who had no samples collected in frequency of premature contraction, premature contraction requiring antibiotics treatment, premature rupture of membrane, premature rupture of membrane requiring antibiotics treatment, prolonged rupture of membrane, fever during labor, natural birth, and Cesarean section.

Table 3 shows the results of drug sensitivity tests. Among the 376 strains, 57 (15.2%) were sensitivity to the nine antibiotics tested. In addition, resistance to clindamycin and erythromycin were the highest at 34.6% and 28.5%, respectively. There were no resistance to vancomycin or penicillin. Among foreign pregnant women, clindamycin, erythromycin, and chloramphenicol had the highest rates of resistance, at 44.4%, 27.8%, and 22.2%, respectively; but there were no resistance to ampicillin, vancomycin, cefepime, or penicillin. Chi-square analysis showed no difference between the results of drug sensitivity tests between all pregnant cases and foreign pregnant women ($p >0.05$), therefore, we cannot use drug sensitivity to infer whether the cases were GPSPP or GBSNP.

Table 4 shows the serotypes of GBS strains. GBS in Taiwan were mainly serotypes V (27.1%) and III (19.7%); 9.6% could not be serotyped. Among foreign pregnant women, the main serotypes were III (44.4%), Ib (22.2%), and Ia

(16.7%). Chi-square analysis showed that the difference for serotype III between Taiwanese and foreign pregnant women was significant.

Conclusion

The mortality of GBS infection depends on countries and regions. Studies have shown that mortality of GBS infection is 5.6% in Sweden and 13% in Finland. In the United Kingdom and the United States, it is may be as high as 22% and 33%, respectively [7-9]. In addition, studies have also shown that mortality of GBS infection were associated with birth weight and gestational age. Yang gathered cases from 1988 to 1996 at the National Cheng-Kung University Hospital to find risk factors of early and late onset GBS infection among neonates, and showed that early onset GBS infection were predominantly in neonates with premature birth and low birth weight [10]. In this study, among newborn of GBSPP, 0% had birth weight ≤1500 g; 3.6% had birth weight 1500–2500 g, 96.4% had birth weight >2500 g. In addition, 0% was born ≤34 weeks; 3.9% were born 35–37 weeks; and 96.1% were born >38 weeks. Because 89.7% of GBSPP had antibiotics treatment during pregnancy, there were no GBS infection among the 2,193 newborns in this study.

Even though this study provided free service, some pregnant women were still not willing to have samples taken. Therefore, only medical histories were collected. The differences between those who had samples taken and those who did not could provide information for future expansion of public policy and education programs. The histories showed that older, more educated, foreigners, and women in their first pregnancy were more willing to provide samples. Furthermore, 33 (6.5%) women who did not provide samples were in the high risk group by history. The reasons for their unwillingness remain to be

investigated. Governing authorities should consider policies on free prenatal GBSP screening and use of antibiotics to prevent neonatal GBSP.

The rates of vaginal bacterial carriage differ by country. It is 2-29% in the United Sates, 18.6% in Brazil, 5.8% in India, 2.9% in Japan, and 19% in Hong Kong; carrier rates of neonates are similar to those of pregnant women [2-5]. Liu showed that GBS infection among non-pregnant adults was 1.6‰ [6]. Our study showed that vaginal carriage rates among pregnant women in was 17.2% (18.3% in central Taiwan, 16.1% in northern Taiwan, and 16.7% in southern Taiwan.) This is the first investigation on vaginal GBS carriage in pregnant women, which will provide helpful information for public health practice and disease prevention in Taiwan.

Penicillin is the drug of choice for GBSPP, but, in 1998, Fernandez showed that 7.4% and 3.4% of invasive GBS was resistant to penicillin and erythromycin, respectively [11]. Yang also showed that sensitivity of GBSP strains to penicillin, ampicillin, and erythromycin was 83%, 74%, and 75%, respectively, and all 36 strains were resistant to gentamicin and tetracycline [10]. Liao tested 8 strains isolated from the blood and cerebrospinal fluid, and showed that all were sensitive to penicillin, ampicillin, vancomycin, and cefotaxime; only 62% and 75% were sensitive to erythomycin and clindamycin, respectively [12]. In this study, we showed that 34.6% and 28.5% were resistant to erythomycin and clindamycin, respectively, and resistance to penicillin was not found.

GBS was grouped by Lancefield in 1933 using type-specific capsular polysaccharides [13]. Hulse, Schuchat, and Liao showed that type III often causes meningitis in neonates [12, 14, 15]. Jelinkova and Harrison showed that serotypes Ia, Ib, II, III, V, and non-typable GBS causes early onset infection in neonates, and late onset infection and meningitis are mainly caused by serotype III [16, 17].

Furthermore, Harrison found infection by serotypes Ia, Ib, II, III, and V occur more frequently in the Americas [17[. Lachenauer showed that serotypes VI and VIII were predominant among pregnant women in Japan, and serotypes IV and VII were rare [18]. In a study of 351 cases collected over 8 years, Ko showed that serotypes III and V predominated (28.5% and 17.1%, respectively), and 34.6% and 25.7% of severe infections were caused by serotypes III and V, respectively [19]. The results were similar to the findings of the current study. Literature review showed that GBS strains in Taiwan are mainly serotypes V and III, and these strains may cause severe infections.

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References

1. Schrag S, Gorwitz R, Fultz-Butts K, et al. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. MMWR Recomm Rep. 2002; 16; 1-22.
2. CDC. Adoption of prenatal group B streptococcal disease prevention recommendations by prenatal-care providers—Connecticut and Minnesota. 1998. MMWR 2000; 49: 228-32.
3. CDC. Early-onset group B streptococcal disease, United States, 1998-1999.MMWR 2000; 49: 793-6.
4. CDC. Laboratory practices for prenatal group B streptococcal screening and reporting—Connecticut, Georgia, and Minnesota, 1997-1998.MMWR 1999;

48: 426-8.

5. Zangwill KM, Schuchat A, Wenger JD. Group B streptococcal disease in the United States, 1990: report from a multistate active surveillance system. MMWR 1992; 41: 25-32.
6. Liu JW, Wu JJ, Ko WC, et al. Clinical characteristics and antimicrobial susceptibility of invasive group B streptococcal infections in nonpregnant adults in Taiwan. J Formos Med Assoc 1997; 96: 628-33.
7. Baker GJ, Edwards MS. Group B streptococcal infections. In: Remington TA, Klein JO, eds. Infectious diseases of the fetus and newborn infant. Philadelphia Saunders, 1990: 742.
8. Franciosi RA, Knostman JD, Zimmerman RA. Group B streptococcal neonatal and infant infections. J Pediatr 1973; 82; 707-18.
9. Ho MY, Wu CT, Ku YT, et al. Group B Streptococcal infection in neonates: an 11-year review. Acta Paediatr Taiwan 1999; 40: 83-6.
10. Yang YJ, Liu CC, Wang SM. Group B streptococcus infection in children: the changing spectrum of infections in infants. J Microbiol Immunol Infect 1998; 31: 107-21.
11. Fernandez M, Hickman ME, Baker CJ. Antimicrobial susceptibilities of group B streptococci isolated between 1992 and 1996 from patients with bacteremia or meningitis. Antimicrob Agents Chemother 1998; 42: 1517-9.
12. Liao CH, Huang LM, Lu CY, et al. Group B streptococcus infection in infancy: 21-year experience. Acta Paediatr Taiwan 2002; 43: 326-9.
13. Baker GJ, Barrett FF, Gordon RC, et al. Suppurative meningitis due to streptococci of Lancefield group B: a study of 33 infants. J Pediatr 1973; 82: 724-9.
14. Hulse ML, Smith S, Chi EY, et al. Effect of type III group B streptococcal

capsular polysaccharide on invasion of respiratory epithelial cells. Infect Immun 1993; 61: 4835-41.

15. Schuchat A. Epidemiology of group B streptococcal disease in the United States: shifting paradigms. Clin Microbiol Rev 1998; 11: 497-513.
16. Jelinkova J, Motlova J. Worldwide distribution of two new serotypes of group B streptococci: type IV and provisional type V. J Clin Microbiol 1985; 21: 361-2.
17. Harrison LH, Elliott JA, Dwyer DM, et al. Serotype distribution of invasive group B streptococcal isolates in Maryland: implications for vaccine formulation. Maryland Emerging Infections Program. J Infect Dis 1998; 177: 998-1002.
18. Lachenauer CS, Kasper DL, Shimada J et al. Serotypes VI and VIII predominate among group B streptococci isolated from pregnant Japanese women. J Infect Dis 1999; 179: 1030-3.
19. Ko WC, Lee HC, Wang LR, et al. Serotyping and antimicrobial susceptibility of group B Streptococcus over an eight-year period in southern Taiwan. Eur J Clin Microbiol Infect Dis 2001; 20: 334-9.

Table 1. Past histories of pregnant cases

Past history (%)	GBSPP[1]	GBSNP[2]	no samples taken[3]
Allergy to penicillin	2（0.5%）	21（1.2%）	0 (0%)
Smoking	8（2.1%）	50（2.7%）	5 (1.0%)
Alcohol consumption	1（0.3%）	11（0.6%）	1 (0.2%)
Diabetes mellitus	1（0.3%）	5（0.3%）	1 (0.2%)
Hypertension	0（0%）	4（0.2%）	2 (0.4%)
Had low birth weight baby	1（0.3%）	13（0.7%）	3 (0.6%)
Premature rupture of membrane	6（1.6%）	36（2.0%）	4 (0.8%)
Premature contraction	14（3.7%）	75（4.1%）	14 (2.7%)
Prolonged rupture of membrane (> 18 hours)	7（1.9%）	34（1.9%）	7 (1.4%)
Fever during labor	0（0%）	8（0.4%）	1 (0.2%)
Had GBSP baby	0（0%）	2（0.1%）	0 (0%)
Had baby died after birth	2（0.5%）	15（0.8%）	0 (0%)
Stillbirth	2（0.5%）	22（1.2%）	0 (0%)
No premature babies	369（98.1%）	1,764（97.1%）	505 (99.2%)
Had premature babies	7（1.9%）	53（2.9%）	4 (0.8%)
Singleton	7（1.9%）	50（2.7%）	1 (0.2%)
Twins	0（0%）	3（0.2%）	2 (0.4%)
Triplets	0（0%）	0（0%）	0 (0%)

Chi-square analysis showed $p > 0.05$ for all parameters

[1]GBSPP: Group B streptococcus positive patient; total GBSPP: 376.

[2]GBSNP: Group B streptococcus negative patient; total GBSNP: 1817.

[3] 509 cases had no samples taken

Table 2 current histories of pregnant cases

Current history (%)	GBSPP[1]	no samples taken[2]
GBS urinary tract infection	49 (13.6%)	0 (0%)
Premature contraction	14 (3.9%)	20 (3.9%)
Premature contraction requiring antibiotics treatment	37 (10.3%)	59 (11.6%)
Premature rupture of membrane	5 (1.4%)	7 (1.4%)
Premature rupture of membrane requiring antibiotics treatment	34 (9.4%)	22 (4.3%)
Prolonged rupture of membrane	7 (1.9%)	8 (1.6%)
Late stage abortion	1 (0.3%)	0 (0%)
Fever during labor	6 (1.7%)	1 (0.2%)
Normal vaginal delivery	270 (75%)	342 (67.2%)
Cesarean section	90 (25%)	167 (32.8%)
Current pregnancy		
≤ 34 weeks	0 (0%)	
35-37 weeks	14 (3.9%)	
≥ 38weeks	346 (96.1%)	
Birth weight		
≤ 1499 g	0 (0%)	
1500-2500 g	13 (3.6%)	
≥ 2501 g	347 (96.4%)	

Chi-square analysis showed that premature contraction, premature contraction requiering antibiotics treatment, premature rupture of membrane, premature rupture of membrane requiring antibiotics treatment, prolonged rupture of membrane, fever during labor, normal vaginal delivery, and Cesarean section had $p > 0.05$.

[1]GBSPP: Group B streptococcus positive patient；total GBSPP: 360

[2]cases had no samples taken: 509

Table 3. Results of drug sensitivity tests

Antimicrobial Agent		
Clindamycin	130 (34.6%)	8 (44.4%)
Erythromycin	107 (28.5%)	5 (27.8%)
Ampicillin	7 (1.9%)	0 (0%)
Cefepime	12 (3.2%)	0 (0%)
Vancomycin	0 (0%)	0 (0%)
Penicillin	0 (0%)	0 (0%)
Chloramphenicol	32 (8.5%)	4 (22.2%)
Cefotaxime	3 (0.8%)	0 (0%)
Ofloxacin	17 (4.5%)	1 (5.6%)

Chi-square showed that for all parameters $p > 0.05$

[1]total pregnant cases: 376

[2]foreigners: 18

Table 4. Serotypes of GBS strains

Serotype	Strains from Taiwanese, n (%)	Strains from foreigners, n (%)
Ia	23 (6.1%)	3 (16.7%)
Ib	63 (16.8%)	4 (22.2%)
II	43 (11.4%)	0 (0%)
III	74 (19.7%)	8 (44.4%)*
IV	18 (4.8%)	0 (0%)
V	102 (27.1%)	2 (11.1%)
VI	8 (2.1%)	0 (0%)
VII	5 (1.3%)	0 (0%)
VIII	4 (1.1%)	0 (0%)
Nontypable	36 (9.6%)	1 (5.6%)
Total positive strains:	376	18

*chi-square analysis showed $p < 0.05$