

MATERNAL TO CHILD GROUP B *STREPTOCOCCUS* TRANSMISSION RATE AT THAMMASAT UNIVERSITY HOSPITAL, THAILAND

Wanwarang Hiriote¹, Siripen Tor-Udom¹ and Pharuhath Tor-Udom²

¹Department of Preclinical Sciences, Faculty of Medicine, Thammasat University

²Department of Clinical Sciences, Obstetrics and Gynecology, Faculty of Medicine, Thammasat University, Pathum Thani, Thailand

Abstract. Group B *Streptococcus* (GBS) or *Streptococcus agalactiae* is a major cause of pneumonia and sepsis in newborns. In Thailand, no studies have been done on GBS transmission rate from mothers to newborns during delivery. In this study, we determined the prevalence of maternal GBS infection, its transmission rate and antibiotic susceptibility profiles. A total of 421 vaginal/rectal swabs were collected from 421 pregnant women during labor and umbilical cord/ear canal/nasal swab specimens taken from 421 newborns. All specimens were cultured for GBS and antibiotic susceptibility testing was performed using the Kirby-Bauer disk diffusion method. The prevalence of maternal GBS infection was 15.0% and the transmission rate of GBS was 31.8%. For the cases of GBS transmission, 95% delivered by normal vaginal delivery and 5% delivered by cesarean section. The transmission rate among GBS positive women who had spontaneous rupture of the amniotic sac was 43.8% and among women who had artificial rupture was 17.2% ($p < 0.05$). All GBS isolates among the women in this study were susceptible to penicillin, ampicillin, vancomycin, cefotaxime, ceftriaxone and linezolid, 87% were susceptible to clindamycin, 86% to erythromycin and 6% to tetracycline. The prevalence of maternal GBS infection and vertical transmission rate were high in our study. Routine screening for GBS at 35-37 weeks gestation and provision of antibiotic prophylaxis to those who are positive is warranted in this study population.

Keywords: Group B *Streptococcus*, prevalence, vertical transmission rate, drug susceptibility

INTRODUCTION

Streptococcus agalactiae (Group B *Streptococcus*, GBS) is a part of the normal flora of the rectum and vagina in 10-30%

of pregnant women (Huber *et al*, 2011). Early-onset disease (EOD) in neonates is associated with GBS colonization in the maternal genital tract during delivery (vertical transmission) (Verani *et al*, 2010). EOD presents with pneumonia and sepsis in the first week of life and has been reported to cause 4-6% infant fatalities (Alemseged *et al*, 2015). Routine screening for GBS between 35 and 37 weeks of gestation and the use of intrapartum antibiotic

Correspondence: Wanwarang Hiriote, Department of Preclinical Sciences, Faculty of Medicine, Thammasat University, 95 Paholyotin Road, Khlong Luang, Pathum Thani 12120, Thailand. Tel: +66 (0) 2926 9710
E-mail: hiriote@gmail.com

prophylaxis (IAP) for women with GBS colonization has been recommended to prevent EOD (Verani *et al*, 2010). IAP has resulted in a nearly 90% reduction in EOD among neonates born to GBS colonized women (Schrag *et al*, 2002). This strategy has been largely successful in the USA and some European countries (Lin *et al*, 2001; Schrag *et al*, 2002; Di Renzo *et al*, 2015).

In Thai studies, the prevalence of GBS colonization among pregnant women has been reported to range from 12% to 18% (Thinkhamrop *et al*, 2003; Tor-Udom *et al*, 2006; Kovavisarach *et al*, 2007; *idem*, 2008); however, there is no standardized GBS screening for pregnant women in Thailand. Pregnant women who deliver at < 37 weeks gestation, amniotic membrane rupture for ≥ 18 hours and an intrapartum temperature $\geq 38.0^{\circ}\text{C}$ are all positively associated with increased risk for EOD (Verani *et al*, 2010). Therefore, IAP is administered to all women with these factors. Antibiotic prophylaxis increases the risk for antibiotic side effects; therefore, is unnecessary if there is no GBS colonization. A recent study from Thailand (Villanueva-Uy *et al*, 2015) reported a low incidence of EOD (0.2 cases/1,000 live births; 95% confidence interval (CI): 0.1 - 0.8); of these, there were only 2 cases of GBS infection out of 8,409 live births. Reasons for this low incidence could be study population, study design, study length (6 months) and loss to follow-up with the infection presenting after discharge. Further studies are needed to clarify the incidence of GBS infection EOD in Thailand to guide screening and prophylaxis policies.

We conducted this study to determine the GBS transmission rate from mothers to newborns at a tertiary-care hospital and determine the isolated GBS antibiotic susceptibility profiles. We hypothesized implementing GBS screening among preg-

nant Thai women is warranted to prevent EOD and neonatal mortality.

MATERIALS AND METHODS

We conducted this cross sectional study at Thammasat University Hospital between January and March 2014. All pregnant women with a gestational age > 28 weeks admitted to the labor room, were aged ≥ 18 years and gave written informed consent were included in this study. Women with a history of antibiotic use within 2 weeks of study recruitment were excluded. Ethical approval for the study was obtained from the Human Research Ethics Committee, Thammasat University (MTU-EC-DS-2-059/56).

Vagina and rectal swabs were obtained from each participating woman. Umbilical cord, ear canal and nasal cavity swabs were obtained from the neonate of each participating women within one hour of birth. The swabs were placed in Amies Transport Medium with charcoal and delivered to the laboratory within 24 hours.

The swabs were directly inoculated into Todd-Hewitt broth containing 10 $\mu\text{g}/\text{ml}$ of colistin and 5 $\mu\text{g}/\text{ml}$ oxolinic acid (Oxoid, Hampshire, UK) and incubated at 37°C in 5% CO_2 for 18-24 hours. The samples were subcultured onto 5% sheep blood agar and incubated at 37°C in 5% CO_2 overnight. If a culture was negative, subculture plates were re-incubated for an additional 24 hours and re-examined. Presumptive identification of beta-hemolytic and non-hemolytic resembling GBS was performed using Gram stain, catalase test, CAMP test and a latex agglutination test using the Strepptococcal Grouping Kit (Oxoid, Hampshire, UK). All GBS isolates were tested for susceptibility to penicillin (10 U), ampicillin (10 μg), erythromycin (15 μg), tetracycline (30 μg), cefotaxime

(30 µg), ceftriaxone (30 µg), vancomycin (30 µg), clindamycin (2 µg), and linezolid (30 µg) by disk diffusion method according to Clinical and Laboratory Standards Institute Guidelines (CLSI, 2013).

Data were analyzed using SPSS version 18 (IBM, Armonk, NY). The Pearson's chi-square (χ^2), Fisher's exact test and *t*-test were used to compare the GBS negative and GBS positive groups. A $p < 0.05$ was considered statistically significant.

RESULTS

A total of 421 participants were included in the study. GBS was isolated from 63 (15.0%) participants. The association of demographics and clinical characteristics with participants who were negative and positive for GBS were analyzed as shown in Table 1. There was no significant difference ($p > 0.05$) in age, education level, occupation, household income, gravida, parity, gestational age at birth, duration of rupture of membranes, rupture of amniotic sac, number of vaginal exams, type of delivery, presence of a perineal laceration and birth weight of infant.

Of the 421 infants born to the 421 study women, 20 infants (4.8%) had a positive culture for GBS giving a maternal to child transmission rate of GBS of 31.8%. Comparing women with and without transmission of GBS to their infants, there was no significant difference in age, education level, occupation, household income, gravida, parity, gestational age at birth, duration of rupture of membranes, number of vaginal exams, presence of a perineal laceration and birth weight (Table 2). However, the following features were significantly associated with transmission of GBS: vaginal delivery ($p = 0.047$), spontaneous rupture of membranes ($p = 0.026$).

All 63 GBS isolates obtained from

the pregnant women were susceptible to penicillin, ampicillin, vancomycin, cefotaxime, ceftriaxone and linezolid. The susceptibilities to clindamycin, erythromycin and tetracycline were: 87%, 86%, and 6%, respectively. All 20 GBS isolates obtained from the neonates were susceptible to penicillin, ampicillin, vancomycin, cefotaxime, ceftriaxone and linezolid. The susceptibilities to erythromycin, clindamycin and tetracycline were 95%, 90% and 10%, respectively (Table 3).

DISCUSSION

The prevalence of GBS among pregnant women in this study was 15%, similar to previous Thai studies (12-18%) (Thinkhamrop *et al*, 2003; Tor-Udom *et al*, 2006; Kovavisarach *et al*, 2007). However, the transmission rates of GBS from the mothers to their infants were not examined in those studies. One study from Thailand (Werawatakul *et al*, 2001) reported the prevalences of GBS in pregnant women and in their infants to be 6.22% and 1.55%, respectively. The prevalences of a positive culture for GBS in their study were low, possibly because they used blood agar instead of 5% sheep blood agar for sub-culturing after specimen inoculation in selective broth culture media (Todd-Hewitt).

In our study, the prevalence of GBS in neonates was 4.8% and the transmission rate was 31.8%, similar to previous international studies: Al-Sweih *et al* (2005) reported a transmission rate in Kuwait of 35.5% with the prevalences of GBS among mothers and infants of 14.6% and 8.7%, respectively. Seoud *et al* (2010) reported a transmission rate in Lebanon of 30% with the prevalences of GBS among mothers and infants of 17.7% and 7.3, respectively. Barcaite *et al* (2012) reported a transmis-

Table 1
Association of selected variables with GBS colonization in pregnant women.

Variable	GBS negative (n = 358)	GBS positive (n = 63)	p-value
Mean (\pm SD) age in years	28 \pm 6	28 \pm 5	0.957 ^a
Education level			
Primary or below	66 (16%)	10 (2.4%)	0.608 ^b
Secondary or vocational	199 (48.1%)	34 (8.2%)	
Post secondary	86 (21%)	19 (4.6%)	
Occupation			
Civil servant	16 (3.8%)	4 (1%)	0.794 ^b
Employed	160 (38.3%)	30 (7.2%)	
Housewife	79 (19%)	11 (2.6%)	
Others (self-employed, student, etc)	100 (23.9%)	18 (4.3%)	
Average monthly income per household in Thai Baht			
< 10,000	91 (22%)	13 (3.1%)	0.620 ^b
10,001 - 25,000	163 (39.3%)	26 (6.3%)	
25,001 - 50,000	81 (20%)	20 (4.8%)	
> 50,000	18 (4.3%)	3 (1%)	
Gravida			
Primigravida	161 (38.2%)	22 (5.2%)	0.138 ^b
Multigravida	197 (46.8%)	41 (9.7%)	
Parity			
Nullipara	175 (41.6%)	26 (6.2%)	0.265 ^b
Primipara	183 (43.5%)	37 (8.8%)	
Gestational age			
28 - 36 weeks 6 days	38 (9.0%)	7 (2%)	0.912 ^b
37 - 42 weeks	319 (76.0%)	56 (13%)	
Duration from rupture of membranes to delivery			
\geq 12 hours	31 (8.6%)	3 (1%)	0.227 ^b
< 12 hours	272 (75.3%)	55 (15%)	
Rupture of amniotic sac			
Spontaneous	162 (42.0%)	32 (8.3%)	0.708 ^b
Artificial	163 (42.2%)	29 (7.5%)	
Number of vaginal examinations			
\geq 4	208 (50.7%)	38 (9.3%)	0.955 ^b
< 4	139 (33.9%)	25 (6.1%)	
Type of delivery			
Normal delivery	249 (59.3%)	50 (12%)	0.120 ^b
Cesarean	108 (25.7%)	13 (3.1%)	
Perineal laceration			
No	225 (62.8%)	37 (10%)	0.234 ^b
Yes	87 (24%)	9 (3%)	
Birth weight of infant in grams			
< 2,500	29 (6.9%)	2 (1%)	0.375 ^c
2,500 - 3,999	317 (75.3%)	60 (14%)	
\geq 4,000	12 (2.9%)	1 (0%)	

^at-test; ^bPearson chi-square; ^cFisher's exact test; GBS, group B *Streptococcus*.

Table 2
Association of selected variables with transmission of GBS from mothers to newborns.

Variable	Transmission of GBS		p-value
	Negative (n = 43)	Positive (n = 20)	
Mean (\pm SD) age in years	28 \pm 6	28 \pm 5	0.786 ^a
Education level			
Primary or below	5 (8%)	5 (8%)	0.109 ^b
Secondary or vocational	27 (43%)	7 (11%)	
Post secondary	11 (18%)	8 (13%)	
Occupation			
Civil servant	4 (6%)	0 (0%)	0.367 ^c
Employed	22 (35%)	8 (13%)	
Housewife	6 (10%)	5 (8%)	
Others (self-employed, student, etc)	11 (18%)	7 (11%)	
Average monthly income per household in Thai Baht			
< 10,000	7 (11%)	7 (11%)	0.082 ^c
10,001 - 25,000	18 (29%)	8 (13%)	
25,001 - 50,000	17 (27%)	3 (5%)	
> 50,000	1 (2%)	2 (3%)	
Gravida			
Primigravida	15 (24%)	7 (11%)	0.904 ^b
Multigravida	28 (44%)	13 (21%)	
Parity			
Nullipara	16 (25%)	10 (16%)	0.461 ^b
Primipara	24 (43%)	10 (16%)	
Gestational age			
28 - 36 weeks 6 days	4 (6%)	3 (5%)	0.669 ^c
37 - 42 weeks	39 (62%)	17 (27%)	
Duration from rupture of membranes to delivery			
\geq 12 hours	1 (2%)	2 (3%)	0.271 ^c
< 12 hours	37 (64%)	18 (31%)	
Rupture of amniotic sac			
Spontaneous	18 (30%)	14 (23%)	0.026 ^b
Artificial	24 (39%)	5 (8%)	
Number of vaginal examinations			
\geq 4	23 (37%)	15 (24%)	0.104 ^b
< 4	20 (32%)	5 (8%)	
Type of delivery			
Normal delivery	31 (49%)	19 (30%)	0.047 ^b
Cesarean	12 (19%)	1 (2%)	
Perineal laceration			
No	25 (54%)	12 (26%)	0.410 ^c
Yes	8 (17%)	1 (2%)	
Birth weight of infant in grams			
< 2,500	1 (2%)	1 (2%)	0.234 ^c
2,500 - 3,999	42 (67%)	18 (29%)	
\geq 4,000	0 (0%)	1 (2%)	

^at-test; ^bPearson chi-square; ^cFisher's exact test; GBS, group B *Streptococcus*.

Table 3
Antimicrobial susceptibility of GBS isolated from pregnant women and their neonates.

Antimicrobial agent	Percent of GBS isolates sensitive to tested antibiotics	
	Mothers	Neonates
Penicillin	100	100
Ampicillin	100	100
Vancomycin	100	100
Erythromycin	86	95
Clindamycin	87	90
Tetracycline	6	10
Ceftriaxone	100	100
Cefotaxime	100	100
Linezolid	100	100

GBS, group B *Streptococcus*.

sion rate in Lithuania of 28.4% with the prevalences of GBS among mothers and infants of 15.3% and 6.4%, respectively. Namavar *et al* (2008) reported a transmission rate in Iran of 60%, with a prevalence of GBS among mothers of 9.1%. Some countries reported lower transmission rates: Eren *et al* (2005) reported a transmission rate in Turkey of 15.2% with the prevalences of GBS among mothers and infants of 9.2% and 1.6%, respectively. A transmission rate in Greece of 22.5% with the prevalences of GBS among mothers and infants of 6.6% and 2.4%, respectively was reported by Tsoia *et al* (2003). Overall, the literature reports maternal-neonate GBS transmission rates ranging from 22% to 60%. These high GBS transmission rates indicate a greater risk for developing GBS infection in neonates, which can lead to sepsis and pneumonia.

The GBS transmission rate was higher among women who had a normal delivery than women who had a cesarean section. The transmission of GBS was significantly more common among women who had spontaneous rupture of membranes than women with artificial rupture of mem-

branes. No other maternal factors were significantly associated with the transmission of GBS.

In this study, all of GBS isolates from the mothers were sensitive to penicillin and ampicillin, similar to previous studies (Barcaite *et al*, 2008; Lu *et al*, 2014; Alemseged *et al*, 2015; Eskandarian *et al*, 2015). These results supported the use of penicillin or ampicillin for intrapartum antibiotic prophylaxis in pregnant women with GBS. There is no GBS screening at the study hospital. According to the US CDC recommendations of the GBS status of a woman in labor is unknown, intrapartum antibiotic prophylaxis should be given if any of the following criteria are present: delivery at < 37 weeks estimated gestation age; if the amniotic membranes are ruptured for ≥ 18 hours or there is a maternal intrapartum temperature of $\geq 38.0^{\circ}\text{C}$ (Schrag *et al*, 2002). For penicillin-allergic women, the CDC recommends using clindamycin or erythromycin after confirmation by antimicrobial susceptibility testing (Schrag *et al*, 2002).

In our study, 13% and 14% of maternal GBS isolates were resistant to

clindamycin and erythromycin, respectively. GBS resistance rates to clindamycin and erythromycin differ by geographical area. In one study from Europe, the resistance rates to clindamycin and erythromycin were reported to be 2.7 - 20% and 3.8 - 21.2%, respectively (Barcaite *et al*, 2008). In a study from China, Lu *et al* (2014) reported GBS resistance rates to clindamycin and erythromycin to be 55.7% and 66.2%, respectively. Infants born to penicillin allergic mothers who receive clindamycin or erythromycin should be monitored carefully in Thailand due to lack of susceptibility testing data. The management of pregnant women at high risk for GBS in Thailand may be challenging due to a lack of susceptibility data. Therefore, GBS screening should be considered in Thailand and susceptibility testing needs to be performed and the results available to clinicians managing these cases. Other strategies also need to be considered, such as use of prophylactic vaginal chlorhexidine which has been shown to reduce mortality in neonates (Stray-Pedersen *et al*, 1999; Facchinetti *et al*, 2002; Goldenberg *et al*, 2006). Rapid result real-time polymerase chain reaction (PCR) or other nucleic acid amplification tests (NAAT) have been added as screening tests at the onset of labor under European guidelines (Di Renzo *et al*, 2015), due to their high sensitivity and specificity, fully automated processing, easy performance and interpretation, and short turnaround time (< 1 hour) in cases of patients who are not allergic to penicillin. Antenatal vaginal-rectal GBS culture screening and susceptibility testing is also performed at 35 - 37 weeks for the patients who are allergic to penicillin following these guidelines (Di Renzo *et al*, 2015).

In conclusion, the prevalence of maternal GBS infection, and the vertical

transmission rate, were high in this study. The factors significantly associated with vertical transmission rate of GBS were a normal vaginal delivery and spontaneous rupture of membranes. There was notable resistance to clindamycin, erythromycin and tetracycline in both maternal and neonatal GBS isolates. The association between finding GBS in infants and the prevalence of EOD need to be investigated in large epidemiological studies in Thailand. These may support the screening for and treatment of GBS among pregnant Thai women.

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