

Choice of Antibiotic for Group B *Streptococcus* in Women in Labour Based on Antibiotic Sensitivity Testing

Eliane M. Shore, MD, FRCSC,^{1,2} Mark H. Yudin, MD, MSc, FRCSC^{1,2}

¹Department of Obstetrics and Gynecology, University of Toronto, Toronto ON

²Department of Obstetrics and Gynecology, St. Michael's Hospital, Toronto ON

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Abstract

Objective: To determine whether pregnant women testing positive for Group B *Streptococcus* (GBS) are receiving appropriate antibiotic prophylaxis in labour based on sensitivity testing.

Methods: We performed a retrospective chart review of all women who delivered at our institution from January 1 to December 31, 2008. We identified all GBS-positive women, and then abstracted data regarding demographic characteristics, method of GBS detection (recto-vaginal or urine culture), prevalence, and antibiotic use. The main outcome measure was the proportion of GBS-positive women who were managed appropriately.

Results: During the study period 628 (22%) of 2878 women were identified as having GBS-positive cultures. Sensitivity testing was available for 481 of the recto-vaginal cultures. All were sensitive to penicillin. The rates of resistance for recto-vaginal culture were 22% for erythromycin, 19% for clindamycin, and 18% for both. Four hundred eighty-one women (93%) were treated with penicillin, 30 (6%) with clindamycin, three with cefazolin, and two with vancomycin. One hundred nine women (17%) who were GBS-positive did not receive antibiotics. Forty-four women (9%) did not receive appropriate antibiotic prophylaxis based on sensitivity testing.

Conclusion: Most GBS-positive women at our institution received an appropriate antibiotic during labour based on sensitivity testing. Our population reflects the Canadian GBS-positivity rate, which is similar to those observed in published studies from other populations. Future work should focus on developing strategies that re-emphasize GBS testing and treatment guidelines for prenatal care providers and on systems to ensure GBS-positive women are given the appropriate antibiotics during labour.

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Résumé

Objectif : Déterminer si les femmes enceintes obtenant un résultat positif au dépistage des streptocoques du groupe B (SGB) reçoivent une antibioprofylaxie appropriée pendant le travail, en fonction de l'épreuve de sensibilité.

Méthodes : Nous avons mené une analyse rétrospective des dossiers de toutes les femmes qui ont accouché au sein de notre établissement entre le 1^{er} janvier et le 31 décembre 2008. Nous avons identifié toutes les femmes séropositives pour les SGB, puis nous avons résumé les données sur les caractéristiques démographiques, la méthode de dépistage des SGB (culture recto-vaginale ou urinaire), la prévalence et l'utilisation d'antibiotiques. Le principal critère d'évaluation était la proportion des femmes séropositives pour les SGB qui ont fait l'objet d'une prise en charge appropriée.

Résultats : Au cours de la période d'étude, 628 (22 %) des 2 878 femmes ont été identifiées comme présentant des cultures positives pour les SGB. Des épreuves de sensibilité étaient disponibles pour 481 des cultures recto-vaginales. Elles étaient toutes sensibles à la pénicilline. Les taux de résistance pour ce qui est de la culture recto-vaginale étaient de 22 % dans le cas de l'érythromycine, de 19 % dans celui de la clindamycine et de 18 % dans le cas de ces deux agents. Quatre cent quatre-vingt-une femmes (93 %) ont été traitées à la pénicilline, 30 (6 %) femmes ont été traitées à la clindamycine, trois femmes ont été traitées à la céfazoline et deux femmes ont été traitées à la vancomycine. Cent neuf des femmes (17 %) qui étaient séropositives pour le SGB n'ont pas reçu d'antibiotiques. Quarante-quatre femmes (9 %) n'ont pas reçu une antibioprofylaxie appropriée fondée sur l'épreuve de sensibilité.

Conclusion : Au sein de notre établissement, la plupart des femmes séropositives pour les SGB ont reçu une antibiothérapie appropriée pendant le travail, en fonction de l'épreuve de sensibilité. Notre population reflète le taux de séropositivité pour les SGB au Canada, lequel est semblable à ceux qui sont constatés dans les études publiées qui ont été menées auprès d'autres populations. Les futurs efforts de recherche devraient être axés sur la conception de stratégies permettant de réitérer aux fournisseurs de soins prénataux l'importance du dépistage des SGB et des lignes directrices quant au traitement, ainsi que sur les systèmes permettant d'assurer que les femmes séropositives pour les SGB reçoivent une antibiothérapie appropriée pendant le travail.

INTRODUCTION

Group B *Streptococcus* is a leading cause of sepsis and meningitis in the first week of life.¹ Intrapartum therapy is the most effective strategy for preventing early neonatal disease.¹⁻³ The current gold standard for detecting GBS colonization is universal screening with a recto-vaginal culture at 35 to 37 weeks' gestation, because cultures taken within five weeks of delivery are most reflective of GBS status at the time of delivery.²⁻⁵ Screening is omitted in women with GBS bacteriuria or a previous infant with GBS sepsis.^{2,3} The presence of GBS bacteriuria during pregnancy is a marker for heavy genital tract colonization; this should be treated at the time of the culture and intrapartum with antibiotic prophylaxis. Vaginal colonization has been associated with Black and Hispanic ethnicities, young maternal age, sexual activity, tampon use, and infrequent handwashing.^{2,3,6,7}

Algorithms have been developed to guide intrapartum antibiotic choice. Penicillin is first-line therapy because of its narrow spectrum of activity and low likelihood of resistance.^{3,8} Approximately 12% of pregnant patients report an allergy to penicillin.⁹ Cefazolin is used for patients at low risk of anaphylaxis, and achieves high intra-amniotic concentrations.^{3,8} Given the rising resistance rates to clindamycin (3% to 15%) and erythromycin (7% to 25%), the CDC in the United States and the American Congress of Obstetricians and Gynecologists have recently amended their guidelines.^{3,6,8} Erythromycin is no longer recommended in cases of penicillin allergy. Clindamycin is recommended in cases of penicillin allergy only if the isolate is susceptible to both clindamycin and erythromycin.^{3,8} Vancomycin is reserved for women with a history of anaphylaxis to penicillin, resistance to both clindamycin and erythromycin, or unknown susceptibility.^{3,8} Despite these algorithms, women may be treated with inappropriate antibiotics if sensitivities are unknown or overlooked.

The primary objective of this study was to determine whether GBS-positive pregnant women at our institution receive appropriate antibiotic prophylaxis in labour, based on sensitivity testing, in order to further characterize the Canadian experience. The secondary objectives were to determine (1) the prevalence of GBS and (2) the proportion of GBS in our centre that is sensitive to one or more of penicillin, erythromycin, and clindamycin.

ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
GBS	Group B <i>Streptococcus</i>
PROM	premature rupture of the membranes

MATERIALS AND METHODS

We performed a retrospective review of the electronic hospital charts of all women who delivered at our institution in Toronto, Ontario, from January 1 to December 31, 2008, to identify those who were GBS-positive. Women were excluded from the study if they did not have GBS testing during pregnancy.

St. Michael's Hospital is an inner city tertiary care centre serving a multi-ethnic population of varied socioeconomic status. At our institution, pregnant women are routinely screened for GBS with a single recto-vaginal culture (first in the vagina and then in the rectum) between 35 and 37 weeks of gestation, following recommendations from the Society of Obstetricians and Gynaecologists of Canada.² Urine cultures are performed on all women at the first antenatal visit and again at 28 weeks of gestation. For all positive recto-vaginal cultures, antibiotic sensitivity testing is performed automatically by the hospital microbiology laboratory, and sensitivity or resistance to penicillin, clindamycin, and erythromycin is itemized on the culture report. Inducible resistance to clindamycin is also tested for automatically. During the time of the study period, routine sensitivity testing was not performed on positive urine cultures.

For all GBS-positive women, we collected the following information: age, gravidity, parity, race, country of birth, expected date of confinement, date of delivery, gestational age at delivery, and mode of delivery. We also documented whether GBS-positivity was determined by recto-vaginal or urine culture, gestational age at positive test, antibiotic sensitivities and resistance profile, allergies to medications, and which antibiotic was administered in labour. All data were abstracted by one author (E.S.) and entered into an Excel spread sheet. Descriptive statistics were used to describe the study population. The proportion of women who were GBS-positive during the study period, the proportion of GBS that was sensitive to each antibiotic (penicillin, clindamycin, and erythromycin), the type of antibiotic used, and the appropriateness of the antibiotic choice based on sensitivity testing were calculated.

Prior to study initiation, approval was granted by the Research Ethics Board at St. Michael's Hospital.

RESULTS

During the one-year study period, 628 women who delivered at our institution had a culture that was positive for GBS (either recto-vaginal, urine, or both) out of a total of 2878 deliveries. This resulted in an overall prevalence

Table 1. Demographic information

	Mean (Range)
Age	31.3 (16 to 48)
Gravidity	2.2 (1 to 2)
Parity	0.8 (0 to 7)
Gestational age at delivery	39+3 (34 to 42+1)
Race	n (%)
Caucasian	231 (37)
Asian	104 (17)
Black	81 (13)
Hispanic	68 (11)
South East Asian	52 (8)
Other	9 (1)
Unknown	83 (13)
Country of birth	
Canada	160 (25)
Other	279 (44)
Unknown	189 (30)

of 22%. Five hundred seventy-five (92%) had a positive recto-vaginal culture, 40 (6%) had a positive urine culture, and 13 (2%) had both recto-vaginal and urine cultures that were positive.

Patient characteristics are presented in Table 1. The ethnic diversity and the large number of women who were born outside Canada reflect our multi-ethnic inner-city population. Four hundred eighty-one GBS recto-vaginal cultures were analyzed at our institution and therefore had sensitivity and resistance profiles reported. One hundred forty-seven women with GBS-positive recto-vaginal cultures had no sensitivity profiles available because their cultures were performed by care providers who used laboratories outside the hospital. For the 481 hospital-based cultures, the rates of sensitivity, resistance, and intermediate resistance to each antibiotic are presented in Table 2. All cultures were sensitive to penicillin. There was a 22% resistance rate to erythromycin, a 19% resistance rate to clindamycin, and an 18% resistance rate to both erythromycin and clindamycin.

Of the 628 women who were colonized with GBS, 516 received antibiotic prophylaxis during labour. Four hundred eighty-one (93%) were treated with penicillin, 30 (6%) were treated with clindamycin, three with cefazolin, and two with vancomycin. One hundred nine women (17%) who were GBS positive did not receive antibiotic prophylaxis. Of these, 75 had a scheduled elective Caesarean section with standard administration of cefazolin (or equivalent in cases of allergy) prior to skin incision, 15 had precipitous vaginal deliveries with no time for antibiotic administration, 10

Table 2. Rates of antibiotic resistance and intermediate resistance in 481 patients

	Resistance Patients, n (%)	Intermediate Patients, n (%)
Penicillin	0 (0)	0 (0)
Erythromycin	104 (22)	4 (1)
Clindamycin	91 (19)	0 (0)
Both clindamycin and erythromycin	86 (18)	0 (0)

women were booked for Caesarean section but presented either in labour or with premature rupture of membranes and did not receive antibiotics, five women had unknown GBS status at the time of delivery, two women were labelled as GBS-negative on their antenatal forms when in fact they were GBS-positive, and two women refused antibiotic prophylaxis. The management for two women was unknown as their hospital charts were unavailable for review at the time of this study. During the study period, there were no cases of neonatal GBS disease.

Drug allergies were based on patient report. Of all GBS-positive women, 40 (6%) reported an allergy to penicillin, four (1%) reported an allergy to erythromycin, and one reported an allergy to clindamycin. The antibiotic treatment of the 40 women who reported an allergy to penicillin is shown in Table 3. Of these women, 30 were treated with clindamycin, three were treated with cefazolin, two were treated with vancomycin, and five did not receive any antibiotic prophylaxis. Four of the 30 women treated with clindamycin had GBS isolates that were resistant to clindamycin.

Of the 628 GBS-colonized women, 44 (9%) were identified as having not received appropriate antibiotic therapy. The reasons for lack of appropriate antibiotic treatment are presented in Table 4.

During the study period 2035 women were GBS-negative and 215 women (7.5%) had unknown GBS status at the time of delivery and were thus excluded from the study. Women with unknown GBS status were 82 who were scheduled for elective Caesarean section and did not have cultures performed, 76 who had a preterm delivery, 30 who delivered at term but did not have GBS testing done, nine who delivered in the previable period, eight who had no prenatal care, five who declined GBS testing, two who had intrauterine fetal deaths determined before delivery, one who did not have any electronic medical chart available for review, one whose culture was mislabelled and not repeated, and one whose recto-vaginal culture was “performed incorrectly” and therefore could not be processed.

Table 3. Antibiotic treatment of patients with penicillin allergy

	Resistant	Treatment		
		Clindamycin	Cefazolin	Vancomycin
Penicillin, erythromycin, clindamycin	None	17	1	
Penicillin, clindamycin	Erythromycin	3		
Penicillin, erythromycin	Clindamycin		1	
Penicillin	Erythromycin, Clindamycin	4	1	1
Unknown	Unknown	6		1

Five patients who were penicillin allergic and had recto-vaginal cultures sensitive to all three antibiotics did not receive any antibiotics.

Table 4. Reasons for inadequate antibiotic prophylaxis

Reasons for inadequate prophylaxis	Patients
Precipitous vaginal delivery	15
Scheduled Caesarean section, presenting in labour or with PROM	10
Unknown GBS status at time of labour, but actually were GBS-positive	5
Penicillin allergic and unknown sensitivities	6
Treatment with antibiotic despite documented resistance	4
Antenatal record documented GBS-negative but patient was GBS-positive	2
Refused prophylaxis	2
Total number of patients	44

DISCUSSION

In this study of 628 women who tested positive for GBS, we found that 44 (9%) were not treated with an appropriate antibiotic based on sensitivity testing and 109 (17%) did not receive any antibiotics. The most common scenarios for inappropriate antibiotic treatment were women presenting with precipitous vaginal deliveries and women with scheduled Caesarean section presenting with labour or PROM. Overall, only four women (0.6%) received an antibiotic to which their GBS isolate was resistant, and all of these women were self-identified as allergic to penicillin.

GBS is a gram-positive organism that colonizes the lower gastrointestinal tract with common secondary spread to the genitourinary tract.³ The Canadian experience is reflected in the prevalence of GBS in our population of 22%. This is consistent with reported values of 10% to 30% of adult women being colonized with GBS.^{2,3} At our institution we follow the SOGC guidelines with universal screening of all patients between 35 and 37 weeks of gestation.²

The prevalence of resistance to clindamycin and erythromycin among invasive GBS isolates is increasing, with reported rates of 3% to 15% and 7% to 25%, respectively.^{3,6,8} Resistance to erythromycin is frequently associated with resistance to clindamycin. If a woman is

allergic to penicillin, this should be stated on her recto-vaginal culture requisition together with a request to perform sensitivity testing.^{2,3} In our population, we found that resistance rates were 19% for clindamycin, 22% for erythromycin, and 18% for both clindamycin and erythromycin. At our institution during this study period, antibiotic sensitivity testing was performed automatically by the microbiology laboratory for positive cultures, and sensitivity or resistance to penicillin, clindamycin, and erythromycin was reported. Sensitivity testing is required to prevent treatment with antibiotics to which the patient's GBS isolate is resistant. In centres where routine sensitivity testing is not performed, it may be missed in patients who are allergic to penicillin. In the event that routine sensitivity testing is not performed, certain safety checks should be put in place so this vital information is not missed. For example, the culture should not be submitted for analysis unless the patient's allergy profile is listed. One study showed that only 11% of patients allergic to penicillin received antibiotic sensitivity testing.¹⁰ Routine sensitivity testing significantly decreases the likelihood of human error, although errors can still occur even when it is in place, with four patients in this study receiving clindamycin for documented clindamycin-resistant GBS. Six patients out of 106 (5.7%) who did not have automatic sensitivity testing were allergic to penicillin. Surprisingly, although cefazolin

is recommended as first-line treatment in patients with non-anaphylactic penicillin allergies, only three patients received cefazolin.^{3,8} It is important to educate obstetric care providers on this point, because pharmacologic data suggest that cefazolin is more reliable than clindamycin to achieve effective intra-amniotic concentrations.^{3,8}

Of the 628 GBS-colonized women, 44 (9%) were identified as having not received appropriate antibiotic therapy. Perhaps the finding of most concern was the 82 women who had a scheduled elective Caesarean section at term with no GBS cultures performed, accounting for 38% of the women with unknown GBS status. In addition to this, 10 women who were known to be GBS-positive presented either in labour or with PROM and did not receive antibiotic prophylaxis because they were scheduled to undergo a Caesarean section; they accounted for 24% of the women who were inappropriately treated with antibiotics. Two women were GBS-positive but were labelled as GBS-negative on their antenatal records. Future efforts need to focus on the importance of GBS screening and proper documentation of results in all patients at 35 to 37 weeks, regardless of whether or not they are booked for delivery by Caesarean section, and on prophylaxis for patients with a scheduled Caesarean section who are GBS-positive at the time of presentation in labour or with PROM, as per CDC guidelines.^{3,8} We suggest that women who present in labour or with PROM and who are scheduled for Caesarean section begin treatment with antibiotics at the time of their presentation, especially in the situation where their Caesarean section will not be performed imminently.

The strengths of this study were the large sample size and our ability to comprehensively evaluate all women who delivered at our institution over a one-year period. Separate data sources were reviewed, including the antepartum chart, the electronic laboratory database, and the intrapartum charts, which were all stored electronically. The routine reporting of sensitivities for GBS recto-vaginal cultures allowed for a detailed assessment of GBS sensitivity and resistance patterns. The findings of the study can be used to highlight areas for improvement, both at our institution and elsewhere, in GBS screening and prophylaxis. The importance of screening all women, regardless of plan for delivery, must be re-emphasized. Further, if practitioners do not use a laboratory that routinely reports sensitivity profiles for GBS-positive isolates, then a request to test for antibiotic-sensitivity in women allergic to penicillin is important. Finally, despite the recommendation that cefazolin be used as the antibiotic of choice in women with penicillin allergies,^{3,4} the majority of women in this cohort

received clindamycin, which is consistent with a study from the United States that found the majority of patients allergic to penicillin received clindamycin.¹⁰ This finding suggests a need for continuing education in this area.

Our study was a retrospective chart review, and this design may have limitations. We were restricted to the information that was available in the chart, and we therefore had areas of incomplete data collection, particularly in relation to ethnicity and country of origin. As well, the sensitivity reports were limited to those women whose health care providers used our hospital microbiology laboratory. We lacked this information for 106 women (18%) who attended midwives, general practitioners, and one obstetrician who used a laboratory that does not routinely report sensitivity and resistance profiles. Our multi-ethnic population and the fact that the data were collected from a single institution may limit generalizability. Rates of reported penicillin allergy are higher in the general population (12%)¹¹ than in our population (6%); therefore, our study may underestimate the likelihood of penicillin-allergic patients being treated with antibiotics to which their isolate is resistant or whose GBS-sensitivity profiles are unknown. In addition, we were unable to determine the nature of the penicillin allergies from the medical charts. More information would have allowed us to determine which patients would have been appropriate for cefazolin treatment.

We found a high proportion of women did not undergo screening at 35 to 37 weeks because they were booked for elective Caesarean section. The SOGC guidelines state that all women should be offered GBS screening at 35 to 37 weeks, and they do not make an exception for those undergoing elective Caesarean section.² As this was a study performed at a single institution, it is unclear whether this concern exists at other sites as well.

CONCLUSION

GBS colonization is common and can lead to serious neonatal complications if not appropriately treated. In our cohort, 22% of women were GBS-positive and 9% of these were not managed with the appropriate antibiotic prophylaxis. Future work should focus on developing both strategies that re-emphasize GBS testing and treatment guidelines for prenatal care providers and systems to ensure that GBS-positive women are given the appropriate antibiotics during labour. Routine sensitivity testing of all GBS-positive isolates can increase the likelihood of choosing an appropriate antibiotic, and such testing should be encouraged.

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