

Revised Abstract

Background: *Streptococcus agalactiae* (GBS) is a major cause of neonatal and perinatal infections as well as a causative pathogen of bacteremia, respiratory, skin and skin structure and urinary tract infections. Although all GBS reported to date remain susceptible to penicillin, resistance to erythromycin and clindamycin has been documented. The Tigecycline Evaluation and Surveillance Trial (TEST) examines the susceptibility of this pathogen isolated from patients in countries worldwide. **Methods:** Clinically significant GBS were obtained from the following infection sites: blood, genital/urinary, respiratory, skin and skin structure and fluids. MICs were determined by the local investigator for 2,176 isolates of GBS isolated from a cumulative total of 322 sites in 49 countries during 2009-2010 utilizing supplied broth microdilution panels. Results were interpreted according to CLSI or FDA (tigecycline) guidelines. **Results:** The % Susceptible and MIC₉₀ (mcg/ml) for six selected antimicrobial agents is shown in the following table for 2009-2010:

Drug	<i>S. agalactiae</i> – %S/MIC ₉₀ (mcg/ml)				
	Blood	Skin/Structures	Genital/Urinary	Respiratory	Fluids
Ampicillin	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Ceftriaxone	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Linezolid	100/2.0	100/2.0	100/1.0	100/2.0	100/1.0
Meropenem	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12
Tigecycline	100/0.12	100/0.12	100/0.25	100/0.12	100/0.12
Vancomycin	100/1.0	100/0.5	100/0.5	100/0.5	100/0.5
N =	426	410	1002	138	200

Conclusions: All GBS isolated in 2009-2010 remained 100 percent susceptible to the studied antimicrobials with the MIC₉₀ for each antimicrobial remaining constant regardless of infection site. Global GBS isolated from a variety of clinical specimens continue to demonstrate complete susceptibility to the studied antimicrobials and stable MIC₉₀.

Introduction

Streptococcus agalactiae or Group B streptococcus (GBS) is the leading infectious cause of both early and late onset neonatal morbidity and mortality in developed countries worldwide. Clinical trials conducted in the 1980 demonstrated that administration of antibiotics prior to childbirth while women who were at risk of GBS colonization were in labor could prevent invasive disease [1]. Penicillin or other beta-lactam antibiotics remain the antibiotic agents of choice for prophylaxis. Frequently macrolides or lincosamides may be prescribed to women who are penicillin or beta-lactam allergic. To date there have been no reported cases of isolates resistant to either penicillin or ampicillin. However in the United States between 5-25% of isolates have demonstrated *in vitro* resistance to erythromycin and between 3-17% resistance to clindamycin [2-5]. Resistance to ceftioxin has been reported but still remains rare. Vancomycin is used as an alternative to ampicillin and penicillin in patients with documented beta-lactam allergies where anaphylaxis is of concern and where resistance to erythromycin or clindamycin is documented.

Alternatives to standard treatment regimens have not been examined but surveillance studies examining the *in vitro* activities of carbapenems, glycolcyclines and cephalosporins to GBS will help define the role of these agents in the future.

GBS furthermore can also cause infections of the bloodstream, central nervous system, respiratory tract, urinary tract and skin/skin structures.

The Tigecycline Evaluation and Surveillance Trial (TEST) has examined the activity of tigecycline and comparative agents against over 170,000 pathogens collected worldwide since 2004. This report documents the *in vitro* activity of tigecycline, ampicillin, ceftriaxone, linezolid, meropenem and vancomycin to 2,176 isolates of GBS isolated worldwide 2009-2010.

Materials & Methods

- All isolates were derived from a variety of clinical specimens/infectious processes including blood, respiratory, and skin/skin structure, but predominantly genital/urinary worldwide. Only one isolate per patient was accepted into the study. Clinical isolates were collected and tested between 2009 and 2010 from 322 cumulative study centers in 49 countries. Isolates were identified to the species level and MICs determined at each site by the participating laboratory.
- Organism collection, transport, confirmation of organism identification, and development and management of a centralized database, were coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- Minimum inhibitory concentrations were determined by the CLSI recommended broth microdilution testing method [6]. Panels were manufactured by MicroScan (Siemens Medical Solutions Diagnostics, West Sacramento, CA, USA) or TREK (TREK Diagnostic Systems, Cleveland, OH, USA).
- The panel used for MIC determinations contained the following antimicrobial agents and concentrations (expressed in mcg/ml): amoxicillin-clavulanic acid (0.12-32); ampicillin (0.5-32); piperacillin-tazobactam (0.06-128); levofloxacin (0.008-8); ceftriaxone (0.06-64); linezolid (0.5-8); penicillin (0.06-8); meropenem (0.06-16); minocycline (0.5-16); tigecycline (0.008-16); and vancomycin (0.12-32).
- QC of broth microdilution panels followed manufacturers' and CLSI guidelines using *Streptococcus pneumoniae* ATCC 49619.
- Quality controls were performed by each testing site on each day of testing and results were included in the analysis only when corresponding QC isolates tested were within the acceptable range according to CLSI (2011) guidelines [7].

References

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Results

Figure 1. Group B *Streptococcus* infection site distribution
N=2,176

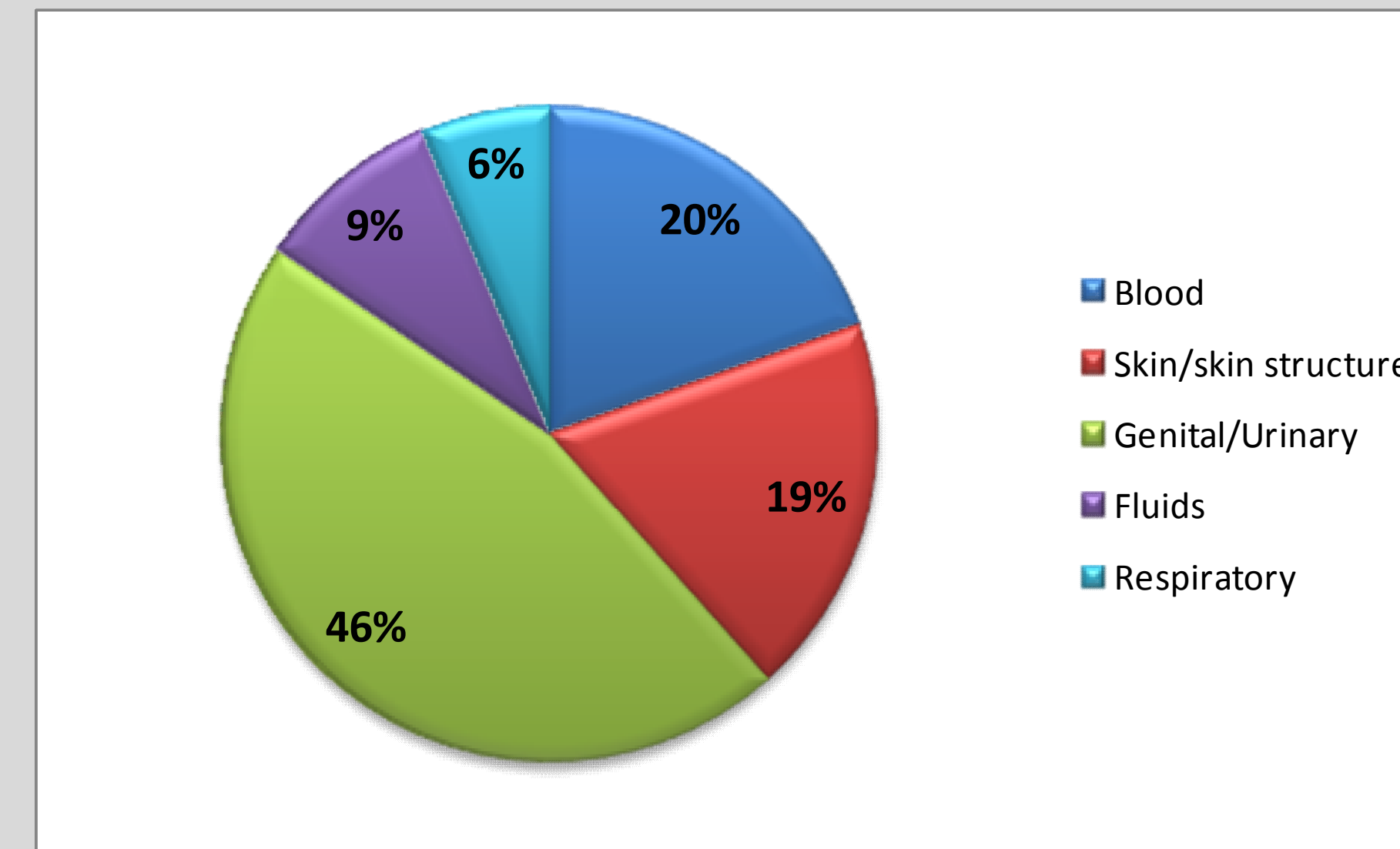


Table 2. 2010

Drug	<i>S. agalactiae</i> – %S/MIC ₉₀ (mcg/ml)				
	Blood	Skin/Structures	Genital/Urinary	Respiratory	Fluids
Ampicillin	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Ceftriaxone	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Linezolid	100/2.0	100/2.0	100/1.0	100/2.0	100/1.0
Meropenem	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12
Tigecycline	100/0.12	100/0.12	100/0.25	100/0.25	100/0.12
Vancomycin	100/1.0	100/1.0	100/1.0	100/0.5	100/0.5
N =	107	109	250	44	53

Percent Susceptible and MIC₉₀ are illustrated in the following tables: 2009, 2010 and 2009-2010.

Table 1. 2009

Drug	<i>S. agalactiae</i> – %S/MIC ₉₀ (mcg/ml)				
	Blood	Skin/Structures	Genital/Urinary	Respiratory	Fluids
Ampicillin	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Ceftriaxone	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Linezolid	100/1.0	100/1.0	100/1.0	100/1.0	100/1.0
Meropenem	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12
Tigecycline	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Vancomycin	100/1.0	100/0.5	100/0.5	100/0.5	100/0.5
N =	319	301	752	94	147

Table 3. 2009-2010

Drug	<i>S. agalactiae</i> – %S/MIC ₉₀ (mcg/ml)				
	Blood	Skin/Structures	Genital/Urinary	Respiratory	Fluids
Ampicillin	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Ceftriaxone	100/0.12	100/0.12	100/0.12	100/0.12	100/0.12
Linezolid	100/2.0	100/2.0	100/1.0	100/2.0	100/1.0
Meropenem	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12	100/≤0.12
Tigecycline	100/0.12	100/0.12	100/0.25	100/0.12	100/0.12
Vancomycin	100/1.0	100/0.5	100/0.5	100/0.5	100/0.5
N =	426	410	1002	138	200

Conclusions

- No resistance to any antimicrobials tested was detected in GBS over the 2 year study period for any specimen sources.
- There were slight variations in MIC₉₀ (by one doubling dilution) for linezolid, tigecycline, and vancomycin; however, this represented no clinical significance.
- Surveillance of over 2,000 GBS between 2009-2010 documents the continued *in vitro* activity of ampicillin and comparator antimicrobials.