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ABSTRACT
Background: Tigecycline, the initial representative of the glycyclines, presents a therapy option for emerging multidrug-resistant (MDR) pathogens. India, a nation rarely monitored in global surveillance programs, appears in need of a baseline against MDR isolates of Enterobacteriaceae (ESBLs), Acinetobacter (carbapenem-resistant) and Gram- positive cocci (MRSA, VRE). Numerous sites were sampled and monitored in the 11 medical centers.

Methods: Eleven sites forwarded 1,714 strains to a regional monitor (WICH, Adelaide, Australia) that susceptibility testing was performed. Four methods were used to identify isolates: CLSI, NCCLS, bioMerieux Vitek 2 Compact, and Vitek 2. Identification was confirmed and interpreted/screening criteria were followed by ESBL (n = 1,498), and VRE (n = 1,714). CLSI susceptibility testing was followed by the United States Food and Drug Administration breakpoints. Major pathogens were S. aureus (250), coagulase-negative staphylococci (228), Enterobacteriaceae (76), E. coli (217), K. pneumoniae (206), Salmonella spp. (65) and Acinetobacter spp. (108).

RESULTS
Tigecycline was active against 99.0% of indicated/tabulated species, lowest for Acinetobacter spp. S. aureus tigecycline MIC50 values were not influenced by oxacillin susceptibility patterns (2.53 mg/L; 100%). Increased resistance patterns noted were tetracycline-resistant (4-100%: average 53%), AmpC, ESBL- and fluoroquinolone resistant Enterobacteriaceae (87-10, 14-78, 91-97, respectively), VRE (1%), MRSA (36%) and Acinetobacter carbapenem-resistant (38%). S. typhi and S. paratyphi were sensitive to tigecycline (MIC50 0.25 mg/L; 85%). Nalidixic acid-resistant. Carbapenem-resistant Enterobacteriaceae (1-7%) was consistent with harbouring metallo-ß-lactamases; confirmed by PCR testing.

Conclusions: Although MDR rates across Gram-positive and -negative species (particularly among enteric bacilli and Acinetobacter) was high, in India, tigecycline remained active (MIC50 1 mg/L overall) against these MDR strains. Tigecycline exhibited promising spectrum/potency against isolates currently available agents sampled isolates from India.

INTRODUCTION
Tigecycline is a semisynthetic glycycline derivative from minocycline that induces its bacteriostatic effect by binding to a large ring of intracellularly located on the bacterial 3OS-ribosome, thus blocking entry of amino-acyl tRNA molecules into the A site of the ribosome and preventing further protein synthesis. The drug is highly concentrated in the lung and is substantially less excreted at position 9. Thus, tigecycline possesses documented activity against tetracycline-resistant Gram-positive and -negative pathogens refractory to treatment by efficacious and/or resist-protective mechanisms. In addition, this antimicrobial agent has demonstrated excellent activity against multidrug-resistant (MDR) pathogens, including oxacillin-resistant (MRSA) and glycopeptide-intermediate Staphylococcus aureus (VISA), vancomycin-resistant enterococci (VRE), penicillin-resistant Streptococcus pneumoniae, extended-spectrum ß-lactamase (ESBL)-producing Enterobacteriaceae and some non-fermentative Gram-negative bacilli, such as Acinetobacter spp. and Stenotrophomonas maltophilia.

The objective of this study was to evaluate the potency and spectrum of tigecycline activity tested against bacterial pathogens isolated during 2006 from medical centers located in India.

MATERIALS AND METHODS
Isolates of 1,714 bacterial isolates collected during 2006 in 22 medical centers located in India were evaluated as part of the SENTRY Antimicrobial Surveillance Program (ASP). The isolates were consecutively collected from bloodstream infections, skin and soft tissue infections, urinary tract infections and patients in hospitalized patients according to a common protocol. Only isolates from documented infections were included in the study. Species identification was confirmed by standard biochemical tests and the VITEK 2 Compact (bioMerieux, Hazelwood, MO), when necessary.

Antimicrobial susceptibility testing. All isolates were susceptible tested using the broth microdilution method as described by the Clinical and Laboratory Standards Institute (CLSI) broth dilution methods. Tigecycline (0.03 mg/L; 100%) fresh cation-adjusted Mueller-Hinton broth was used in validated panels manufactured by TREK Diagnostics (Cleveland, OH). Categorical interpretations for comparator antimicrobials were those found in M100-S18; breakpoints for tigecycline were those of the United States Food and Drug Administration (FDA). Quality control (QC) was performed using Escherichia coli ATCC 25922, S. aureus ATCC 29213 and Pseudomonas aeruginosa ATCC 27853; all QC results were within specified ranges as published in M100-S19.

RESULTS
• Tigecycline showed pronounced activity against Gram-positive clinical isolates, with 100.0% susceptibility for S. aureus and Enterococcus spp. (Table 1).
• Tigecycline potency against oxacillin-resistant S. aureus (MIC50 0.25 mg/L) was the same as the potency for oxacillin-susceptible strains.
• Among Gram-negative isolates, tigecycline demonstrated 100.0% activity against E. coli, and various species of Enterobacter and Salmonella (Table 1).
• The activity of tigecycline against K. pneumoniae and Acinetobacter spp. was slightly lower at 98.5 and 98.1%, respectively, and only 0.7 to 0.9% of strains were categorized as resistant (Table 1).
• Tigecycline was very active against tetracycline-resistant strains that were observed in 4.0 to 100.0% (average 50.3%) of isolates.
• Overall, tigecycline remained active (MIC50 1 mg/L) against isolates harbouring important resistance mechanisms including: AmpC, ESBL-producing strains, fluoroquinolone resistant Enterobacteriaceae, VRE, MRSA and carbapenem-resistant Acinetobacter spp.
• Among Salmonella spp. isolates, 54.5% were S. typhi and 38.2% were S. paratyphi. A total of 84.2% were nalidixic acid-resistant (1.8% susceptible to ciprofloxacin); tigecycline (MIC50 0.5 mg/L) showed good activity and potency against these isolates.
• Carbapenem resistance in Enterobacteriaceae was low and most resistant isolates were carbapenemase-producers.

CONCLUSIONS
• Antimicrobial activity of tigecycline was largely unaffected by mechanisms that most commonly occur in Gram-positive and Gram-negative organisms in India.
• This novel compound could be a valuable therapeutic option for the treatment of infections caused by these troublesome pathogens in this nation.

ACKNOWLEDGEMENT
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Table 1. In vitro activity of tigecycline in comparison to selected antimicrobial agents tested against 1,714 clinical isolates from India collected in 2006 as part of the SENTRY Antimicrobial Surveillance Program (ASP).

<table>
<thead>
<tr>
<th>Organism</th>
<th>Tigecycline</th>
<th>Ciprofloxacin</th>
<th>Amikacin</th>
<th>Gentamicin</th>
<th>Linezolid</th>
<th>Teicoplanin</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus</td>
<td>0.12 0.25 0.5 1 2 4</td>
<td>0.12 0.25 0.5</td>
<td>&gt;32 &gt;32 &gt;32</td>
<td>&gt;32 &gt;32 &gt;32</td>
<td>2 4 8 16 32 64</td>
<td>1 2 0.5 – 2</td>
<td></td>
</tr>
<tr>
<td>E.coli</td>
<td>0.06 – 0.12 0.25 – 1 4 – 8</td>
<td>0.06 – 0.12 0.25 – 1 4 – 8</td>
<td>&gt;16 &gt;16 &gt;16</td>
<td>&gt;16 &gt;16 &gt;16</td>
<td>2 4 8 16 32 64</td>
<td>1 2 0.5 – 2</td>
<td></td>
</tr>
<tr>
<td>S. typhi</td>
<td>0.12 0.25 0.5 1 2 4</td>
<td>0.12 0.25 0.5</td>
<td>&gt;32 &gt;32 &gt;32</td>
<td>&gt;32 &gt;32 &gt;32</td>
<td>2 4 8 16 32 64</td>
<td>1 2 0.5 – 2</td>
<td></td>
</tr>
<tr>
<td>A. baumannii</td>
<td>0.5 1 2</td>
<td>0.5 1 2</td>
<td>&gt;32 &gt;32 &gt;32</td>
<td>&gt;32 &gt;32 &gt;32</td>
<td>2 4 8 16 32 64</td>
<td>1 2 0.5 – 2</td>
<td></td>
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</tbody>
</table>