Time Trends in the Epidemiology of Microbial Infections at a Tertiary Care Center in West India Over Last 5 Years

Atul K Patel¹², Ketan K Patel¹², Kamlesh R Patel³, Sanjiv Shah³, Pratibha Dileep⁴

Abstract

Introduction: Microbiological surveillance data is of crucial importance in appropriate management of patients with infectious diseases. The current study was conducted to study the microbiological surveillance data along with antibiotic sensitivity patterns for isolates collected at a single tertiary care center from Western India over last four years and to analyze the change in the patterns of nosocomial infections seen over the last four year period.

Methods: Design: Retrospective study. Culture reports data were retrospectively collected from microbiology department of Sterling hospital Ahmedabad. Isolates from clinical specimen from blood cultures, surgical site swabs, abdominal drain fluid, urine samples and bronchoscopy samples were analysed in present study. Isolates from respiratory secretions including endotracheal, tracheostomy and sputums were excluded from analysis. Frequency of different organisms which were isolated as well as the sensitivity patterns to major antibiotics were recorded.

Results: Among the blood isolates there was a clear trend regarding the emergence of gram positive organisms with Staphylococcus being the most common isolate from 149 blood culture specimens in the period 2008-09 (27.4%). Majority (>85%) of gram negative isolates causing blood stream infections were sensitive to Amikacin, Cefoperazone-Sulbactam, Piperaciln-Tazobactam, Meropenem and Colistin. On the other hand, sensitivity of gram negative isolates from other sites to these antibiotics was much more variable. Incidence of candidemia went down from 20.3% to 13.4% in 2005-6 and in 2008-09 respectively.

Conclusion: Staphylococcus aureus has emerged as the dominant pathogen causing the blood stream infections in last two years. Piperaciln-tazobactum, cefaperazone-sulbactum or meropenem may be appropriate as empiric antibiotic choice for gram negative blood stream infections along with Amikacin for patients with serious infections.

Introduction

Microbiological surveillance data is of critical importance in appropriate management of patients with serious life threatening infections. Emergence of newer pathogenic strains as well as multi-drug resistant strains has brought into focus the immense importance of microbiologic surveillance.¹ Role of this data can not be overemphasized while choosing empirical antibiotics in patients with critical illnesses. Several studies have shown that outcomes of critically ill patients are improved with appropriate empiric antibiotic.²⁻⁴ Incidence of different organisms in infections acquired in the community or the health care set up vary across different countries and sometimes even different studies. Further, even the microbiological flora as well as the sensitivity pattern to different antibiotics tends to change over time in a particular health care set up. All these factors have a bearing on the choice of empiric antibiotic protocols. In addition, knowledge about these data can also result in reduction in use of inappropriate antibiotics and thereby reduce emergence of resistant microorganisms.¹

The current study was conducted to study the microbiological surveillance data along with antibiotic sensitivity patterns for isolates collected at a single tertiary care center from Western India. We also analyze the change in the patterns seen over the last four year period.

Material and Methods

In this retrospective study, data from the Department of Microbiology at the Sterling Hospital, Ahmedabad collected from the year 2005-2009 was reviewed. Sterling Hospital is 285 bed multispeciality tertiary care center. There are 10,000 in patients admissions yearly with more than 500 annual ICU admissions and 3000 surgeries per year. Data on isolates and the sensitivity patterns were available for three different time frames: 2005, 2006, and 2008-09. However the data on isolates from 2007 was not available and could not be analysed. Further, some data was missing regarding few isolates especially from earlier years. Missing data and incomplete information were removed from final analysis.

Isolates from all submitted clinical specimen including blood cultures, surgical site swabs, abdominal drain fluid, urine samples and bronchoscopy samples were analysed. Samples had been received from inpatients from intensive care units (Medical, surgical, cardiac, neuro and pediatric) and floors. Respiratory secretions like sputum, endotracheal and tracheostomy aspirate samples were not analysed as many isolates from these sources tend to represent colonizers rather than true pathogens. Frequency of different organisms which were isolated as well the sensitivity patterns to major antibiotics was recorded.

All samples submitted for suspected or confirmed infections acquired in the community or healthcare set up was included. Decision to submit the samples for culture was at the discretion of the treating physician and this was not impacted for the purpose of the study. All the cultures were submitted for culture and antimicrobial sensitivity testing in accordance with Clinical and Laboratory Standard Institute Guidelines.⁵ Species identification and susceptibility testing was performed by mini API system biomeurix and Simens microscan system. No patient data was analyzed for the purpose of this report.
Results

Frequency of organisms isolated as well as the sensitivity patterns has been variable during the three time frames that were studied. Results were analyzed separately for isolates from blood specimens. Among the blood isolates there was a clear trend regarding the emergence of gram positive organisms. Gram negative bacilli tended to dominate the isolates in 2005 (n=148) with more than a quarter isolates being Pseudomonas and Staphylococcus being isolated in less than 10% of the specimens (Figure 1). However, Staphylococcus was the most common isolate from 149 blood culture specimens in the period 2008-09 (27.4%). Interestingly frequency of Candida spp also went down from 20.3% to 13.4% whereas E. coli did not change.

Interesting trends were noted regarding the sensitivity patterns of the gram negative bacilli isolated from the blood cultures. Sensitivity to almost all the antibiotics improved over the last four years (Table 1). Based on the antibiogram from 2008-09, Amikacin Cefoperazone-Sulbactam, Piperacillin-Tazobactam, Meropenem and Colistin were all dependable empiric antibiotic options for gram negative bacilli. All these antibiotics were consistently effective against a large majority (>85%) of the isolates. Amongst staphylococcus isolates 25% (7 out of 28 isolates) were MRSA. We havenot performed vancomycin MIC for MRSA. Among the isolates from other sites (surgical site, abdominal drains, urine and bronchoscopy samples), overall trend remained the same as for blood isolates with consistent improvement in the sensitivity patterns to almost all analyzed antibiotics (Table 2). However, the efficacy of different antibiotics was more variable among these isolates. None of the antibiotic was consistently effective though Meropenem tended to do better than others. However, the sensitivity of Pseudomonas isolates in 2008-09 to Meropenem was less than 70%. Similarly though Colistin appeared to be effective for >85% of the Pseudomonas

![Figure 1: Carbapenemase production in gram negative organisms, Intermediate susceptibility is reported here as resistant](image)

Table 1 : Frequency of Isolation and sensitivity patterns of gram negative blood stream isolates

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Amikacin</th>
<th>Cefipime</th>
<th>Cefaperazone + Sulbactam</th>
<th>Cipro</th>
<th>Meropenem</th>
<th>Pipera-cillin+ Tazo</th>
<th>Colistin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 n= 33</td>
<td>30</td>
<td>12</td>
<td>12</td>
<td>15</td>
<td>36</td>
<td>15</td>
<td>48</td>
</tr>
<tr>
<td>2006 n=8</td>
<td>25</td>
<td>12</td>
<td>50</td>
<td>12</td>
<td>50</td>
<td>62</td>
<td>62</td>
</tr>
<tr>
<td>2008-9 n=53</td>
<td>76</td>
<td>15</td>
<td>85</td>
<td>9</td>
<td>100</td>
<td>85</td>
<td>100</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 n=16</td>
<td>62</td>
<td>NA</td>
<td>6</td>
<td>37</td>
<td>25</td>
<td>6</td>
<td>NA</td>
</tr>
<tr>
<td>2006 n=5</td>
<td>100</td>
<td>NA</td>
<td>100</td>
<td>NA</td>
<td>100</td>
<td>100</td>
<td>NA</td>
</tr>
<tr>
<td>2008-9 n=22</td>
<td>100</td>
<td>23</td>
<td>100</td>
<td>5</td>
<td>100</td>
<td>100</td>
<td>100</td>
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<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 n=14</td>
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<td>36</td>
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<td>14</td>
<td>NA</td>
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<td>2006 n=2</td>
<td>NA</td>
<td>NA</td>
<td>100</td>
<td>NA</td>
<td>100</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>2008-9 n=25</td>
<td>96</td>
<td>8</td>
<td>88</td>
<td>8</td>
<td>100</td>
<td>88</td>
<td>100</td>
</tr>
</tbody>
</table>

All values are in percentages. Values in columns are mutually not exclusive; NA: Not available

Table 2 : Frequency and sensitivity patterns of gram negative isolates from other sites (surgical site, abdominal drains, urine and bronchoscopy samples)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Amikacin</th>
<th>Cefipime</th>
<th>Cefaperazone /sulbactam</th>
<th>Cipro</th>
<th>Meropenem</th>
<th>Pipera-cillin+ Tazo</th>
<th>Colistin</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 n= 177</td>
<td>19.8</td>
<td>7.3</td>
<td>19.8</td>
<td>10.2</td>
<td>21.5</td>
<td>10.2</td>
<td>45.3</td>
</tr>
<tr>
<td>2006 n=73</td>
<td>20.5</td>
<td>15.1</td>
<td>31.5</td>
<td>6.8</td>
<td>41.1</td>
<td>43.9</td>
<td>72.6</td>
</tr>
<tr>
<td>2008-9 n= 155</td>
<td>50.3</td>
<td>10.32</td>
<td>53.3</td>
<td>5.2</td>
<td>69.7</td>
<td>70.3</td>
<td>86.6</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 n= 204</td>
<td>68.1</td>
<td>19.1</td>
<td>40.2</td>
<td>45.6</td>
<td>54</td>
<td>22.5</td>
<td>NA</td>
</tr>
<tr>
<td>2006 n=59</td>
<td>78</td>
<td>10.2</td>
<td>79.7</td>
<td>8.5</td>
<td>100</td>
<td>49.1</td>
<td>NA</td>
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<tr>
<td>2008-9 n=164</td>
<td>81.7</td>
<td>4.2</td>
<td>86.6</td>
<td>3.7</td>
<td>96.7</td>
<td>61.6</td>
<td>53.1</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005 n= 64</td>
<td>54.7</td>
<td>9.4</td>
<td>26.6</td>
<td>37.5</td>
<td>46.9</td>
<td>11</td>
<td>NA</td>
</tr>
<tr>
<td>2006 n=25</td>
<td>24</td>
<td>0</td>
<td>40</td>
<td>0</td>
<td>100</td>
<td>8</td>
<td>NA</td>
</tr>
<tr>
<td>2008-9 n=87</td>
<td>75.9</td>
<td>2.3</td>
<td>64.4</td>
<td>2.3</td>
<td>96.6</td>
<td>63.2</td>
<td>71.3</td>
</tr>
</tbody>
</table>

All values are in percentages. Values in columns are mutually not exclusive; NA: Not available
isolates, it performed poorly against E. coli.

We also found appearance of carbapenem resistance in gram negative isolates, Figure 1.

Recently 3 isolates of klebsiella resistant to carbapenems were subjected for further evaluation and found to be New Delhi Metalobeta lactamase producers.

Discussion

Frequency and species of infective microbial organism and their antimicrobial susceptibility depends on three main factors namely the types of patients catered by the hospital such as neurosurgical, solid organ and bone marrow transplant, intensive care units etc, the hospital infection control policies and frequency and use of antibiotics to treat infections. For many years, medical practice in India was mainly limited to small nursing homes. In last few years it has changed to big corporate hospitals in the major cities of India. Because of better medical care facility at these hospitals many immunocompromised patients like those with diabetes, solid organ transplant, and collagen vascular diseases are surviving longer. This may contribute to development of drug resistance. Further, extensive use of quinolones and 3rd generation cephalosporines in community from family physicians and consultants has contributed to increase in extended spectrum beta lactamases in gram negative organisms and methicillin resistant Staphylococcus aureus (MRSA) and vancomycin resistant enterococcus.

We report our experience regarding the trends in the isolates from different clinical specimen collected over the last 4 year period. One of the most pertinent information to emerge from the current analysis was the shift in the predominant isolates in the organisms causing blood stream infections. Staphylococcus seems to be emerging as the dominant organisms in blood stream infections with 25% MRSA isolates. Similar trend has been reported in the data from the West over the last two decades. Nosocomial infection due to Staphylococcus aureus constitutes a major part of the total annual nosocomial infections. Moreover, the prevalence of MRSA has since then been on the rise. In fact, MRSA prevalence approached 50-60% by 2006. However, the same had not been reported earlier in data from India. In the study by Vergheese et al, among patients with central venous catheter associated infections, staphylococcus was not associated with bacteremia or septicemia. Gram negative organisms including Klebsiella species, Enterobacter species, E. coli species, Serratia and non-fermenting Gram negative bacilli formed the predominant isolates in this study. However, this trend might be changing and the findings from current report should be confirmed in a larger prospectively designed study.

It was seen that over the last four years, sensitivity of all gram negative isolates to major antibiotics tended to improve. Significant improvements were documented across the board. Some of these findings were intriguing and opposite to what has generally been observed. Although a close surveillance with proactive infection control policies including restriction and rationalization of antibiotic use along with aggressive antibiotics cycling at the institution level may have contributed to these trends, they are unlikely to explain the dramatic improvements in the sensitivity. It is possible that these findings reflect a local institute level phenomenon and can not be generalisable.

On the other hand, the latest data on isolates from 2008-09 throw up interesting results with pertinent clinical ramifications. Multiple antibiotic options may be available for choosing appropriate empiric coverage for patients with suspected gram negative blood stream infection with Amikacin, Cefoperazone-Sulbactam, Piperacillin-Tazobactam, Meropenem and Colistin all having excellent efficacy against all the major isolates. However, an appropriate empiric choice of antibiotic for suspected gram negative infections from other sites may be tricky. No single antibiotic appears to have good enough activity against all the isolates. It may be appropriate to use a combination of two antibiotics for empiric coverage for such patients. It may be reasonable to use aminoglycoside in combination with Cefoperazone-Sulbactam, or Piperacillin-Tazobactam or Meropenem for enhancing the odds of covering the culprit organism in seriously ill patients. However, it is important to emphasize that this approach needs to be validated in prospectively designed studies.

There are several limitations of the current report. Being a single center study the results can not be widely extrapolated. Moreover, extrapolation of surveillance data to other set ups is always fraught with danger as institutional antibiotic protocols as well as the practices in the community by the private physicians tend to impact the microbiologic flora as well as the sensitivity patterns. Also, some of the data was found to be missing or incomplete in the review of the database. All such data was excluded and may have lead to selection bias. Further, data regarding the isolates from tracheostomy and endotracheal aspirates were discarded and this may have confounded results of some of the sensitivity results. However, we would like to believe that this helped us to focus on isolates of definite pathogenic significance and thereby improve the robustness of the antibiotic protocol recommendations.

It is concluded that, there was a shift from gram negative pathogens to gram positive pathogens over the last two years in blood stream isolates and Staphylococcus aureus has emerged as the dominant pathogen causing the blood stream infections in last two years. Metalobetalactamase – a new variant New Delhi Metalobetalactamase (NDM) is coming up in nosocomial Gram negative pathogens. Piperacillin-tazobactum, cefaperazone-sulbactum or meropenem may be appropriate for choosing antibiotic choice for gram negative blood stream infections along with Amikacin for patients with serious infections.

Acknowledgement

Authors would like to acknowledge Pfizer India for supporting data analysis.

References


