Antimicrobial resistance among bacterial pathogens is a global problem, but in Egypt data are sparse. We reviewed the antimicrobial susceptibility patterns of bloodstream isolates of Gram-positive cocci and Gram-negative bacilli in five hospitals in Cairo, Egypt, from 1999 to 2000. In addition, susceptibilities of non-bloodstream isolates of Streptococcus pneumoniae and Enterococcus spp. were analysed. High rates of resistance were found in most of the bacteria studied. In the hospitals, a variety of methods were used for identification and susceptibility testing, but in the laboratories quality controlled strains were utilized routinely, to ensure accurate performance of the assays. Only 29% of Staphylococcus aureus isolates and 23% of coagulase-negative staphylococcal isolates were oxacillin susceptible. Both groups of staphylococci were also highly resistant to erythromycin, co-trimoxazole, clindamycin and doxycycline; all isolates were susceptible to vancomycin. Susceptibility of S. pneumoniae isolates to penicillin, ceftriaxone and fluoroquinolones was 63%, 84% and 82%, respectively. Vancomycin susceptibility of the enterococci was 96%; susceptibility to high-level gentamicin and streptomycin was 54% and 48%, respectively. Resistance to most relevant antimicrobials was commonplace among the Gram-negative bacilli; however, most remained susceptible to imipenem. The percentage of bloodstream isolates of Escherichia coli susceptible to common antimicrobial agents was as follows: ampicillin (6%), ampicillin–sulbactam (38%), co-trimoxazole (38%) and aminoglycosides (52%). The susceptibility of isolates of E. coli, Klebsiella and Enterobacter spp. to ceftazidime was 62%, 40% and 46%, respectively. This suggests a potentially high rate of extended-spectrum β-lactamase (ESBL) and/or Amp-C enzyme production. These results call for a nationwide surveillance programme to monitor microbial trends and antimicrobial resistance patterns in Egypt.

Keywords: resistance, Egypt, bacterial susceptibility testing, Gram-negative bacilli, Gram-positive cocci

Introduction

Infections caused by resistant pathogens result in significant morbidity and mortality, and contribute to escalating healthcare costs worldwide. Despite the availability of newer antibiotics, emerging antimicrobial resistance has become an increasing problem in many pathogens throughout the world.1–3 For practising physicians, clinical microbiologists and public health officials, knowledge of local antimicrobial resistance patterns is essential to guide empirical and pathogen-specific therapy. This information is also critical for optimal decisions regarding hospital formulary and infection control policies, for the rational formulation of public healthcare policies, and national and international research agendas in this area. Unfortunately, data regarding endemic antimicrobial resistance are unavailable in many parts of the world, especially from areas where over-the-counter antibiotic use is common.

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Few papers have examined endemic antimicrobial resistance in Egypt, although several reports have studied the occurrence and resistance patterns of specific respiratory and enteric pathogens, and a few small, short-term studies from individual institutions have been reported in Egyptian medical journals. This study was therefore undertaken to identify regional endemic antimicrobial resistance patterns among common bacterial isolates from patients in five hospitals in Cairo.

Materials and methods

Study design

This was a retrospective, multicentre study, conducted utilizing microbiology laboratory records from 1 July 1999 to 30 June 2000, from five hospitals in the greater Cairo region. These hospitals included Cairo University Pediatric Hospital (CUPH; 350 beds), Dar Al Fouad Hospital (DAF; 40 beds), Manial University Hospital (MUH) of Cairo University (1200 beds), Manial Specialized Hospital of Cairo University (MSUH; 300 beds) and the Specialized Hospital of Ain-Shams University (AS; 800 beds). These hospitals, collectively, admit patients from all socioeconomic strata from Cairo and the surrounding rural areas, although patient populations vary among individual institutions.

Microbiology data

Microbiology records were reviewed by two of the authors (A.E.K. and H.B.). The isolates studied were confined to unrelated first isolates from different patients, and did not include multiple isolates from the same patient. All isolates were recovered from blood cultures; some coagulase-negative staphylococcal isolates were single isolates from blood cultures and thus of uncertain clinical significance. Specific antimicrobials tested varied from one institution to another. Information regarding the isolate, its source and antimicrobial susceptibility profile was collected and recorded. Data from different institutions were pooled. Because of lack of medical records, information regarding the clinical significance of each isolate and whether infection was community- or hospital-acquired was not available; however, by restricting our analysis to blood isolates and isolates of enterococci and pneumococci from other sites, we attempted to increase the likelihood of the clinical significance of most isolates other than coagulase-negative staphylococci.

Organism identification and susceptibility testing

All isolates were identified at the participating institution by standard laboratory methods. Confirmation of species identification of Gram-negative bacilli was performed with Microscan Walkaway System (Dade MicroScan, Inc., W. Sacramento, CA, USA), Sensititre (TREK Diagnostics Inc., Westlake, OH, USA) or BBL Crystal (Becton Dickinson Microbiology Systems, Sparks, MD, USA) products. Each laboratory performed susceptibility testing according to their own standardized techniques based on current NCCLS guidelines. The Kirby–Bauer disc diffusion method, which is the predominant method employed in Egypt, was used at CUPH, DAF and MUH. In MSUH, the Sensititre semi-automated instrument (TREK) was used, and the Micoscan Walkaway (Dade) automated system was employed at AS. Quality control strains were utilized routinely in all laboratories to ensure accurate performance of the assays. For data analysis, resistance included combined, intermediate and resistant results.

Results

Sources of isolates

One thousand five hundred and twenty-nine isolates were recovered from blood cultures of patients over the course of this 1 year retrospective study. An additional 51 isolates of Streptococcus pneumoniae and 69 of Enterococcus spp. over the same period from sites other than blood were analysed.

Resistance

As can be seen in Table 1, 442 staphylococci were isolated from blood cultures. The rate of oxacillin resistance was similar among both Staphylococcus aureus and coagulase-negative staphylococcal isolates, at 71% and 77%, respectively. The non-susceptibility to ciprofloxacin was 49% and 50%, respectively, for S. aureus and coagulase-negative staphylococci.
Antimicrobial resistance in Cairo, Egypt

Table 2. Percentage susceptibility of non-bloodstream isolates of Gram-positive cocci

<table>
<thead>
<tr>
<th>Isolates (n)</th>
<th>S. pneumoniae (% S)</th>
<th>Enterococcus spp. (% S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>84</td>
<td>69</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>82</td>
<td>80</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>82</td>
<td>63</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>49</td>
<td>54</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>63</td>
<td>48</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>45</td>
<td>43</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>43</td>
<td>35</td>
</tr>
<tr>
<td>Gentamicin (HL)</td>
<td>63</td>
<td>54</td>
</tr>
<tr>
<td>Penicillin</td>
<td>100</td>
<td>96</td>
</tr>
</tbody>
</table>

HL, high-level; provides for detection of high-level aminoglycoside resistance.

coccal isolates. Higher rates of susceptibility were demonstrated for S. aureus as compared with coagulase-negative staphylococcal isolates versus clindamycin (64% and 55%), co-trimoxazole (66% and 29%) and doxycycline (70% and 58%). All isolates of staphylococci were susceptible to vancomycin. Percentage susceptibilities of non-bloodstream isolates of Streptococcus pneumoniae and Enterococcus spp. are shown in Table 2.

There were 532 isolates of Enterobacter spp. and 303 of Pseudomonas aeruginosa, as compared with a total of 252 for all other Gram-negative bloodstream isolates. Susceptibility to imipenem for the Enterobacteriaceae was >98.7%. For P. aeruginosa, 98.7% were susceptible to imipenem, as compared with only 89.7% of the Acinetobacter spp. Susceptibility to ciprofloxacin was >79.2% for all groups tested. Ampicillin–sulbactam and cefazolin demonstrated a 38% and 40% susceptibility, respectively, versus E. coli, but had 100% resistance versus the other Gram-negative bacilli. Cefazidime and cefotaxime susceptibilities were <72% for all groups (Table 3).

Discussion

The striking finding in this 1 year retrospective study at five major teaching hospitals in Cairo is the high degree of antimicrobial resistance among the isolates studied. Our isolates represented both nosocomial- and community-acquired pathogens, and were collected from five different hospitals in Cairo. Although data stratified by hospital are not presented in detail, resistance among Gram-positive cocci and Gram-negative bacilli was widespread between the participating hospitals. We do not have epidemiological or clinical data to evaluate further the extent to which these resistance patterns reflect endemic antimicrobial resistance within the community, versus nosocomial spread of resistant organisms within and between various hospitals. But we know that each facility had its own infection control programme. Nevertheless, we believe that these data highlight the fact that widespread antimicrobial resistance exists in Cairo.

Staphylococcal isolates were highly resistant to all antimicrobials tested, except vancomycin. Nearly five times as many coagulase-negative staphylococci were isolated, as

Table 3. Percentage susceptibility of bloodstream isolates of Gram-negative bacilli

<table>
<thead>
<tr>
<th>Isolates (n)</th>
<th>E. coli (% S)</th>
<th>Klebsiella spp. (% S)</th>
<th>Enterobacteriaceae spp. (% S)</th>
<th>Citrobacter spp. (% S)</th>
<th>P. aeruginosa (% S)</th>
<th>Acinetobacter spp. (% S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftriaxone</td>
<td>84</td>
<td>88</td>
<td>94</td>
<td>79</td>
<td>62</td>
<td>54</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>52</td>
<td>42</td>
<td>30</td>
<td>42</td>
<td>62</td>
<td>31</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>84</td>
<td>88</td>
<td>94</td>
<td>79</td>
<td>62</td>
<td>31</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>52</td>
<td>42</td>
<td>30</td>
<td>42</td>
<td>62</td>
<td>31</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>46</td>
<td>38</td>
<td>36</td>
<td>54</td>
<td>62</td>
<td>31</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>52</td>
<td>42</td>
<td>30</td>
<td>42</td>
<td>62</td>
<td>31</td>
</tr>
</tbody>
</table>
compared with S. aureus. Although some of the coagulase-
negative staphylococci were probably the cause of true bac-
teraemia, many could have represented skin contamination.
Among bloodstream isolates of staphylococci, 71% of strains
of S. aureus and 77% of strains of coagulase-negative staphylo-
cocci were resistant to oxacillin. The S. aureus resistance
rates were higher than those in the USA and Canada, reported
in the SENTRY Antimicrobial Surveillance Program, in
which 26.2% of bloodstream isolates from the USA and 2.7%
of similar isolates from Canada were methicillin resistant.2
Compared with our isolates, the Canadian isolates of S. aureus
were also more susceptible to gentamicin, fluoroquinolones,
macrolides and co-trimoxazole.2

Resistance rates among staphylococci have been reported
from other geographical areas with results similar to ours. In
the study of Melo-Cristino in Portuguese hospitals, methi-
cillin resistance was found in 48.2% of S. aureus isolates, and
in 71–84% of coagulase-negative staphylococci, rates similar
to those found in our study.13 Among staphylococci from 19
European hospitals, methicillin resistance was found in 28%
and 68% of S. aureus and coagulase-negative staphylococci,
respectively.14

Penicillin resistance among our isolates of S. pneumoniae
was comparable to other parts of the world, although higher
than previous reports from Egypt.6 In our study, 63% of
isolates were susceptible to penicillin, compared with 71% in
a prior study from Egypt.6 Eighty-four per cent and 82%,
respectively, of isolates were susceptible to ceftriaxone and
ciprofloxacin. The high rate of resistance in our isolates is
consistent with many studies. Results of the SENTRY study
in the USA and Canada showed decreased susceptibility of
pneumococci to penicillin, to a degree similar to our isolates.
Both USA and Canadian isolates remained susceptible to
fluoroquinolones (96–100%) and vancomycin (100%).2
Fluoroquinolone resistance among pneumococci has been
considered rare.15,16 Ciprofloxacin is known to possess only
borderline activity against pneumococci, as compared with
the activity of other fluoroquinolones, such as levofloxacin,
gatifloxacin or moxifloxacin; however, 18% is quite high.17
Since it was the only fluoroquinolone reported in the present
study, it is difficult to speculate what the level of fluoro-
quinolone resistance truly is versus S. pneumoniae. Further
study is needed to define the epidemiology of these infections
and what effect the high resistance of ciprofloxacin will
have on the use of other more active fluoroquinolones versus
S. pneumoniae.

In contrast to reports from many parts of the world, <5% of
our enterococcal isolates were vancomycin resistant.18,19 Our
rate was similar, however, to that reported by Araj & Kanji20 in
Lebanon. Similar to other geographical areas, high levels of
resistance to gentamicin and streptomycin were identified in
about half of our isolates.2

Antimicrobial resistance among Gram-negative bacilli in
our study was significant. Among isolates of E. coli, only 6%
were susceptible to ampicillin, 38% to ampicillin–sulbactam,
38% to co-trimoxazole and 52% to the aminoglycosides. All
isolates were susceptible to imipenem. E. coli isolates in our
study were more resistant to the fluoroquinolones than those
from the USA and Canada.2

Antibiotic resistance among isolates of Klebsiella, Enterobacter,
Citrobacter, Acinetobacter and P. aeruginosa was common
in the present study, and comparable to reports from other
parts of the world.21–24 Imipenem and ciprofloxacin
retained activity against most of these isolates, except for
Ceftobacter and Acinetobacter spp. Perhaps one of the most
striking findings in our study was the high level of ceftazidine
and/or ceftotaxime resistance among our isolates of Klebsiella
and E. coli. Thirty-eight per cent of the E. coli isolates and
60% of Klebsiella spp. were ceftazidime resistant, with simi-
lar findings when compared with cefotaxime. Ceftazidime
and ceftotaxime resistance are markers for the presence
of extended-spectrum β-lactamases (ESBLs). Aztreonam
resistance is also defined by the NCCLS as a potential marker
for the presence of an ESBL-producing organism; in our
study, resistance to aztreonam among isolates of E. coli and
Klebsiella spp. was high at 44% and 64%, respectively.
Whereas we did not perform confirmation tests or genetic
analyses to confirm the presence of ESBL enzymes in these
isolates, the high MIC results suggest that ESBL enzymes
are endemic in Cairo. Further epidemiological studies are
necessary to determine whether such isolates exist in the com-
munity, or remain largely confined to tertiary hospitals where
they produce nosocomial infections.

The prevalence of ESBL enzymes has been increasing
in many parts of the world. Infections caused by ESBL-
producing isolates are difficult to treat, because they confer
resistance to all currently available β-lactam agents, except
imipenem, and in some cases piperacillin–tazobactam.24–26 In
addition, ESBL production is usually associated with resist-
ance to other classes of antimicrobial agent, such as amino-
glycosides and fluoroquinolones.27

Enterobacter spp. were highly resistant to ceftazidime,
ceftotaxime and aztreonam as well in the present study. In a
study published in 1998 by Jones et al.25 from the USA, 33.4%
of Enterobacter isolates were resistant, or immediately sus-
ceptible, to ceftazidime. In a more recent study, Mathai et al.28
reported that among pulmonary isolates of Enterobacter spp.
from the USA, only 79.6% were susceptible to ceftazidime,
whereas 100% remained susceptible to imipenem. These
results can be explained by the high prevalence of ESBL- and
AmpC-induced resistance among Enterobacter isolates, which
render the use of third-generation cephalosporins ineffect-
ive.29 Our data suggest the presence of similar resistance
mechanisms in Egyptian isolates. We cannot explain why
the number of Enterobacter spp. exceeded all other Enterob-
Antimicrobial resistance in Cairo, Egypt

bacteriaceae; however, this may be another reflection of the increased resistance among Gram-negative bacilli, since Enterobacter spp. are among the most resistant of the group.

The susceptibility of bloodstream isolates of P. aeruginosa and Acinetobacter spp. isolates in the present study was low to ceftazidime, piperacillin, aztreonam and aminoglycosides; however, susceptibility of isolates in our study to imipenem and ciprofloxacin was higher than in published reports from the USA.2,22

In conclusion, our data suggest that antimicrobial resistance among Gram-positive cocci and Gram-negative bacilli is common and significant in Cairo. One of the explanations for these high resistance rates could be antibiotic usage in the respective institutions. el-Teheawy et al.31 in Egypt in 1988 reported that >80% of admitted patients were prescribed antibiotics, and in many cases without documented proof of infection. Among these patients, >30% received repeated courses, with no apparent reasons for doing so. Whether this would still be the practice today is unknown by the authors of the present paper.

Particularly alarming are the high rates of ceftazidime resistance among E. coli, Klebsiella spp. and Enterobacter spp., which suggest the presence of ESBL and AmpC enzymes. Our results have important implications for practising physicians in the region, with regard to empirical antibiotic selection. They also have important implications for authorities involved in hospital formulary decisions, and in the development of policies regarding antibiotic utilization, infection control and public healthcare. Our results call for further epidemiological studies to define whether ESBLs are highly endemic in the community and, on a larger scale, for the implementation of a regional and nationwide surveillance system to monitor antimicrobial resistance trends in Egypt.

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References


