Community-acquired bacteraemia in a rural area: predominant bacterial species and antibiotic resistance

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The invasion of the bloodstream represents one of the most important sequelae of infection. This study was conducted over an 18-month period to determine the predominant bacterial agents of a community-acquired bacteraemia seen at health centres in a rural area of Jordan, and their antibiotic susceptibilities. Blood samples were collected and cultured from 215 patients who presented with fever and presumed diagnosis of a bacteraemia. Isolates were identified and tested for antibiotic susceptibility. The variables included the age and sex of the patients, aetiology, sources of the bacteraemia, risk factors, treatment and outcome. One hundred and twenty-six (58.6 %) blood cultures were positive. Children less than 14 years old accounted for 34.9 % of these, and 38 % were from patients that were more than 50 years old. The most frequent aetiologic agents were Staphylococcus aureus, followed by Brucella melitensis and Streptococcus pneumoniae. A wide range of resistance to commonly used antimicrobial agents and multidrug resistance was documented in 44.4 % of the isolates. The most frequent sources of the bacteraemia were urinary (15.9 %), respiratory (14.3 %), no source of the bacteraemia identified (primary bacteraemia) (13.5 %), gastrointestinal (12.7 %) and soft-tissue infection (7.9 %). No identifiable risk factor for infection could be determined in 34 % of the patients. The predominant pathogens identified and the relatively high prevalence of antibiotic resistance of the isolates are most probably due to the nature and lifestyle of this rural population and the use of empiric treatment. Characteristics permitting recognition of patients with such strains would aid infection control efforts in the community.

INTRODUCTION

It has been recognized that the presence of living microorganisms in the blood of a patient carries with it considerable morbidity and mortality (Reimer et al., 1997). Despite all the advances in medical practices in recent years, bacteraemia continues to be a serious problem that needs immediate attention and treatment. In addition, it is still one of the main causes of mortality despite the existence of numerous antimicrobial agents and an increase in means of support. Patients with community-acquired bacteraemia have diseases with a differing spectrum of pathogens and prognosis. A variety of factors, such as the type of micro-organism, age, the underlying disease and where the bacteraemia was acquired, can change the prognosis of the infection (Cisterna et al., 2001). Bloodstream infections in hospitalized patients are usually attributable to the use of central venous lines. However, in cases of community-acquired bacteraemia, the underlying disease is usually unknown and investigators have attempted to define the factors that influence the outcome of these infections. The bacteraemia in certain infections is considered the best practical way to identify the causative organism because the invasion of the bloodstream represents one of the most important sequelae of infection. The isolation of bacteria from blood cultures is usually indicative of a serious invasive infection that requires immediate antibiotic treatment (Anthony et al., 2000). The most frequent aetiologic agents of bacteraemia cases include Staphylococcus spp., Streptococcus spp., Enterobacter spp., Escherichia coli, Klebsiella pneumoniae and Pseudomonas spp. (Reimer et al., 1997; Cisterna et al., 2001).

The study was conducted in a rural area in the north east of Jordan, where inhabitants are recently settled Bedouins. To the best of our knowledge, this is the first study of bacteraemia in this area. Thus the objectives of this study were to determine the predominant bacterial agents of a community-acquired bacteraemia, the risk factors, clinical outcomes and the antibiotic susceptibilities of the causative agents.

METHODS

Study area and patients. Two hundred and fifteen patients presenting with fever and presumed diagnosis of a bacteraemia seen between September 1999 and September 2001 were enrolled in the study.
Patients had other symptoms depending on the underlying disease, e.g. cough, chest pain and joint pain; rash was observed in 12 cases. The patients were settled Bedouins from a rural area in north east Jordan who were seen as outpatients and were physically examined by a physician in one of the four main health centres in that area. A nurse at the centre recorded the demographic and clinical data from the patients using a structured questionnaire in addition to laboratory tests performed.

All patients consented to the collection of the specimens and the study was approved by the University ethical review committee for human investigations.

The primary focus of infection was defined as a culture-positive site and/or a clinically evident site of infection concomitant with bacteraemia.

**Blood cultures.** Blood was withdrawn and immediately inoculated under strict aseptic conditions in broth media (Bloodgrow; Medical Wire & Equipment Co. Ltd, Corsham, UK) or diphasic blood culture bottles (Hemolene performance diphasique; bioMérieux). These cultures were incubated at 37 °C for 1–4 weeks depending on the appearance of signs of growth.

Subcultures on selective media were done after 10, 20 and 30 days or whenever growth was noticed. An aliquot of the positive blood bottles was aseptically taken by a syringe for Gram staining and subcultured on enriched media and media selective for a wide variety of pathogens.

All positive specimens were aliquoted into 1-5 ml microcentrifuge tubes when a Gram-stained-smear showed the presence of bacteria.

Organisms from the positive blood cultures yielding pathogens were identified by microbiological and biochemical methods, including the API 20E system (bioMérieux).

**Review of medical records.** The demographic and clinical data collected for each patient included sex, age, immune status, acquisition of a polymicrobial bacteraemia, underlying disease, a history of hospitalization within the previous month, admission to an intensive care unit, and finding of the origin of the bacteraemia in these patients.

The increasing frequency of *Staphylococcus aureus* bacteraemia, coupled with increasing rates of antibiotic resistance, has renewed interest in this serious, common infection (Finkelstein et al., 1984; Petti & Fowler, 2002). In this study, the most probable primary sites of infection were superficial skin wounds or skin abscesses.

The recovery of *B. melitensis* from 20 blood cultures was not surprising; in fact this is considered low since the study area is highly endemic for brucellosis (Nimri, 2003). The prevalence of this pathogen in that rural population is due to contact with infected animals, and habits of drinking unpasteurized milk and consuming home-made soft cheese.

Seven of the *Streptococcus pneumoniae* cases were children less than 15 years. The recent focus of clinical attention on community-acquired pneumonia is because a subgroup of patients has severe disease with a differing spectrum of pathogens and prognosis (Cassiere & Fein, 1996). However, pneumococcal bacteraemia may be a primary infection in susceptible patients or may accompany the acute phase of one of several other pneumococcal infections such as pneumonia, meningitis or middle ear infections. The rash that was observed in 12 cases was highly suggestive of sepsis due to *Streptococcus spp.* or *Staphylococcus aureus*, which were isolated from the blood cultures of these patients. The median duration from a symptom onset to initiation of effective antibiotics among patients was 4 days.

**RESULTS AND DISCUSSION**

One hundred and twenty-six out of 215 (58.6 %) blood cultures were positive. The mean age of the patients was 44 years (range 10 months to 87 years), 44 (34.9 %) were children less than 14 years old, and 48 (38 %) were older than 50 years. The incidence in males and females was 56 (44.4 %) and 70 (55.6 %), respectively.

Five (4 %) of these blood cultures were polymicrobial and yielded double isolates. The double isolates included: two *Staphylococcus aureus* and *Streptococcus pyogenes*; one *Staphylococcus aureus* and *Escherichia coli*; one *E. coli* and *Klebsiella spp.*; one group B *Streptococcus sp.* and *Staphylococcus epidermidis*. No pathogens were recovered from the other 89 (41-4 %) cultures.

*Staphylococcus aureus* (40 isolates; 31.7 %) was the most common bacterial agent isolated from the positive cultures, followed by *Brucella melitensis* (20 isolates; 15.9 %), *Streptococcus pneumoniae* (14 isolates; 11.1 %), β-haemolytic streptococci, e.g. groups A, B and G *Streptococcus spp.* (13 isolates; 10.3 %), and *E. coli* (10 isolates; 7.9 %). These results, except those for *B. melitensis*, were in agreement with another study that reported on a community-acquired bacteraemia in Spain (Cisterna et al., 2001). The isolates were assessed as clinically relevant based on physical examination, symptoms and finding of the origin of the bacteraemia in these patients.

Susceptibility testing of the isolates to at least eight out of 15 antibiotics was performed on each isolate on Mueller–Hinton agar by a standard disc diffusion assay, following National Committee for Clinical Laboratory Standards (1999) guidelines. Antibiotics tested were ampicillin, carbenicillin, ceftriaxone, clindamycin, chloramphenicol, doxycyclin, gentamicin, kanamycin, lincomycin, methicillin, penicillin, tetracycline, erythromycin and vancomycin (for the Gram-positive isolates) and trimethoprim-sulfamethoxazole.

"Non-susceptible" refers to resistant and intermediately resistant, and multidrug resistance refers to resistance of the isolates to two or more antibiotics.

Characteristics permitting recognition of patients with such strains would aid infection control efforts and choice of empiric therapy pending culture and susceptibility results (Rezende et al., 2002). Therefore, in most instances the physician initiates empiric antibiotics on the basis of epidemiologic data. If an aetiologic pathogen is identified (either initially or at a later time), then the antibiotic spectrum can be narrowed. When no pathogen is discovered, broad-spectrum empiric antibiotics are continued (Cassiere & Niederman, 1998).

Despite the increase in the incidence of group B streptococcal bacteraemia in adults in recent years, particularly in patients with severe underlying diseases, it remains an unusual...
common blood isolates that always or nearly always represent true infection include Staphylococcus aureus, members of the Enterobacteriaceae, Pseudomonas aeruginosa and Strep-tococcus pneumoniae. More problematic are viridans group streptococci, enterococci and CoNS, which represent true bacteraemia 38, 78 and 15 % of the time, respectively (Weinstein et al., 1997; Raimundo et al., 2002). Staphylococcus epidermidis was the only CoNS isolated in this study from immunocompetent children and old patients. Although CoNS are often reported as nosocomial pathogens, recent reports support the view that they are significant community-acquired pathogens (Anthony et al., 2000), where 88 % of the CoNS cases were assessed as clinically relevant (Towns et al., 1993). The ascendance of this group of staphylococcus has created increased interpretative difficulties for clinicians, since the great majority of CoNS (85 %) continue to represent contamination rather than a true bacteraemia (Mirrett et al., 1994; Raimundo et al., 2002). The most probable origins of the bacteraemia due to CoNS were soft-tissue infections (12 %) and puncture wounds due to various reasons (e.g. walking barefooted), which were reported in another study (Miller et al., 1996). The most probable sources of infection in the bacteraemia cases due to β-haemolytic streptococci (Streptococcus pyogenes) were pharyngitis, tonsillitis, or wound or skin infections.

Three isolates of non-typhi Salmonella (S. enteritidis) were associated with soft-tissue infections and abscess. One patient was younger than 5 years and two were more than 65 years old. The incidence of these rare infections is reported to be higher in these age groups (Canut Blasco et al., 1992).

The recovery of Chryseobacterium indologenes (two isolates; 1-6 %) and Stenotrophomonas (Xanthomonas) maltophilia (two isolates; 1-6 %) along with Y. pseudotuberculosis from blood cultures of immunocompetent patients is unusual since they have been rarely reported in nosocomial and immunocompromised patients (Ljungberg et al., 1995; Muder et al., 1996; Hsu et al., 1997; Nulens et al., 2001), and are usually seen in patients with underlying disorders such as diabetes and wound sepsis, which might have played a role in each of these cases.

Although almost any localized infection can disseminate into the bloodstream (Weinstein et al., 1997; Raimundo et al., 2002), the most probable common origins of the bacteraemia based on physical examination, signs and symptoms supported by positive cultures in most of the cases were urinary (20 isolates; 15.9 %), respiratory (18 isolates; 14.3 %), no source of the bacteraemia identified (a primary bacteraemia) (17 isolates; 13.5 %), gastrointestinal (16 isolates; 12.7 %), soft-tissue infection, e.g. wound and superficial skin infections (10 isolates; 7.9 %), or meningitis (2 isolates; 1.6 %).

Risk factors for infection could not be identified in 43 (34.1 %) of the patients. Studies have shown that despite the best efforts of clinicians, the source of bacteraemia or fungaemia cannot be determined in one-quarter to one-third of patients (Anthony et al., 2000).

No mortality was reported in association with bacteraemia in these patients. A study in Israel reported an overall mortality of 29 % (Weinstein et al., 1997). Other studies suggest that the mortality associated with bacteraemia may be decreasing, and that receiving a conservative treatment significantly increased survival (Hanon et al., 2002).

Factors that might affect the epidemiology of diseases in that area include the socio-economic status, where some are still living in tents or very small crowded houses, and the lack of health education, which influence personal hygiene, and certain practices, e.g. walking barefooted and drinking unpasteurized milk.

The isolates recovered showed a wide range of resistance to commonly used antimicrobial agents (Table 1), and multidrug resistance was documented in 56 (44.4 %) of the isolates. Fifteen (37.5 %) of the Staphylococcus aureus isolates were resistant to penicillin, and 10 (25 %) were resistant to methicillin, aminoglycosides, erythromycin, lincomycin and clindamycin. Eight of 10 E. coli isolates, all three Salmonella isolates, 32 of 40 (80 %) Staphylococcus aureus isolates and 3 of 4 (75 %) Klebsiella isolates were susceptible to gentamicin.

Rates of resistance of Streptococcus pneumoniae to ampicillin, ceftriaxone, clindamycin, erythromycin, penicillin and trimethoprim-sulfamethoxazole were 22.2, 24, 50, 61, 35.7 and 38.9 %, respectively.

This wide range of resistance of the isolates is most probably due to the empiric treatment used in invasive and recurrent infections and reflects an uncontrolled use of antibiotics. Results indicate that therapeutic options for community-acquired bacteraemia have not yet become seriously limited by the prevalence of acquired antibiotic resistance. The prevalence of antibiotic resistance among blood isolates from patients with community-acquired bacteraemia in a Danish study was also related to antibiotic consumption (Pedersen et al., 2000). Periodic reviews of pathogen frequency and the impact of susceptibility patterns on appropriate antimicrobial usage will lead to more effective prescribing practices (Mathai et al., 2001).

In conclusion, our study reports on the relatively different predominant aetiological agents of bacteraemia in a rural area, which are most probably due to the lifestyle and health practices in that area. It demonstrates the importance of
characterizing patients with such strains to permit recognition of groups at increased risk for bacteraemia, and characterizing the antibiotic susceptibility distribution of isolates to develop appropriate policies for the treatment and prevention of these diseases in the community. Furthermore, results confirm that appropriate empirical antimicrobial treatment increases the survival of bacteraemic patients since no mortality was reported in these cases.

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REFERENCES


