Klebsiella pneumoniae Bacteremia in the Community Hospital

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The purpose of this study was to elicit the circumstances of occurrence and organism sensitivities of Klebsiella pneumoniae *bacteremia in the community hospital, since data on this illness from the community hospital are rare. All records of documented* Klebsiella pneumoniae *bacteremia (46 cases) at Alachua General Hospital, Gainesville, Florida, over the period July 14, 1982, through July 27, 1985, were reviewed in detail. Fifty-nine percent (27 organisms) were nosocomial, whereas 41% (19 organisms) were community acquired. The most common predisposing disorders in these patients were, in decreasing order, malignancy; following gastrointestinal or biliary surgery; biliary tract obstruction; diabetes; and unknown. Twenty-two percent (10) of the patients died from bacteremia. The majority of organisms tested were sensitive to mezlocillin, cephalothin, cefoxitin, tetracycline, tobramycin, gentamicin, co-trimoxazole and ceftizoxime. Therapy was considered to be appropriate in 89% (41) of the patients and inappropriate in 10.9% (5) of the patients. Contrary to previous thought,* Klebsiella pneumoniae *bacteremia is a relatively common problem in the community hospital and may be community acquired as well as nosocomial. There are many characteristics of this disease in the community that are different from those reported in studies on* Klebsiella pneumoniae *bacteremia from large referral centers.*

It is known that bacteremia secondary to the genus *Klebsiella* is a common problem in tertiary care centers, and it has also been noted that *Klebsiella* rarely causes infection in the community.[1] This genus is a member of the family Enterobacteriaceae and is reported to be second only to *Escherichia coli* as a cause of gram-negative bacteremia.[2,3] *Klebsiella* has been reported to be responsible for 5.4%[4] to 29.6%[5] of cases of gram-negative bacteremia in various university hospitals. *Klebsiella pneumoniae* is commonly thought of as a nosocomial organism that causes opportunistic infection.[3,6–11] Infection due to this organism has classically been felt to be difficult to treat, and bacteremia due to the organism causes high mortality rates (eg, 52%,[10] 37%[1]).[1,10–13] It is thought that the large polysaccharide capsule surrounding this gram-negative rod enhances the virulence of the organism.[6,7]

Klebsiella bacteremia, with the exception of two series from large referral hospitals,[1,14] has usually been reviewed as part of studies devoted to gram-negative bacteremia or reported together with bacteremia for *Enterobacter* and *Serratia* species. The study reported here was on *K pneumoniae* bacteremia specifically and was undertaken with the hypothesis that *K pneumoniae* bacteremia is also a common problem in the community hospital and that a substantial portion of cases are community acquired. The purpose of this study was also to identify predisposing factors to *K pneumoniae* bacteremia in the community hospital, to compare these factors with descriptions from the tertiary care center, and to elicit the antibiotic sensitivities of the organisms.

METHODS

All 46 charts from cases of documented *K pneumoniae* bacteremia that occurred from July 14, 1982, through July

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TABLE 1. PORTALS OF ENTRY FOR *Klebsiella pneumoniae* BACTEREMIA (N = 46)

Portals of Entry	No. (%)	Mortality No. (%)
Gastrointestinal or biliary	14 (30.3)	2 (14.3)
Genitourinary	12 (26.1)	1 (8.3)
Pulmonary	10 (21.7)	3 (30.0)
Unknown	9 (19.6)	3 (33.3)
Dialysis fistula	1 (2.2)	1 (100.0)

TABLE 2. UNDERLYING DISORDERS AND DEATHS ASSOCIATED WITH *Klebsiella pneumoniae* BACTEREMIA (N = 46)

Disorder	No. (%)	Deaths No.	(%)
Malignancy, advanced	10 (21.7)	3	(30.0)
Following gastrointestinal or biliary surgery	4 (8.7)	0	(0)
Biliary tract obstruction	3 (6.5)	0	(0)
Diabetes mellitus	3 (6.5)	1	(33.3)
None known	3 (6.5)	1	(33.3)
Neurological disease, severe, with respiratory compromise	2 (4.4)	1	(50)
Alcoholism, advanced	1 (2.2)	0	(0)
Anemia, severe	1 (2.2)	0	(0)
Catheter, indwelling urethral, for prostatic hypertrophy	1 (2.2)	0	(0)
Catheterization, urethral, recent	1 (2.2)	0	(0)
Cirrhosis, Laennec's, severe	1 (2.2)	0	(0)
Congestive heart failure, severe	1 (2.2)	1	(100)
Diverticulosis	1 (2.2)	0	(0)
Goodpasture's syndrome	1 (2.2)	1	(100)
Ileal conduit	1 (2.2)	0	(0)
Immunosuppression, pharmacologic	1 (2.2)	0	(0)
Malnutrition, severe	1 (2.2)	0	(0)
Obstructive pulmonary disease, chronic	1 (2.2)	0	(0)
Paraplegia with neurogenic bladder	1 (2.2)	0	(0)
Pneumonia, aspiration	1 (2.2)	0	(0)
Post cerebrovascular accident status	1 (2.2)	0	(0)
Postsurgical status	1 (2.2)	1	(100)
Renal failure or dialysis	1 (2.2)	1	(100)
Splenectomy, previous	1 (2.2)	0	(0)
Superior mesenteric artery syndrome	1 (2.2)	0	(0)
Urinary retention secondary to prostatic hyperplasia	1 (2.2)	0	(0)
Urolithiasis	1 (2.2)	0	(0)

27, 1985, at Alachua General Hospital, Gainesville, Florida, were reviewed with regard to multiple factors. Alachua General Hospital is a 453-bed acute care general hospital that serves Gainesville, Florida, and the surrounding rural areas. All blood cultures positive for *K pneumoniae* were found by reviewing laboratory records. Blood cultures were generally obtained by needle puncture of an antecubital vein after sterilization of the area with an iodine solution. Organisms were identified by standard laboratory techniques described by Edwards and Ewing.[15]

The organism was considered nosocomial if it was found on a culture taken 3 or more days after the patient had been admitted to the hospital. The organism was considered community acquired if found on a culture taken from a patient who had been in the hospital less than 3 days.[16] Blood cultures in all cases were drawn within 24 hours of detection of fever. Fever was defined as an oral temperature of $\geq$100.5 °F within 24 hours prior to drawing blood for cultures that were positive for *K pneumoniae*. A normal range for blood leukocyte count was defined by the hospital as 5×10^9 to 10×10^9 L.

The portal of entry of the organism was considered to be that organ system of the body from which the organism entered the blood stream. Portals of entry were defined clinically and were often, though not always, microbiologically proved. For example, if 1×10^5 colonies of *K pneumoniae* were cultured from a patient's urine sample that was taken at the same time as the blood culture positive for the same organism (by antibiotic susceptibility studies), the portal of entry was considered to be genitourinary.

The underlying disorder was defined as the underlying illness the patient had that might predispose him or her to severe infection.[12] If the patient had more than one predisposing illness, the disorder considered the most serious was listed. For example, if the patient had both diabetes mellitus and a systemic malignancy, the malignancy was listed as the underlying illness. Shock was defined as a systolic blood pressure of $\leq$75 mmHg at any point during the bacteremic episode. The underlying diseases of all patients were divided into three prognostic groups according to the classification of McCabe and Jackson[3]: (1) rapidly fatal disease, eg, advanced intracranial hemorrhage, (2) ultimately fatal, eg, adenocarcinoma of the pancreas, and (3) nonfatal, eg, ileal conduit with frequent urinary tract infections. Patients were considered to have died from their episodes of bacteremia if they died within 7 days of the day on which the blood cultures were drawn for culture and in the absence of any intervening events during that time that could explain the patients' deaths.[17] Organism sensitivities were determined by the method of Bauer et al.[18]

Appropriate therapy was defined as one or more antibiotics to which the organism was susceptible (generally a cephalosporin or aminoglycoside) administered intravenously in high doses after bacteremia was suspected and for at least 3 days following this period. Inappropriate therapy was defined as any treatment that did not meet the above criteria. Fisher's exact test was used as a test of statistical significance where indicated with $P \leq .05$ considered significant.

RESULTS

There were approximately 47,000 adult admissions to the hospital during the study period, giving a rate for *K pneumoniae* bacteremia of approximately 0.98 cases per 1000 admissions for this study. The incidence of *K*

TABLE 3. ANTIBIOTIC SENSITIVITIES OF *Klebsiella pneumoniae* ISOLATES, BY THE METHOD OF BAUER ET AL[18]

Antibiotics	Sensitive No. (%)	Intermediate No. (%)	Resistant No. (%)	Total Performed
Carbenicillin	1 (2.2)	2 (4.4)	42 (93.3)	45
Mezlocillin	13 (86.7)	2 (13.3)	0 (0.0)	15
Cephalothin	28 (90.3)	0 (0.0)	3 (9.7)	31
Cefoxitin	42 (97.7)	0 (0.0)	1 (2.3)	43
Tetracycline	42 (93.3)	0 (0.0)	3 (6.6)	45
Tobramycin	40 (95.2)	0 (0.0)	2 (4.8)	42
Gentamicin	29 (96.7)	0 (0.0)	1 (3.3)	30
Co-trimoxazole	12 (85.7)	1 (7.1)	1 (7.1)	14
Ampicillin	0 (0.0)	0 (0.0)	45 (100.0)	45
Ceftizoxime	13 (100.0)	0 (0.0)	0 (0.0)	13

pneumoniae bacteremia increased with age with the highest number, ten cases (21.7% of cases), taking place in the 8th decade. The median patient age was 66 years with an age range of 28 to 93 years. Six of the 10 deaths occurred in the 8th and 9th decades. Thirty-nine percent (18) of the bacteremic patients were men, and 60.9% (28) of the patients were women. Fifty-six percent (26) of the patients were single, and 43.5% (20) of the patients were married. Of the 46 blood cultures positive for *K pneumoniae*, three isolates were found in cultures positive also for a second organism. Fifty-nine percent (27) of the isolates were nosocomial, and 41.3% (19) of the isolates were community acquired by the aforementioned criteria. Twenty-six percent (7) of the patients with nosocomial infections died, and 5.8% (3) with community-acquired infections died.

Fifty-seven percent (26) of the patients had fever at the onset of bacteremia, and 37% (17) had no fever. Blood cultures were drawn in the latter group of patients because they exhibited other clinical signs of bacteremia such as confusion, a drop in blood pressure, or an increased respiratory rate. Febrile status was undetermined in 6.5% (3) of the patients. Leukocyte count was elevated by study criteria in 56.5% (26) of the patients, low in 10.9% (5), normal in 15.2% (7), and not determined in 17.4% (8).

The portals of entry with respective mortality rates for the organisms are listed in Table 1. In decreasing order, the most common portals of entry for the organisms were gastrointestinal, genitourinary, pulmonary, and source unknown. Apart from the one case of the patient who died as a result of an infectual dialysis fistula, the highest mortality was from the unknown source of entry followed by pulmonary. The cause of death in the latter group was related primarily to sepsis and shock, not to respiratory problems. The underlying disorders for the patients are listed in Table 2. The most common underlying disorders, in decreasing order, were malignancy, following gastrointestinal or biliary surgery, and (equal for) biliary tract obstruction, diabetes mellitus, and none known. Of the patients with advanced malignancy, 30.0% (3) died. One patient was thought to have had rapidly fatal disease, 19 patients had ultimately fatal disease, and 26 patients had nonfatal disease as underlying illnesses. Significantly more patients in the ultimately fatal disease group died (42.2%) than in the nonfatal disease group (7.7%) ($P<.01$).

Ten of the patients died of their bacteremia by study criteria, for a 21.7% mortality rate. Seven cases were associated with septic shock and three of these patients died. One case was associated with *K pneumoniae* meningitis and subsequently disseminated intravascular coagulation. Pyogenic metastatic foci were not detected in this study either visually or by radiographic methods. The antibiotic sensitivities for the isolates are listed in Table 3. A large majority of the organisms were sensitive to mezlocillin, cephalothin, cefoxitin, tetracycline, tobramycin, gentamicin, co-trimoxazole, and ceftizoxime. Most of the organisms were resistant to carbenicillin and ampicillin. Only two strains (4.3%) resistant to multiple antibiotics (including gentamicin or tobramycin and first-generation cephalosporins) were noted, and neither of these were nosocomial organisms as defined by the study criteria.

Therapy was considered to be appropriate by study criteria in 89.1% (41) of the patients and inappropriate in 10.9% (5) of the patients. Of those treated inappropriately (often, when an antibiotic was administered to which the organism was not sensitive), three died, whereas of those treated appropriately, seven died.

DISCUSSION

A MEDLINE search for the period 1975 through 1985 revealed only two other studies that dealt specifically with *K pneumoniae* bacteremia. (No relevant studies were found on a review of the recent infectious disease literature.) One study by Montgomerie and Ota[1] had 41 cases and the other by García de la Torre et al,[14] in Madrid, had 100 cases. Both studies were done in large referral centers. Despite the overseas location, most comparisons of the present data were made with the latter study because it was well controlled and had a large sample size.

The rate for *K pneumoniae* bacteremia in Alachua General Hospital (0.98 cases per 1000 admissions) was lower than for the study by García de la Torre et al (2.3 cases per 1000 admissions),[14] perhaps because there was a larger

percentage of patients with malignancy and other severe illnesses in the latter referral center. The present study indicates not only that serious infection caused by this organism can occur in the community hospital (almost 1 per 1000 admissions), but that the infection may often be community acquired (41.3% of the isolates). The percentage of organisms in this study that were nosocomial was actually lower than in the study by García de la Torre et al (75%). Other studies show that bacteremias tend to occur in the very old and the very young.[1,12] Not surprisingly, then, *Klebsiella* bacteremia in this study tended to occur in the elderly, with the greatest number of cases occurring in the 8th decade of life. Patient mortality appeared to follow the incidence of bacteremia (with 6 of 10 deaths occurring in the 8th and 9th decades). García de la Torre et al reported more men than women (1.5:1) with *Klebsiella* bacteremia in his referral center,[14] almost the opposite of the present study. The percentage of *Klebsiella* isolated with a second organism in this study (6.5%) was slightly lower than that found in the study by García de la Torre et al (12%).[14] That there were no cases in children in the present study can be attributed to two possible circumstances: first, though there is a small pediatric and newborn nursery section at Alachua General Hospital, the hospital is not equipped with neonatal intensive care facilities; second, one study showed outbreaks of *K pneumoniae* bacteremia in neonates tended to occur in clusters[1] with long periods of pathogen inactivity in between.

While all blood cultures were drawn because of suspected bacteremia, 37% of the patients had no fever at detection of their bacteremia, which suggests that though fever may be one sign of *Klebsiella* bacteremia, fever is not necessarily present. The percentage of patients with fever in this study (56.5%) is considerably lower than the percentage in the García de la Torre et al study (96%). The present study shows that, although leukocyte counts are usually high at detection of *K pneumoniae* bacteremia, they may be low or normal also. The lack of fever and leukocytosis would not be atypical in older, debilitated patients in whom the only clues to their infection may be altered mental status, slight drop in blood pressure, or an increase in respiratory rate.

The most frequent portals of entry for the organism (gastrointestinal or biliary, genitourinary, pulmonary, and unknown) are similar to those reported for *Klebsiella* bacteremia in other studies. At one tertiary care center the order was genitourinary (27%), gastrointestinal (24%), intravenous site (20%), and pulmonary (15%).[1] García de la Torre et al reported genitourinary (31%), respiratory (15%), and biliary (10%). It is possible that some of the organisms in this study whose portals of entry were unknown actually entered through intravenous sites. The order of portal of entry for this study contrasts with urinary tract, wound, and respiratory tract for one study of hospital-acquired *Klebsiella* bacteremia[11] and with urinary tract, lung, abscess or wound, and upper respiratory tract for a study of gram-negative bacteremia in a university hospital.[19]

Not surprisingly, advanced malignancy was the most common underlying disorder for *Klebsiella* bacteremia. Some patients with malignancy were or had been treated with chemotherapeutic agents, which would increase their propensity for bacteremia.[20,21] The frequency of underlying disorders for this study (malignancy, following gastrointestinal or biliary surgery, biliary tract infection, diabetes mellitus, and none known) contrasts with neoplasia (25%), cardiovascular disease (14%), cholelithiasis (10%), chronic obstructive pulmonary disease (8%), gastrointestinal diseases (7%), and cirrhosis (6%) in the García de la Torre et al study; with prior antibiotic use following surgery, infected intravenous catheter, and urinary tract manipulation in the study on nosocomial *Klebsiella* bacteremia[11]; and with malignancy-cardiac disease, urinary obstruction, diabetes mellitus, and alcoholism in the previously mentioned study of gram-negative bacteremia in a university hospital.[19]

Klebsiella bacteremia has been associated with a high mortality rate. The mortality rate for this study in a community hospital (21.7%) is low compared with other studies for *Klebsiella* bacteremia (67%,[5] 52%,[10] 37%,[1] 35%,[12] 32%,[13] 30%,[11] and 25%[14]) and compares favorably with mortality rates of 19.6%[12] and 20.3%[20] in two general studies of bacteremia in community hospitals and 24% in a study on gram-negative bacteremia.[19] A possible explanation (although data could not be found to support it) for a lower mortality rate for *K pneumoniae* bacteremia in the community hospital is that there may be fewer patients with malignancies and other serious illnesses in the community hospital than in the tertiary care center. Another explanation might be that the criteria used by other authors to attribute patient mortality to this organism were less rigorous in their studies than in this study. For example, this study defined death due to bacteremia as a patient death within one week of the day on which the blood culture was determined to be positive with no intervening events that could explain the death, whereas most other studies did not specify these criteria.

The percentage for cases of *Klebsiella* bacteremia associated with septic shock (15.2%) is similar to the 22% found in the García de la Torre et al study, though the latter authors defined shock somewhat less strictly than in this study. There were two other interesting incidental contrasts with the García de la Torre et al study. There was one case of disseminated intravascular coagulation associated with *Klebsiella* bacteremia in the present study, but none reported by García de la Torre et al. Although not so defined, 5% of the 100 *Klebsiella* bacteremia cases in the García de la Torre et al study were associated with pyogenic metastatic foci. Assuming the latter entity to be purulent abscesses in the skin or other organs, no cases in the present study were found.

This study confirms the findings of others[1,6,7,22,23] that pathogenic strains of *K pneumoniae* are usually sensitive to cephalothin, tetracycline, gentamicin, and tobramycin, and resistant to carbenicillin. Since the organisms appear to be uniformly resistant to ampicillin, this agent should

never be used as a single-choice antimicrobial in *K pneumoniae* infection. It appears that most of the strains of *K pneumoniae* in this study were sensitive to first-, second-, and third-generation cephalosporins and the aminoglycosides gentamicin and tobramycin. Three strains of the organism were found that were resistant to cephalothin.

One strain was resistant to gentamicin and two strains were found to be resistant to tobramycin. While only two (4.3%) of the *K pneumoniae* species in this study demonstrated resistance to multiple antibiotics (and neither of them, interestingly, were nosocomial strains), 24% of the *Klebsiella* organisms identified by García de la Torre et al demonstrated multiple resistance. It is possible that bacteria with multiple resistance have a propensity for larger referral centers, where patients may be more severely ill and use of many antibiotics is common. Most experience exists with first-generation cephalosporins in treating this organism, though second-generation cephalosporins have been shown to be equally or more effective.[23] Other authors recommend treating severe *Klebsiella* infections with an aminoglycoside and a cephalosporin to take advantage of the synergistic bactericidal effect of these two agents in combination.[6,7,23,24] The data of the present study, however, are consistent with data of others demonstrating that this genus has developed very little new antibiotic resistance over many years.[25,26] Until the organism is identified, however, therapy of *Klebsiella* bacteremia must be initiated considering all possible etiological organisms.

That only seven of 41 appropriately treated patients died and three of five patients treated inappropriately died suggests that appropriate treatment as defined by this study is effective, though the numbers did not reach statistical significance (P=.06), probably because of the small sample size.

One must also be cautioned in interpreting these figures that ethical, moral, and other circumstances for individual patients were not taken into consideration in patients defined as being treated appropriately. For example, a patient who is terminally ill may not be treated as vigorously with antibiotics as one who is not. That an "inappropriately treated" patient may have been appropriately managed, however, should have had no effect on the outcome of the study.

In summary, *K pneumoniae* bacteremia is an important cause of morbidity and mortality in the community hospital as well as the tertiary care center; it may be community acquired as well as nosocomial; and when compared with the large referral center, there may be differences in the characteristics of this illness in the community hospital. Common portals of entry for the organism in the community hospital are the gastrointestinal and genitourinary tracts and common underlying problems are malignant neoplasms and postoperative states. *Klebsiella* bacteremia may be treated with cephalosporin or aminoglycoside antibiotics alone or in combination. Mortality for this illness may be lower in community hospitals than tertiary care centers, possibly because there are more critically ill patients in the latter institutions.

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