

ORIGINAL

Bacteraemia in Bahrain. A Study of Aetiological Conditions, Clinical Presentation and Antibiotic Therapy

By Sujata Kumar * and F. Al-Hilli**

ABSTRACT

Bacteraemias other than those due to enteric fever were studied in 257 patients in Bahrain most of whom had an underlying condition. The common isolates in decreasing order were *S typhi*, *Strept pneumoniae*, *Staph aureus*, *E coli* and *Klebsiella*. The clinical features of bacteraemias due to gram negative organisms were similar to each other irrespective of the aetiological agent. But those due to gram positive cocci were suggestive of the causative agent. Although antibiotic thereapy was associated with low mortality rate in patients with nonfatal underlying conditions, the outcome of bacteraemia was dependant on the gravity of these condition and the appropriateness of the antibiotic therapy rather than on the aetiological agent.

Bacteraemia is the microbial invasion of the blood stream. It may be transient and self-limiting or may be associated with serious clinical manifestations depending on the predisposing factors and the aetiological agent. Its hospital incidence varies from 20 to more than 200 cases per 10,000 admissions^{1, 2} also depending on the prevalence ratio of organisms, the patient population and the type of hospital service. The common aetiological agent may therefore vary from staph aureus in some hospitals to *Ps aeruginosa* in others^{3, 4, 5}, and at present, gram negative bacilli are increasingly reported as the most frequent aetiological agents of bacteraemia⁶. The aim of this study is to investigate the bacteriological spectrum, source of organisms, predisposing factors, clinical features and outcome of bacteraemia in Bahrain.

METHODS

The study was based on the review of results of all of 14044 blood culture samples processed at the Department of Pathology, Salmaniya Medical Centre (SMC), Bahrain, during the period January 1984 to December 1985. The case files of the patients with positive bacteriological results were studied for information concerning the onset of symptoms, clinical features, underlying conditions, prior invasive procedures and the response to antibiotic

* Jaslok Hospital & Research Centre
15 Peddar Road
Bombay, India

** Consultant
Pathology Department
Salmaniya Medical Centre
State of Bahrain

therapy. Each bacterial culture isolate was evaluated to decide whether it was a pathogen or contaminant by taking into consideration the number of positive blood cultures obtained at different times, the bacterial species, isolation of similar organisms from other affected sites, other laboratory data, clinical picture, and the final outcome with and without appropriate antibiotic therapy. The antibiotic therapy was considered appropriate if the organism was sensitive to the antibiotic given to the patient after in-vitro susceptibility tests. Only patients whose clinical details were consistent with bacteraemia were included in the study. Bacteraemias due to *S typhi* and *S paratyphi A* were not included.

All bacteraemias occurring on or after the fifth day of admission were considered nosocomial in origin, whereas those occurring before this time were regarded as community acquired, except for those cases which were clearly related to a procedure performed after hospital admission.

Bacteriological Methods

Blood cultures were performed by inoculating the blood samples drawn under aseptic conditions directly into taurocholate broth and cooked meat medium. The bottles were incubated at 37°C and routine aerobic and anaerobic subcultures were done 24 and 48 hours after incubation. The cooked meat medium, however, was held for 7 days and a third subculture was carried out. When the clinical details indicated the presence of slow growing organisms, the media were further incubated for 3 to 4 weeks and subcultured at regular intervals. The bacterial isolates were identified and antimicrobial susceptibility tests were done employing standard methods^{7, 8, 9}.

Source of Organisms

The primary site of origin of the organisms was determined on the basis of its isolation with identical antibiogram from local pathological lesions prior to or simultaneously with those of blood culture. When the organism was not isolated from any site, the probable source was determined on the basis of the clinical details. Thus the lung was regarded as the source of organism in patients with clinical features of pneumonia whose blood culture grew streptococci, whereas the gallbladder was considered as the primary site in patients who underwent

cholecystectomy for cholecystitis and in whom culture of gallbladder's bile was not done but blood culture grew gram negative bacilli.

RESULTS

Out of the 14044 samples of blood culture reported at SMC during the two-year period of this study, there were 794 positive samples and the type of bacterial isolates in these samples were as follows; 532 (67%) pathogens, 166 (20.9%) contaminants, and in 96 (12.1%) specimens no details were available to ascertain either of these categories. The contaminants were staph epidermidis, staph aureus, enterococci, coliform bacilli, and non-fermenting gram negative bacilli. Of the 532 pathogenic samples there were 171 (32.1%) specimens with *S typhi* and 13 (2.4%) with *S paratyphi A*. The remaining 348 (65.5%) specimens were obtained from 257 patients.

Incidence, Probable Source and Outcome of Bacteraemia : (Table 1). Out of the 257 patients with bacteraemia surveyed in this study, there were 205 (79.6%) patients with community acquired infections and 52 (20.4%) with hospital related infections. Furthermore, it was possible in 214 (83.2%) patients to ascribe the source of organisms to a recognizable primary anatomical site, and in the remaining 43 (16.8%) patients, the source could not be ascertained. The overall fatal outcome of bacteraemia in this study was seen in 53 (20.6%) patients.

Streptococci was the most common aetiological agent of bacteraemia in this study reported in 68 (26.5%) patients. All these infections were community acquired. An underlying condition namely sickle cell disease (SCD), G-6-PD deficiency, leukaemia, heart disease, and measles was identified in the majority of these patients. In 42 (68.8%) patients there were clinical features of pneumonia at the time of admission, and in 8 (11.8%) there were signs of pyogenic meningitis.

In a majority of patients with pneumonia, culture of sputum or other aspirate from the respiratory tract was not done. The organism was also isolated from the peritoneal exudate in 2 (2.9%) patients with primary peritonitis. Both were 8 years old, previously healthy, girls and both recovered with antibiotic therapy alone; one received penicillin and the other was given penicillin and gentamycin. All the patients with pyogenic meningitis due to

TABLE 1
Aetiological Agents, Probable Tissue Source of Infection and Outcome of Bacteraemia.
* *Salmonella* Species Other Than *S* Typhi and *S* Paratyphi A

Organism	Lung	Urinary	Skin	Intestine	Meninges	Bone	Heart	Genital	Upper Respiratory	Gall bladder	Ear	Peritoneum	Unknown	Patients		Mortality	
														No.	%	No	%
<i>Strept pneumoniae</i>	42	—	1	—	8	1	—	—	5	—	4	2	5	68	26.5	5	7.3
<i>Staph aureus</i>	2	—	12	2	—	12	2	—	—	—	1	—	1	34	13.2	6	17.6
<i>E coli</i>	3	22	2	1	—	—	—	1	—	1	—	—	2	32	12.5	7	21.9
<i>Klebsiella</i>	7	6	1	3	—	—	—	3	—	4	—	—	4	30	11.7	12	40.0
<i>Salmonella</i> *	—	—	—	14	—	1	—	—	—	—	—	—	4	19	7.4	2	10.5
<i>B haem streptococci</i>	—	—	5	—	—	—	—	2	1	—	—	—	6	18	7.0	4	22.2
Coliforms	3	2	1	—	—	—	—	1	—	1	—	—	5	13	5.0	5	38.5
Enterococci	1	—	3	—	—	—	3	1	—	—	—	—	2	10	3.8	2	20.0
<i>N meningitidis</i>	—	—	—	—	—	—	—	—	—	—	—	—	3	5	1.6	1	20.0
<i>Strept viridans</i>	—	—	—	—	—	—	2	—	—	—	—	—	2	4	1.5	—	—
<i>Proreus</i>	2	1	1	—	—	—	—	—	—	—	—	—	—	4	1.5	3	75.0
<i>H influenzae</i>	—	—	—	—	3	—	—	—	—	—	—	—	—	3	1.2	—	—
<i>Ps aeruginosa</i>	—	2	—	—	—	—	—	—	1	—	—	—	—	3	1.2	1	33.3
<i>Staph epidermidis</i>	—	—	2	—	—	—	—	—	—	—	—	—	1	3	1.2	1	33.3
<i>Alkaligenes</i>	1	—	—	—	—	—	—	—	—	—	—	—	—	1	0.4	—	—
<i>Acinetobacter</i>	—	—	—	—	—	—	—	—	—	—	—	—	1	1	0.4	—	—
<i>Bacteroides</i>	—	—	—	1	—	—	—	—	—	—	—	—	—	1	0.4	1	100.0
<i>Candida albicans</i>	—	—	—	—	—	—	—	—	—	—	—	—	—	1	0.4	1	100.0
<i>C hommannii</i>	—	—	—	—	—	—	1	—	—	—	—	—	—	1	0.4	—	—
Mixed infections	3	—	—	—	—	—	—	—	—	—	—	—	3	6	2.3	2	33.3
TOTAL	64	33	28	21	11	14	8	8	7	6	5	2	40	257	100.0	53	20.6

strept pneumoniae also recovered with appropriate antibiotic therapy. Finally all the 68 isolates of this organism were found to be sensitive to penicillin and the outcome of this form of bacteraemia was fatal in 5 (7.3%) patients.

Bacteraemia due to *staph aureus* was seen in 34 (13.2%) patients and the most common sources of infection were the skin and bone. Complications were seen in 7 patients; 2 developed endocarditis, 2 had meningitis, and one patient each with disseminated intravascular coagulation, shock, and pneumonia with pleural effusion. The outcome was fatal in 6 (17.6%) patients; 5 of whom expired despite the administration of the appropriate antibiotic therapy.

E coli bacteraemia was seen in 32 (12.5%) patients and the most common source of this organism was the urinary tract. The outcome was fatal in 7 (21.9%) patients; 5 of whom had an ultimately fatal underlying condition such as terminal stage of lung cancer, thalassaemia major with liver

failure and obstructed hernia, severe myocardial infarction, SCD with pulmonary embolism, and liver cirrhosis associated with pneumonia and urinary tract infection. The other 2 patients had no underlying fatal disease; one was an alcoholic with neutropnia and the other was a 70 years old man with ulcerative colitis.

Bacteraemia due to *klebsiella* was seen in 30 (11.7%) patients and the outcome was fatal in 12 (40%) patients. All of the expired patients had an ultimately fatal underlying condition; 2 extremely premature infants, 2 premature infants with necrotising enterocolitis, one premature infant with meningitis and pneumonia, and one patient each with multiple myeloma, bile duct carcinoma with metastasis, post-splenectomy thalassaemia major, hemiplegia and pneumonia in a geriatric patient, multiple fractures due to road traffic accident, multiple congenital abnormalitis in a newborn, and liver cirrhosis with renal failure in a geriatric patient.

Salmonella bacteraemia was seen in 19 (7.4%) patients; 8 with *S typhimurium*, 7 with *Salmonella*

group C, 3 with *S enteritidis*, and one with *Salmonella* group E. The outcome was fatal in 2 (10.5%) patients both of whom had *S typhimurium*; one was a 2 month old infant with thalassemia and necrotising enterocolitis with perforation, and the other was a 60 years old man under chemotherapy for lung cancer.

Bacteraemia due to B-haemo streptococci was seen in 18 (7%) patients and the outcome with this infection was fatal in 4 (22.2%) patients. Five of these isolates were group A.

Bacteraemia due to Coliforms (*Citrobacter*, *Enterobacter* and other coliforms) was seen in 13 (5.1%) patients and the outcome was fatal in 5 (38.5%) patients. Four of the expired patients had received appropriate antibiotic therapy and the respective underlying conditions in these patients were acute leukemia, pregnancy with heart disease and renal failure, acute pancreatitis with shock, and SCD with renal failure and disseminated intravascular coagulation. The fifth patient had pneumonia and the culture results in this patient became positive only after the antibiotics were withdrawn.

Bacteraemia due to anaerobic organisms (*Bacteroides*) was fatal in one patient; a child who developed peritonitis following appendicitis.

Bacteraemia due to infection by more than one organism was seen in 6 (8.8%) patients; 2 with *klebsiella* and coliform bacilli, one each with strept pneumoniae and *klebsiella*, strept pneumoniae and *coliform bacilli*, *E coli* and *staph aureus*, and one with 2 sequential episodes of bacteraemias; *E coli* followed by *klebsiella*. The outcome of mixed bacteraemia was fatal in 2 (33.3%) patients and good in the remaining 4. The underlying conditions were as follows; 2 cancer patients, and one patient each with systemic lupus erythematosus and renal failure, pneumonia, splenectomy and multiple liver abscess, and SCD associated with G-6-PD deficiency and hyperbilirubenemia.

Age of patients, Bacterial Species and Outcome of Bacteraemia: (Table 2). Out of the 68 patients with bacteraemia due to strept Pneumoniae, 45 (66.2%) were children below the age of 10 years. On the other hand infection due to staph aureus occurred with almost equal frequency in all age groups. Bacteraemias due to *E coli* and *Klebsiella* were most commonly seen in the age group of 21-60 years. The majority of case of bacteraemia due to B haemo streptococci were infants and none of these isolates belonged to group A.

TABLE 2
Bacterial Agents, Age of Patients, and Outcome of Bacteraemia

ORGANISM	A G E G R O U P S						Total	
	<1 m	< 1 yr	<10 yr	<20 yr	<60 yr	>60 yr	No	%
Strept pneumoniae	1	10	34	7	12	4	68	26.5
Staph aureus	9	5	6	8	4	2	34	13.2
E coli	2	2	2	4	17	5	32	12.5
Klebsiella	8	1	2	1	10	8	30	11.7
Salmonella (*)	—	6	9	2	2	—	19	7.4
B haemo streptococci	8	3	—	—	4	3	18	7.0
Coliforms	—	2	1	3	7	—	13	5.1
Enterococci	4	1	2	—	2	1	10	3.8
N meningitidis	—	4	1	—	—	—	5	1.9
Strept viridans	—	—	3	—	1	—	4	1.5
Proteus	—	—	—	—	1	3	4	1.5
H influenzae	—	2	1	—	—	—	3	1.2
Staph epidermidis	—	—	—	1	2	—	3	1.2
Uncommon organisms	3	—	1	—	2	2	8	3.1
Mixed infections	1	—	—	1	3	1	6	2.3
Total	36	36	62	27	67	29	257	100.0
OUTCOME								
Good	28	29	54	18	50	12	191	74.3
Slow recovery	—	2	2	4	2	1	11	4.3
Fatal	8	5	6	5	14	15	53	20.6
No %	22.2	13.9	9.7	18.5	20.9	51.7	20.6	—
Unknown	—	—	—	—	—	1	1	0.8

* See table 1

High mortality rate was seen at both extremes of age. Thus the rate in infants below the age of one month was 22.2%, whereas that in patients above the age of 60 years was 51.7%. Underlying Conditions of the Patients : The most common underlying conditions were SCD, G-6-PD deficiency, heart disease, urinary tract infection, renal stones, gall-bladder disease, malignancy, diabetes mellitus, pyogenic meningitis, pneumonia, osteomyelitis and septic arthritis. Other less common conditions include gastroenteritis, cellulitis, otitis media, thalassaemia, hyperbilirubinaemia, prematurity, and trauma.

There were 30 patients with SCD and the outcome of bacteraemia in these patients was fatal in 5 (16.7%) cases despite the administration of the appropriate antibiotic therapy (Table 3). The common aetiological agents in these patients were gram negative bacilli of the Enterobacteriaceae family isolated from 14 patients, 6 (20%) of whom had bacteraemia due to salmonellae other than enteric fever group. Strep pneumoniae was isolated from 11 (36.7%) patients.

TABLE 3
Bacterial Isolates and Fatal
Outcome in 30 Patients with Sickle
Cell Disease

	<i>All patients</i>		<i>Fatal outcome</i>	
	No	%	No	%
Strep Pneumoniae	11	36.7	1	20.0
Salmonella *	6	20.0		
E coli	4	13.4	1	20.0
Coliform bacilli	3	10.0	1	20.0
N meningitidis	2	6.7	1	20.0
Klebsiella	1	3.3	1	20.0
H influenzae	1	3.3		
Staph epidermidis	1	3.3		
Strep viridans	1	3.3		
TOTAL	30	100.0	5	100.0

* See table 1

There were also 13 cancer patients, 9 of whom had gram negative bacilli of the Enterobacteriaceae family. The neoplastic condition and bacterial isolates of the remaining 5 patients were as follows : one patient with Hodgkin's disease and staph epidermidis, one with cancer of the urinary bladder and Ps aeruginosa, one with breast cancer and mixed infection of Strep pneumoniae and coliform bacilli, and two patients with leukemia; one with strept pneumoniae and the other with strept pyogenes. The outcome of bacteraemia associated with malignancy was fatal in 6 (46.2%) patients, good in 5 (38.5%) patients, and with no improvement in 2 (15.3%) patients.

Bacteraemia associated with bone and joint involvement was seen in 14 patients, 9 of whom were children below the age of 10 years. Staph aureus was isolated from 12 (85.8%) patients, 8 of whom had osteomyelitis and septic arthritis. The other isolates were strept pneumoniae in one (7.1%) patient with septic arthritis, and salmonella in another patient (7.1%) with osteomyelitis. The outcome was good in 11 (78.6%) patients, slow in 2 (14.3%), and fatal in one diabetic patient (7.1%).

There were 4 patients, all infants below the age of 2 months, with fatal necrotising enterocolitis confirmed by surgery and histopathology. The bacterial isolates were as follows: 2 patients with klebsiella, one with S typhimurium, and one with staph aureus. In addition there were also two adult patients with bacteraemia associated with gangrene of the intestine, one of whom had a fatal outcome.

Bacteraemia associated with endocarditis was seen in 8 patients, 2 of whom were in prosthetic valves. In one, the valve was placed 10 years before the development of the Enterococcus endocarditis, and in the other, the valve was placed 7 months before the development of endocarditis due to corynebacterium hofmannii. The remaining 6 patients had either congenital or rheumatic heart disease. The bacterial isolates were as follows; 3 patients with enterococci, 2 with strept viridans, 2 with staph aureus, and one with corynebacterium hofmannii. Although all the patients received appropriate antibiotic therapy, the outcome was fatal in 2 patients; one had staph aureus and developed shock and disseminated intravascular coagulation, and the other had enterococci and multiple congenital abnormalities.

There were 21 patients with bacteraemic meningitis, 16 of whom were below the age of 10 years. The outcome of this condition was fatal in 2 (9.5%) patients, one with non group A B-haemo streptococci, and the other with klebsiella. Strept pneumoniae was the most common aetiological agent isolated from 8 (38.1%) patients. Infection due to non group A B-haemo streptococci was seen in 4 (19%) infants all of whom were below the age of 2 months; one was given ampicillin, and the remaining 3 received combination of ampicillin and gentamycin. Staph aureus was the causative agent in 2 (9.5%) patients, in one of whom the organism was isolated from 3 blood cultures collected at different times, from the CSF, and from an abscess in the leg. The latter patient was first given a combination of cloxacillin and gentamycin, and then methicillin and amikacin. The other patient in whom the staph aureus was isolated from ear discharge was a 20 days old infant, and was given a combination of cloxacillin and cerfuruxine. Meningitis due to klebsiella was seen in 2 (9.5%) patients; one was a 3-day-old infant with obstructed uropathy and hydronephrosis and was given ampicillin and gentamycin, and the other was a 6-day-old premature infant who died before the culture results were ready. The other agents responsible for bacteraemic meningitis in this study were H influenzae isolates from 3 (14.3%) patients and N meningitidis isolates from 2 (9.5%) patients.

Bacteraemia following prior Invasive Procedures: (Table 4). There were 21 patients who had been

TABLE 4
Bacterial Isolates and Outcome
in 21 Patients with Bacteraemia following Prior
Invasive Procedures

	<i>All patients</i>		<i>Fatal outcome</i>	
	No	%	No	%
Klebsiella	8	38.1	6	60.0
E coli	4	19.0		
Coliforms	4	19.0	2	20.0
Ps aeruginosa	2	9.5		
Alkaligenes	1	4.8		
C albicans	1	4.8	1	10.0
Mixed organisms	1	4.8	1	10.0
TOTAL	21	100.0	10	100.0

subjected to various prior invasive procedures ranging from cholecystectomy and laparotomy to catheterization and artificial ventilation. Gram negative organisms were responsible for bacteraemia in 20 (95.2%) patients. The outcome was fatal in 10 (47.6%) patients. Clinical Presentation : The majority of the patients presented with more than one clinical feature depending on the causative organism and the body organ/system involved. These included fever, vomiting, diarrhoea, cough, dyspnoea, tachypnea, pneumonia, drowsiness, dysuria, weakness, coma or semiconsciousness, joint or bone pain, poor feeding in infants, cellulitis, chills, convulsions, abdominal pain, excessive crying in children, chest pain, gastrointestinal haemorrhage, tachycardia, hypertension, jaundice, hepatomegaly, splenomegaly, skin rashes and petichiae, headache, neurological signs, hypothermia, leucocytosis, and leucopenia. The variability of the symptoms and signs were not helpful in distinguishing the patients with gram negative bacteraemia from those with gram positive bacteraemia, except in patients with infection due to strept pneumoniae, staph aureus and E coli.

The most common presenting features of bacteraemia in this study were fever followed by tachycardia (66 and 38 patients respectively). On the other hand, hypothermia was observed in 3 patients, all of whom were infants below the age of one month.

Hypotension with BP less than 90/60 mm Hg in previously normotensive individuals, and a drop of systolic pressure by 70 mm Hg or more in hypertensive patients was seen more commonly in patients with gram negative bacteraemia than in patients with gram positive organism like strept pneumoniae.

In all the patients with osteomyelitis and septic arthritis, there was a local suppuration near the involved bone and there was also abrupt onset of fever. The isolated organism in these conditions were staph aureus.

Bacteraemia associated with dysuria and abdominal pain and occurring in adults was found to be commonly due to E coli.

In children with neurological signs such as neck rigidity, Kernig's sign and other features of meningitis, the isolates were Strept pneumoniae, H influenzae, and N meningitidis.

The total blood count in patients with bacteraemia was found to be high in 195 (75.9%) patients, within normal range in 49 (19%) patients, and low in 13 (5.1%) patients. In the 29 patients who received prior antibiotics, chemotherapy or corticosteroids, the count was high in 18 patients, within normal range in 5 patients and low in 6 patients. Prior Drugs and "Breakthrough" Bacteraemia : The underlying conditions in patients who received antibiotics, chemotherapy or corticosteroids prior to blood culture were cancer, systemic lupus erythematosus, prematurity, SCD, obstructive uropathy, and post-operative procedures. The isolated organisms were as follows; 6 patients with each of *klebsiella* and *E coli*, 4 with *Coliforms*, 2 with each of *S typhimurium*, *B haemo streptococci*, *staph aureus*, *Ps aeruginosa* and other mixed infections, and one patient each with *alkaligenes*, *staph epidermidis* and *candida albicans*. In 6 of these patients the bacteraemia was due to organism sensitive to the same antibiotic given before blood culture, 3 were receiving the antibiotic at the time the blood was collected for culture, and in 3 the antibiotic was given 1 to 7 days before the detection of bacteraemia. All these 6 patients died. Antibiotic Susceptibility Patterns and Treatment : Out of the 257 patients with bacteraemia surveyed in this study 232 (90.3%) were given the appropriate antibiotic therapy, 23 (8.9%) were not given such therapy, and in 2 (0.8%) no antibiotic was administered resulting in a fatal outcome.

232 patients who were given appropriate antibiotic therapy, 40 (17.2%) died.

The outcome in the cases of 23 patients who were not given the appropriate antibiotic therapy was fatality in 11 (47.8%), recovery in 10 (43.5%) and unknown in 2 (8.7%) cases. In the recovery group, 8 patients received ampicillin alone, one was given ampicillin and cephalothin, and one received ampicillin and gentamycin. The isolated organisms in this group were as follows: 4 patients with *klebsiella*, 3 with *coliform bacilli*, and one patient each with *E coli*, *acinetobacter*, and *salmonella*.

All of the strept pneumoniae, the commonest organism responsible for bacteraemia in this study, and isolated from 68 patients, were sensitive to the penicillin group of antibiotics. Ampicillin alone was given to 34 (50%) patients and the outcome in this cluster was fatal in 3 patients. Good outcome was

observed, however, in 16 (23.5%) patients who were given penicillin alone as well as in remaining 18 (26.5%) who received ampicillin in combination with other antibiotics such as gentamycin. The overall response to this organism was good, except in 9 patients; 5 of whom had a fatal outcome and recovery was slow among the remaining 4 patients.

Bacteraemia due to *staph aureus* was isolated from 34 patients all of whom were sensitive to cloxacillin. The outcome was good in 6 (17.6%) patients who took cloxacillin alone, as well as in 24 (70.6%) other patients who received a combination of cloxacillin, fucidin, erythromycin and gentamycin. The outcome was, however, fatal in 4 (11.6%) patients.

E coli was isolated in 32 patients in this study; 14 (43.8%) of whom were given single antibiotic, 17 (53.1%) received a combination of antibiotics, and in one (3.1%) no therapy was given. The most commonly used antibiotics were ampicillin and gentamycin, and only in 4 patients there was resistance to gentamycin. The outcome was fatal for 7 (21.9%) patients.

Bacteraemia due to *klebsiella* was seen in 30 patients, 19 of whom received appropriate antibiotic therapy. The outcome was good in 14 (46.7%) patients who received single antibiotic. On the other hand combination of antibiotics was given to 16 (53.3%) patients and the outcome in this group was fatal for 8 patients. Only 8 of the *klebsiella* species isolated in this study were resistant to gentamycin.

Bacteraemia due to *salmonella* species was seen in 19 patients, 16 (84.2%) of whom were given a single antibiotic (mostly ampicillin) with good outcome, and 3 (15.8%) received combination of antibiotics with 2 fatalities.

DISCUSSION

S typhi was the commonest organism responsible for bacteraemia in this study, followed by strept pneumoniae, *staph aureus*, and gram negative bacilli of the Enterobacteriaceae family. The various aspects of bacteraemia in Bahrain as well as their aetiological agents, underlying conditions and management are discussed below. However, since enteric fever is regarded as a distinct entity, analysis of

data concerning the source of the organisms, clinical features or treatment of salmonellal bacteraemia will not be considered.

Pneumococcal Bacteraemia

The results of this study showed that strept pneumoniae was the most common agent responsible for bacteraemia in children and that most of the patients had an underlying condition such as leukaemia, SCD, G-6-PD deficiency, thalassaemia, kidney and heart diseases, and infections such as measles. The response to therapy in these patients was good and the bacterial strains resistant to penicillin which caused bacteraemia in other countries were not seen in Bahrain. On the other hand, the mortality rate of pneumococcal bacteraemia in this study was 7.3% while in other countries it was 10% among children, 17% among adults, and 44% in all age groups^{10,11}. These population differences are influenced however, by the number of patients with fatal or ultimately fatal underlying conditions. The course and outcome of pneumococcal bacteraemia is determined therefore by the presence and gravity of the underlying condition.

Bacteraemia in SCD

There were 30 patients with SCD in the present study and strept pneumoniae was responsible for 36.7% of bacteraemia in these patients, while Salmonellae species other than those of Enteric fever group were accountable for 20% of the cases. In a study from Saudi Arabia on 40 children with SCD, Mallouh and Salamah¹² reported bacteraemia in only 16 patients; 7 with Salmonella, 3 with strept pneumoniae, and 6 with other organisms. The incidence of salmonellal bacteraemia in Saudi Arabia is higher than that in Bahrain because bacteraemias due to *s typhi* and *s paratyphi A* were excluded from the present study. But if infection due to these organisms were to be included, then the incidence in Bahrain would be higher.

Patients with SCD are 600 times more susceptible to pneumococcal infection than normal individuals¹³. In the present study however, only 11 (16.2%) out of the 68 patients with pneumococcal bacteraemia had SCD, and none of these received pneumococcal vaccine prior to the infection. The reason for this low incidence of strept pneumoniae infection is attributed to the initiation of the vaccina-

tion program in Bahrain for patients with SCD. The pneumococcal polysaccharide vaccine has been shown to be highly effective in reducing the incidence of bacteraemic and non-bacteraemic pneumococcal infection^{14, 15, 16} although the study of Broom et al.¹⁷ suggested that the effectiveness of the vaccination would depend on the underlying condition. The other factor responsible for such low incidence may be related to the mild course of SCD in the Eastern parts of the Arabian peninsula^{18, 19, 20, 21, 22}.

The second common cause of bacteraemia in patients with SCD was salmonella. Salmonella infections are common in Bahrain²³ and patients with SCD seem to be particularly prone to infection by these organisms. This is because the microinfarcts produced in the intestinal wall, and the decreased serum opsonization activity would favour the invasion of the organisms into the blood stream^{24, 25}.

Non-Enteric Salmonellal Bacteraemia

Salmonellal gastroenteritis associated with bacteraemia is common in Bahrain²³. On the other hand, acute gastroenteritis is also common but the disease is usually self-limiting and rarely associated with long term sequelae. However the study of Meadow and Schneider²⁶ on a group of patients with gastroenteritis and bacteraemia and on another group with gastroenteritis and with no bacteraemia showed no difference in the severity of illness, clinical course and eventual outcome between the two groups. In Bahrain SCD is also common and since these patients are immunocompromised, the possibility of haematogenous spread from the intestine as well as from the bone must always be considered while assessing the prognosis of these patients. The outcome of bacteraemia seems therefore to depend on the underlying condition. In this study both of the expired patients with salmonellal bacteraemia had a severe underlying condition; one was an infant with necrotising enterocolitis and the other was a 60-year-old patient under chemotherapy for lung cancer. It is possible however, to control and reduce the incidence of salmonellal infection in Bahrain as well as the morbidity and mortality by effective public health measures.

Other Gram-negative Bacteraemias

In this study gram negative bacilli were responsible for bacteraemia in 113 patients, whereas gram

positive cocci caused infection in 137 patients. However, if the cases of Enteric fever were to be accounted for, then gram negative organisms become the main cause of bacteraemia in Bahrain. Reports from other countries also showed a high frequency of gram negative bacteraemias⁶. But in these countries, the high incidence was not due to Enteric fever, but to other gram negative bacilli associated with severe underlying disease such as frequency of cardiac surgery and manipulative procedures, and the frequent and prolonged use of antimetabolites and corticosteroids⁶. This again emphasizes the role of population differences and the type of hospital service in the aetiology and outcome of bacteraemia.

E coli and *klebsiella* were the most frequent aetiological agents responsible for gram-negative bacteraemia in this study and the mortality rate was particularly high with *Klebsiella* infection. But when the underlying conditions were considered, no difference was found in the mortality rates between bacteraemias caused by individuals species. All the patients in this study with *klebsiella* bacteraemia had fatal underlying conditions, and 5 of the 6 patients with polymicrobial infection including those with *klebsiella* were immunocompromised.

Age related differences were observed in the aetiology of bacteraemia. Thus, while gram-positive organisms (e.g. *strept pneumoniae*) caused infection mainly in children, gram-negative bacteraemias were more common in adults. The mortality rate was also higher in older patients as well as in patients with serious underlying conditions.

The urinary tract was the most common source of gram negative bacteraemia in this study. Krieger et al.²⁷ reported that 2.7% of patients with nosocomial bacteriurea develop bacteraemia, and Strand et al.²⁸ observed septicemia secondary to urinary tract infection in immunocompromised patients who had no urinary symptoms (e.g. dysuria) and from whom low colony count of urine culture was seen. Since it is the practice in most laboratories not to report the bacteriological spectrum and antibiotic sensitivity of these isolates in the absence of clinical information which may influence the colony count, it is possible to ascribe cases of bacteraemia of unknown source to the urinary tract.

Although the source of bacteraemia could not be determined in 16.8% of the cases in this study, intravenous catheterization may probably be the responsible factor in some patients even though the relevant information concerning the use of catheters and the subsequent appearance of local inflammatory reaction at the site of administration could not be ascertained due to inadequate data in the patients' file. It is interesting to note that 20.4% of bacteraemias in this study were hospital acquired.

Staph aureus Bacteraemia

The common sources of this organism in this study were the skin, subcutaneous tissue, and bone. However, in the majority of patients with osteomyelitis and septic arthritis, no other primary focus of infection was found. It is therefore most likely that in these cases the organisms were situated in a colonized foci in the bones and joints, and were disseminated into the blood stream following mild or even unrecognized trauma to these sites. On the other hand, infection of these sites must have resulted from seeding of the bacteria from the blood stream itself.

Except for those patients with osteomyelitis or septic arthritis where local signs were present, in most other cases the signs and symptoms were not helpful in distinguishing patients with staphylococcal bacteraemia from those with other bacteraemic infections.

According to Nolan and Beaty²⁹, bacteraemic patients with identified source of infection usually respond better to treatment than those with an unrecognized primary source, who not only require prolonged courses of antibiotics, but are also prone to develop clinical complications. In the present study 7 of such patients developed complications; 2 had endocarditis and the others developed thrombocytopenia, bleeding, shock, pneumonia, pleural effusion, and meningitis.

Staph epidermidis, an organism usually considered non pathogenic, caused bacteraemia in 3 patients in this study, all of whom were immunocompromised. Similar findings have also been reported in studies from other countries³⁰.

Infective Endocarditis

All of the 8 patients with infective endocarditis in this study had an underlying heart disease. However, since it is often difficult to identify the source of organisms responsible for this condition, it would seem that its occurrence is not preventable³¹. One of the patients with prosthetic valve endocarditis in this study had infection due to a diphtheroid, an organism usually considered non-pathogenic commensal of the throat and skin. This is a rare and uncommon cause of endocarditis in prosthetic valves^{32, 33}.

Bacteraemic Meningitis

It has been pointed out that 90% of cases with pyogenic meningitis occur between the age of one month to 5 years,^{34, 35} and in the present series, 76.2% of the patients were children below the age of 10 years. The route of infection could either be haematogenous, or direct invasion from a nearby infection such as mastoiditis. In two patients the organisms were isolated from other foci; in one from a subperiosteal abscess in the leg, and in the other from ear infection.

Non group A B-haemo streptococci probably belonging to Lancefield group B, was responsible for meningitis in 4 infants in this study. This is one of commonest causes of meningitis in infants^{36, 37} and their most likely source is the birth canal. The newborn infant is highly susceptible to infection due to immaturity of host defense mechanisms.

Necrotising Enterocolitis

This is the most common acquired gastrointestinal emergency in neonatal intensive care units³⁸ and its outcome in the present study was fatal in all of the 4 infants who developed it. The disease has multiple causes and many contributory factors, and the associated bacteraemia is attributed to the direct vascular invasion of the intestinal organisms and the absorption of their toxins through friable intestinal mucosa³⁸.

Primary Peritonitis in Children

Peritonitis not related to any intra-abdominal pathological lesion is very rare and occurs most commonly in girls. Over a period of 22 years, Freij et al.³⁹ described the disease only in 7 previously

healthy children, and in this study which 2 additional cases with similar history occurring among 8-year-old girls are described. The disease however, is common in the developing countries⁴⁰ and caused most commonly by strept pneumoniae. The possible route of infection is usually haematogenous, but other routes e.g. through the genital or lymphatic systems as well as transmurally across the wall of the intestine must also be considered. The response to antibiotic therapy is good and surgery is rarely indicated.

Since SCD is common in Bahrain, and since these patients are more susceptible to infection by strept pneumoniae, it may be possible in these conditions to predetermine the pathogenesis of primary peritonitis by examining the blood, peritoneal exudate, vaginal discharge and surgically excised specimens from suspected sites.

Antibiotic Therapy

The mortality rate with appropriate antibiotic therapy in this study was 17.2%, and the patients who did not improve with therapy had fatal or ultimately fatal underlying conditions. Appropriate antibiotic therapy alone is therefore inadequate and the outcome of bacteraemia seems to depend on the gravity of these conditions. The general guidelines of optimal therapy are; prompt recognition of bacteraemia and its tissue source, identification of the aetiological agents and its antibiogram, appropriate parenteral doses of bactericidal antibiotics, drainage of purulent collections, and prompt attention to complications. However, some bacteraemic patients in this study recovered without appropriate antibiotic therapy. These may probably be transient forms of bacteraemias which are known to occur spontaneously as well as after manipulation of the urinary tract. On the other hand there were many other patients who received a combination of antibiotics with no indication as to the efficacy of such regime. Combinations of antibiotic are indicated in empiric regimes when the culture and sensitivity results are not available, and in some infections such as infective endocarditis.

"Breakthrough bacteraemia", the blood stream infections which occur during treatment with presumably adequate dosage of appropriate antibiotics to which the isolated organism is susceptible in

vitro, was fatally seen in 6 cases in this study all of whom had an underlying condition. The phenomenon appear to be related to adverse host factors such as the presence of primary focus of infection elsewhere in the body, and inadequate serum antibiotic level. It also shows the limitation of the antimicrobial therapy when used alone for the treatment of bacteraemia. Other supportive measures are therefore equally important.

CONCLUSION

The bacteriological spectrum and antibiogram pattern of bacteraemia vary from one geographic area to another, and its outcome with appropriate antibiotics depends on the gravity of the underlying conditions of the patient, and the supportive measures of treatment of such conditions. Other detrimental factors include the age of the patient, the state of vaccination, and proper attention to the source of organisms and to complication.

REFERENCES

1. McCabe WR, Wolff SM, Bennett JV. Incidence of gram-negative bacteraemia. *N Engl J Med* 1975;292:111.
2. McGowan JE, Barnes MW, Finland M. Bacteraemia at Boston City Hospital: Occurrence and mortality during 12 selected years (1935-1972), with special reference to hospital acquired cases. *J Infect Dis* 1975;132:316-35.
3. Armstrong D, Young LS, Meyer RD, et al. Infectious complications of neoplastic disease. *Med Clin North Am* 1971;55:729-45.
4. Winston DJ, Gale RP, Meyer DV, et al. Infectious complications of human bone-marrow transplantation. *Medicine* 1979;58:1-31.
5. Duggan JM, Oldfield GS, Ghosh HK. Septicemia as a hospital hazard. *J Hosp Infect* 1985;6:406-12.
6. Kreger BE, Craven DE, Carling PC, et al. Gram-negative bacteraemia III. Reassessment of etiology, epidemiology and ecology in 612 patients. *Am J Med* 1980;68:332-43.
7. Baur AW, Kirby WMM, Sherrie JC, et al. Antibiotic susceptibility testing by a standardized single disk method. *Am J Clin Pathol* 1966;45:493-96.
8. Edwards PR, Ewing WH. Identification of Enterobacteriaceae. 3rd ed. Minneapolis: Burgess Publ Co, 1972.
9. Sonnenwirth AC, Jerett L. Gradwohl's clinical laboratory methods and diagnosis. Vol 2, 8th ed. St Louis: CV Mosby Co, 1980.
10. Esposito AL. Community acquired bacteremic pneumococcal pneumonia. Effect of age on manifestations and outcome. *Arch Inter Med* 1984;144:945-48.
11. Ruben FL, Norden CW, Korica Y. Pneumococcal bacteraemia at a medical surgical hospital for adults between 1975 and 1980. *Am J Med* 1984;77:1091-94.
12. Mallouh AA, Salamah MM. Pattern of bacterial infections in homozygous sickle cell disease. A report from Saudi Arabia. *Am J Dis Child* 1985;139:820-22.
13. Barrett-Conner E. Bacterial infection and sickle cell anaemia. *Medicine* 1971;50:97-112.
14. Amman AJ, Addiego J, Wara DW, et al. Polyvalent pneumococcal polysaccharide immunization of patients with sickle cell anaemia and patients with splenectomy. *N Engl J Med* 1977;297:897-900.
15. Austrian R. Prevention of pneumococcal infection by immunization with capsular polysaccharide of streptococcus pneumoniae: Current status of polyvalent vaccines. *J Infect Dis* 1977;136:838-41.
16. Riley ID, Tarr PI, Andrew M, et al. Immunization with a polyvalent pneumococcal vaccine. Reduction of adult respiratory distress syndrome in a New Guinea Highlands community. *Lancet* 1977;1:1338-41.
17. Broome CV, Facklam RR, Fraser DW. Pneumococcal disease after pneumococcal vaccination. *N Engl J Med* 1980;303:549-52.
18. Perrine RP, Brown MJ, Chgg JB, et al. Benign sickle cell anaemia. *Lancet* 1972;2:1163-67.
19. Perrine RP, Penbery ME, John P, et al. Natural history of sickle cell anaemia in Saudi Arabia. A study of 270 subjects. *Ann Intern Med* 1978;88:1-6.
20. Perrine RP, John P, Penbery ME, et al. Sickle cell disease in Saudi Arabia in early childhood. *Arch Dis Child* 1981;56:187-92.
21. Al-Awamy B, Wilson WA, Pearson HA, et al. Spleen function in sickle cell disease in the eastern province of Saudi Arabia. *J Paediatr* 1984;104:714-17.
22. Mallouh AA, Burke GM, Salamah MM, et al. Spleen function in Saudi children with sickle cell disease. *Ann Tropic Paediatr* 1984;4:87-91.
23. Kumar S, Al-Hilli F. Bacterial and antimicrobial sensitivity pattern in Bahrain. *Bahrain Med Bull* 1984;6:81-89.
24. Hand WL, King NL. Serum opsonization of Salmonella in sickle cell anaemia. *Am J Med* 1978;64:388-95.
25. Adiyokunu AA, Hendrickse RG. Salmonella osteomyelitis in childhood. A report of 63 cases seen in Nigerian children of whom 57 had sickle cell disease. *Arch Dis Child* 1980;55:175-84.

26. Meadow WL, Schneider H. Salmonella enteritidis bacteremia in childhood. *J Infect Dis* 1985;152:185-89.
27. Krieger JN, Kaiser DL, Wenzel RP. Urinary tract etiology of blood stream infection in hospitalized patients. *J Infect Dis* 1983;148:57-62.
28. Strand CL, Bryant JK, Sutton KH. Septicemia secondary to urinary tract infection with colony counts less than 10 cfu/ml. *Am J Clin Pathol* 1985;83:619-22.
29. Nolan CM, Beaty HN. Staphylococcus aureus bacteremia: Current clinical patterns. *Am J Med* 1976;60:495-500.
30. Leon SPD, Wenzel RP. Hospital acquired blood stream infection with Staphylococcus epidermidis. *Am J Med* 1984;77:639-44.
31. Griffin MR, Wilson WR, Edwards WD. Infective endocarditis, Olmsted County, Minnesota, 1950 through 1981. *JAMA* 1985;254:1199-1202.
32. Van Sevoy RE, Cohen SN, Geraci JE, et al. Coryneform bacterial endocarditis. *Mayo Clinic Proc* 1977;52:216-19.
33. Eliakim R, Silkoff P, Lugassy G, et al. Corynebacterium xerosis endocarditis. *Arch Inter Med* 1983;143:1995.
34. Parke JC, Schneerson R, Robbins JB. The attack rate, age incidence, racial distribution and case fatality rate of Haemophilus influenzae type b meningitis in Mecklenburg County, North Carolina. *J Paediatr* 1972;81:765.
35. Fraser DW, Darby CP, Koehler RE, et al. Risk factors in bacterial meningitis, Charleston County, South Carolina. *J Infect Dis* 1973;127:271.
36. Baker CJ, Barnett FF, Gorden RC, et al. Suppurative meningitis due to streptococci of Lancefield group B. A study of 33 infants. *J Pediatr* 1973;82:724.
37. Franciosi RA, Knostman JD, Zimmerman RA. Group B streptococcal neonatal and infant infections. *J Pediatr* 1973;82:707.
38. Louvois JD. Necrotising enterocolitis. *J Hosp Infect* 1986;7:4-12.
39. Freij BJ, Votteler TP, McCracken GH. Primary peritonitis in previously healthy children. *Am J Dis Child* 1984;138:1058-61.
40. Sen S, Laitha MK, Fenn AS, et al. Primary peritonitis in children. *Ann Trop Paediatr* 1983;3:53-56.