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Extended spectrum *Beta-Lactamase*-producing *Klebsiella pneumoniae* septicaemia outbreak in the Neonatal Intensive Care Unit of a tertiary hospital in Nigeria.

KC Iregbu and U Anwaal

Department of Medical Microbiology and Parasitology, National Hospital, Abuja, Nigeria

Summary

Between March and August 2002 a cluster of nosocomial septicaemia associated with Extended Spectrum beta lactamase (ESBL)-producing *Klebsiella pneumoniae* was observed in 11 neonates from the neonatal intensive care unit of a 200-bed tertiary hospital in Abuja, the Federal Capital territory of Nigeria. An investigation was conducted to identify the possible reservoirs and mode of transmission. Infection control measures and epidemiologic surveillance were executed. The environment was investigated by collecting and processing several swab samples for microbiological studies. Antibiogram tests and extended spectrum beta lactamase production test were performed on all *K. pneumoniae* isolates from both the environment and the patients, and all bacteraemic and environmental isolates of *K. pneumoniae* compared. A total of 30 *K. pneumoniae* isolates made up of 17 from the patients and 13 from the environment were analysed. An identical antibiogram was found in 24 isolates, which included all the 17 from the patients and the 7 from the hands of staff, sink and incubator surface in the NICU. Mortality rate from the outbreak was 36.4% and constituted 10.8% of all deaths in the unit in 2002. Overall mortality in the unit for 2002 was 28.9%. The outbreak significantly caused more deaths than usual in the unit. The nosocomial septicaemia was caused by a single ESBL-producing strain of *K. pneumoniae* brought into the hospital by a neonate delivered and admitted from an external health institution. Sink and the incubator were also contaminated by the same strain.

Keywords: *Extended spectrum beta lactamase, Klebsiella pneumoniae, neonatal intensive care unit, outbreak, septicaemia*

Résumé

Entre Mars et Août 2002, une septicémie nosocomiale associée avec le pneumonie klebsiella était observée chez 11 nouveaux nés dans l'unité des soins intensif des nouveaux nés du centre hôpitalier tertiaire d'Abuja ; capitale fédérale du Nigeria. Une investigation était conduite pour identifier les réservoir possibles et mode de transmission, des mesures de contrôles d'infections et une surveillance épidémiologique était exécutée. les testsd'antibiogrammes et test de production du Bêta lactamase étaient faites sur tout les isolant de *K pneumonie* de l'environnement et des patients, au total, 30 isolats de *K pneumonie* (17 des patients et 13 de l'environnement étaient analysées) . Un antibiogramme identique était trouvé dans 24 isolats (17 patients et 7 environnements). Le taux de mortalité de l'épidémie était de 36,4% et constituaient 10,8% des morts (décès dans cette unité en 2002. le taux de mortalité annuel dans cette unité en 2002 était de 28,9%. L'épidémie causait significativement plus de morts dans cette unité que d'habitude. La septicémie nosocomiale était causée par les soins de type *K pneumonie* apportés à l'hôpital aux nouveaux nés admis des centres de santé externe. Les réservoirs et les incubateurs étaient contaminés par le même sous type d'espèce.

Introduction

Klebsiella pneumoniae is associated with life threatening nosocomial infections such as septicaemia, meningitis and pneumonia especially in the newborn [1-4] and has been implicated in a number of reports and studies [5,6]. The organism is a well documented producer of extended spectrum beta lactamase (ESBL) enzyme which confers multiple resistance property to it, particularly to third generation cephalosporins [7-11]. The ESBL producing strains of *K. pneumoniae* have emerged as important agents of nosocomially acquired pathogens [5,12,13], and have been isolated in a number of nosocomial sepsis and outbreaks [6,14,15].

Mortality rates associated with *K. pneumoniae* septicaemia ranging from 5.7% to 80% have been documented in some reports [6,16-18]. The resistance of ESBL-producing strains of *K. pneumoniae* to third generation cephalosporins poses

Correspondence: Dr. K.C. Iregbu, Department of Medical Microbiology and Parasitology, National Hospital, Plot 132 Central District (Phase II), PMB 425, Garki, Abuja, Nigeria. E-mail: keniregbu@yahoo.co.uk.

Table 1: Antibiogram of K. pneumoniae implicated in the outbreak

Drugs Source of isolate	No tested	AMC No R (%)	XM No R (%)	CAZ No R (%)	CRO No R (%)	CN No R (%)	CIP No R (%)	AK No R (%)	IP No R (%)	CAZ-AMC No R (%)	CAZ-AMC No S (%)
Patients	17	17 (100)	17 (100)	17 (100)	17 (100)	17 (100)	17 (100)	17 (100)	17 (100)	0 (0)	17 (100)
Staff	2	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	0 (0)	2 (100)
Incubator	2	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	2 (100)	0 (0)	2 (100)
Sink	3	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	2 (100)	0 (0)	3 (100)
Total	24	24 (100)	24 (100)	24 (100)	24 (100)	24 (100)	24 (100)	24 (100)	24 (100)	0 (0)	24 (100)

AMC - Amoxycillin-clavulanic acid; XM - Cefuroxime; CAZ - Ceftazidime; CRO - Ceftrixone; CN - Gentamicin; CIP - Ciprofloxacin; AK - Amikacin; IP - Imipenem; R - Resistance; S - Sensitive

a formidable challenge in the management of patients especially infected neonates and calls for surveillance and regular reporting of clinically significant cases. Generally, there is paucity of nosocomial infection data in Nigeria particularly for hospitalised neonates. Here we present the report of an ESBL-producing *K. pneumoniae* septicaemia outbreak involving eleven patients over a five-month period.

Patients and method

The neonatal intensive care unit (NICU) of our hospital admits patients with asphyxia and low birth weight delivered within and outside the hospital. Diagnosis of septicaemia in infected neonates was made based on presenting clinical features and positive blood cultures. The blood cultures were carried out using the Oxoid 103 BC system (Oxoid, Basingstoke UK). Growths in the blood broths were sub-cultured onto appropriate media and isolates subsequently identified by established methods [19]. Properly collected cord swabs from the patients were also processed. Antibiotics sensitivity tests were performed on all isolates by disk diffusion technique and results interpreted using the National Committee for Clinical Laboratory Standards (NCCLS) criteria [20]. Antibiotics tested were amoxicillin-clavulanic acid, cefuroxime, ceftazidime, ceftriaxone, imipenem, gentamicin, amikacin and ciprofloxacin. ESBL production was established by the disk approximation technique using ceftazidime (30ìg) and amoxicillin-clavulanic acid (20/10ìg). *Escherichia coli* ATTC 29232 was used for control.

A review of our Medical Microbiology records showed that for more than one year prior to this outbreak no *K. pneumoniae* was isolated from any blood sample from any NICU patient. The isolation of *K. pneumoniae* strains with identical antibiotic resistance/sensitivity profile from the blood samples of NICU patients prompted a discussion with medical staff of the Paediatrics Department, which culminated in the investigation and control of the outbreak. Samples were taken from the hands of staff, water sink, water tap handles, suction tubes and equipment, feeding trolleys and utensils, humidifiers, storage bottles, incubators, and other surfaces and items of equipment. The antibiogram of all isolated *K. pneumoniae* from these samples were determined as stated above, and compared with those isolated from the patients. Appropriate infection control measures, including temporary ward closure and fumigation and surveillance were instituted.

Results

The outbreak was presumed to have started from a patient admitted into the ward from an outside health institution. Eleven patients were then shown to have been involved in the outbreak which lasted for five months from March 2002 to August 2002. A total of 35 *K. pneumoniae* strains were isolated from both the patients and the environment – 17 from patients, 2 from the hands of staff, 2 from the incubator surface and 3 from different parts of the sink. Of the 17 strains from the patients 11 were from blood, 5 from cord swabs and one from cerebrospinal fluid.

All the 24 *K. pneumoniae* strains isolated from the patients, members of staff, the sink, as well as the incubator had an identical antibiogram; all of them being resistant to amoxicillin-clavulanic acid, cefuroxime ceftazidime, ceftriaxone, gentamicin and ciprofloxacin, and sensitive to imipenem and amikacin as well as to a combination of amoxicillin-clavulanic acid and ceftazidime (Table 1), and demonstrated the production of extended spectrum beta-lactamase (ESBL).

Four of the 11 (36.4%) patients died. The dead included the index patient and one other patient who was readmitted with meningitis eight days after discharge. The outbreak accounted for 10.8% of all deaths in the unit in 2002. Overall mortality in the unit was 28.9% in 2002. The death rate due to the outbreak was significantly higher than the endemic rate for the unit for the year ($\div^2 = 0.400$, $p<0.05$, 95% confidence limit).

After nine months of active surveillance following the institution of control measures no further case was found.

Discussion

The outbreak was facilitated by breach in the infection control practices by the ward staff. The patient brought in from outside was not isolated as is the practice in the NICU. This made it possible for the outbreak strain to contaminate staff, sink and incubator creating reservoirs and sources for other patients. A similar finding was reported in a study in China by Su *et al* [12]. The high pathogenicity and virulence of *K. pneumoniae* coupled with the multiply-resistant nature of ESBL strains and the age of the patients accounted for the high case fatality rate of 36.4% recorded in the outbreak. Although this rate would appear to fall with the range reported in previous studies [6,16-18] the outbreak was largely preventable if infection control measures were adhered to. The percentage mortality of the outbreak was more than the 28.9% annual rate for the unit in 2002 (unpublished report from the medical records department of the hospital), and contributed substantially to the year's rate. This emphasises the need to plan and strictly implement infection control programmes in healthcare institutions.

The sensitivity of the outbreak strain to amikacin and imipenem was not surprising because these two drugs have been rarely used in Nigeria. There is thus little or no selective pressure against them. In our hospital the drugs can only be dispensed on the advice of the Consultant Clinical Microbiologist, which advice is often based on the result of antibiotics sensitivity testing.

The control measures adopted to control the outbreak included the use of a combination of ceftazidime and amoxicillin-clavulanic acid to which the strains were found susceptible to treat the patients. Amikacin and imipenem were not used because they were unavailable at the time of the outbreak. Other measures were the disposal of all disposable items, sterilization and disinfection of all items and equipment as necessary and a review of infection control procedures including adequate and effective hand-washing by the staff, as well as a 48-hours temporary closure of the ward and fumigation. The absence of any other case nine months after the last control measures is indicative of the effectiveness of the measures. It is concluded that the outbreak and isolation of a single clone of *K. pneumoniae* with ESBL activity highlights the need for a functional infection control programme and practices with necessary policies and guidelines as well as behaviour change on the part of the staff in order to prevent or mitigate further outbreaks.

References

1. Abbot SL. Klebsiella, Enterobacter, Citrobacter, Serratia, Plesimonas and other Enterobacteriaceae. In: Murray PR, Baron EJO, Jorgensen JH, Pfaller MA, Yolken RH eds. Manual of Clinical Microbiology, Washington DC 2003: 684-700.
2. Nawshad Uddin Ahmed ASM, Azad Chowdhury MAK, Mahbul Hoque and Darmstadt GL. Clinical and Bacteriological Profile of Neonatal Septicaemia in a Tertiary level Paediatric Hospital in Bangladesh. Indian Paediatrics 2002: 39: 1034-1039.
3. Al-Rabea AA, Burwen DR, Eldeen MA, Fontaine RE, Tenover F and Jarvis WR. Klebsiella pneumoniae bloodstream infections in neonates in a hospital in the Kingdom of Saudi Arabia. Infect Control Hosp Epidemiol 1998 Sep; 19(9): 674-679.
4. Malik A, Hasani SE, Shahid M, Khan HM and Ahmad AJ. Nosocomial Klebsiella infection in neonates in a tertiary care hospital: Protein profile by SDS-page and klebocin typing as epidemiological markers. Indian J Med Microbiol 2003; 21: 82-86.

5. Gupta P, Murali P, Murali MV, *et al.* Clinical Profile of Klebsiella septicaemia in neonates. Indian J Paediatr 1993; 60: 565-572.
6. Arredondo-Garcia JL, Diaz-Ramos R, Solorzano-Santos F, Sosa-Gonzalez IE and Beltran-Zuniga M. Neonatal septicaemia due to Klebsiella pneumoniae in newborn infants. Nosocomial outbreak in an intensive care unit. Rev Latinoam Microbiol. 1992 Jan-Mar; 34(1): 11-16.
7. Podschun R and Ullmann U. Klebsiella spp. as nosocomial pathogens: epidemiology, taxonomy, typing methods and pathogenicity factors. Clin Microbiol Rev 1998; 11(4): 589-603.
8. Martinez-Aguilar G, Alpuche-Aranda CM, Anaya C, *et al.* Outbreak of nosocomial sepsis and pneumonia in a newborn intensive care unit by multiresistant extended-spectrum beta-lactamase-producing Klebsiella pneumoniae: high impact on mortality. Infect Control Hosp Epidemiol 2001 Nov; 22(11): 725-728.
9. Yunsong Yu, Weilin ZHOU, Yagang CHEN, Yongxiang DING and Yilin MA. Epidemiological and antibiotic resistant study on extended-spectrum â-lactamase-producing Escherichia coli and Klebsiella pneumoniae in Zhejiang Province. Chin Med J 2002; 115(10): 1479-1482.
10. GalesAC, Bolstrom A, Sampaio J, Jones RN and Sader HS. Antimicrobial Susceptibility of Klebsiella pneumoniae producing Extended-Spectrum beta-lactamase (ESBL) isolated in Hospitals in Brazil. Braz J Infect Dis 1997 Aug; 1(4): 196-203.
11. Del Carmen Rodriguez M, Vera DE, Ramirez-Ronda CH and Saavedra S. Phenotypic confirmation of extended-spectrum â-lactamase (ESBL) in clinical isolates of Escherichia coli and Klebsiella pneumoniae at the San Juan Veterans Affairs Medical Centre. P R Health Sci J 2004 Sep; 23(3): 207-215.
12. Su LH, Wu TL, Chiu YP, *et al.* Infection Control Group. Outbreaks of nosocomial bloodstream infections associated with multiresistant Klebsiella pneumoniae in a paediatric intensive care unit. Chang Gung Med J 2001 Feb; 24(2): 103-113
13. Kuruvilla KA, Pillai S, Jesudasan M and Jana AK. Bacterial profile of sepsis in a neonatal unit in South India. Indian J Paediatr 1998; 35: 851-858
14. Gupta A. Hospital-acquired infections in the neonatal intensive care unit- Klebsiella pneumoniae. Semin Parinatol 2002 Oct; 26(5): 340-345
15. Kim YK, Pai H, Lee HJ, *et al.* Antimicrob Agents Chemother 2002 May; 46(5): 1481-1491.
16. Misallati A, El-Bargathy S and Shembesh N. Blood-culture-proven neonatal septicaemia: a review of 36 cases. Eastern Mediterranean Health Journal 2000; 6: 483-486.
17. Shanmuganathan C, Ananthakrishnam A, Jayakeerthi SR, *et al.* Learning from an outbreak: ESBL- the essential points. Indian J Med Microbiol 2004; 22: 255-257.
18. Al-Zwaini EJ. Neonatal septicaemia in the neonatal care unit, Al-Anbar governorate, Iraq. East Mediterr Health J 2002 Jul-Sep; 8(4-5): 509-514
19. Farmer III JJ. Enterobacteriaceae: Introduction and Identification. In: Murray PR, Baron EJO, Jorgensen JH, Pfaller MA, Yolken RH eds. Manual of Clinical Microbiology, Washington DC 2003: 636-653
20. Jorgensen JH and Turnidge JD. Susceptibility Test Methods: Dilution and Disk Diffusion Methods. In: Murray PR, Baron EJO, Jorgensen JH, Pfaller MA, Yolken RH eds. Manual of Clinical Microbiology, Washington DC 2003: 1108-1127

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