

Original Research Article

***Klebsiella pneumoniae* Outbreak in Paediatric Ward: Detection and Prevention**

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A B S T R A C T

Septicemia is one of the important causes of mortality and morbidity in neonates and children. Emergence of multidrug resistant *Klebsiella pneumoniae* bacterial strains is a major problem in the management of sepsis. The study was conducted in the Department of Microbiology, JNMCH, AMU, Aligarh from June 2104 to September 2014. to describe an outbreak of multidrug resistant *Klebsiella pneumoniae* in Neonatal ward and the strategies to barge in the same. Blood for culture was collected from patients taking all sterile precautions. Survey of environmental samples was also conducted in HDU. Cultures showing growth of *Klebsiella pneumoniae* were identified using standard biochemical procedures. Antimicrobial susceptibility testing was done on Mueller Hinton's agar by Kirby Bauer Disc diffusion method as per the CLSI guidelines. Detection of ESBL and Amp C production was done. A total of 90 isolates were identified as *Klebsiella pneumoniae*. Majority of the isolates were multidrug resistant, 17 (18.8%) were ESBL producers and 59 (65.5%) were Amp C positive. One isolate (1.1%) was MBL producer. Multidrug resistant strains of *Klebsiella* species were obtained from HDU samples. *Klebsiella pneumoniae* solates from the hospital environment had antibiogram similar to the patient samples. All the isolates from the environmental samples were found to be multidrug resistant and amp C positive. *Klebsiella pneumoniae* is an important cause of neonatal sepsis and cross transmission can occur from the hospital environment. Following proper infection control measures, segregation of waste and proper disinfection and cleaning of the hospital wards can help barge such infections.

Keywords

Klebsiella;
bacterimia;
NICU;
antimicrobial
resistance

Introduction

Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30-50% of total neonatal deaths each year in developing countries. It is estimated that 20% of all neonates develop sepsis and approximately 1% die of sepsis related causes (Bhattacharjee *et al.*, 2008).

Klebsiella pneumoniae has been identified as one of the most frequent causes of outbreaks reported in neonatal intensive care units (NICUs) (Skogberg *et al.*, 2008). It can easily survive in hospitals, reproduce on environmental surfaces and colonize the human skin, bowels, bladder and respiratory

tract (Struve and Krogfelt, 2004; Macrae *et al.*, 2001). Once introduced these infections are very difficult to treat due to the high level of drug resistance particularly the strains producing extended spectrum β -lactamases ESBL and AmpC (Paterson *et al.*, 2003).

As evident from various studies, *Klebsiella pneumoniae* account for nearly 50% outbreaks in NICUs but there are also evidences that these can be controlled by applying a mix of different infection control measures (Gastmeier *et al.*, 2003). More recently the importance of correct antibiotics policies, less use of invasive procedures, hand disinfection/hand washing before and after patient management and isolation precautions have been underlined by several authors (Gill *et al.*, 2009). This study was done to describe an outbreak of multidrug resistant *Klebsiella pneumoniae* in Neonatal ward and the strategies to barge in the same.

Material and Methods

Study group: The study was conducted in the Department of Microbiology, JNMCH, AMU, Aligarh from June 2104 to September 2014. Samples were received for blood culture in brain heart infusion broth. Repeated subcultures were done on 5% sheep Blood agar and Mac-Conkeys agar after 24 hours, 48 hours and 7 days of incubation at 37°C. Cultures showing growth were identified by standard biochemical procedures (Collee *et al.*, 2006).

Cultures showing growth of *Klebsiella pneumoniae* from blood (collected after 48 hours of hospital admission) with signs and symptoms of BSI (fever > 38°C) were included in the study.

Antimicrobial susceptibility testing: Antimicrobial susceptibility testing was

done on Mueller Hinton's agar by Kirby Bauer Disc diffusion method as per the Clinical and Laboratory Standards Institute guidelines (CLSI, 2014) for the following antimicrobials -amikacin (30 μ g), gentamycin (10 μ g), cefoperazone (75 μ g) ceftriaxone+sulbactam (25 μ g/75 μ g), cefoperazone+sulbactam (75 μ g/75 μ g), levofloxacin(5 μ g), piperacillin+tazobactam (100 μ g /10 μ g) and imipinem (10 μ g).

Detection of extended spectrum beta lactamases: Screening of possible ESBL production was done by using ceftriaxone (30 μ g) and cefoperazone (75 μ g). Those isolates with zone diameters less than 25mm for ceftriaxone and less than 22mm for cefoperazone were subsequently confirmed for ESBL production. Confirmation was done by noting the potentiation of the activity of cefoperazone in the presence of cefoperazone sulbactam (Rizvi *et al.*, 2009).

Detection of inducible and derepressed AmpC beta lactamase: Detection of AmpC betalactamase was done on isolates resistant to ceftriaxone (30 μ g), cefixime (15 μ g), cefoperazone (75 μ g) and cefoperazone sulbactam (75/75 μ g). Induction of AmpC synthesis was based on the disc approximation assay using imipenem as inducer (Rizvi *et al.*, 2009).

Detection of metallobeta-lactamases: Detection of MBL was done by Hodge test and Double Disc synergy test using EDTA. The method was as described by Lee *et al.* (2001).

Environmental survey: Environmental samples were taken from various sites including bed, drug table, laryngoscope, air conditioner and monitor in the HDU. Samples were inoculated on 5% sheep blood agar and tee-pol lactose agar. Antimicrobial susceptibility testing was done by Kirby bauer disc diffusion method on Mueller

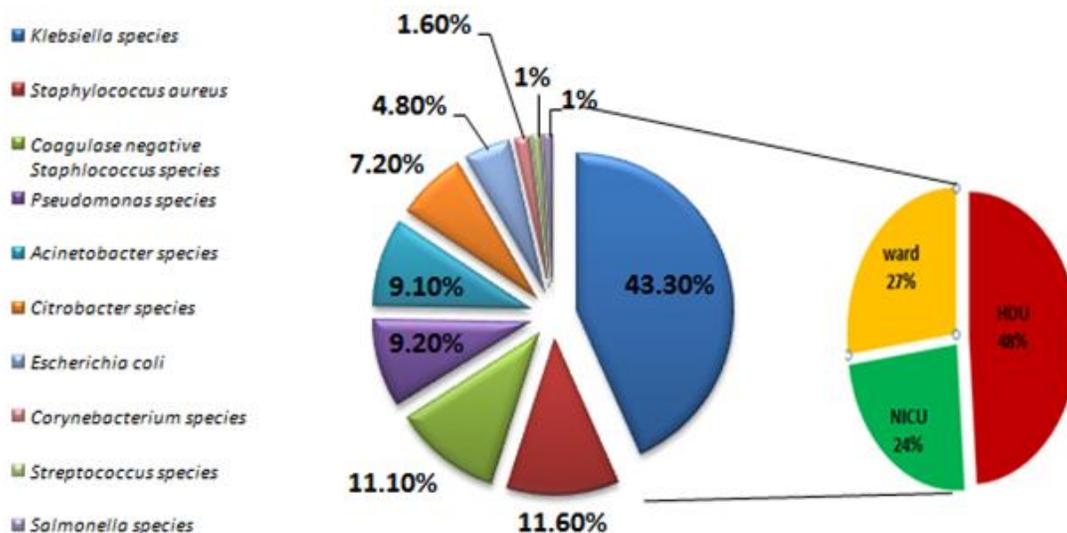
Hinton Agar as per the CLSI guidelines. The antibiograms were compared to the patient isolates and intensive measures were taken to implement the infection control procedures and proper cleaning and disinfection of the ward.

Results and Discussion

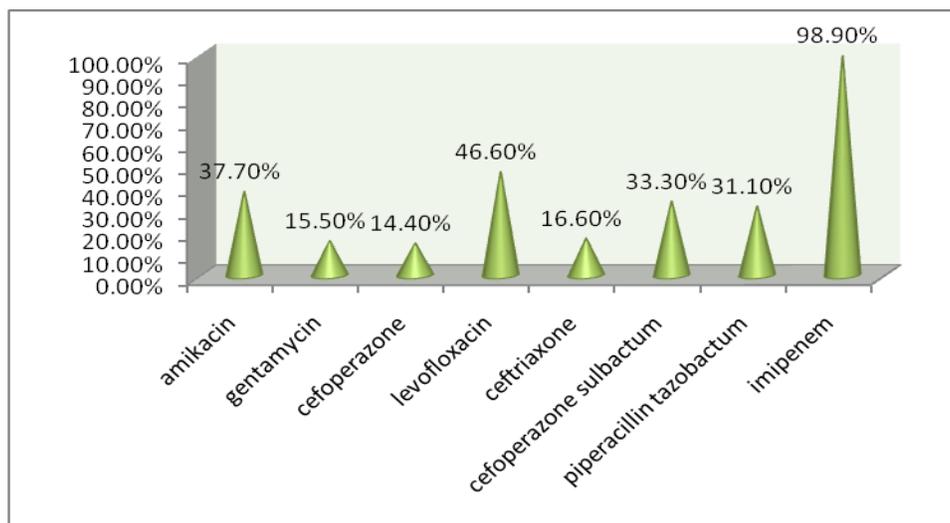
Over a period of four months a total of 90 (43.3% of all isolates) *Klebsiella pneumoniae* strains were isolated from blood culture of patients admitted in paediatric ward (Graph 1). The other pathogens isolated during this period were *Staphylococcus aureus* (24, 11.6%), Coagulase negative *Staphylococcus* species (23, 11.1%) and *Pseudomonas* species (19, 9.2%), *Acinetobacter* species (19, 9.1%), *Citrobacter* species (15, 7.2%), *Escherichia*

coli (10, 4.8%), *Streptococcus* species (2, 1%), *Salmonella typhi* (2, 1%) & *Coryneform* species (3, 1.6%). Out of the 90 *Klebsiella pneumoniae* isolates 43 (47.7%) were from the patients admitted in high dependency unit (HDU), 21 (23.3%) from the neonatal ICU & the remaining 24 (26.6%) from the paediatric ward. On antimicrobial sensitivity testing of the *Klebsiella pneumoniae* isolates were sensitive to amikacin (37.7%), gentamycin (15.5%), cefoperazone (14.4%) ceftriaxone (16.6%) cefoperazone+sulbactam (33.3%) , levofloxacin (46.6%), piperacillin+tazobactam (31.1%) and imipinem (98.9%) (Graph 2). Forty isolates (45.5%) isolates were multidrug resistant, 17 (18.8%) were ESBL producers and 59 (65.5%) were Amp C positive. One isolate (1.1%) was MBL producer.

Graph.1 Bacteria isolated from blood culture of paediatric patients and distribution of *Klebsiella pneumoniae* in various wards



Graph.2 Antimicrobial susceptibility profile of *Klebsiella pneumoniae* isolates from blood culture



Amongst the specimens drawn from the environment, *Klebsiella pneumoniae* was the most frequent isolate (7 out of 16 isolates, 43.7%) (Table 1). The other bacteria isolated included *Staphylococcus aureus*, *Coagulase negative Staphylococci*, *Citrobacter* species and *Escherichia coli*. On antimicrobial susceptibility testing of the *Klebsiella pneumoniae* isolates from the environment samples it was noted that they were resistant to all the antimicrobials tested except imipenem. All these strains were found to be amp C positive.

Multidrug resistant gram-negative bacilli are frequently associated with infections in the patients admitted to intensive care units of hospitals. *Klebsiella pneumoniae* has been identified as one of the most frequent causes of outbreaks reported in neonatal intensive care units (NICUs) (Viswanathan *et al.*, 2011; Rastogi *et al.*, 2010). In our study, we noted a sudden rise in the *Klebsiella pneumoniae* (n=90, 43.3%) isolates from blood culture of patients admitted in paediatric ward. *Klebsiella* is a known cause of sepsis and had been reported in other

studies as the commonest blood culture isolates (Shah and Desai, 2012).

The isolates in our study were mainly from high dependency unit (HDU). This may be due to the fact that *Klebsiella* affects immunocompromised subjects as an opportunistic pathogen, and newborns are more prone to the risk of infection due to their immature immune systems, their low weight at birth, and the frequent use of invasive devices and antibiotics (Ruiz *et al.*, 2010) and the patients in HDU are high risk with severe illness, many times on multiple antibiotics.

On antimicrobial susceptibility testing of the *Klebsiella pneumoniae* for different group of drugs it was noted that amongst the various antimicrobial group tested (aminoglycosides, cephalosporins, flouroquinolones) except the carbapenems showed sensitivity below 50%. Out of the 90 isolates tested Forty 45.5% were multidrug resistant, 17 (18.8%) were ESBL producers and 59 (65.5%) were Amp C positive.

Table.1 Pathogens isolated from the environmental cultures of HDU and their antimicrobial susceptibility pattern

S.No.	Site	Organism isolated	Susceptibility profile												
			Amikacin	Gentamycin	Cefoperazone	Cefoperazone+sulbactam	Ceftriaxone+sulbactam	Levofloxacin	Piperacillin+tazobactam	Imipinem	Oxacillin	Azithromycin	Clindamycin	Vancomycin	Cotrimoxazole
1	Air	<i>S aureus</i>	S	S	-	-	-	S	-	-	S	S	S	S	S
		<i>CONS</i>	S	S	-	-	-	S	-	-	S	S	S	S	S
2	Air Conditioner	<i>S aureus</i>	S	R	-	-	-	R	-	-	R	S	S	S	S
		<i>CONS</i>	S	S	-	-	-	S	-	-	S	S	S	S	S
		<i>Klebsiella Sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
3	Monitor	<i>E coli</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
4	Bed	<i>Klebsiella sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
5	Laryngoscope surface	<i>Klebsiella sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
6	Table	<i>Klebsiella sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
		<i>Citrobacter sp.</i>	R	R	R	R	R	R	S	S	-	-	-	-	-
7	Door Handle	<i>Klebsiella sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
		<i>S aureus</i>	S	R	-	-	-	S	-	-	R	S	S	S	S
8	Table 2	<i>Klebsiella sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-
9	Monitor 2	<i>Citrobacter sp.</i>	R	R	R	S	R	R	S	S	-	-	-	-	-
10	Table 3	<i>Citrobacter sp.</i>	R	S	R	S	R	R	S	S	-	-	-	-	-
		<i>Klebsiella sp.</i>	R	R	R	R	R	R	R	S	-	-	-	-	-

One isolate (1.1%) was MBL producer. Imipenem was the only antimicrobial tested to which majority of the isolates were sensitive. The high rate of antimicrobial resistance in our study may be because of the fact that we are a tertiary referral centre, where majority of patient come after already taking treatment from quacks or other non-professional doctors. Study from a tertiary care hospital from Gujarat had reported uniform susceptibility to imipenem, although they reported a high rate of ESBL (75.9%) but less amp C (7.54%) (Modi *et al.*, 2012).

In view of the outbreak of multidrug resistant *K. pneumoniae* in HDU, environmental surveillance was done from various sites like bed, table, laryngoscope, door handle and monitor of HDU. All the strains of *K. pneumoniae* isolated had antibiogram similar to the patient strains. All were AmpC producing and were resistant to all the drugs tested except imipenem. Our set up is a tertiary referral teaching centre with high patient load, entry of medical students in hospital wards for teaching purposes and interchange of duties among the paramedical staff which leads to breach in infection control practices. After this episode, reinforcement for following proper infection control measures was done with stress on simple measures such as hand disinfection/hand washing before and after patient management, isolation precautions, less use of invasive procedures, set-up of a dedicated tray with daily-use medical and hygienic instruments (stethoscope, thermometer, diapers, gauzes, ointments), correct reprocessing of multi-use semi-critical medical devices, implementation of a pathway dedicated to hygienic manoeuvres and waste disposal from infected infants. Repeat screening was done. Results of repeat screening of potential environmental

sources were negative. Implementation of infection control measures further lead to the cessation of outbreak of *K. pneumoniae*.

In conclusion, our study highlights that a sudden increase in the isolation of multidrug resistant pathogens should be taken as a challenge and prompt action should be taken. There is an urgent need for early detection of these isolates for better treatment outcomes. Routine environmental surveillance although not recommended routinely, plays a vital role in identifying the source of outbreak and in motivating the healthcare workers for following the infection control measures.

References

- Bhattacharjee, A., Sen, M.R., Prakash, P., Gaur, A., Anupurba, S. 2008. Increased prevalence of extended spectrum β -lactamase producers in neonatal septicaemic cases at a tertiary referral hospital. *IJMM.*, 26(4): 356–60.
- Clinical and Laboratory Standards Institute, 2014. Performance standards for antimicrobial susceptibility testing: Twenty fourth informational supplement: Approved standards M100-S24. Clinical and Laboratory Standards Institute, Baltimore, USA.
- Collee, J.G., Fraser, A.G., Marmion, B.P., Simmons, Mackey, A. 2006. McCartney practical medical microbiology. In: Collee, J.G., Miles, R.S., Watt, B., (Eds). Tests for the identification of Bacteria, 14th edn. Elsevier, New Delhi, India. Pp. 131–49.
- Gastmeier, P., Groneberg, K., Weist, K., Ruden, H. 2003. A cluster of nosocomial *Klebsiella pneumoniae* bloodstream infections in a neonatal intensive care department: Identification of transmission and

- intervention. *Am. J. Infect. Control.*, 31: 424–430.
- Gill, C.J., Mantaring, J.B., Macleod, W.B., Mendoza, M., Mendoza, S., Huskins, W.C., Goldmann, D.A., Hamer, D.H. 2009. Impact of enhanced infection control at 2 neonatal intensive care units in the Philippines. *Clin. Infect. Dis.*, 48: 13–21.
- Lee, K.Y., Chong, H.B., Shin, Y.A., Yong, K.D., Yum, J.H. 2001. Modified Hodge test and EDTA disc synergy tests to screen metallo beta lactamase producing strains of *Pseudomonas* and *Acinetobacter* species. *Clin. Microbiol. Infect.*, 7: 88–91.
- Macrae, M.B., Shannon, K.P., Rayner, D.M., Kaiser, A.M., Hoffman, P.N., French, G.L. 2001. A Simultaneous outbreak on a neonatal unit of two strains of multiply antibiotic resistant *Klebsiella pneumoniae* controllable only by ward closure. *J. Hosp. Infect.*, 49: 183–192.
- Modi, D.J., Patel, B.V., Patel, M.H., Bhatt, S.S., Sood, N.K., Vegad, M.M. 2012. A Study of Extended Spectrum β -Lactamase (ESBL) and AmpC β -Lactamase Producing *Klebsiella Pneumoniae* in Neonatal Intensive Care Unit at Tertiary Care Hospital, Ahmedabad. *Natl. J. Commun. Med.*, 3(3): 523–8.
- Paterson, D.L., Hujer, K.M., Hujer, A.M. 2003. Extended-spectrum betalactamases in *Klebsiella* bloodstream isolates from seven countries: dominance and widespread prevalence of SHV- and CTXM-type beta-lactamases. *Antimicrob. Agents Chemother.*, 47: 3554–3560.
- Rastogi, V., Nirwan, P.S., Jain, S., Kapil, A. 2010. Nosocomial outbreak of septicaemia in neonatal intensive care unit due to extended spectrum β -lactamase producing *Klebsiella pneumoniae* showing multiple mechanisms of drug resistance. *Indian J. Med. Microbiol.*, 28: 380–384.
- Rizvi, M., Fatima, N., Rashid, M. 2009. Extended spectrum AmpC and metallo-beta-lactamases in *Serratia* and *Citrobacter* spp. in a disc approximation assay. *J. Infect. Dev. Ctries.*, 3(4):285-94.
- Ruiz, E., Rojo-Bezares, B., Sáenz, Y., Olarte, I., Esteban, I., Rocha-Gracia, R., Zarazaga, M., Torres, C. 2010. Outbreak caused by a multi-resistant *Klebsiella* strain of new sequence type ST341 carrying new genetic environments of aac(6₋)-Ib-cr and qnrS1 genes in a neonatal intensive care unit in Spain. *Int. J. Med. Microbiol.*, 300: 464–469.
- Shah, M.N., Desai, P.B. 2012. Emergence of multi-drug-resistant *Klebsiella* in Neonatal Intensive Care Units: concern about antimicrobial policies. *Res. J. Recent Sci.*, 1: 275–280.
- Skogberg, K., Lyytikäinen, O., Ruutu, P. 2008. Increase in bloodstream infections in Finland, 1995–2002. *Epidemiol. Infect.*, 136: 108–114.
- Struve, C., Krogfelt, K.A. 2004. Pathogenic potential of environmental *Klebsiella pneumoniae* isolates. *Environ. Microbiol.*, 6: 584–590.
- Viswanathan, R., Singh, A.K., Mukherjee, S., Mukherjee, R., Das, P., Basu, S. 2011. An outbreak of neonatal sepsis presenting with exanthematous rash caused by *Klebsiella*. *Epidemiol. Infect.*, 139: 226–228.