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Outbreak of Neonatal Septicemia by *Klebsiella* Species in NICU

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Klebsiella **species is an important pathogen responsible for various hospital-acquired infections. They are isolated from various sites in the hospital or from the health care workers. These hospital strains can be resistant to various antibiotics. They are also known to cause neonatal septicemia. A sudden increase in *Klebsiella* isolates from NICU prompted this study. Retrospective and prospective data were analyzed from the months of September 2013 to March 2014 i.e., before and after the outbreak. During that period a total of 249 blood culture samples from NICU were collected for analysis. Culture and sensitivity was performed for the isolates. Samples were also collected from the environment, water and health care personnel to identify the source.Out of the 249 blood samples 35 (14%) yielded bacterial growth on primary & secondary sub culture. The remaining 100 (86%) yielded no growth. *Klebsiella* species accounted for 29% , Coagulase Negative Staphylococci (CONS) for 37% , Enterococci 11 %, along with these various other bacteria were also isolated. Many of the *Klebsiella* strains were ESBL producers, and a clustering of cases was seen in the months of December 2013 and January 2014. *Klebsiella* was also isolated from the water sample used for humidification. The present study emphasizes the importance of good infection control practices and rationale use of antibiotics especially in high risk settings like the NICU.**

Key words: Late onset neonatal septicemia, hospital acquired infection, *Klebsiella* spp., ESBL producers.

Klebsiella is an important pathogen responsible for late onset neonatal sepsis among hospital born neonates[1]. It is a capsulated Gram negative bacterium which is prone to develop resistance, especially in the hospital environment. Due to selection pressure *Klebsiella* strains quickly acquire genes for ESBL production. Rampant use of third- generation cephalosporins is associated with the selection of the resistant mutants[2] Pre-term neonates with low birth-weight are especially prone for these pathogens. Initially they colonize the gut later they establish infection[3]. These bacteria easily thrive in moist environments & ground water and have access to these neonates via aerosols and droplet nuclei which are produced during various procedures like ventilation, suctioning, bathing and humidification. They also enter the blood stream directly via the peripheral and central line catheters through the skin or environmental surfaces. Prompt environmental cleaning and partaking in good ventilation care bundles help reduce the burden of infection in such critical care settings.

Ours is a tertiary care hospital with a well equipped laboratory, labor room & NICU. This investigation was prompted following a sudden and unusual clustering of *Klebsiella* septicemia cases from the months of December 2013 & January 2014 among pre- term neonates

MATERIALS AND METHODS

Following a sudden increase in the isolation of *Klebsiella* species from neonatal blood cultures, a prompt investigation was undertaken to identify the source of infection and to contain it. Retrospective and prospective data were

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analyzed from the months of September 2013 to March 2014 i.e., before and after the outbreak. During that period a total of 249 blood culture samples from NICU were sent for analysis. The blood samples were collected with all aseptic precautions in Brain Heart Infusion (BHI) broth following which primary, secondary & tertiary subculture were done on 48 hrs, 72 hrs & 96 hrs respectively on blood & Mac Conkey agar. Growth was identified by standard laboratory methods and antibiotic susceptibility testing was done by Kirby Bauer's disc diffusion techniques according to the latest Clinical Laboratory Standards Institute (CLSI) guidelines and interpreted. Extended Spectrum Beta Lactamase (ESBL) detection was done using Ceftazidime & Ceftazidime + Clavulanic acid disc method. The various other parameters like the birth weight, CRP levels, place & mode of delivery along with the gestational age was analyzed.

Table 1. Distribution of positive blood culture isolates

Positive Blood Culture (35)	Isolates	No	%
Fungal growth(2)	Candida	2	6
Bacterial growth (33)	Klebsiella*	10	29
	CONS	13	37
	Pseudomonas	3	9
	Enterococci	4	11
	Acinetobacter	2	6
	S. aureus	1	3
Total (35)		35	

* Out of ten Klebsiella isolates six were ESBL producing strains

To trace the source of infection active surveillance was done and samples were collected from the skin of health care personnel, various environmental surfaces, tap water, stored RO water, RO water plant and disinfectants.

RESULTS

Out of the 249 blood samples 35 (14%) yielded bacterial growth on primary & secondary sub culture. The remaining 100 (86%) yielded no growth.

Of the bacterial isolates *Klebsiella* species accounted for 29% (10/35), Coagulase Negative Staphylococci (CONS) for 37% (13/35), Enterococci 11 %(4/35), Pseudomonas 9%(3/35) Acinetobacter 6%(2/35)& one case of Methicillin resistant Staphylococcus aureus (MRSA) 3%. Among the ten *Klebsiella* strains six were ESBL producing strains, having similar antibiotic sensitivity pattern.

A sudden appearance and peaking of *Klebsiella* spp. was noted during the months of December 2013 and January 2014 with only one case in February 2014. The CRP levels were elevated for all the neonates from whom *Klebsiella* was isolated in December 2013 and January 2014. Four of neonates with CONS had raised CRP values and the remaining had normal CRP values.

Of the ten *Klebsiella* positive neonates, eight were delivered in our hospital and the other two were outside deliveries. The ten neonates were preterm and underweight except for two with normal weight. C -reactive protein level was elevated in nine out of ten neonates. No definite

Table 2. Month-wise distribution of positive isolates

Month	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Total	Normal CRP	Increased CRP
POS B/C	3	4	3	12	5	5	3	35	18	17
Klebsiella	0	0	0	5	3	2	0	10(6 ESBL4 non ESBL)	1	9
Acinetobacter	1	0	0	0	0	1	0	2	2	0
Pseudomonas	1	0	1	1	0	0	0	3	2	1
S. aureus	0	0	0	0	0	0	1	1(MRSA)	1	0
CONS	1	2	0	5	2	1	2	13	8	5
Enterococci	0	2	1	0	0	1	0	4	4	0
Candida	0	0	1	1	0	0	0	2	2	0

maternal risk factors could be identified.

Klebsiella species was also isolated from the tap water, stored reverse osmosis (RO) water & environmental surfaces. The water from the RO plant had no growth. Hence the source was identified to be the stored RO water in cans, which was used for humidification of oxygen. The reusable cans which were used to store RO water after cleaning with disinfectants were rinsed with the tap water, which contaminated the RO water and acted as a source of infection. Once identified this was immediately rectified. Strict environmental cleaning was done which in turn reduced the number of cases by February 2014.

DISCUSSION

Hospital acquired infection contributes significantly on morbidity, mortality and increased health care costs. *Klebsiella* is an important bacterium which easily acquires drug resistance especially to various penicillins, cephalosporins and aminoglycosides. ESBL was first isolated in *Klebsiella* species[2,4]. The prevalence of ESBL in India varies from 6-87%[5]. In such a scenario the only treatment option remaining would be the carbapenems[1]. Non fermentor bacteria like Acinetobacter and some members of

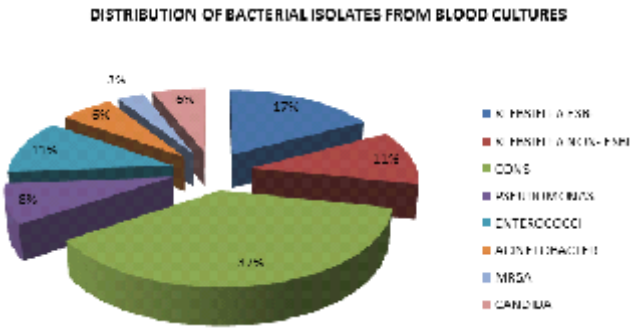

Fig. 1. Distribution of Bacterial isolates from blood cultures

Table 3. Antibiogram of Klebsiella isolates

Sample	1	2	3	4	5	6	7	8	9	10	Tap water	Stored RO Water	Environmental sample
Imipenem	R	S	R	S	S	S	S	S	S	S	S		S
Meropenem	R	R	R	S	S	S	S	S	R	S	S		S
Ciprofloxacin	R	R	R	S	S	S	S	S	R	S	S		S
Levofloxacin	R	R	R	S	S	S	S	S	R	S	S		S
Amikacin	S	S	S	S	S	S	S	S	S	S	S		S
Tigecycline	S	S	S	S	S	S	S	S	S	S	S		S
Cotrimoxazole	S	R	S	R	R	R	R	R	R	R	R		R
Ceftazidime	R	R	R	R	R	R	R	R	R	R	R		R
Cefipime	R	R	R	R	R	R	R	R	R	R	R		R
Cefixime	R	R	R	R	R	R	R	R	R	R	R		R
Cefoxitin	R	R	R	S	S	S	S	S	R	S	S		S
CeftazidimeClavulanic acid	R	R	R	S	S	S	S	S	R	S	S		S
Amoxycillin clavulanic acid	R	R	R	R	R	R	R	R	R	R	R		R
Cefazolin	R	R	R	R	R	R	R	R	R	R	R		R
Ceftriaxone	R	R	R	R	R	R	R	R	R	R	R		R
				*	*	*	*	*		*	*		*
B.wt (kg)	3.5	1.2	1.4	1.1	2	1.2	2	2	3	2	2		
CRP	12.5	23.6	38	9.3	18	11.8	45	25	31	30.5	2.9		

Enterobacteriaceaea are also developing resistance to these drugs[6]. That would mean that we are progressing to the pre-antibiotic era very soon with very few drugs remaining in our armamentarium. The only means to prevent this would be the judicious use of antibiotics both in the hospital & community setting and strict adherence to infection control practices. It is the need of the hour to develop national and local antibiotic policies. ICU are places where immunocompromised patients are exposed to various antibiotics for long duration of time. This selects the various commensal bacteria to develop resistance[7]. It is not rare to isolate bacteria from the environment which are multi drug resistant as we have isolated ESBL producing *Klebsiella* from the tap water.

The most important bacteria to cause neonatal sepsis in India are K. pneumonia and *E.coli*[1].Other bacteria responsible are Group B *Streptococci, S. aureus*, CONS, Enterococci, *Listeria* etc[8,9]. Late onset sepsis is development of septicemia after 72 hours of life and the most common bacteria responsible is K. pneumonia. About 4% of neonates develop late onset sepsis with *Klebsiella*[6]. Mode of acquiring the pathogen is from the external environment, as is seen in our study[3].These bacteria contaminate the inanimate patient care surfaces as well as the hand of health care workers. One study has reported the use of artificial nails to out-break of *Klebsiella* pneumonia in the NICU[10]. In our study the source of infection was the contamination of stored RO water with tap water. All these highlight the importance of simple but effective techniques like hand hygiene and common sense.

These neonates developing neonatal septicemia usually have low birth weight as seen in our study[3]. Other factors like delay in feeds (breast milk), premature rupture of membrane (PROM), maternal factors, mechanical ventilation and various invasive procedures may all contribute to the development of septicemia. The mortality (7-55%) and morbidity with *Klebsiella* septicemia is very high, which contributes to increased hospital stay and costs[11].

The old adage, prevention is always better than cure cannot be overemphasized. Infection control practices like hand hygiene, environmental cleaning with standard products at correct dilution, continued health education, use of personal protection equipment whenever necessary go a long way in reducing the rate of infection[2]. In the event of outbreak prompt isolation of index case & following of transmission based precautions with environment sampling help in identifying and limiting the source of infection. Restriction in the use of antibiotics, with formulation of antibiotic policy help in reducing the selective pressure needed for the development of resistant bacteria.

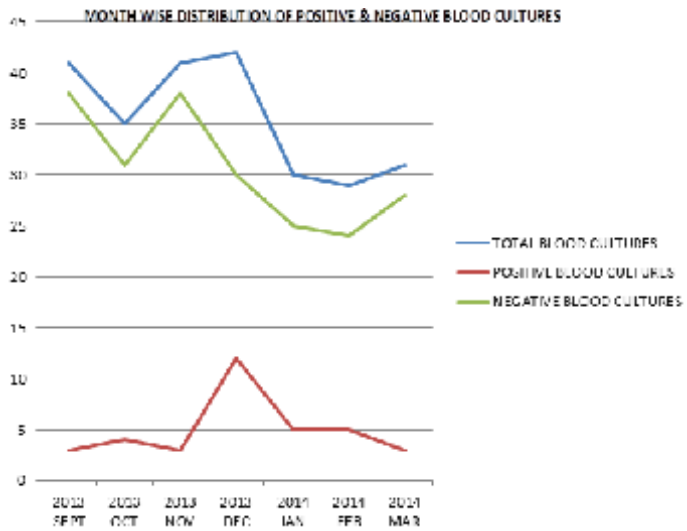

Fig. 2. Month wise distribution of positive & negative blood cultures

Key note

Health education of health care workers at all levels

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