Analysis of two different outbreaks in PICU of a tertiary care centre in two different time zones

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ABSTRACT

Klebsiella pneumoniae is one of the common cause of nosocomial outbreak. With the emergence of multi-drug resistance, clinical management has become a serious challenge. The present study is a comparative analysis of changing trends of antimicrobial resistance (AMR) between two outbreaks of *Klebsiella pneumoniae* in PICU occurring over a gap of 8 years.

Materials & Methods: 1054 Blood culture samples received from paediatric patients over a period of 6 months were tested by BacT/Alert-3D & VITEK-2 system. Survey of environmental samples was also conducted in Paediatric ICU. All the findings were then analysed with the data from another outbreak of MDR *Klebsiella pneumoniae* in PICU reported from the same institute in the year 2015.

Result: From 154 (14.6%) positive paediatric blood samples, Gram-negative bacilli was most commonly isolated (75/154, 48.7%), followed by Gram-positive cocci (53, 34.4%). Amongst gram-negative isolates *Klebsiella pneumoniae* was commonest (40/75, 53.3%), followed by *Pseudomonas* speices (17.3%), *Escherichia coli* (16%), *Burkholderia cepacia*-complex (6.7%), and *Acinetobacter baumanii*-complex (4%). Out of 40 *Klebsiella pneumoniae,* 90% were extensively-drug resistant (XDR), i.e resistant to cephalosporins, carbapenems, aminoglycosides, fluoroquinolone, Co-trimaxazole as well as Tigecyclin. 45% of these patients were admitted in the PICU. However, previous outbreak reported 90 *Klebsiella pneumoniae* (43.3% of all isolates) over a period of 4 month, out of which 45.5% were MDR & 18.8% were ESBL producers. However,

Carbapenems were effective in majority of them (98.9%), which is a contrast to our present finding (97.5% resistance). Moreover, multiple MDR strains of *Klebsiella* species (7/16 isolates, 43.7%) were obtained from PICU samples in previous outbreak, with antibiogram similar to that of patient samples. Similarly PICU sampling in the current outbreak also yielded XDR *Klebsiella pneumoniae* from medicine table, with similar profile that is seen in patients sample.

Conclusion: On analysis of two outbreaks from same hospital in two different time zones, we observed changing trend in resistance pattern, as Carbapenems were effective in previously isolated MDR strains, but now XDR stains are isolated which are resistant to carbapenems as well. Urgent and effective measures are needed to restrain emergence and transmission of XDR strains within the hospital. Stringent infection control practices should be advocated and strictly followed.

KEYWORDS: Outbreak, Klebsiella pneumoniae, PICU, MDR, XDR

Introduction

Bloodstream infections (BSI) are common cause of febrile illness and is associated with high morbidity and mortality worldwide. The bacterial pathogen *Klebsiella pneumoniae* is a major cause of nosocomial infections, especially in immunocompromised individuals (1). Increasing antimicrobial resistance among these notorious bacteria, particularly with emergence of carbapenem resistance seen in recent years (2), and their worldwide dissemination (3), possess serious threat to public health worldwide. Because infections caused by these Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) are difficult to treat (4), and are associated with high mortality (5). CRKP strains produces a variety of Cabapenamases enzymes and/or Extended-spectrum Beta-lactamases (ESBLs) along with porin loss and efflux pump overexpression, leading to emergence of multi-drug resistant (MDR), extensively-drug resistant (XDR) and pan-drug resistant (PDR) bacteria. (6)

Another aggravating factor is the tendency of *Klebsiella pneumoniae* to cause outbreaks in healthcare facilities, particularly in ICUs (7–9). Moreover, *Klebsiella pneumoniae* has propensity to silently colonize patients and hospital personnel, without causing any sign of infections. These carriers function as reservoirs and help in its dissemination, making control of outbreak a difficult challenge (9). Furthermore, because of extensive use of antibiotics in hospital setting, multiple

drug resistance have selective advantage in perseverance of such nosocomial bacteria in hospitalised patients as well as in hospital environment (7).

To apply productive infection control measures, it is crucial to know relevant environmental contamination and in-hospital transmission routes. Therefore the present study was done to describe changing pattern of antimicrobial resistance (AMR) between two outbreaks of *Klebsiella pneumoniae* associated with bacteriemia in paediatric patients reported from the same institute occurring over a gap of 8 years (10).

Materials & Methods:

The study was conducted in a tertiary care centre in two different time zone. Present data was taken from July 2022 to December 2022. Blood samples for culture were collected from paediatric patients taking all sterile precautions. Blood culture positive samples identified by BacT/ALERT 3D (bioMérieux) automated system were plated on 5% sheep Blood agar, MacConkey agar and Chocolate agar. Bacterial identification as well as antimicrobial sensitivity of positive growth was done by VITEK-2 (bioMérieux) automated system.

Survey of environmental samples was also conducted in Paediatric ICU. Environmental samples were taken from various sites including patient bed, door handle, medicine table, medicine basket, Ventilator knob, suction pipe, warmer and disinfectant bottle. Air culture was done by settle plate method. Samples were inoculated on brain heart infusion broth, from which subculture was done next day on 5% sheep blood agar and MacConkey agar. Bacterial identification was done by conventional methods and confirmed by VITEK-2.

All the findings of present outbreak was then compared & analysed with another outbreak of MDR *Klebsiella pneumoniae* reported in paediatric blood culture isolates from the same institute 8 years back in the year 2015. (10)

Result & Discussion:

A total of 1834 blood samples were received in the enteric lab over the period of 6 months, out of which 1054 (57.5%) were from paediatric patients. Out of these 1054 paediatric blood samples,

154 (14.6%) were identified positive. Gram negative bacilli was most commonly isolated (75/154, 48.7%), followed by Gram positive cocci (53, 34.4%), then yeast like fungi (24, 16.9%). Amongst gram negative bacilli, maximum isolates were of *Klebsiella pneumoniae* (40/75, 53.3%), followed by *Pseudomonas* speices (13/75, 17.3%), *Escherichia coli* (12, 16%), *Burkholderia cepacian* complex (5, 6.7%), *Acinetobacter baumanii* complex (3, 4%), *Citrobacter* species (1, 1.3%), and *Enterobacter cloacae* complex (1, 1.3%) as depicted in Figure1.

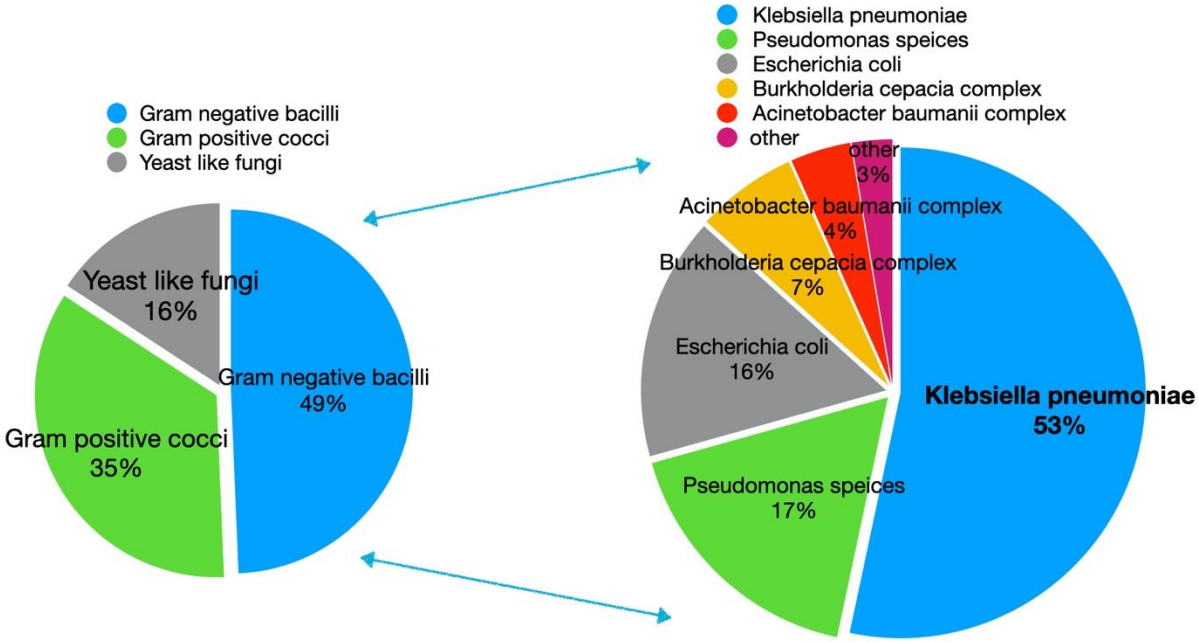

Figure1

Out of 40 paediatric samples from which *Klebsiella* was isolated 27 (67.5%) were of infants, which includes 17 neonates (42.5%). 45% of these patients were admitted in the PICU, and 36.8% of patients were intubated and were on mechanical ventilation.

Antimicrobial susceptibility profile by VITEK-2 system showed 97.5% (n=39) of total 40 *Klebsiella pneumoniae* were resistant to beta lactams antibiotics (namely Ampicillin, Amoxicillin/clavulanic acid, Piperacillin/Tazobactum, Cefuroxime, Ceftriaxone,

Cefoperazone/Sulbactum, Cefepime, Ertapenem, Imipenem, Meropenem), Tigecyclin, as well as aminoglycosides (Amikacin & Gentamicin). Ciprofloxacin resistance was seen in 95% (n=38), and Co-trimaxazole resistance in 90% (n=36). Thus, 90% of the strains were Extensively drug resistant (XDR), which is defined as non-susceptible to at least one agent in all but two or fewer antimicrobial categories (6).

Another outbreak of MDR *Klebsiella pneumoniae* was reported 8 years back in the year 2015 in paediatric blood culture isolates from the same institute (10). In the previous outbreak 90 *Klebsiella pneumoniae* (43.3% of all isolates) were isolated over a period of 4 month. Out of which 71.1% were from PICU. Antimicrobial susceptibility testing showed resistance rates of 62.3% to amikacin, 84.5% to gentamycin, 83.4% to ceftriaxone, 85.6% to cefoperazone, 66.7% to cefoperazone+sulbactum, 68.9% to piperacillin+tazobactum and 53.4% to levofloxacin (10). 45.5% were reported as MDR. Fortunately, Imipinem was resistant in only 1.1% isolates, which is contrast to our present study, where carbapenems are resistant in 97.5% of Klebsiella isolates. Figure 2 depicts increasing trend of resistance pattern from 2015 outbreak to the present outbreak, especially to Carbapenems. Alarming rise in resistance rates of Carbapenems seen over 8 years, is a cause of concern as this leaves us with only few available treatment options (11).

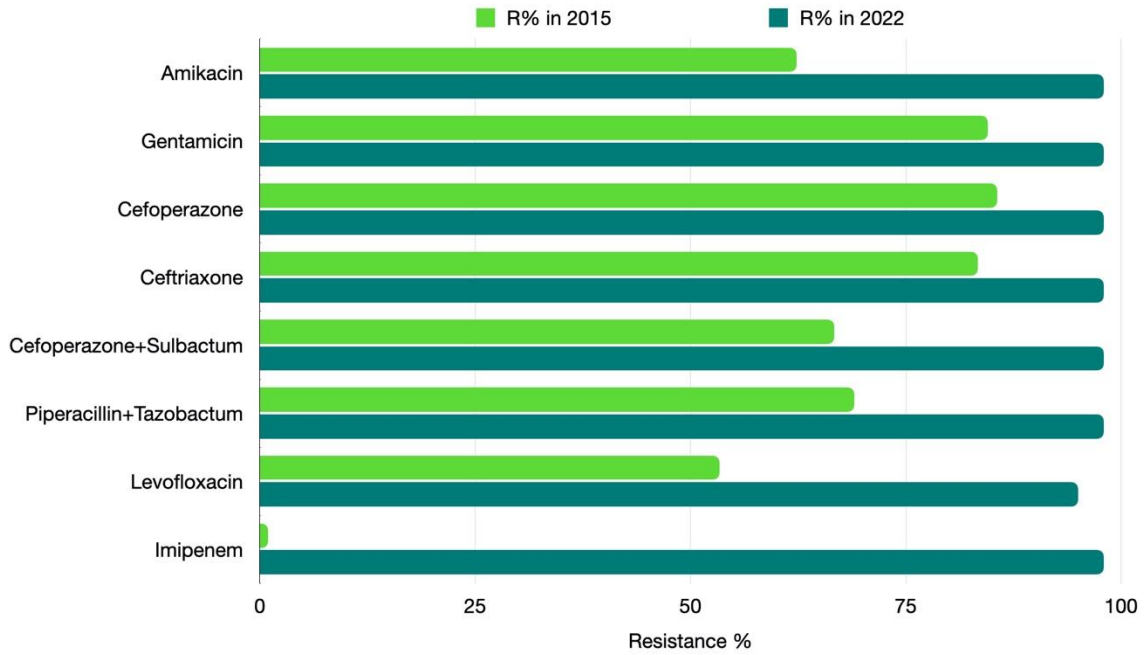

Figure2

For successful containment of an outbreak it is very important to understand how transmission is occurring. To identify the source of contamination within the PICU environmental samples were taken. Air culture by settle plate method grew Bacillus and Coagulase negative Staphylococcus species. No growth was seen in sample from patient bed side and disinfectant bottle. Different bacteria isolated from different samples were Bacillus, Coagulase negative Staphylococcus species (CONS), Acinetobacter baumanii complex, Klebsiella pneumoniae, Pseudomonas stutzeri, and Enterococcus species (Table). Apart from variety of different bacteria isolated from different sites, XDR *Klebsiella pneumoniae* was isolated from medicine table, with similar antimicrobial resistance profile that is seen with patients samples, which could be source of contamination. Strict infection control practices were advocated to stop any further cross contamination to the patients.

Table 1

S.No.	Site	Organism isolated	Susceptibility profile											
			Amikacin	Aztreonam	Gentamicin	Ceftriaxone	Cefoperazone +Sulbactum	Cefepime	Imipenem	Meropenem	Ciprofloxacin	Cotrimaxazole	Tigecyclin	Minocyclin
1.	Air	Bacillus	-	-	-	-	-	-	-	-	-	-	-	-
		CONS	-	-	-	-	-	-	-	-	-	-	-	-
2.	Medicine Table	Pseudomonas stutzeri	S	R	S	-	-	R	-	S	-	S	-	S
		Klebsiella pneumoniae	R	-	R	R	R	R	R	R	R	R	R	-
3.	Medicine Basket	Pseudomonas species	S	S	R	-	-	S	-	R	-	R	-	R
		Bacillus	-	-	-	-	-	-	-	-	-	-	-	-
4.	Syringe tray	CONS	-	-	-	-	-	-	-	-	-	-	-	-
		Enterococcus species	-	-	-	-	-	-	-	-	-	-	-	-
5.	Ventilator knob	**Acinetobacter baumanii complex**	-	-	R	R	R	R	R	R	R	R	R	-
6.	Suction pipe	**Klebsiella pneumoniae**	S	-	S	R	S	R	S	S	R	S	R	-
7.	Warmer	**Acinetobacter baumanii complex**	-	-	S	R	R	R	R	R	R	R	I	-
8.	Door handle	Pseudomonas species	S	S	R	-	-	R	-	S	-	S	-	S

		Bacillus	-	-	-	-	-	-	-	-	-	-	-	-

Similarly in the previous outbreak of 2015, multiple MDR strains of *Klebsiella* species (7/16 isolates, 43.7%) were obtained from environmental sampling, with antibiogram similar to that of patient samples (10). Most of the environmental MDR strains were still susceptible to Imipenem, which is contradictory to our present study where carbapenems are ineffective. Presence of such XDR strains in healthcare environment is unsettling, since cross contamination of these organisms may cause grave danger to patients. It warrants the need to create improved cleaning protocols and ensuring strict adherence to infection control practices within the PICU.

Our hospital is a tertiary referral centre as well as a teaching hospital. Environment such as ours, with enormous burden of patients, unrestrained movement of medical as well as paramedical students inside wards for teachings and rounds and duty exchange within nursing staff, lead to reduced compliance with infection prevention practices and facilitate transmission of multidrug resistant organisms (MDRO), from either hospital environment or hands of healthcare staff to the patients (12). Poor hand hygiene practices among staff is the most plausible reason. Strict infection prevention practices among healthcare staff have been described as an effective tool to combat MDRO transmission within the healthcare system (13).

In recent years *Klebsiella pneumoniae* have been identified as major cause of nosocomial outbreaks in the ICU (8,9). Patients admitted in the Intensive critical units of hospitals are always at a risk of acquiring nosocomial infections, because of their critical condition, low immunity and prolonged hospitalisation (14). Furthermore, infants and newborns admitted in PICU are at greater risk due to their immature immune system, low birth-weight and regular usage of antimicrobials and invasive devices (15).

Numerous studies have described *Klebsiella pneumoniae* as most common etiological agent of outbreak within ICU (16,17) and Neonatal ICUs (NICU) (18,19). Similar to our report, nosocomial outbreak of XDR *Klebsiella pneumoniae* have been reported worldwide, like report of nosocomial BSI by XDR *Klebsiella pneumoniae* in a teaching hospital in China by Wenzi B et al (20), and by Gasper et al in Brazil in 2022 (21) and so on. XDR isolates show high resistance to beta-lactams antibiotics (including carbapenems and beta-lactam/ beta-lactamase inhibitors combination),

aminoglycosides, fluoroquinolones, tigecycline and/or polymyxins, and may lead to emergence of pan drug-resistant (PDR) isolates. (22,23). The rising prevalence and worldwide dissemination of these XDR isolates, especially in healthcare system, is a major public health threat, as there are very few effective therapeutic options left (24) and are associated with high mortality (25).

Conclusions

Our study describes an outbreak of XDR *Klebsiella pneumoniae* associated with bacteriemia in paediatric patients. On comparative analysis of two outbreaks from same hospital in two different time zones, we observed changing trend in resistance pattern seen in nosocomial pathogen. In the present outbreak XDR stains are isolated which are resistant to carbapenems as well, which were effective in previously isolated MDR strains. This makes us wonder, from here, where do we go next? Urgent and effective measures are needed to restrain emergence and transmission of XDR strains within the hospital. Vigorous infection control practices should be advocated and strictly followed. Also, high mortality associated with BSIs caused by XDR *Klebsiella pneumoniae* should alert clinicians to institute effective and rational antibiotic policy.

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