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ORIGINAL ARTICLE

Investigation and management of *Klebsiella Pneumoniae* Outbreak in Intensive Care Unit of Tanta University Emergency Hospital

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ABSTRACT

Background: *Klebsiella pneumoniae infection is responsible for a wide range of infections including pneumonia, bacteremia, wound infections, and urinary tract infections.* ***Objective:*** *To investigate and manage the occurrence of multi-drug resistant Klebsiella pneumoniae outbreak in Intensive Care Unit of Tanta University Emergency Hospital.* ***Methodology:*** *The investigation of the outbreak included isolates identification and typing while management included implementation of infection prevention and control precautions; establishment of an Outbreak Control Team; epidemiological investigations; and decontamination of environment.* ***Results:*** *During September 2020, five patients in the Intensive Care Unit in Emergency Hospital of Tanta University had multi drug-resistant Klebsiella pneumoniae identified in samples obtained from a variety of specimens. The fifth case was identified 10 days following confirmation of the first case. The Microbiology laboratory confirmed the five cases had identical Klebsiella pneumoniae strains. This suggests that there was a patient-to- patient spread of multi-drug resistant Klebsiella pneumoniae.* ***Conclusion:*** *This investigation revealed the importance of proactive recognition of a possible outbreak, screening of patients transferred from other hospitals, early identification of any unusual microorganisms and implementation of early infection control interventions.*

INTRODUCTION

In 1882, Carl Friedlander described *Klebsiella pneumoniae* for the first time after isolating it from lungs of patients of pneumonia. It was described as an encapsulated bacillus, originally named Friedlander's bacillus until 1886 when it gained the name *Klebsiella*. *Klebsiella pneumoniae* is a gram-negative, encapsulated, non-motile bacterium found in the environment and typically colonizes human oropharyngeal and gastrointestinal mucosal surfaces. Once it enters our body, it displays extraordinary degree of virulence and antimicrobial resistance[1,2].

Today, pneumonia caused by *K. pneumoniae* is considered the most common cause of hospital-acquired pneumonia in the United States, and the organism accounts for 3% to 8% of all bacterial nosocomial infections[3].

Virulence of the bacterium is delivered by a wide range of factors e.g. the polysaccharide capsule of the organism which is the most important virulence factor and permits the bacteria to escape opsono-phagocytosis and serum killing by the host. To date, 77 capsular types have been considered. Another virulence factor is the lipopolysaccharide coating the Gram-negative outer surface and responsible of releasing an inflammatory cascade in the host causing the major sequelae of sepsis and septic shock. Other virulence factors include, fimbriae which help the organism adhere to host cells, siderophores which acquire iron from host cells to allow breeding of the organism[4].

Klebsiella pneumoniae is subjected to high rate of antimicrobial resistance due to alterations in the core genome of the organism. It has shown to produce a beta-lactamase and Extended-spectrum beta-lactamase (ESBL) which can hydrolyze oxyimino cephalosporins rendering the third-generation cephalosporins ineffective in its treatment where carbapenems become the drug of choice[5]. However, the Centers for Disease Control and Prevention (CDC) reported that 80% of carbapenem-resistant Enterobacteriaceae were due to *K. pneumoniae* which was associated with up-regulation in efflux pumps, alteration of the outer membrane, and increased production of ESBL enzymes[6].

Both the presence of multi-virulent and multi-drug resistance mechanisms contribute to the maintenance of *Klebsiella pneumoniae* in the hospital setting, and may explain its ability to cause extended outbreaks and different types of nosocomial infections such as hospital acquired pneumonia, bloodstream infections, lung abscesses, empyema, bacteremia, catheter-related infections, wound or surgical site infections, upper and

lower urinary tract infection, liver abscess, and meningitis[7].

K. pneumoniae accounts for approximately 11.8% of all hospital-acquired pneumonia worldwide. In ventilated patients it is responsible of about 8 to 12%, and about 7% in non-ventilated patients. Mortality ranges from 50% to 100% in patients with alcoholism and septicemia[8].

The bacterium enters the host by direct inoculation or following oropharyngeal aspiration. The main route of transmission is through direct or indirect contact. Many host factors may contribute to the colonization and infection with *Klebsiella pneumoniae* e.g. admission to ICUs, poor infection control measures, immune-compromised states especially alcoholics and diabetics, prolonged use of broad-spectrum antibiotics and co-presence of burn sites, wounds, or invasive devices[9].

In this article, we tried to lead an investigation process together with infection prevention and control management of an outbreak of multi-drug resistant Extended Spectrum Beta Lactamase (ESBL) producing *Klebsiella pneumoniae* (*ESBLK.p*) affecting five patients in ICU of Tanta University Emergency Hospital.

METHODOLOGY

Description of the outbreak:

In September 2020, an outbreak comprising 5 cases of *ESBLK.p* were identified on a 30-bedded ICU (table 1). The ICU mainly deals with surgical and trauma patients and consists of six wards each containing five beds. The first three cases were discovered in the same ward then the next two cases were discovered 6-10 days later, in the ward directly next to the first ward.

Table 1: Characteristics of the five cases confirmed with ESBL positive *Klebsiella pneumoniae* in the intensive care unit

Patient no.	Cause of admission	Age/sex	Condition admitted with*	Lenghth of ICU stay	Day when *ESBLK.p* isolated	*ESBLk.p* initially isolated from	Antibiotic therapy
Patient 1	Major Surgery (transferred from other facility)	63/ male	Peritonitis	12	Day 0	Endo-Tracheal swab	Imipenem
Patient 2	Accident & Emergency (A&E)	66/ male	Respiratory problems	30	Day 2	Endo-Tracheal Swab, sputum	Imipenem
Patient 3	A&E	37/ male	Road traffic accident	25	Day 4	Endo-Tracheal swab, sputum	Imipenem
Patient 4	A&E	50/ male	Spinal injury	29	Day 6	Endo-Tracheal swab, sputum	Imipenem
Patient 5	A& E	34/ male	Road traffic accident	10	Day 10	Wound swab	Imipenem

**All patients were subjected to the same risk factors e.g. mechanical ventilation, use of intravascular lines (central and peripheral), severe illness, long ICU stay, prolonged empirical antibiotic therapy.*

Subjects:

Outbreak Investigations:

Specimen collection and processing:

Following identification of the five cases of multi-drug resistant *Klebsiella pneumoniae* through the routine ICU laboratory investigations, patients' specimens were sent to the Medical Microbiology and Immunology laboratory, Faculty of Medicine, Tanta University to ask for typing of these isolated multi-drug resistant *Klebsiella pneumoniae* strains.

Isolates typing:

Antibiotic susceptibility testing: that was performed by the Kirby-Bauer disk diffusion method according to the criteria set by the Clinical and Laboratory Standards Institute (CLSI)[10]. Antibiotics tested (Oxoid) were: Ampicillin (10), Amoxicillin (20), Amoxicillin /clavulanic acid (20/10), Amikacin (30), Cefotaxime (30), Ceftazidime(10), Ceftriaxone (30), Chloramphenicol (30), Ciprofloxacin (5), Imipenem (10), Gentamicin (10), Piperacillin (100), Piperacillin/ tazobactam (100/10), Trimethoprim/ sulfamethoxazole (1.25/23.75) as shown in table (2)

Table 2: Antimicrobial susceptibility zones interpreted according to the criteria set by the Clinical and Laboratory Standards Institute (CLSI)

Antibiotic	Zone diameter (mm)		Zones of inhibition in (mm)				
	R<	S≥	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5
Ampicillin (10)	14	14	13	12	13	12	13
Amoxicillin (20)	14	14	10	11	11	10	10
Amoxicillin -clavulanic acid(20/10)	16	16	16	15	16	16	15
Amikacin (30)	18	18	17	18	17	18	17
Cefotaxime (30)	17	20	16	15	15	16	15
Ceftazidime(10)	19	22	18	18	17	17	17
Ceftriaxone (30)	22	25	20	19	19	19	20
Chloramphenicol (30)	17	17	18	18	17	17	17
Ciprofloxacin (5)	22	25	22	21	22	21	21
Imipenem (10)	19	22	25	26	26	25	26
Gentamycin (10)	17	17	17	16	17	16	17
Piperacillin (100),	20	20	18	17	17	17	18
Piperacillin/tazobactam (100/10),	20	20	19	18	19	19	19
Trimethoprim/ sulfamethoxazole (1.25/23.75).	11	14	11	12	11	11	11

Serological identification of capsular antigen K1 and K2 of K. pneumoniae: was performed by Quellung test using specific antibodies purchased from Statens Serum Institute, Copenhagen, Denmark**.** The antigen-antibody reactions were observed microscopically.

Communication:

On confirmation of the outbreak of *ESBLK.p* in the ICU, the incident was reported to Infection Control Committee (ICC) and Infection Control Team (ICT) which directed to form an immediate Outbreak Control Team (OCT), following a certain systematic agenda that was continuously monitored and reviewed along the progress of the outbreak investigation based on the data available at each phase. That included environment /equipment decontamination and screening, potential Source Detection (Patients and Staff screening) and root cause analysis.

The OCT was established immediately, its membership included director of Infection Prevention and Control (IPC) team, chief nurse of IPC, medical microbiologist, housekeeping worker, responsible clinicians, infection control link nurse of ICU, epidemiologist and an infectious diseases consultant. The OCT agreed to adopt the case definition advised by the World Health Organization Regional Office for the Eastern Mediterranean[11].

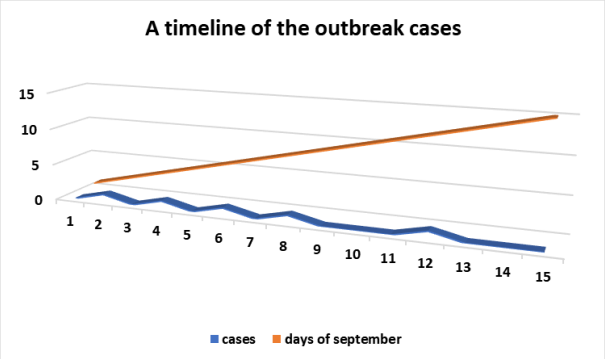

Fig. 1: A timeline and epidemiological curve of the outbreak

Environment /equipment decontamination

A twice daily environmental and equipment decontamination was initiated with either high level disinfectant (1000 ppm chlorine) or 70% alcohol wipes according to the type of surfaces decontaminated.

All patient washbasins were discarded and disposable washbasins were used instead. Any bed-side equipment was decontaminated and only an emergency kit was left in each bed-side. All trolleys were carefully decontaminated. Ventilators, bed linens and pillows

have been also recognized as significant or potential sources of outbreaks[12], therefore careful decontamination of the ventilation system was done manually or by the aid of a washer-disinfector machine together with the use of disposable bed linens and pillow covers as an alternative option.

Potential Source Detection (Patients and Staff screening)

In addition to the standard screening of any infected sites, wounds and lesions, all patients and staff members gave nose and sputum specimens to be screened for *ESBLK.p*. To reduce possible *ESBLK.p* skin colonization, 4% chlorhexidine solution or 1% triclosan solution daily body washes was highly recommended for all ICU patients and staff for 5 days.

Environmental screening: Environmental screening was not undertaken following identification of *ESBLK.p* as a negative sample would not exclude the presence of the organism.

Root cause analysis: Following confirmation of the fifth case of *ESBLK.p*, a root cause analysis (RCA) was directed on the five patients. The RCA was undertaken by the link clinician and nurse who reported the possible causes that may have attributed to the occurrence of the outbreak.

Outbreak management:

Management of *ESBLK.p* outbreak was commenced in three different phases. Phase 1 management (days 0–14) was occupied with the identification of the first two patients diagnosed with *ESBLK.p*. Phase 2 management (days 15–30) was triggered when the third case was identified and included extraordinary decontamination measures. Phase 3 management (days 31–60) began on the re-opening of the ICU following the improved decontamination policy.

Phase One management: an evaluation process to the environmental decontamination level in the ICU was carried out by the IPC nurses, which included environmental auditing with the help of the audit tool published by World Health Organization Regional Office for the Eastern Mediterranean[10]. Another audit was implemented on the ICU staff compliance to hand hygiene.

Phases Two and Three: in addition to the auditing process implemented in phase one, weekly auditing was commenced to categorize areas of poor practice in hand hygiene, isolation/cohorting, nursing and environmental decontamination. Penalties were undertaken on identification of any misbehavior regarding previous issues. Results were immediately sent to the ICU director for taking actions.

RESULTS

The findings of the RCA determined that all five patients had risk factors associated with acquiring *ESBLK.p* which included prolonged empirical antimicrobial therapy, major surgeries, presence of multiple invasive devices, mechanical ventilation, environmental contamination, severe illness or debilitation and finally being transferred from other private healthcare facilities.

It was hypothesized at this stage that cross-infection had occurred between the initial case owing to poor hand-hygiene compliance in an emergency situation that usually occurs. The last case was probably a result of environmental contamination. This was supported by the subsequent confirmation from isolate typing using antimicrobial sensitivity pattern, which identified that all cases had identical strains. The five patients had no direct contact with each other. Therefore, indirect contact transmission of infection through the ICU staff or the environment was highly assumed.

The RCA reported the possible causes that attributed to the occurrence of the outbreak. These causes included that the ICU did not have an isolation facility, poor hand hygiene compliance as the auditing system revealed 65% compliance (pass rate 85%), dusty ventilation systems and delayed rate of bed line and pillow covers alteration. Table (3) shows different infection prevention and control measures implemented in response to these findings.

Table 3: Infection prevention and control measures implemented in response to outbreak control team findings

Isolation facility	• Transmission-based contact precautions were activated. • One dedicated nurse to one bed space in the affected areas
Poor compliance to hand hygiene	• The significance of decontaminating hands with either soap and water, or with an alcohol hand-rub at the five moments for hand hygiene was re-enforced • Hand hygiene educational sessions in the ICU was started.
Environmental decontamination	The environment was decontaminated using 1000ppm hypochlorite twice daily
Equipment decontamination	Equipments were decontaminated using either 1000ppm hypochlorite or 70% isopropyl alcohol wipes twice daily as suitable for the equipment material
Linen and laundry	All linen was handled as infected and bagged in a leak-proof bag and sent to the laundry daily

DISCUSSION

Following identification of five patients with *ESBLK.p* in ICU, an OCT was immediately formed and outbreak investigation was commenced. IPC precautions, which had been identified in previous published reports and outbreaks[12,13,14,15] were also integrated into the action plan to reduce the risk of spread to further patients. It was anticipated that actions implemented in order to protect ICU patients from *ESBLK.p* were successful as the next phase (phase three) passed without further transmission to other patients.

However, other outbreak investigations and management reported by Adams D. et al revealed that sometimes the management measures undertaken may not be sufficient as after 1 month a new case was identified. That's when the OCT re-convened and the outbreak management plan restarted with enhanced decontamination strategies and a review of IPC interventions[16].

In response to the any possible future transmission of *ESBLK.p* owing to potential environmental contamination, an enhanced decontamination strategy was implemented during phase three that extended for one month after the ICU patients were re-located in theatre

Trust was learned from this experience and developed an operational strategy which will be used for any future emergency situations involving closure of the ICU.

HOCl is a major component of bleaching agents or detergents and is also commonly used to disinfect tap or swimming pool water because of its strong sterilizing power.[8,9]

In vivo, it is produced by the action of H_2O_2 and neutrophil-derived myeloperoxidase and exhibits a strong antibacterial activity as a potent toxic or oxidizing agent.[6,10,11]

HOCl can be produced in many ways, and in this experiment we produced HOCl with the Salicid device.

CONCLUSION

The outbreak investigated in this article describes the occurrence of repetitive *ESBLK.p* infections in ICU. Lessons learnt from this investigation revealed that proactive recognition of a possible outbreak is mandatory in limiting the potential risk and spread of any infection. Moreover, requesting a full screening from all patients transferred from other hospitals to ensure early identification of any unusual microorganisms and implementation of early IPC intervention. It is also important to continuously monitor the effectiveness of those interventions and wherever risk is assessed, put additional action plans ensuring patient safety.

We finally highlight the importance of the presence of an isolation facility at each ICU together with implementing a policy for ensuring effective communication with the local community and make sure that patients and their relatives are aware of what is happing in hospitals with the aim of calming fears and promoting effective policies.

- The design of the study was approved by the ethical committee of Tanta University.
- The authors declare that they have no financial or non-financial conflicts of interest related to the work done in the manuscript.
- Each author listed in the manuscript had seen and approved the submission of this version of the manuscript and takes full responsibility for it.
- This article had not been published anywhere and is not currently under consideration by another journal or a publisher.

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