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Outbreak of CTX-M-15 and SHV-12 extended-spectrum β-lactamase (ESBL) co-producing *Klebsiella pneumoniae* in a neonatal intensive care unit (NICU), in Ha'íl, Saudi Arabia

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Introduction

Neonates are at a very high risk of developing life-threatening bacterial infections in intensive care settings. In the majority of cases these healthcare-associated infections are associated with *Klebsiella pneumoniae* and *Escherichia coli* and require the administration of antibiotic therapy. *E. coli* is a common cause of community and healthcare associated infections and over the past few decades, *E. coli* strains isolated from community-acquired infections have become increasingly resistant to antibacterial drugs. Bloodstream infections caused by *K. pneumoniae* are also often reported in the neonatal intensive care units (NICUs). Additionally, there has been a rapid and global dissemination of extended-spectrum-β-lactamase (ESBL) producing *E. coli* and *K. pneumoniae* in the hospital settings, which complicates and limits current antibiotic treatment options. This increase has been mainly due to the successful dissemination of CTX-M-15 gene-carrying bacterial isolates via mobile genetic elements [1-5].

Objectives

The aim of the this study was to characterize 40-ESBL-positive *Klebsiella pneumoniae* and 19-ESBL-positive *Escherichia coli* isolates obtained from a neonatal intensive care unit (NICU) outbreak in Ha'il region of Saudi Arabia.

Methods

During April 2014, an outbreak of 3rd generation cephalosporin resistant infections was reported within a neonatal intensive care ward in a maternity hospital at Haíl, Saudi Arabia. A total of 821 samples were screened, including 407 patients and 414 others (comprising healthcare workers, staff and swabs from the NICU environment). The bacteria cultured were identified by routine automated identification system as well as MALDI-TOF mass spectrometry (Bruker). Antibiotic resistance testing was performed using VITEK 2 and Microscan. PCR was performed to determine the presence of *blaTEM, blaSHV* and *blaCTX-M* antibiotic resistance genes. Isolate genotyping was performed using pulsed field gel electrophoresis (PFGE) protocol adapted for PulseNet.

Results

A total of 47 *K. pneumoniae* isolates were cultured from neonates, with the majority of isolates 85.1% (40/47) being ESBL positive (Fig-1) and resistant to 3rd generation cephalosporins. Overall 90.2% of the *K. pneumonaie* isolates were resistant to aminoglycosides. However all of the *K. pneumonaie* isolates were susceptible to ciprofloxacin, levofloxacin, carbapenems, colistin and tigecycline. A total of 95% (38/40) of *K. pneumonaie* were co-producers of CTX-M-15 and SHV-12. Further, 63.4% were positive for TEM-1 (Table-1).

A total of 24 *E. coli* isolates were cultured from neonates, with the majority of isolates (19/24) being ESBL-positive (Fig-1) and resistant to 3rd generation cephalosporins. However, all of the isolates were sensitive to aminoglycosides, cefoxitin, amikacin, nitrofurantoin, levofloxacin, piperacillin / tazobactam, carbapenems, colistin, and tigecycline. A total of 15% were co-producers of CTX-M-15 and SHV-12. Further, 57.9% were TEM-1 positive (Table-1). The majority (31/40) of *K. pneumoniae* isolates belonged to a single genotypic lineage at the 85% similarity level, while *E. coli* isolates grouped into 2 genetic clusters at 80% similarity (18/19 isolates) [Fig-2 and Fig-3].

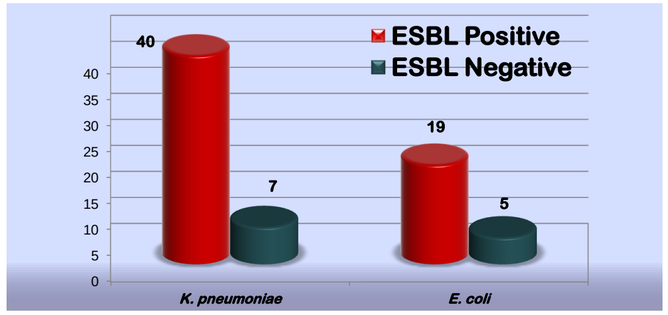

Fig-1: Distribution of ESBL resistance in *K. pneumoniae* and *E. coli* isolates from an NICU in Ha'il, Saudi Arabia.

Species	TEM-1	SHV-12	CTX-M-15
K. pneumoniae	37	40	40
E. coli	12	3	19

Table-1: The prevalence of ESBL β-lactamase genes in *K. pneumonia* and *E. coli* isolates from an NICU in Ha'il, Saudi Arabia.

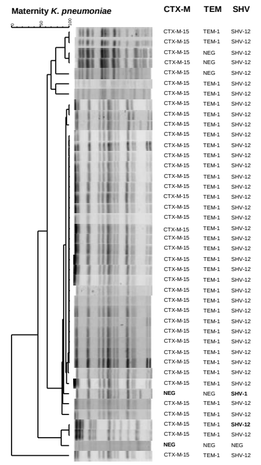

Fig-2: PFGE patterns obtained from 42 *K. pneumoniae* isolates cultured from NICU outbreak from Saudi Arabia. Cluster analysis was performed using the method of DICE with UPGMA with band tolerances set to 1.0%.

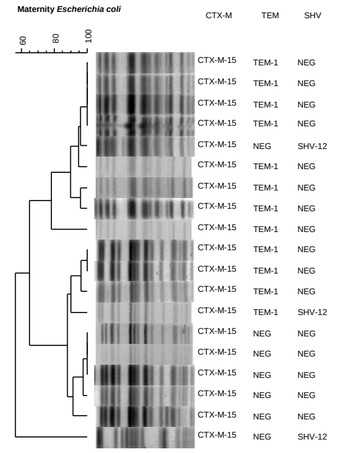

Fig-3: PFGE patterns obtained from 19 *E. coli* isolates cultured from NICU outbreak from Saudi Arabia. Cluster analysis was performed using the method of DICE with UPGMA with band tolerances set to 1.0%.

Conclusions

This is the first report of CTX-M-15-positive, ESBL *K. pneumoniae* and *E. coli* isolates recovered from an outbreak in an NICU in Ha'il, Saudi Arabia. It is alarming to note the high rate of outbreak isolates with simultaneous production of CTX-M-15 and SHV-12 conferring high level resistance to oxyimino-cephalosporins.

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