

Frequency of Carbapenem, Colistin and Tigecycline Resistant Enterobacteriaceae in Medical ICU of a Tertiary Care Hospital in Karachi

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ABSTRACT

BACKGROUND: Resistance to antibiotics among Enterobacteriaceae represents a serious therapeutic and infection control challenge. The objective of this study was to determine the frequency of carbapenem, colistin and tigecycline resistant Enterobacteriaceae isolates obtained from patients admitted in medical intensive care unit (ICU) of a tertiary care hospital in Karachi, Pakistan.

METHODS: This was a descriptive cross sectional study that was conducted at Liaquat National Postgraduate Medical Centre, Karachi, Pakistan during December 2015 to May 2016. Patients admitted in the medical ICU with systemic inflammatory response syndrome were included. The culture positive samples were analyzed for further identification and antimicrobial

sensitivity was performed according to clinical laboratory standard institute (CLSI) 2014 guidelines.

RESULTS: Of the 748 samples, 177 were positive for Enterobacteriaceae. Most samples were taken from blood 75(42.2%) or tracheal secretions 67(37.9%). Most common organism isolated were Klebsiella pneumoniae 77(43.5%) and Escherichia coli 71(40.1%). Out of these 10.7% organisms were resistant to meropenem, while 2.8% and 20.3% were resistant to colistin and tigecycline respectively.

CONCLUSION: Increasing spread of drug resistance among Enterobacteriaceae reflects an important problem that can be controlled with effective policies of infection control, surveillance and antimicrobial stewardship.

Keywords: Antibiotic Resistance; Carbapenem; Colistin; Tigecycline; Enterobacteriaceae

INTRODUCTION

With an increasing use of antibiotics worldwide, there is a parallel rise in the prevalence of antibiotic resistant organisms. This challenging antimicrobial resistance is highly problematic among Gram negative bacteria. Carbapenems and polymyxins were highly effective treatments but now bacteria have developed resistance mechanisms against these antibiotics [1]. The infections caused by these organisms result in high mortality and morbidity and potential for transmission of resistance through mobile genetic elements to other bacteria [1,2]. Enterobacteriaceae, which produces serine carbapenemases and metalloproteinases such as KPC, VIM, NDM etc.

are resistant to majority of the antibiotics [3,4]. There is limited data from Pakistan on the frequency of drug resistant Enterobacteriaceae isolated from the ICUs. The aim of this study was to determine the frequency of carbapenem, colistin and tigecycline resistant Enterobacteriaceae isolated from clinical specimens in medical ICU of a tertiary care hospital.

METHODS

This was a cross sectional study conducted in medical ICU and microbiology department, Liaquat National Hospital Karachi, Pakistan from December 2015 to May 2016. All patients above

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12 years of age admitted in the medical ICU with the signs of systemic inflammatory response syndrome (SIRS) were included in the study. SIRS was defined as having 2 or more of the following; fever of more than 38°C (100.4°F) or less than 36°C (96.8°F), heart rate of more than 90 beats per minute, respiratory rate of more than 20 breaths per minute or arterial carbon dioxide tension (PaCO₂) of less than 32 mm Hg, abnormal white blood cell count (>12,000/μL or < 4,000/μL or >10% immature [band] forms[5].

The clinical specimens from suspected site of infections from these patients were sent to microbiology laboratory where they were processed using standard methods [6]. All samples, except urine samples, were inoculated on blood agar, MacConkey agar. The respiratory secretions were additionally inoculated on chocolate agar and Sabouraud dextrose agar (SDA). The urine was inoculated on cysteine lactose electrolyte deficient (CLED) agar. These plates were incubated aerobically at 35±2°C for 24 hrs. After incubation, established microbiological methods, which include colonial morphology, Gram's staining and biochemical characteristics were used for identification.

Semi-quantitative cultures were performed on tracheal aspirates to decrease the chance of reporting colonizers. After incubation, colony count was done and ≥10⁵ colony forming unit were considered significant and reported for tracheal aspirate. If many organisms were isolated from one sample, it was considered contamination and growth were only reported after clinical correlation [7].

Antimicrobial susceptibility testing of the isolated organisms was performed by the disk diffusion technique according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) [6]. Extended spectrum beta lactamase (ESBL) production was detected by using disc of ceftazidime (30mg), cefotaxime (30mg) and amoxicillin/clavulanic acid (20+10) as recommended by CLSI and British Society of Antimicrobial Chemotherapy (BSAC) [6,8]. The non ESBL producing isolates were excluded from this study. The zone diameter breakpoint for Enterobacteriaceae for meropenem was interpreted according to the CLSI standards and zone size < 19 mm was taken as resistant [6]. For tigecycline BSAC breakpoints were used and zone size < 18 mm was taken as resistant [8].

Colistin susceptibility was determined using MIC and E strip was used with MIC <2 as sensitive and MIC > 4 as resistant [6,8]. The colistin disc

was not used if colonies of Serratia or Proteus were isolated and tigecycline disc was not used to determine the sensitivity of Proteus because Proteus and Serratia are intrinsically resistant to colistin and Proteus is resistant to tigecycline.

The data was analyzed using SPSS version 20 and the values obtained were expressed in terms of frequencies and percentages. The study was approved by the ethical committee of the hospital.

RESULTS

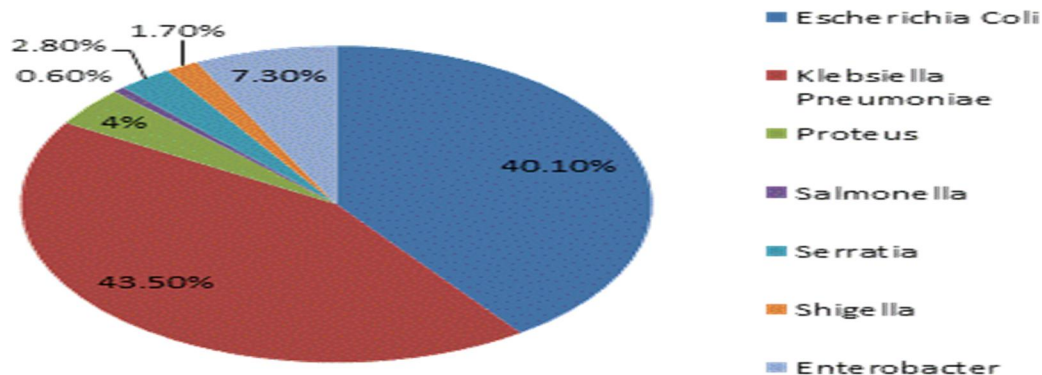
Of the 748 samples sent from medical ICU to the microbiology lab during the study period, 177(23.6 %) were positive for Enterobacteriaceae which were ESBL producers. The frequency of different Enterobacteriaceae isolated is shown in Figure 1. The most common bacterium was *Klebsiella pneumoniae* (43.50%) followed by *E.coli* (40.10%) and *Enterobacter* (7.30%) respectively. The most common sample which yielded growth for Enterobacteriaceae was blood (42.4%) followed by tracheal secretions (37.9%) and urine (7.9%).

Most isolates were resistant to ciprofloxacin (62.1%) and piperacillin-tazobactam (54.8%) followed by gentamicin (40.1%) and cefepime (40.1%). Meropenem resistance was present in 10.7% isolates, tigecycline resistance, excluding Proteus, in 20.3% isolates, and 2.8% were resistant colistin except *Serratia* and *Proteus*. During the study period, 3 isolates of *Klebsiella pneumoniae* were panresistant: resistant to all available antibiotics including tigecycline and colistin.

DISCUSSION

In our study, most frequently isolated organism was *Klebsiella pneumoniae* followed by *Escherichia coli*, *Enterobacter*, *Proteus*, *Serratia*, *Shigella* and *Salmonella* (0.6%). We also found that the resistance rate for piperacillin-tazobactam was very high in our study and one in five samples were resistant to tigecycline

Infections caused by drug-resistant Gram-negative pathogens have become a global threat [9]. Enterobacteriaceae and particularly *Klebsiella pneumoniae* strains producing carbapenemases cause infections that have high mortality rates ranging between 23% and 75% [10]. These organisms have now become resistant to the antibiotic of last resort i.e. colistin and tigecycline as well and unfortunately no therapeutic options are available if such an

Figure1: Frequency of different Enterobacteriaceae isolated n=748

extensively drug resistant organism is isolated from a clinical specimen [11]. Fakhruddin et al, in 200 samples of Enterobacteriaceae, found that the most common isolated organism was E. coli (65.5%) followed by K. pneumoniae (21%), Proteus spp. (5%), C. freundii (1.0%) and E. cloacae (5.5%), similar to our study and they found that 12% of their isolates were resistant to carbapenem [12]. Another study from India reported the similar frequency of isolates [13].

In a large multicenter global surveillance (The Tigecycline Evaluation and Surveillance trial) between 2004 to 2006, the susceptibility to tigecycline was reported up to 99% among Enterobacteriaceae [14]. But the situation has changed now and numerous studies have reported rising resistance rates for carbapenems, colistin and tigecycline [15, 16]. In contrast to our study, Azzab et al did not find such a high level of resistance in patients with ventilator associated pneumonia in ICU. They found that the most common Gram negative bacteria were Klebsiella and all isolates were sensitive to colistin and 94.6% were sensitive to tigecycline [17]. Another study found that among ESBL and AMP C producers, which constituted 73% of the isolates, 89% of the isolates of Enterobacteriaceae were resistant to piperacillin /tazobactam, 22% were resistant to amikacin, 6% were resistant to gentamicin, 100% were resistant to ciprofloxacin and 22% were resistant to tigecycline while 0% were resistant to colistin and meropenem [18]. All the metallo-beta-lactamase (MBL) producers (27%) were resistant to meropenem while the

sensitivity to tigecycline was 50% and none of the isolates were resistant to colistin [18]. The determination of AMP C, KPC and MBL production was not done in our study. Another limitation of our study is that it was conducted in a single ICU of a tertiary care hospital in Karachi and the antibiotic susceptibility was tested by disc diffusion method and MICs for most antibiotics was not determined due to unavailability of Vitek or E-strip at our facility.

CONCLUSION

Antibiotic resistance in Enterobacteriaceae is a serious problem in health care settings and contributes to high mortality and morbidity. Resistance to carbapenems, colistin, tigecycline is worrisome as these are the antibiotics of last resort.

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