KPC- PRODUCER GRAM NEGATIVE BACTERIA AMONG BURNED INFANTS IN MOTAHARI HOSPITAL, TEHRAN: FIRST REPORT FROM IRAN


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SUMMARY. To the best of our knowledge, this is the first report of Klebsiella, Acinetobacter and Pseudomonas-producing Klebsiella pneumoniae Carbapenemase (KPC) among burn infants in Iran. The objective of this study was to determine the phenotypic detection of these KPC among isolated Pseudomonas aeruginosa, Acinetobacter baumannii and Klebsiella spp. A cross-sectional study was performed (February to September 2011) at a tertiary burn hospital in Tehran, Iran. Sixty-four strains were isolated from 20 patients. Strain and genus of isolates were confirmed, antibiotic susceptibility testing was implemented, and KPC determined by Modified Hodge Test. Fifteen of 36 strains (six Pseudomonas aeruginosa, six Acinetobacter baumannii, and three Klebsiella pneumoniae) were resistant to imipenem. Ten strains of 36 Gram negative isolates were resistant to all tested antibiotics except for Colistin. Thirteen of 15 resistant imipenem strains were confirmed as KPC-producer bacteria that isolated from nine patients. Six of 36 isolated strains were extended-spectrum β-lactamase (ESBL)-producing bacteria, of which four strains were both KPC and ESBL. A high percentage of multidrug resistant (MDR) strains in our centre with positive KPC have created a major challenge in terms of mortality and morbidity. The findings of this study highlight the importance of implementing an effective infection control strategy to prevent and decrease the prevalence of KPC-producing organisms.

Keywords: Pseudomonas, Acinetobacter, Klebsiella, KPC, Infant.

Introduction

Intensive care unit (ICU) hospitalized patients such as burned patients are at increased risk for infections with various nosocomial pathogens. Among this critically ill population, infants have more potential for infection by multidrug resistant (MDR) nosocomial bacteria because of their vulnerability and low immune system. It has been suggested that treating nosocomial infectious diseases in this population could be more challenging considering etiologies pertinent to Gram negative bacteria especially MDR strains. Emergence of MDR nosocomial Gram negative bacteria has become a serious concern in health care settings worldwide which could potentially lead to high mortality and morbidity, particularly among children. For example, the sensitivity rate of isolated micro-organisms to imipenem in a study from a developing country was 34.4% in a paediatric haematology/oncology unit.1

The rapid spread of resistance to β-lactam antibiotics among Gram negative pathogens poses a clinical and public health challenge. Carbapenem group antibiotic are a safe and effective treatment for severe Gram negative infections. Resistance to Carbapenems can cause complication in the treatment of patients because there are often limited alternative treating choices available. Carbapenem-resistant Gram negative bacteria have recently evolved as an significant problem in the health care centre.10-13 One of the mechanisms of resistance to carbapenems is related to their ability to produce Klebsiella pneumoniae Carbapenemase (KPC) enzyme. Potential resistance to other classes of antibiotics in addition to carbapenems is of significance, and this can occur among KPC-producing organisms.10,13 The KPC enzyme is a serin carbapenemase that can be produced by Gram negative bacilli such as Enterobacteriaceae.
We performed this study with the aim of determining the phenotypic characteristics of Gram negative bacteria which is producing KPC in burn wound infection in infants in Iran. To the best of our knowledge, this is the first report of its kind from Iran and its findings would certainly contribute to the existing knowledge in this area and to enhance our understating of the current problem we face in burn centres in Iran.

**Materials and methods**

We performed a cross-sectional study from October to December 2011 at Motahari Burn and Reconstruction Center, a tertiary burn care centre in Tehran. Motahari Burn and Reconstruction Center is one of the few large highly equipped tertiary burn centres in Iran, providing care to severely burned patients from the province of Tehran and to complicated cases referred from other centres across the country. All patients were admitted immediately after burn injuries except for referral cases. The policy of the Motahari Burn and Reconstruction Center is to admit: 1) any patient with ≥ 20% total body surface area (TBSA) burns, 2) patients suffering from electrical and chemical burns with any degree of TBSA, and 3) any immunocompromised burn patient such as diabetics. Paediatric ward in this hospital includes one corridor and four rooms (two rooms with six beds and two with two beds). Infant burned wounds are washed with suitable washing solution such as butadiene and hype hypochlorite. Antibiotic prophylaxis is not given unless a clinical setting for infection is warranted (i.e. change in appearance/colour of wounds or positive blood or wound cultures). Treatment generally starts with sephalozine or cephepime and in severe case with carbapenems.

Strain and genus of isolates were confirmed with specific biochemical tests such as oxidase, TSI, SIM, citrate, gelatinase, lysine decarboxilase, and urea. The antibiotic susceptibility testing was performed according to the Clinical and Laboratory Standards Institute’s (CLSI) recommendations with MAST company disk, and for cefotaxime (30µ), ceftazidime (30µ), aztronam (30µ), imipenem (10µ), gentamicin (10µ), amikacin (30µ), tobramycin (10µ), colistin (25µ) and ciprofloxacin (5µ). Resistant imipenem strains were examined for KPC-producing modified Hodge test according to the CLSI guideline using E. coli ATCC 25922 and the Ertapenem disk. Resistant cefotaxime and ceftazidime strains examined for Extended Spectrum Beta-Lactamase (ESBL) production by combination disk method.

**Results**

Sixty-four strains were isolated from 20 patients with TBSA between 15 and 40%, age range 0-6 yr. The isolated strains include 28 Gram positive bacteria, 16 *Enterobacteriacea*, 12 *Pseudomonas* and seven *Acinetobacter baumannii*. Ten of 36 Gram negative isolates were resistant to all tested antibiotics except Colistin and ten strains were susceptible to at least one aminoglycoside. Fifteen of 36 strains (6 *Pseudomonas aeruginosa*, 6 *Acinetobacter baumannii* and 3 *Klebsiella pneumoniae*) were resistant to imipenem. Thirteen of 15 resistant imipenem strains were confirmed as KPC-producing bacteria that isolated from nine patients (Fig. 1). Four out of six imipenem-resistant *Pseudomonas* were producing KPC. All six *Acinetobacter baumannii* and three *Klebsiella pneumoniae* imipenem-resistant were KPC-producers. Six of the 36 isolated strains were ESBL producers. Among observed cases, 4 strains were KPC and ESBL combined positive.

**Discussion**

Gram negative bacteria are usually the predominant cause of bloodstream and wound infections among the paediatric population. On the other hand, strains that can produce KPC could also be resistant to broad spectrum antibiotics, especially betalactames. For instance, *Klebsiella pneumoniae* was isolated from 17 female patients who had septicaemia in a study after transplantation. These isolates
were KPC-producing strains and resistant to all tested antibiotics except Colistin and Tigecycline. Further, among 13 KPC-producing strains, eight isolates (60%) were resistant to all antibiotics except Colistin. This resistance to broad spectrum antibiotics can represent a major challenge in the treatment of these types of infections. Rastgar Lari et al. reported a case related to MDR strains with KPC-producer that led to the death of 22 infants. In a study from Greece, two out of the 19 cases studied of Klebsiella pneumoniae reported KPC positive strains. These bacteria were isolated from blood and bronchia obtained from two children aged respectively 14 and 4.5 yr. In a separate study from the USA, one out of 6 cases that were isolated from a 17-yr-old patient was a Klebsiella KPC-producer. Moreover, in 2011 in the USA, three cases of KPC-producer Enterobacteriaceae were reported to have been isolated from children.

The results of the current study indicated that the rate of resistance to Carbapenems could be due to producing KPC in Gram negative bacteria. The high prevalence of KPC-producer strains is important and serious in infants. In this study, 87% of imipenem-resistant strains were confirmed as KPC-producers. Our incidence rate among infants is higher than in other studies. The high rate in our setting could be related to antibiotic susceptibility, hospitalization conditions (i.e., infection control measures) and use of broad spectrum antibiotics in infants. The increase of nosocomial Gram negative KPC-producer bacteria, especially in burn care centres, should be taken into serious consideration. The results of this study can be useful to determine antibiotic resistance patterns and potentially lead to more functional and effective prevention and treatment protocols.

Conclusion

In brief, there appears to be a high percentage of multidrug resistant strains in our centre with positive KPC. This has resulted in a major challenge in terms of mortality and morbidity. The findings of this study highlight the importance of implementing an effective infection control strategy to prevent and decrease the prevalence of KPC-producing organisms.

RÉSUMÉ. Au meilleur de notre connaissance, le nôtre est le premier rapport sur Klebsiella, Acinetobacter et Pseudomonas productrices de Klebsiella pneumoniae carbapenemase (KPC) chez les nourrissons atteints de brûlure en Iran. Les Auteurs de cette étude ont voulu établir l’individuation phénotypique de ces KPC entre les cas de Pseudomonas aeruginosa, Acinetobacter baumannii et Klebsiella spp. Une étude transversale a été réalisée (février à septembre 2011) dans un hôpital tertiaire des brûlures à Téhéran, en Iran. Soixante-quatre-quatre souches ont été isolées chez 20 patients. La souche et le genre des isolats ont été confirmés, les tests de sensibilité aux antibiotiques ont été mis en œuvre, et KPC a été déterminée par le test modifié de Hodge. Quinze des 36 souches (Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae) étaient résistantes à l’imipénème. Dix souches des 36 isolats à Gram négatif étaient résistantes à tous les antibiotiques testés à l’exception de la colistine. Treize des 15 souches résistantes à l’imipénème ont été confirmées comme KPC-producteurs bactéries isolées à partir de neuf patients. Six des 36 souches isolées ont été étendues à spectre β-lactamase (ESBL)-bactéries productrices, dont quatre souches étaient KPC et BLSE. Un pourcentage élevé de multirésistance aux médicaments (MRM) des souches dans notre centre avec KPC positifs ont créé un défi majeur en termes de mortalité et de morbidité. Les résultats de cette étude soulignent l’importance de la mise en œuvre d’une stratégie efficace de contrôle des infections dans le but de prévenir ou réduire la prévalence des organismes producteurs de KPC.

Mots-clés: Pseudomonas, Acinetobacter, Klebsiella, KPC, enfant.

BIBLIOGRAPHY


BIBLIO TO FINISH


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