ORIGINAL ARTICLE

Carbapenemases classes of Carbapenem-Resistant Organisms from Tertiary Care Hospital

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Abstract

Due to extensive utilization of carbapenem as anti-antimicrobial agents in treatment, carbapenem-resistant organisms have drastically expanded and turn into a genuine general medical problem. Classes A (KPC), B (IMP, NDM, and VIM) and D with its variations (OXA-48, OXA-162, OXA-181, etc.) are the three significant classes of carbapenemase producing genes, all around the world, in carbapenem-resistant organisms. To maintain a strategic procedure to prevent additional spread of these dangerous bacteria between the hospital patients, quick recognizable proof of the patients colonized with carbapenem-resistant organisms is an absolute necessity to actualize suitable infection control measures. All selected isolates were examined by the Cepheid Xpert Carba-R assay (Cepheid, Sunnyvale, CA, USA) for the detection and differentiation of the most prevalent carbapenemase producing genes; KPC, NDM, VIM, IMP-1, and OXA-48. The genes were detected in 85 out of 156 patients (54%);55 out of 85 (64.7%) harbored OXA-48 gene, whereas; 30 out of 85 (35.3%) harbored NDM gene. All isolated organisms had no IMP, VIM and KPC genes. In conclusion, carbapenem-resistant organisms with OXA-48 and NDM genes still the most prevalent strains in our region.

Keywords

Carbapenemases; Carbapenem; Resistant; blaOXA; blaNDM

Introduction

Gram-negative bacteria (GNB) and *Enterobacterales* are the most common pathogenic organisms causing various life threatening infections. *Carbapenems* are one of the best known treatments for diseases brought about by multi-drug resistant GNB (MDR-GNB)[1,2]. With the wide use of *carbapenem* antibiotics in clinical therapy, *carbapenem*-resistant organisms (CRO) have dramatically increased and become a serious public health issue[3].

Classes A (KPC), B (IMP, NDM, and VIM) and D with its variations (OXA-48, OXA-162, OXA-181, etc.) are the three significant classes of *carbapenemases* all around the world in CRO strains[4]. The cepheid Xpert Carba-R assay (Cepheid, Sunnyvale, CA, USA) is a rapid and sensitive automated *in vitro* diagnostic test for the qualitative detection of the *bla*KPC, *bla*NDM, *bla*VIM, *bla*OXA-48, and *bla*IMP genes. The sensitivity and specificity of the Carba R were 95.0% and 98.1%, respectively[5,6]**.** To stay away from additional spread of these genuine microbes to the clinical patients, fast detection of colonized patients with CROs is an absolute necessity to actualize appropriate infection control measures.

The aim of this study is to identify the resistance mechanisms of *carbapenem*-resistant gram-negative bacteria that will be isolated from clinical specimens.

Materials and Methods

This study included 156 *carbapenem*-resistant isolated clinical strains; from a (500 beds) tertiary care hospital; during the period from November 2020 till March 2021. Species identification and antimicrobial susceptibility were performed using the VITEK 2.0 (bioMérieux, USA). The results were interpreted according to the MIC breakpoints for *carbapenems* (≤ 1 *u*g/ml for sensitive, 2 *u*g/ml for intermediate and 4 ≥ *u*g/ml for resistant) as mentioned in the Clinical and Laboratory Standards Institute (CLSI) guidelines (2019). *Carbapenem* resistance was defined as a resistance to at least one of the *carbapenem* antibiotics (*meropenem*, *doripenem*, or *imipenem*)[7].

Table 1. The sources of the isolates

Source	n	%
Sputum	62	40%
Wound	52	33%
Blood	25	16%
Urine	10	6%
Body fluid	4	3%
IV catheter tip	3	2%
Total	**156**	**100%**

All isolates were examined by the Cepheid Xpert Carba-R assay (Cepheid, Sunnyvale, CA, USA) for the qualitative detection of the *bla*KPC, *bla*NDM, *bla*VIM, *bla*OXA-48, and *bla*IMP genes.

Results

A total 156 CRO clinical isolates were examined for *carbapenemase* genes. These organisms were isolated from 105 (67%) males, the sources were sputum (40 %) followed by wound and blood (33% and 16%) respectively (Table 1). The most prevalent strains were *K. pneumonia (*43%) -followed by *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (36% and 14%) respectively (Table 2).

The genes were detected in 85 out of 156 patients (54%); 55 out of 85 (64.7%) harbored OXA-48 gene, whereas; 30 out of 85 (35.3%) harbored NDM gene. All isolated organisms had no IMP, VIM and KPC genes. In conclusion, *carbapenem*-resistant organisms with OXA-48 and NDM genes still the most prevalent strains in our region.

Discussion

As global spread of CROs, including the *carbapenemase*-producing *Enterobacteriaceae, Pseudomonas aeruginosa* and *Acinetobacter* species, has become a matter of concern worldwide[8], detection of CROs turned out to be a critical issue for clinical laboratories to provide guidance of infection control activities leading to a targeted therapy[9]. We investigated 156 CROs isolates from a tertiary care hospital for the detection of the *bla*KPC, *bla*NDM, *bla*VIM, *bla*OXA-48, and *bla*IMP genes.

Firstly, Carbapenem-resistant *K. pneumonia* were the most prevalent strains (43%). It has been stated by many authors that Carbapenem-resistant *K. pneumonia* has been found in many areas in the Gulf Cooperation Council Countries[10,11]. Sabrina *et al.*[12] showed that *Klebsiella pneumonia* is the most bacterial species found in Carbapenem-resistant Enterobacteriaceae [48.6%].

Table 2. The carbapenemase genes

	n	%	NEGATIVE (n)	%	NDM(n)	%	OXA(n)	%
Klebsiella	67	43%	10	15%	18	27%	38	57%
Acinetobacter	56	36%	44	79%	6	11%	6	11%
Pseudomonas	22	14%	12	55%	3	14%	7	32%
Enterobacter	6	4%	2	33%	2	33%	2	33%
E. coli	3	2%	1	33%	1	33%	1	33%
Citrobacter	2	1%	2	100%	0	0%	1	50%
Total	**156**	**100%**	**71**	**46%**	**30**	**19%**	**55**	**35%**

The most common species of *Enterobacteriaceae* harboring transmissible *carbapenemase* genes are K. *pneumoniae*[13].

Klebsiella pneumoniae isolates producing *bla*OXA-48 carbapenemase was first identified in the Middle East (in Turkey) and has rapidly spread globally[14], whereas; *bla*OXA-48 is considered the most common carbapenemase in the Middle-Eastern countries. Although; NDM was first reported in India and its dissemination varies geographically, Middle Eastern countries have been described as the second reservoir of NDM producing isolates[4].

In our study (35%) of all isolates harbored *bla*OXA-48, whereas; (19%) were positive for *bla*NDM. These findings are consistent with those which showed that NDM, OXA-48 and KPC are the most common carbapenemase producing genes worldwide[4, 15]. Regarding Saudi Arabia, Abdalhamid *et al.*[16] stated that OXA-48 and NDM-1 are the most common carbapenemases produced in Enterobacteriaceae reported in Saudi Arabia. In hospitals at Southern (Asir) Province, it is showed that *K. pneumoniaee* that produces OXA-48 and NDM carbapenemases were the most prevalent isolates[10]. Our results were also in accordance with studies from Riyadh, Zaman *et al*.[18] that showed K. *pneumoniaee* OXA-48 gene was detected in (67.6%) isolates NDM-1 alone in (12.7%) isolates [18] and Al-Agamy *et al*.[19] who showed that blaOXA-48-type and blaNDM were the only detected in the K. *pneumoniaee* and E. *coli* isolates.

K. *pneumoniaee* was shown to be the most isolated species by many authors e.g. Memish *et al.*[20], Zowawi *et al.*[21], Zaman *et al*.[22] and Al-Agamy *et al.*[17]. The prevalence of blaOXA-48 and blaNDM strains in Saudi Arabia may be explained by the fact that it receives a large number of visitors and migrant workers from the OXA-48 and NDM endemic countries such as Turkey, India, and Pakistan[10].

Regarding all examined organisms**,** our results showed that, there was no isolate that had the genes of IMP, VIM and KPC (See Table 2). This result was in accordance with Al-Zahrani and Alsiri[10] whose results showed no producers of blaIMP and blaKPC among all tested isolates but (VIM) was detected only in one isolate. On the other hand, Zowawi *et al.*[21] found that, no KPC-type, VIM-type, or IMP-type carbapenemase producers were detected. In addition, Zowawi *et al.*[21] found 17 strains with no carbapenemase enzymes or carbapenemase-producing genes that may have different ways of resistance, for example, loss of porin and extended-spectrum beta-lactamase (ESBL) creation, in addition to loss of penetrability of the outer membrane, were proposed [21].

Conceivable use of the the Xpert Carba-R assay on tested strains may be considered as an extra examination tool for CROs from different clinical samples to decide whether they have carbapenemases-producing genes. The affirmation of the outcomes *via* genetic examination helps the infection control to improve its procedures, for example, the utilization of contact precaution measures or cohorting of the suspected patients with comparative diseases, and possibly therapeutic protocols[8].

The correct identification of carbapenemase genes is necessary to address therapeutic options using the newer beta-lactam–beta-lactamase inhibitors which have activity against serine-based carbapenemases e.g. avibactam has no activity against MBLs, varborbactam covering only KPCs, and relebactam may have a different degree of efficacy related to the presence of particular genes)[23], whereas cefotriaxone-sulbactam is active against class B(MBL) :NDM, IMP and VIM

Conclusion

Carbapenem-resistant organisms are dangerous with genuine health wellbeing concerns if they spread around the world. Carbapenem-resistant organisms represent an expanding danger to all patients. Early identification of this worldwide general health wellbeing danger should be through genetic approaches, epidemiologic investigations, and surveillance; which may be considered as appropriate methodologies in their prevention and control. CROs with *bla*OXA-48 and *bla*NDM genes still the most prevalent strains in our region.

Conflict of Interest

The authors declared that there is no conflict of interest that is related to this study and this article.

Disclosure

The authors did not receive any type of commercial support either in the form of compensation or financial

support for this case report. The authors have no financial interest in any of the products, devices, or drugs mentioned in this article.

Ethical Approval

The study design was reviewed and approved by the Ministry of Halth Institutional Review Board.

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فئات الميكروبات المقاومة للمضادات الحيوية من نوع الكاربابينيم المعزولة من أحد مستشفيات التخصصية

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المستخلص. إن الاستخدام الواسع لمضادات الكاربابينيم الحيوية في العلاج السريري قد زاد من الميكروبات المقاومة للكاربابينيم بشكل كبير ومن ثم أصبحت مشكلة صحية عامة وخطيرة. لقد وضح أن الفئة (أ) (بشكل رئيسي) ، والفئة (ب) والفئة (د) هي الفئات الرئيسية الثلاثة المنتشرة على مستوى العالم. ولتجنب المزيد من انتشار هذه البكتيريا الخطيرة بين مرضى المستشفى ، فإن التشخيص السريع للمرضى المصابين بالكائنات المقاومة للكاربابينيم وعزلهم أمر لا بد منه لتنفيذ تدابير مناسبة لمكافحة العدوى. تم فحص جميع العزلات المختارة بواسطة جهاز Cepheid Xpert للكشف النوعي عن الجينات المسببة للمقاومة للمضادات الحيوية من فئة كاربابينيم blaKPC و blaNDM و blaVIM و blaOXA-٤٨ و blaIMP. تم الكشف عن الجينات المسببة لمقاومة المضادات الحيوية من فئة كاربابينيم في (٥٤٪) ؛ و(٦٤,٧٪) من جميع العزلات كانت تحتوي على النوع blaOXA-٤٨ ، بينما (٣٥,٣٪) كانت موجبة للنوع blaNDM ، ولم يتم الكشف عن أي من الميكروبات من blaIMP و blaVIM و blaKPC بين جميع العزلات المختبرة. ومن نتائج البحث نخلص الى ان الجينات المسببة لمقاومة المضادات الحيوية من فئة كاربابينيم blaOXA-٤٨ و blaNDM لا تزال السلالات الأكثر انتشارًا في منطقتنا.