SHORT REPORT

High prevalence of carbapenem-resistant Acinetobacter baumannii associated respiratory tract infections in Pakistani hospitals

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Abstract

Acinetobacter baumannii is one of the most common causes of nosocomial infections in developing countries. It has a better ability to get antimicrobial resistance due to plasticity in genome. The recent emergence of carbapenem-resistant A. baumannii isolates in several countries narrows down the spectrum of options to treat A. baumannii infections. The WHO has placed carbapenem-resistant A. baumannii on the top of priority organisms against which novel antibiotics are required. A systematic evaluation of carbapenem-resistant A. baumannii infections in three tertiary care hospitals in Pakistan is presented here. A total of 2270 positive culture samples were collected over a period of two years. Of which 1642 (72.33%) were respiratory tract specimens. A. baumannii was identified in 681 (41 %) cases. Of which 583 (85.5%) were carbapenem-resistant. Our findings suggest that the burden of carbapenem-resistant A. baumannii infections is alarmingly high in Pakistan.

Keywords: Carbapenem-resistant; Acinetobacter baumannii; API 20NE; Respiratory tract infections;

DOI: https://doi.org/10.5455/JPMA.35384

Introduction

Acinetobacter baumannii has recently emerged as one of the most common causes of hospital-associated infections. Till 1971, genus Acinetobacter was not definitively established as a human pathogen and therefore, ignored whenever isolated from clinical specimen. Its better ability to acquire antibiotic resistance enables it to earn the status of a common human pathogen. Acinetobacter has now been separated from diverse clinical specimens and often from hospitalised patients' sputum, bronchial lavage, wounds, and urine. Colonisation rates are higher in the Intensive Care Unit (ICU) patients, especially of the respiratory tract.[1]

Half a century ago, it was thought that A. baumannii retained at least intermediate susceptibility against the third and fourth generation cephalosporins, fluoroquinolones, semisynthetic aminoglycosides, and carbapenems, with almost 100% isolates retained sensitivity to imipenem. During the late 1980s and 1990s, however, worldwide emergence and spread of Acinetobacter isolates resistant to imipenem further limited the therapeutic use. By the late 1990s, carbapenems were the only useful antimicrobial agents of choice that could combat many serious Acinetobacter infections. But in recent years, the frequent reports on the emergence of carbapenem-resistant A. baumannii further narrow down the therapeutic options. Carbapenem-resistant phenotype of A. baumannii seems to play an essential role in its ability to persist and spread in the hospital environment along with the ability to colonise living and non-living surfaces, to grow as biofilm and survive for a more extended period of time on abiotic surfaces under desiccated conditions.[2]

The status of carbapenem-resistant A. baumannii in Pakistan is currently under-explored and limited studies on smaller population size have occasionally been reported. Here, we present a systematic evaluation of the status of carbapenem-resistant A. baumannii infections and their antimicrobial susceptibility pattern in three tertiary care hospitals of Lahore, Pakistan.

Methodology

An observational cross-sectional analysis was done and samples were obtained randomly (non-duplicated).All Acinetobacter isolates which have been confirmed to be A. baumannii by API 20-NE were included in the study while all Acinetobacter species other than A Baumannii were excluded.

Identification of A. baumannii was based on the morphology of the colony found on culture plates, Gram stain, catalase, oxidase and API 20 NE (Analytical Profile Index).

Antimicrobial susceptibility testing was performed by standard Kirby-Bauer disk diffusion method using cation adjusted Mueller-Hinton agar (MHA) (Oxoid UK), according to Clinical Laboratory Standards Institute (CLSI) guidelines, 2017. Inhibition zones were defined by reference to the breakpoints set out in the CLSI 2017 Guidelines.Nevertheless, there are no conditions for the disk diffusion process for polymyxin B and colistin. As a

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result, their sensitivity was assessed by the MIC as specified in the CLSI 2017 Guidelines.

Results

A total of 2270 (H-I 1043, H-II 149, H-III 1078) specimens were positive for bacterial growth in three selected hospitals from January 1, 2015, to December 31, 2016. Out of these 2270 culture-positive specimens, 1642 were respiratory tract specimens, either sputum, tracheal aspirates or bronchial lavage. In 681 (41 per cent) cases, A baumannii was identified in a total of 1642 samples of the respiratory tract. The Hospital's wise frequency of isolated organisms is shown in Table 1.

All of the isolates were found resistant to most of conventional antibiotics, including piperacillin, ampicillin-sulbactam, piperacillin-tazobactam, ticarcillin-clavulanic acid, ceftazidime, ceftriaxone, cefepime and levofloxacin. Interestingly, all isolates were susceptible to polymyxin B. A fraction of isolates were susceptible to doxycycline (73%), Imipenem (13%), gentamicin (1.5%), and co-trimoxazole (0.7%).

Antibiotic susceptibility testing of A. baumannii isolates revealed that 85.5% isolates were resistant to carbapenem drug imipenem, 1.5% were intermediately resistant to imipenem, and 13% were susceptible to it. Frequency of carbapenem-resistant A. baumannii among three different hospitals is given in Table 2.

Table-1: Frequency of respiratory tract infection associated with bacteria in three hospitals.

Organisms	H – I IHT (n=781)	H – II SMDC (n=57)	H – III CMH (n=804)	Total (n=1642)
	n (%)	n (%)	n (%)	n (%)
Acinetobacter baumannii	351 (45)	18 (31)	313 (39)	682 (41)
Pseudomonas aeruginosa	78 (10)	19 (32)	355 (44)	452 (27)
Klebsiella pneumonia	149 (19)	14 (27)	80 (10)	243 (15
Escherichia coli	133 (17)	5 (8)	16 (2)	154 (9)
Staphylococcus aureus (MRSA)	70 (9)	1 (2)	40 (5)	111 (7)

IHT: Ittefaq Hospital Lahore; DMC: Sharif Dental and Medical Complex
CMH: Combined Military Hospital, Lahore.

Table-2: Frequency of carbapenem-resistant Acinetobacter baumannii in respiratory tract infections

	H – I IHT (n=351)	H – II SMDC (n=18)	H – III CMH (n=313)	Total (n=682)
	n (%)	n (%)	n (%)	n (%)
Carbapenem sensitive A. baumannii	46 (13)	-	53 (17)	99 (14.5)
Carbapenem resistant A. baumannii	305 (87)	18 (100)	260 (83)	583 (85.5)

IHT: Ittefaq Hospital Lahore; DMC: Sharif Dental and Medical Complex
CMH: Combined Military Hospital, Lahore.

Discussion

The systematic evaluation of the status of carbapenem-resistant A. baumannii infections in three hospitals suggests that the prevalence of carbapenem-resistant A. baumannii infections is very high in Pakistan.The frequency of hospital-acquired non-fermenter pneumonia was found to be 67% in Pakistan, the highest among the other Asian countries in the region.[3]

Acinetobacter bacteraemia in hospitalised patients causes a challenging problem worldwide. Studies from around the globe have shown a mild to severe situation. A. baumannii has been associated with infections from country to country. Pakistan is one of the major South Asian and South-East Asian countries to bear the burden of carbapenem-resistant A. baumannii. Carbapenem resistant A. baumannii was reported to be more than 60% of A. baumannii isolates in Pakistan.[4]

Different studies recently highlight the increasing burden of A. baumannii infections from different regions of Pakistan. One of such studies conducted in Karachi reported that A. baumannii is the most frequent organism causing both ventilated associated pneumonia (30%) and bloodstream infections (54.2%).[5] The results of three hospitals in Lahore on a relatively larger population indicate that the burden of carbapenemic-resistant A. baumannii infections were higher than previously thought.

Pseudomonas aeruginosa and Klebsiella pneumoniae, among Gram-negative rods, were known to be the most common cause of hospital-related infections in the past. However, A. baumannii infection is now quickly gaining ground among top infections associated with hospital in developing countries. A. baumannii attracts worrying attention due to its robust climate and rapid development of antibiotic resistance.Mortality rate in ICUs was reported to be 34 to 43% from Acinetobacter septicaemia.[6] Our findings suggest that the burden of carbapenem-resistant A. baumannii is even higher than previously thought.

Since all of carbapenem-resistant isolates were additionally resistant to the most conventional antibiotics, the situation is alarming. Although, it is fortunate that all of the carbapenem-resistant isolates were sensitive to Polymyxin B but it needs the attention of concerned professionals and organisations to deal with carbapenem-resistant A. baumannii infections. World Health Organization has already published its first-ever list of antibiotic-resistant "priority pathogens" to secure and guide research and development related to new antibiotics, among which carbapenem-resistant A. baumannii is the most important pathogen for the urgent investigation of new medicines.[7]

Our findings further illustrate that doxycycline could be the second drug of choice for which 73% isolates were found to be susceptible.

This study shows a high rate of A baumannii carbapenem resistant organisms in our hospitals. However, our data are limited to three tertiary hospitals and a more extensive surveillance study involving more hospitals is required to see the actual picture over a more extended period of time to see the changing trends in drug resistance patterns to combat this highly resistant bug.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Sources: None to declare.

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