ORIGINAL ARTICLE

PREVALENCE OF CARBAPENEM-RESISTANT ACINETOBACTER BAUMANNII (CRAB) IN MEDICAL AND SURGICAL INTENSIVE CARE UNITS (ICUS) OF JPMC, KARACHI

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ABSTRACT

Background: Antimicrobial resistance is one of the research priorities of health organizations due to increased risk of morbidity and mortality. Outbreaks of nosocomial infections caused by carbapenem-resistant Acinetobacter Baumannii (CRAB) strains are on the rise worldwide. Antimicrobial resistance to carbapenems reduces clinical therapeutic choices and frequently led to treatment failure. The aim of our study was to determine the prevalence of carbapenem resistance in A. baumannii isolated from patients in intensive care units (ICUs).

Methods: This cross-sectional study was carried out in the Department of Microbiology, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, from December 2016 to November 2017. Total 63 non-repetitive A. baumannii were collected from the patients’ specimens, admitted to medical and surgical ICUs and wards of JPMC, Karachi. The bacterial isolates were processed according to standard microbiological procedures to observe for carbapenem resistance. SPSS 21 was used for data analysis.

Results: Out of the 63 patients, 40 (63.5%) were male. The age of the patient ranged from 15-85 year, with average of 43 year. 34.9% patients had been hospitalized for 3 days. Chronic obstructive pulmonary disease was present in highest number with average of 58.7% for morbidity. Number of patients on mechanical ventilation was highest (65.1%). All isolates were susceptible to colistin. The resistance to ampicillin-sulbactam, ceftazidime, ciprofloxacin, amikacin, piperacillin- tazobactam and meropenem was 82.5%, 81%, 100%, 87.3%, 82.5% and 82% respectively. Out of 82% CRAB, 77% were obtained from ICUs.

Conclusion: This study has revealed the high rate of carbapenem resistance in A. baumannii isolates in ICUs thus leaving behind limited therapeutic options.

Keywords: Acinetobacter Baumannii; Carbapenem Resistant; Nosocomial Infections.

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INTRODUCTION

Acinetobacter infections have received great importance in clinical practice due to organism’s prolonged environmental survival and strong tendency to develop antimicrobial drug resistance1. World Health Organization (WHO) has included the A. baumannii in “ESKAPE” group (includes Enterococcus faecium, Staphylococcus aureus, Kiebsiella pneumoniae, A. baumannii, Pseudomonas aeruginosa and Enterobacter spp.) which is the most dangerous and difficult to treat group of organisms2. Multidrug resistant A. baumannii (MDR-AB) is a serious nosocomial emerging strain, strongly associated with high mortality rate in ICUs patients3. Thus, is a research priority for WHO and other health organizations to combat this health issue. Risk factors associated with A. baumannii infections are, indwelling catheters, invasive procedures such as central venous catheterization, mechanical ventilation, hands of medical technicians and staff, prolonged hospital stay and wide-
spread use of broad-spectrum antibiotics. A. baumannii is ubiquitous in nature, found mainly in hospitals, causing ventilator associated pneumonia, bloodstream infection, urinary tract infection, vasculitis, meningitis and wound infections. It is Gram-negative aerobe, non-lactose fermenting, oxidase-negative bacteria with a deoxyribonucleic acid (DNA) Guanine + Cytosine (G+C) content of 39% to 47% and grows well at 44ºC. One of most highlighted issues is that this bacterium is naturally resistant to commonly used antibiotics such as aminopenicillins, first- and second-generation cephalosporins and chloramphenicol and Erta penem, making it a challenge to effectively treat infection caused by this organism. Carbapenems (imipenem, meropenem and doripenem) were considered as drugs of choice for MDR-AB infections. However, recent reports of resistance to even these drugs have emerged with increasing frequency. Multiple mechanisms are utilized by these bacteria to develop resistance, such as production of enzymes (carbapenemases: beta-lactamase), over expression of efflux pumps, porin loss and alteration in penicillin binding proteins. There can be an alarming increase of infections by carbapenem resistant A. baumannii; further lack of detection may enhance their rapid spread among clinical isolates. Timely appropriate laboratory investigations are essential to avoid delays in the management of these patients.

The data regarding A. baumannii is limited at species level and its resistance pattern needs continuous monitoring for an incident of outbreak. Therefore, this study was designed to determine the prevalence and resistance pattern of carbapenem resistance in A. baumannii isolated from patients in ICUs. This will help the clinicians in prophylaxis and treatment of infection caused by this bug.

METHODS

This cross-sectional study was conducted in the Department of Microbiology, Basic Medical Sciences Institute (BMSI), JPMC, Karachi after ethical approval from Institutional Review Board, JPMC as a part of M. Phil research. Total 63 non-repetitive A. baumannii were collected between December 2016 to November 2017 from the patients admitted to (ICUs), medical and surgical wards of JPMC, Karachi. The samples collected from patients included respiratory secretions, blood, pus and urine. Sample size was calculated by OpenEpi calculator, and confidence level was set at 95%. After taking necessary aseptic measures and verbal consent, the samples were collected and patient history was documented in a proforma. Data collected included age, sex, length of hospital stay, use of invasive medical devices and co-morbidities. Escherichia coli ATCC 25922 was used for quality control of the Gram’s stain, biochemical tests, media preparation and susceptibility testing of tetracycline and trimethoprim-sulfamethoxazole and for another antibiotics Pseudomonas aeruginosa ATCC 27853 was used.

All specimens were processed by standard microbiological procedures including, culture, and biochemical characteristics according to manual of clinical microbiology. A. Baumannii was identified by colony morphology (On MacConkey agar colonies of A. baumannii appeared as non-lactose fermenter and on blood agar colonies were about 1 to 2 mm in diameter, non-pigmented, domed, and mucoid, with smooth to pitted surfaces).

Specification was confirmed by Analytical Profile Index (API) 20NE (Bio-merieux, France), according to manufacturer’s instructions. Antimicrobial susceptibility testing of the isolated organisms was performed by the disc diffusion technique according to the recommendations of the clinical and laboratory standards institute (CLSI, 2015). The minimum inhibitory concentration (MIC) for all isolates to imipenem and meropenem was determined by E-test (Bio-Merieux, France). The results were interpreted according to CLSI guidelines. CRAB was defined as an A. baumannii isolate that was resistant to both imipenem and meropenem (MIC of >8ug/ml as resistant) whereas carbapenem-susceptible A. baumannii possessed carbapenem MIC of ≤ 2 ug/ml.

Colistin and polymyxin B susceptibility was performed by E-test (Biomerieux) and results were confirmed by MIC broth microdilution method. MIC breakpoints for resistant and susceptible were ≥ 4ug/ml and ≤ 2ug/ml respectively. Data was analyzed by SPSS-21. Required statistical tests were applied and p-value <0.05 was considered significant.

RESULTS

Total 63 non-repetitive A. baumannii were isolated from patients, admitted in different wards and ICUs of JPMC, Karachi. The subjects included in this study were of both genders, with age ranging from 15 to 85 years (Table 1). Forty (40; 63.5%) positive samples were collected from males while 23 (36.5%) were from females. Among these 8 (12.7%) were received from the surgery wards, 14 (22.2%) from the medical ward whereas 41 (65.1%) were collected from ICUs. Out of 63 samples 6 (9.52%) samples were taken from UTI patients (urine), 8 (12.7%), samples of pus were taken from patient’s wounds, 36 (57.1%) samples of respiratory secretions (sputum and tracheal aspirates) were collected from patients of lower respiratory tract infections (LRTIs) and 13 (20.6%) samples of blood were taken from patients with suspected septicemia.
Out of total 63 patients included in this study, majority 41 (65.1%) stayed in hospital for more than 3 days while, 22 (34.9%) stayed for < 3 days. Number of patients on mechanical ventilation was higher 41/63 (65.1%), than non-ventilated patients. Of the selected cases, 44 (69.8%) patients were urinary catheterized, 39/63 (61.9%) patients developed hyperpyrexia. CRP (C- reactive protein) of > 8mg/dl was recorded in 45/63 (71.4%) patients while 39/63 (69.1%) patients showed only leukocytosis (WBC >11x10^9/L). COPD (Chronic obstructive pulmonary disease) was present in highest rate 37/63 (58.7%) for morbidity, followed by diabetes mellitus in 33/63 (52.8%) ESRD (End stage renal disease) in 27/63 (42.8%) and hypertension in 19/63 (30.1%) in decreasing order of frequency (Table 2).

Table 1: Clinical characteristics of 63 patients infected with A. baumannii (N=63).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>40</td>
<td>63.5</td>
</tr>
<tr>
<td>Female</td>
<td>23</td>
<td>36.5</td>
</tr>
<tr>
<td>Department</td>
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<td></td>
</tr>
<tr>
<td>ICUs</td>
<td>41</td>
<td>65.1</td>
</tr>
<tr>
<td>Medical ward</td>
<td>14</td>
<td>22.2</td>
</tr>
<tr>
<td>Surgical ward</td>
<td>8</td>
<td>12.7</td>
</tr>
<tr>
<td>Samples</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory secretions</td>
<td>36</td>
<td>57.1</td>
</tr>
<tr>
<td>Blood</td>
<td>13</td>
<td>20.6</td>
</tr>
<tr>
<td>Pus</td>
<td>8</td>
<td>12.7</td>
</tr>
<tr>
<td>Urine</td>
<td>6</td>
<td>9.52</td>
</tr>
</tbody>
</table>

Table 2: Demographic characteristics of patients with A. baumannii infection (N=63).

<table>
<thead>
<tr>
<th>Variables</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital stay (hours)</td>
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<td></td>
</tr>
<tr>
<td>≤ 3 days</td>
<td>22</td>
<td>34.90%</td>
</tr>
<tr>
<td>&gt; 3 days</td>
<td>41</td>
<td>65.10%</td>
</tr>
<tr>
<td>On mechanical ventilation</td>
<td>41</td>
<td>65.10%</td>
</tr>
<tr>
<td>Urinary Catheterization</td>
<td>44</td>
<td>69.80%</td>
</tr>
<tr>
<td>Hyperpyrexia</td>
<td>39</td>
<td>61.90%</td>
</tr>
<tr>
<td>C-reactive Protein &gt;8mg/dl</td>
<td>45</td>
<td>71.40%</td>
</tr>
<tr>
<td>WBC count &gt;11x10^9/L</td>
<td>39</td>
<td>61.90%</td>
</tr>
<tr>
<td>comorbidities:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>19</td>
<td>30.10%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>33</td>
<td>52.80%</td>
</tr>
<tr>
<td>End stage renal disease</td>
<td>27</td>
<td>42.80%</td>
</tr>
</tbody>
</table>

*Chronic Obstructive Pulmonary Disease
Almost all antibiotics exhibited high resistance against A. baumannii except polymyxin-B and colistin which showed 100% sensitivity. Out of 63 A. baumannii isolates 52(82%) were resistant to ampicillin-sulbactam, piperacillin-tazobactam, imipenem, meropenem and tetracycline. Among the cephalosporin, as less as 51(81%) isolates were resistance to both ceftazidime and cefepime while as much as 62(98.4%) were resistant to ceftriaxone and cefotaxime each. The resistance against other antibiotics was as follows: Amikacin 55 (87.3%), levofloxacin 57(96.8%), doxycycline 55(87.3%), minocycline 46 (73%), while 52 (82.3%) were resistant to tetracycline. Resistance to sulfamethoxazole-trimethoprim was found in 58/63 (92.1%) of the isolates. Whereas, all (100%) were found to be resistant to ciprofloxacin (Figure 1).

**DISCUSSION**

Rapid emergence and spread of resistant strains of bacteria are a threat to our health care system. Among serious infections, A. baumannii has emerged as a challenge due to rapid acquisition of resistance to almost all routinely prescribed antimicrobial agents. It has significantly threatened the effectiveness of current available antibiotics.  

In this study 63 A. baumannii were isolated from different clinical specimens and the commonest source of isolation was respiratory secretion 36 (56%) followed by blood 20.54%, pus 12.64% and (9.48%) were from urine. This is in accordance with the study conducted by Begum, showed higher prevalence of A. baumannii in respiratory secretion which were (54%), (50%) and (41.8%) respectively. This suggested that invasive devices such as tracheal tubes are important reservoir involved in A. baumannii transmission. Al-Sehlawi indicated high prevalence of A. Baumannii in urine samples, which is in contrast to our study. This showed that the site of infection is not specific but may be variable depends upon the different factors including infection control practice, environment and mechanical ventilation. These findings are in agreement with study results by Saleema. The frequency of A. baumannii was higher in ICUs patients, similar findings were reported by Begum et al. This is due to the ICU environment and immunocompromised patients favor the adoption, transmission and infection. The majority of patents (65.1%) showed stayed in hospital for more than 3 days. This indicates that the source of infection was hospital, which is reported everywhere in literature.

In the present study A. baumannii infections were more common in males (63.5%) as compared to females. This may be due to the fact that the males reported more frequently to the hospitals compared to females. Islahi also observed high percentage of nosocomial infections present in males, while results from Shoja showed high prevalence in females. Data presented that 100% of isolates were resistant to ciprofloxacin and 96% were resistant to levofloxacin, in accordance to the results reported by Indhar. Present data showed 82% A. baumannii was resistant to ampicillin-sulbactam and same was in the study conducted by Lowings, showed higher resistance rate of Ampicillin-sulbactam in A. baumannii, again supporting our findings. Resistance to ceftazidime, cefepime, ceftriaxone, cefotaxime showed 81%, 98%, 81% and 98% respectively. The resistance against aminoglycosides was lower, which is similar to former studies. Resistance to meropenem and imipenem were 82%, which is in accordance to previous study.
Carbapenem resistance in A. baumannii is mainly due to expression of (OXA) carbapenemases-types, and uncommon mechanisms are impermeability and altering the expressions of porins or efflux pumps and metallo-beta-lactamase (MBL) carbapenemases\textsuperscript{23}. Different studies from Pakistan conducted by Hasan\textsuperscript{24}, Sohail\textsuperscript{20}, and Indhar\textsuperscript{16} showed higher level of carbapenem resistance in A. baumannii. Due to the rapid spread of carbapenem resistant A. baumannii, there is dire need of prevention, rapid detection and appropriate management.

CONCLUSION

This study has revealed that rate of carbapenem resistance in A. baumannii isolates in ICUs patients is at a swift rise. Therefore, it is suggested that continuous evaluation in hospitals should be maintained to avoid the irrational use of antibiotics. The delayed isolation of such strains not only leaves behind limited therapeutic options for treatment but also leads to higher rate of mortality.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST

There was no conflict of interest among the authors.

ETHICS APPROVAL

The study approval was sort from BMSI, JPMC Institutional Board Committee (No.F.2-81-IRB/2017/GEN-L/19809 JPMC).

PATIENTS CONSENT

Verbal and written consent was obtained from all patients.

AUTHORS CONTRIBUTION

ZS conducted the study; RA guided and helped in the write-up, proof read the manuscript completed the final version for publication. FU handled the laboratory technical work and helped in the data collection and MAD was the supervisor of the study.

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