A Study on Burden of Carbapenem-Resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* Infections in a Tertiary Care Hospital of Eastern India

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**ABSTRACT**

**Introduction:** Healthcare associated infections (HAI) by multi-drug resistant organisms (MDRO) are major cause of mortality and morbidity having significant impact on quality of life and economic burden. HAI by carbapenem-resistant *Pseudomonas aeruginosa* (CRPsA) and *Acinetobacter baumannii* (CRAB) are emerging threat for their high antibiotic resistance and spread via mobile genetic elements. Objectives of this study were to detect prevalence of CRPsA and CRAB infections in a tertiary care hospital of Eastern India and to determine their antimicrobial resistance profile.

**Material and methods:** This observational study was done in Department of Microbiology from January 2018-June 2019. From HAI patients, different clinical samples were collected. Culture and identification by standard conventional methods and antimicrobial susceptibility tests by modified Kirby-Bauer disc-diffusion method following CLSI guidelines were performed. CRPsA and CRAB cases were identified when isolates were resistant to ≥1 carbapenem, 10µg imipenem disc (zone diameter ≤15mm for *P. aeruginosa* or ≤18mm for *A. baumanii*) or meropenem disc (≤15mm for *P. aeruginosa* or ≤14mm for *A. baumanii*).

**Result:** From 27,043 clinical samples, 1785 (6.6%) *Acinetobacter baumannii* and 777 (2.87%) *Pseudomonas aeruginosa* were isolated. CRAB and CRPsA prevalence were 74.17% and 62.29% respectively. Carbapenem-resistance were further categorised into imipenem-resistant-meropenem-resistant (IRMR) (*A. baumanii*-63.19%, *P. aeruginosa*-51.61%), imipenem-resistant-meropenem-sensitive (IRMS) (*A. baumanii*-10.48%, *P. aeruginosa*-9.13%), meropenem-resistant-imipenem-sensitive (MRIS) (*A. baumanii*-0.51%, *P. aeruginosa*-1.54%) phenotypes. Fourth category was imipenem-sensitive-meropenem-sensitive (ISMS) (*A. baumanii*-25.82%, *P. aeruginosa*-37.71%). Carbapenem-resistant groups showed significantly high resistance for all antibiotics excepting colistin.

**Conclusion:** Carbapenems are often used for treating MDRO. But high carbapenem-resistance in HAI is alarming, warranting judicious use of antibiotics.

**Keywords:** Carbapenem-Resistant, *Pseudomonas Aeruginosa*, *Acinetobacter Baumannii*, Antimicrobial Susceptibility Test, Multi-Drug Resistant Organisms.

**INTRODUCTION**

Healthcare associated infections (HAI) are a major concern nowadays because of emergence of multi-drug resistant organisms (MDRO). Endemic burden and epidemics of HAI have significant impact on mortality and morbidity, prolonging hospitalization and increasing the economic burden. The introduction of carbapenems in the clinical practice was of great help in case of treatment with serious bacterial infections caused by β-lactam resistant bacteria producing penicillinase or cephalosporinase. *Pseudomonas aeruginosa* is an opportunistic pathogen that frequently causes nosocomial infections. These are difficult to treat as *Pseudomonas aeruginosa* is intrinsically resistant to many antimicrobial drugs as well as it shows various other resistance mechanisms and have different virulence factors, making carbapenems crucial in its clinical management. *Acinetobacter baumannii* can acquire resistance to multiple classes of antimicrobial drugs, making them a major treatment challenge. The spread of these infections are also difficult to control because it can survive for prolonged periods on environmental surfaces. Carbapenems have been the drug of choice for treatment of infections by gram negative bacteria showing multi drug resistance. But now, HAI by carbapenem-resistant *Pseudomonas aeruginosa* (CRPsA) and carbapenem-resistant *Acinetobacter baumannii* (CRAB) are emerging threat for showing high antibiotic resistance, as they are becoming extensive drug resistant (XDR) and are rapidly spreading via mobile genetic elements. The major risk factors for spread of these CRAB and CRPsA, are poor

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**How to cite this article:** Maitreyi Bandyopadhyay, Bipasa Chakraborty, Simit Kumar, Reena Roy Ghosh, Mitali Chatterjee, Prabir K Mukhopadhyay, Manas K Bandyopadhyay. A study on burden of carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections in a tertiary care hospital of Eastern India. International Journal of Contemporary Medical Research 2019;6(12):L5-L13.

**DOI:** http://dx.doi.org/10.21276/ijcmr.2019.6.12.33
adherence to infection control measures and injudicious and overuse of antibiotics. The emergence of MDR and XDR phenotypes are dependent not only on the direct effect of individual antibiotic exposure but also on the indirect effect due to increased bacterial resistance in others. This is because of the higher selection pressure by MDR and XDR bacteria which gets colonized and more likely to be transmitted to other patients, spreading infections, increasing morbidity and mortality. However, CRAB has become common worldwide. Infections with CRAB have been associated with mortality as high as 52%. Mechanisms associated with carbapenem resistance can be plasmid mediated and chromosomal mediated. Carbapenem resistance in *P. aeruginosa* by chromosomal mutations is primarily due to mechanisms that alter porins, modify efflux pump activity, and derepress intrinsic β-lactamases. Whereas carbapenemase enzymes which can hydrolyze imipenem and meropenem and other β lactams are commonly plasmid mediated and carried on mobile genetic elements, so have the potential for rapid dissemination. These are carbapenemase-producing CRPsA (CP-CRPsA). Chromosomal mediated mechanism are specific for each carbapenems, such as, loss of porin (oprD) contributing to imipenem resistance and the overexpression of efflux pumps contributing to meropenem resistance. Depending on these above mechanisms of carbapenem resistance, clinical isolates exhibit different types of resistance phenotypes such as type I (imipenem resistant meropenem susceptible - IRMS), type II (meropenem resistant imipenem susceptible - MRIS) and type III (imipenem resistant meropenem resistant - RMR). Generally, *P. aeruginosa* isolates having plasmid mediated carbapenemase enzyme genes (CP-CRPsA) give rise to type III (IRMR) phenotype whereas type I and II show discrepant carbapenem susceptibility profile where resistance mechanism is specific for imipenem or meropenem. The major CP-CRPsA identified are Verona Integron Mediated (VIM) MBL, the *Klebsiella pneumoniae* carbapenemase (KPC), imipenem (IMP-1) MBL, New Delhi MBL (NDM) and oxacillinases (OXA-48, 181). A study from 14 countries in Europe showed that the prevalence of metallo-β-lactamase (MBL) producing *P. aeruginosa* increased from 12.3% in 2010 to 30.6% in and it is increasing day by day. Carbapenem resistance in *Acinetobacter baumannii* is a big concern and Metallo-β-lactamases (VIM, IMP, SIM) have been reported worldwide, especially in Asia and western Europe, and confer resistance to all β-lactams except aztreonam. The most widespread carbapenemases in *A. baumannii* belong to carbapenem-hydrolysing class D β-lactamases activity which are represented by OXA-23, OXA-24, OXA-40 and OXA-58, that are either plasmid or chromosomally encoded. Carbapenem resistance may also result from combined action of OXA carbapenemases and secondary resistance mechanisms like porin deficiency or over expressed efflux pumps. To date, the epidemiology of CRPsA and CRAB with different types of resistant phenotypes has not been systematically evaluated in the Eastern parts of India. So, the objectives of this study were to detect prevalence of CRPsA and CRAB infections in a tertiary care hospital of Eastern India and determine their antimicrobial resistance profile.

**MATERIAL AND METHODS**

This laboratory-based cross-sectional observational study was done in Microbiology Department for one and a half year from January 2018 to June 2019. From HAI patients with bacteremia, hospital acquired pneumonia, ventilator associated pneumonia, surgical site infections, catheter-related bloodstream infections, urinary tract infections or other HAI's, different clinical samples like blood for culture, respiratory samples (putum, endotracheal tube aspirate, deep tracheal aspirate, bronchoalveolar lavage, endotracheal tube tips), pus, wound swabs, central line tips, urine, pleural fluid, peritoneal fluid, and other infectious body fluids were collected aseptically and transported to laboratory, all following standard operating procedures. For blood culture, 5-10 ml blood from adult patients and 2 ml from paediatric patients were inoculated in brain heart infusion broth. After incubation, if turbidity appeared in the blood culture bottle within 7 days, it was further subcultured in blood agar and MacConkey agar media. All other samples were inoculated in blood agar and MacConkey agar media following standard operating procedures and incubated overnight aerobically at 37°C. Characteristic growth were further identified seeing colony morphology, Grams stain, motility and biochemical tests all following standard conventional methods of isolation and phenotypic identification. The antimicrobial susceptibility tests were done by modified Kirby-Bauer disc-diffusion method in Muller Hinton agar, following CLSI guidelines 2018, 2019 for all antimicrobial agents except for colistin where microbroth dilution test (MBDT) were performed. CRPsA and CRAB cases were identified when isolates were resistant to ≥1 carbapenem, for 10µg imipenem disc (when zone diameter was ≤15mm for *P. aeruginosa* or ≤18mm for *A. baumanii*) or 10µg meropenem disc (with ≤15mm for *P. aeruginosa* or ≤14mm for *A. baumanii*). Multidrug-resistant (MDR) *P. aeruginosa* or *A. baumanii* was defined by resistance to ≥1 agent in ≥3 antimicrobial classes. The other antibiotic discs used were ceftriaxone (30µg only for *A. baumanii*), cefazidine (30µg), piperacillin-tazobactum (100/10µg), ticarcillin-clavulanate (75/10µg), aztreonam (30µg, only for *P. aeruginosa*), ciprofloxacin (5µg), levofloxacin (5µg), lomefloxacin (10µg), amikacin (30µg), trimethoprim-sulfamethoxazole (1.25/23.75µg only for *A. baumanii*), tigecycline (15µg only for *A. baumanii*) and doxycycline (30µg only for *A. baumanii*), all procured from Himedia Laboratories Pvt Ltd. For MBDT, colistin sulphate salt powder was procured from Sigma Life Science Pvt. Ltd. and MBDT was performed as per manufacturer guidelines. Interpretation was done as per Clinical and Laboratory Standards Institute (CLSI) guidelines. 

**STATISTICAL ANALYSIS**

Data analysis of CRPsA and CRAB from different clinical samples and their AST profiles was done using Excel spread
were found to be growth positive. Among them, 1785 Acinetobacter baumannii and 777 Pseudomonas aeruginosa were isolated and identified (Figure-1). CRAB and CRPsA prevalence were 74.17% (n=1324) and 62.29% (n=484) respectively (Table-1). Distribution of Pseudomonas aeruginosa and Acinetobacter baumannii isolates among different clinical samples and proportion of CRPsA and

| Clinical samples (n) | Pseudomonas aeruginosa | Acinetobacter baumannii | Other bacteria isolated | No growth |
|----------------------|-------------------------|-------------------------|-------------------------|-----------|
|                      | Total isolates (n) | CRPsA n (%) | Total isolates (n) | CRAB n (%) | |
| Urine (11590)        | 178                   | 131 (73.59%) | 428                   | 356 (83.18%) | 1578          | 9406          |
| Blood (3554)         | 129                   | 83 (64.34%)  | 339                   | 261 (76.99%) | 548           | 2538          |
| Sputum (3962)        | 191                   | 90 (47.12%)  | 296                   | 212 (71.62%) | 711           | 1198          |
| Endotracheal tube (439) | 19                   | 10 (52.63%)  | 47                    | 38 (80.85%)  | 230           | 296           |
| Deep tracheal aspirate (205) | 12                   | 7 (58.33%)   | 32                    | 21 (65.62%)  | 89            | 72            |
| Central line tips (386) | 9                    | 6 (66.67%)   | 21                    | 17 (80.95%)  | 91            | 265           |
| Pus & wound swabs (4775) | 206                  | 143 (69.41%) | 585                   | 399 (68.21%) | 1177          | 2807          |
| Fluids and others (2132) | 33                   | 14 (42.42%)  | 37                    | 20 (54.05%)  | 112           | 1950          |
| Total (27043)        | 777                   | 484 (62.29%) | 1785                  | 1324 (74.17%)| 4536          | 19945         |

Table-1: Distribution of Pseudomonas aeruginosa and Acinetobacter baumannii isolated from different clinical samples and proportion of CRPsA and CRAB cases among them.

| SN | Antimicrobial disc | Different clinical samples with growth of P. aeruginosa (no of samples tested) | IRMS n/NIRMS (%) | MRIS n/NMRIS (%) | IRMR n/NIRM (% | ISMS n/NISMS (%) | Carbapenem sensitive | P value (two-way ANOVA) |
|----|-------------------|--------------------------------------------------------------------------------|------------------|------------------|----------------|-----------------|-------------------|----------------------|
| 1  | Ceftazidine       | Urine (178)                                                                     | 29/29 (100%)     | --               | 102/102 (100%) | 16/47 (34.04%)  | --                | P<0.0001             |
|    |                   | Respiratory samples (222)                                                       | 12/15 (80%)      | 3/3 (100%)       | 87/89 (97.75%) | 72/115 (62.60%) | --                |                      |
|    |                   | Pus, wound swabs & fluids (239)                                                 | 9/10 (90%)       | 2/2 (100%)       | 145/145 (100%) | 74/82 (90.24%)  | --                |                      |
|    |                   | Blood and central line tips (138)                                               | 13/17 (76.47%)   | 5/7 (71.42%)     | 65/65 (100%)  | 33/49 (67.34%)  | --                |                      |
| 2  | Piperacillin-tazobactam | Urine (178)                                                                    | 15/29 (51.72%)   | --               | 93/102 (91.78%)| 13/47 (27.66%)  | --                | P<0.0001             |
|    |                   | Respiratory samples (222)                                                       | 3/15 (20%)       | 0/3 (0.0%)       | 86/89 (96.62%)| 29/115 (25.21%) | --                |                      |
|    |                   | Pus, wound swabs & fluids (239)                                                 | 7/10 (70%)       | 1/2 (50%)        | 115/145 (79.31%)| 56/82 (68.29%)  | --                |                      |
|    |                   | Blood and central line tips (138)                                               | 9/17 (52.94%)    | 2/7 (28.57%)     | 49/65 (75.38%)| 13/49 (26.53%)  | --                |                      |
| 3  | Ticarcillin-clavulanate | Urine (131)                                                                    | 22/29 (75.86%)   | --               | 97/102 (95.10%)| --               | --                | P<0.0001             |
|    |                   | Respiratory samples (107)                                                       | 4/15 (26.66%)    | 3/3 (100%)       | 86/89 (96.62%)| --               | --                |                      |
|    |                   | Pus, wound swabs & fluids (157)                                                 | 7/10 (70%)       | 1/2 (50%)        | 118/145 (81.38%)| --               | --                |                      |
|    |                   | Blood and central line tips (138)                                               | 13/17 (76.47%)   | 7/7 (100%)       | 62/65 (95.38%)| 23/49 (46.94%)  | --                |                      |
| 4  | Aztreonam         | Urine (131)                                                                     | 24/29 (82.76%)   | --               | 98/102 (96.08%)| --               | --                | P<0.0001             |
|    |                   | Respiratory samples (107)                                                       | 7/15 (46.67%)    | 3/3 (100%)       | 72/89 (80.90%)| --               | --                |                      |
|    |                   | Pus, wound swabs & fluids (157)                                                 | 7/10 (70%)       | 1/2 (50%)        | 98/145 (67.58%)| --               | --                |                      |
|    |                   | Blood and central line tips (138)                                               | 13/17 (76.47%)   | 2/7 (28.57%)     | 58/65 (89.23%)| 20/49 (40.81%)  | --                |                      |
Table-2: Comparison between the resistance profiles of P. aeruginosa isolated from different clinical samples among IRMS, MRIS, IRMR and ISMS phenotypic groups:

| SN | Antimicrobial disc | Different clinical samples with growth of A. baumannii (no of samples tested) | CRAB | Carbapenem sensitive | P value (two-way ANOVA) |
|----|--------------------|-------------------------------|------|----------------------|------------------------|
|    |                    |                               | IRMS n/N (IRMS (%)) | MRIS n/N (MRIS (%)) | IRMR n/N (IRMR (%)) | ISMS n/N (ISMS (%)) |
| 1  | Ceftriaxone        | Urine (428)                   | 95/95 (100%)        | 7/7 (100%)          | 253/254 (99.61%)    | 49/72 (68.05%)       | P<0.0001 |
|    |                    | Respiratory samples (375)     | 37/37 (100%)        | 2/2 (100%)          | 231/232 (99.57%)    | 62/104 (59.61%)      |
|    |                    | Pus, wound swabs & fluids (622) | 31/31 (100%)  | --                | 388/388 (100%)      | 128/203 (63.05%)     |
|    |                    | Blood and central line tips (360) | 24/24 (100%) | --                       | 254/254 (100%)      | 61/82 (74.39%)       |
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|   | Ceftazidime |                         |                         |                         |                         |                         |                         |                         |
|---|-------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
|   |             | Urine (428)             | 94/95 (98.95%)          | 6/7 (85.71%)            | 253/254 (99.61%)        | 42/72 (58.33%)          | P<0.0001                |
|   |             |                         | 36/37 (97.29%)          | 2/2 (100%)             | 231/232 (99.57%)        | 54/104 (51.92%)         |                         |
|   |             |                         | 31/31 (100%)            | --                     | 388/388 (100%)          | 117/203 (57.63%)        |                         |
|   |             |                         | 24/24 (100%)            | --                     | 254/254 (100%)          | 54/82 (65.85%)          |                         |
| 2 |             | Blood and central line  |                         |                         |                         |                         |                         |
|   |             | tips (360)              |                         |                         |                         |                         |                         |
| 3 |             |                         |                         |                         |                         |                         |                         |
|   | Piperacillin-tazobac- |                         |                         |                         |                         |                         |                         |
|   | tam          | Urine (428)             | 74/95 (77.89%)          | 5/7 (71.43%)            | 231/254 (90.94%)        | 24/72 (33.33%)          | P<0.0001                |
|   |             |                         | 18/37 (48.65%)          | 1/2 (50%)              | 221/232 (95.26%)        | 28/104 (26.92%)         |                         |
|   |             |                         | 24/31 (77.42%)          | --                     | 356/388 (91.75%)        | 53/203 (26.11%)         |                         |
|   |             |                         | 18/24 (75%)             | --                     | 241/254 (94.88%)        | 29/82 (35.36%)          |                         |
| 4 |             | Blood and central line  |                         |                         |                         |                         |                         |
|   |             | tips (360)              |                         |                         |                         |                         |                         |
| 5 |             |                         |                         |                         |                         |                         |                         |
|   | Ciprofloxacin | Urine (356)             | 78/95 (82.10%)          | 5/7 (71.43%)            | 243/254 (95.67%)        | --                      | P<0.0001                |
|   |             |                         | 20/37 (54.05%)          | 2/2 (100%)             | 222/232 (96.55%)        | --                      |                         |
|   |             |                         | 27/31 (87.09%)          | --                     | 368/388 (94.85%)        | --                      |                         |
|   |             |                         | 19/24 (79.17%)          | --                     | 245/254 (96.46%)        | 33/82 (40.24%)          |                         |
| 6 |             | Blood and central line  |                         |                         |                         |                         |                         |
|   |             | tips (360)              |                         |                         |                         |                         |                         |
| 7 |             |                         |                         |                         |                         |                         |                         |
|   | Lomefloxacin | Urine (356)             | 84/95 (88.42%)          | 4/7 (57.14%)            | 225/254 (88.58%)        | 19/72 (26.39%)          | P<0.0001                |
|   |             |                         | 22/37 (59.46%)          | 2/2 (100%)             | 201/232 (86.64%)        | 28/104 (26.92%)         |                         |
|   |             |                         | 22/31 (70.97%)          | --                     | 368/388 (94.85%)        | 86/203 (42.36%)         |                         |
|   |             |                         | 18/24 (75%)             | --                     | 223/254 (97.79%)        | 29/82 (35.36%)          |                         |
| 8 |             | Blood and central line  |                         |                         |                         |                         |                         |
|   |             | tips (360)              |                         |                         |                         |                         |                         |
| 9 |             |                         |                         |                         |                         |                         |                         |
|   | Amikacin    | Urine (428)             | 72/95 (75.79%)          | 4/7 (57.14%)            | 236/254 (92.91%)        | 11/72 (15.27%)          | P<0.0001                |
|   |             |                         | 22/37 (59.46%)          | 2/2 (100%)             | 221/232 (95.26%)        | 28/104 (26.92%)         |                         |
|   |             |                         | 23/31 (88.87%)          | --                     | 356/388 (91.75%)        | 79/203 (38.92%)         |                         |
|   |             |                         | 20/24 (83.33%)          | --                     | 231/254 (90.94%)        | 29/82 (35.36%)          |                         |
| SN | Antibiotics                        | Pseudomonas aeruginosa n/N (%) | Acinetobacter baumannii n/N (%) |
|----|-----------------------------------|-------------------------------|---------------------------------|
| 1  | Ceftriaxone                        | 1622/1785 (90.87%)           |                                 |
| 2  | Ceftazidime                        | 1586/1785 (88.85%)           |                                 |
| 3  | Piperacillin-Tazobactam            | 1323/1785 (74.12%)           |                                 |
| 4  | Ticarcillin-Clavulanic acid        | 1264/1406 (89.90%)           |                                 |
| 5  | Aztreonam                          | 1241/1406 (88.26%)           |                                 |
| 6  | Imipenem                           | 327/419 (78.04%)             |                                 |
| 7  | Meropenem                          | 249/1406 (88.83%)            |                                 |
| 8  | Ciprofloxacin                      | 1334/1785 (74.73%)           |                                 |
| 9  | Levofloxacin                       | 1344/1406 (88.90%)           |                                 |
| 10 | Tigecycline                        | 14/533 (2.67%)               |                                 |
| 11 | Colistin                           | 0/533 (0.0%)                 |                                 |

IR- Intrinsic resistance, n- total number of isolates showing resistant for that particular antibiotic, N- total number of isolates tested by AST
type III (imipenem resistant meropenem resistant - IRMR). Fourth category was imipenem sensitive meropenem sensitive - ISMS group after screening their AST reports. Prevalence of IRMS, MRIS, IRMR and ISMS phenotypes of Pseudomonas aeruginosa and Acinetobacter baumannii in our study are represented in Figure-2. After their initial screening, resistance patterns with other antimicrobial agents were systematically studied. From the resistance profiles of P. aeruginosa and A. baumannii isolated from different clinical samples comparison among IRMS, MRIS, IRMR and ISMS phenotypic groups were done using Graph Pad Prism and result was found to be statistically significant (P<0.0001), which is represented in Table-2 and Table-3. Overall burden of resistance shown by P. aeruginosa and A. baumannii from all clinical samples tested are represented in Table-4 and Figure-3.

**DISCUSSION**

In our study, A. baumannii (25.25%) were more common than P. aeruginosa (10.95%) similar to studies by Sarkar M et al., whereas previous studies by Grewal, et al., Benachinmardi, et al. showed P. aeruginosa infection more prevalent indicating a shifting trend towards more infections by A. baumannii in recent time. According to CDC report in a sentinel survey from July – October 2015, CRPsA prevalence was 9.1%, whereas according to WHO survey (2015), 17.8% were CRPSA for European countries and 19.2% CRPSA in USA was reported. Studies by Gonçalves et al (2017) reported 43.9% CRPsA in Brazil. In our studies CRPsA was 62.29% which is even more and alarmingly high. WHO has also reported 49.5% CRAB prevalence in USA. Another study by Su C-H et al., showed that there was a significant increase in the proportion of number of HAIs caused by CRAB from 14% in 2003 to 46% in 2008 (P<0.0001). Whereas in our study 74.17% CRAB were detected from HAI.

Though only 1.54% P. aeruginosa and 3.6% A. baumannii were isolated from urine samples but proportion of CRPSA (73.59%) and CRAB (83.18%) were highest from patients with HA-UTI. From blood culture of patients with bacteremia and septicemia, only 3.63% P. aeruginosa and 9.54% A. baumannii were isolated, with 64.34% CRPSA and 76.99% CRAB. From patients with HA- pneumonia and VAP, 4.8% P. aeruginosa and 8.14% A. baumannii were isolated, of which 48.12% CRPSA and 72.26% CRAB were detected. From pus and wound swabs of wound infections and surgical site infections, 4.31% P. aeruginosa were isolated but CRPSA was 69.41% which is higher than that of bacteremia and HA-pneumonia or VAP. Whereas maximum number of A. baumannii 12.25% were isolated from pus and wound swabs but CRAB was 68.21% which is lower compared to those isolated from HA-UTI, bacteremia and septicemia and HA- pneumonia and VAP patients.

Both imipenem and meropenem resistance (IRMR) was compared to those isolated from HA-UTI, bacteremia and septicemia, only CRPsA was 62.29% which is even more and alarmingly high. WHO has also reported 49.5% CRAB prevalence in USA. Another study by Su C-H et al., showed that there was a significant increase in the proportion of number of HAIs caused by CRAB from 14% in 2003 to 46% in 2008 (P<0.0001). Whereas in our study 74.17% CRAB were detected from HAI.

CRPsA cases among them are shown in Table-I. CRPsA and CRAB cases were further categorised into different types of resistance phenotypes such as type I (imipenem resistant meropenem susceptible - IRMS), type II (meropenem resistant imipenem susceptible - MRIS) and
whereas 53.15% of \textit{P. aeruginosa} and 63.70% \textit{A. baumannii} were resistant to meropenem. This discrepant carbapenem susceptibility profile is due to the two rare phenotypes IRMS(9%-10%) and MRIS (0.5%-1.5%). Carbapenem-resistant groups have shown significantly higher resistance for all antibiotics excepting colistin(0.99%-1.69% resistance). Also \textit{A. baumannii} were in general more resistant than \textit{P. aeruginosa} with increasing resistance pattern for all antibiotics except colistin. (Figure-3)

Carbapenem-resistant gram-negative bacteria are highly transmissible and have a high potential to cause outbreaks in health care settings.\textsuperscript{20} Outbreaks of CRAB have been found to be mainly transmitted via the hands of health care workers, contaminated equipment and the health care environment.\textsuperscript{20} Mortality and clinical outcomes of CRAB and CRPsA can be severe. One meta-analysis found that patients with CRPsA bacteremia had 3.07 higher odds of death compared to those with carbapenem-susceptible \textit{P. aeruginosa} bacteremia.\textsuperscript{20} Another meta-analysis found a significant association between carbapenem resistance and mortality among \textit{A. baumannii} infection patients.\textsuperscript{20}

\textbf{CONCLUSION}

Our study have showed an alarmingly high prevalence of carbapenem resistance among HAI patients, more with \textit{A. baumannii} infections than \textit{P. aeruginosa} infections, along with high antibiotic resistance with all groups of antibiotics except colistin. Carbapenems are often used for treating MDRO infections. But increasing rate of carbapenem-resistance in HAI is warranting judicious use of this group of antibiotics, or our last resort colistin will be increasingly used as saviour drug. This will acquire colistin resistance over carbapenem resistance leading to pan drug resistant isolates, which have already started emerging and leading to clinical failure leaving no treatment options in our hand. This rise in the prevalence of CRAB and CRPsA in current scenario can be severe and strict infection control strategies should be followed to prevent worst outcomes.

\textbf{ACKNOWLEDGEMENT}

We heartily acknowledge Prof. Dr. Suddhadhan Batabyal, Principal of R G Kar Medical College for his kind and constant support and enthusiasm in research works. We are also thankful to all technical staffs and other teaching faculties of Dept. of Microbiology, R G Kar Medical College.

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Source of Support: Nil; Conflict of Interest: None
Submitted: 19-11-2019; Accepted: 15-12-2019; Published: 31-12-2019