Changing Trend of Antimicrobial Resistance in *Acinetobacter baumannii*

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Acinetobacter baumannii is an opportunistic nonfermentative, gram-negative, nonmotile, oxidase-negative bacillus. The natural reservoir still remains to be determined. However, it is found in many health care environments and is a very effective human colonizer in the hospital[1]. The combination of its environmental resilience and its wide range of resistance determinants renders it a successful nosocomial pathogen[2]. *A. baumannii* is mostly a cause of septicaemia, pneumonia and urinary tract infection following hospitalisation of patients with more severe illness. *A. baumannii* is frequently involved in numerous global outbreaks[3], occurring mostly in intensive care units[4].

The microorganisms that are mainly involved in antibiotic resistance are the so called ESKAPE pathogens, standing for *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacteriaceae*, capable of "escaping" from common antibacterial treatments[3]. Among these *A. baumannii* is one of the most challenging nosocomial pathogens due to its widespread emergence of antibiotic resistance.

In 1970 *A baumannii* was sensitive to most antibiotics, but now the pathogen appears to exhibit extensive resistance to most antibiotics[5]. The rapid emergence of multi- and pan drug-resistant strains of Acinetobacter highlights the organism's ability to quickly acclimatize to selective changes in environmental pressures. The up regulation of the organism's innate resistance mechanisms coupled with the acquisition of foreign determinants have played a crucial role in the express route the organism has taken to becoming a multidrug-resistant pathogen[6].

Acinetobacter spp. can acquire and spread antimicrobial resistance through conjugation of plasmids[7,8]. In addition Transposons (mobile genetic elements that are integrated into the chromosome or on plasmids) are also responsible in the dissemination of genetic determinants of resistance in *Acinetobacter* spp.[9, 10]. Many of these transposons contain integrons (predominantly class 1).

Integrons are genetic elements that, although unable to move themselves (they are carried either with plasmid or transposon), contain an *int* gene and gene cassettes that can be mobilized to other integrons or to secondary sites in the bacterial genome [11,12,13]. As in other gram-negative bacteria, an MDR phenotype in *A. baumannii* results when integron-borne resistance determinants against different classes of antibiotics coexist, giving rise to MDR gene cassettes. The selection and dissemination of the mobile elements carrying these resistance genes may be amplified in the clinical setting by the indiscriminate use of antibiotics[14, 15].

Fournier et al.[16] identified an 86-kb region called the AbaR1 resistance island in resistant strains of *A. baumannii* that contained a cluster of 45 resistance genes in the MDR isolates. Among the resistance genes determined were those coding for VEB-1, AmpC, and OXA-10 beta-lactamases, various aminoglycoside-modifying enzymes (AMEs), and tetracycline efflux pumps. Genetic analysis of AbaR1 demonstrated that it had similar mobile genetic elements and other genes previously identified in *Pseudomonas spp.*, *E coli*, and *Salmonella* spp. However, the homologous location in the susceptible strain of *A. baumannii* consisted of a 20-kb genomic island devoid of resistance genes.

Acinetobacter species are becoming a major cause of nosocomial infections and can present major challenges for physicians. Of growing concern is the increase in multidrug resistance exhibited by clinically relevant species[17]. Similar to western countries multidrug-resistant isolates of *A. baumannii* have been reported increasingly during the last decade in Bangladesh, probably as a consequence of indiscriminate use of antimicrobial agents. A study in Bangladesh showed that antibiotic were prescribed on the basis of patient's complaints and also the antibiotics were used in inappropriate doses and durations (18).

A study in Bangladesh demonstrated that among *A baumannii,* MBL encoding genes such as blaNDM-1 (83.33%), blaVIM (66.67%) and blaIMP (41.67%); and ESBL encoding genes such as blaCTX-M-15

(16.67%) and blaOXA-1 (12.50%) were detected by PCR (19). In another study in Dhaka Medical College, 6.37% *A baumannii* were identified from 345 wound swab samples and of them 91% were multidrug resistant. All the identified *A baumannii* were sensitive to colistin and 82% to imipenem. Out of 20 multidrug resistant *A baumannii*, adeB gene was detected in 16 (80%). 4 (18%) of 22 *A baumannii* were imipenem resistant. NDM-1 gene was detected in 2 (50%) of the imipenem resistant strains of *A baumannii*[20].

In a recent study form Bangladesh on *A baumannii* demonstrated that colistin resistance genes *pmr*A (11.11%), *pmrB* (28.89), pmrC (11.11%), *phoP* (8.88%), *phoQ* (4.44%), *mgrB* (11.11%), *lpxA* (28.89%), *lpxC* (28.89), *lpxD* (28.89%), *mcr2* (8.88%), *mcr4* (4.44%) and tigecycline resistance gene *tetA* (8.88%) were detected by PCR using specific primers (21).

The present study was undertaken for identification and susceptibility on 69 isolates of *Acinetobacter* from critical care centers (CCC) from Combined Military Hospital (CMH). In the study, total 17 antibiotics were used to identify resistance pattern of Acinetobacter isolates. Ceftazidime (91.30%), ceftriaxone (91.30%), amikacin (52.20%), gentamicin (33.33%), cotrimoxazole (50%) and ciprofloxacin (65.22%) were mostly resistant. Only colistin appeared as most effective antibiotic with only 7.70% resistance rate.

Restriction of the use of antibiotics, especially those with broad-spectrum activity and those identified as antibiotics of last resort, is a necessary complement to any infection control strategy. The implementation of systems to monitor antimicrobial resistance and its relationship to antimicrobial use, as well as a program of antimicrobial stewardship, has been recommended by WHO. These are likely to have an impact on MDR *A. baumannii*, particularly as specific antimicrobials resistant to this organism were identified.

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