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Original Research Article

A Comparative Study of ICU And Non ICU Bacterial Blood Stream Infections with an emphasis on the role of Non Fermenters: *Acinetobacter* and *Pseudomonas* Species

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ABSTRACT

Background: Emerging trends in non ICUs (Intensive care units) reveal an increase in morbidity and mortality directly proportional to risk factors, virulence capabilities and resistant antibiograms in contrast to the ICU settings.

Aims & Objectives: To determine the bacterial blood pathogens isolated from adult ICUs and compare it with isolates from non ICU (wards) settings in regard to antimicrobial resistance and analyze the role of carbapenems and colistin with special reference to non fermenters like *Acinetobacter* and *Pseudomonas* species.

Methods: A one year prospective cohort study of patients in adult ICUs and non ICUs. Positive bacterial Bactec blood cultures from patients admitted in both these settings and possible risk factors and antibiogram patterns were noted. Analysis was done using SPSS software.

Results: The most significant bacterial blood isolates in both settings was *Staphylococcus aureus*, *Acinetobacter* and *Pseudomonas species* from non ICUs were predominant and demonstrated a higher degree of drug resistance in comparison with ICU strains. The major risk factors in the ICUs were intubations and mechanical ventilations and in non ICU settings were elderly patients with a history of recent hospital admissions requiring central line interventions and third line therapies.

Conclusion: Growing incidence of community acquired multidrug resistant (MDR) non fermenters in non ICUs is a reminder to adopt systematic surveillance and minimize associated risk factors.

Key words: Blood stream infections ICUs, Non ICUs, Non fermenters, Resistant antibiograms.

INTRODUCTION

Blood stream infections (BSIs) are a major cause of healthcare-associated morbidity and mortality. [1] These occur in critically ill patients leading to excess length of stay and extra costs. [2] Intensive antibiotic therapy and mechanical ventilation in ICU's have been associated with adverse outcomes. Considerable differences do exists in a number of bacterial bacteremias that occur outside ICUs. The significance of this study lies in the emergence of an increasing incidence of BSIs under a new entity called healthcare-associated (HCA) community onset disease. The objectives of this study was to

determine the bacterial blood pathogens isolated from adult ICUs and compare it with isolates from non ICU settings in regard to antimicrobial resistance and analyze the effectiveness of third line antibiotics with special reference to non fermenters like *Acinetobacter* and *Pseudomonas* species.

MATERIALS AND METHODS

A prospective cohort study from January to December 2011 of patients from the various adult intensive care units (ICUs) and non ICUs (wards) of a tertiary care teaching institute in South Kanara district of Karnataka, India. During the study period after informed consent blood culture samples were collected from 3604 patients who presented with or developed bacteremia. Polymicrobial bacteremia if at least one Gram negative organism was present was included. Subsequent episodes of bacteremia in study patients and fungal isolates were excluded from the analysis. Positive flagged Bactec 9120 Plus Aerobic/F blood culture bottles were subjected to Gram stain and sub cultures were made to obtain growth which was then identified by standard phenotypic and biochemical methods. The antibiogram was performed by Kirby-Bauer disc diffusion as per the CLSI guidelines. Quality control was assured by concurrent testing with the American Type Culture Collection (ATCC) strains. Isolates with intermediate susceptibility were considered resistant.

RESULTS

Table 1: Age & Sex wise distribution of the cases studied

Age group	Patients with significant isolates	
	ICU	NON ICU
≤ 20	9	17
21-49	29	102
≥ 50	55	109
Total= 321	93	228

Out of the total 3604 cases, 193 males and 128 females had significant blood stream isolates. Their age wise distribution in both settings are depicted in (Table 1).

Most common significant bacterial blood isolates from the ICU was *Staphylococcus* 36 (38.7 %) of which 7 (19.44%) *methicillin resistant staphylococcus aureus (MRSA)* strains showed a clinical response only to either vancomycin, or linezolid. Out of the 12 (12.09%) *E.coli* isolates, 50 % were sensitive to third line drugs. Of the 11 (11.8%) *Acinetobacter* isolates, 4 (36.36 %) were sensitive to only to third line drugs and 2 (18.1%) were pan resistant (susceptible only to Colistin). Out of 7(7.5%) *Klebsiella* isolates, 6 (85.7%) were sensitive to third line and one isolate was pan resistant. Among the 5 (5.3%) *Pseudomonas* isolates only 1(20%) showed sensitivity to third line drugs and 2 (40 %) were found pan resistant.(Figure 1 & 2) and in such cases colistin was the only drug of choice clinically.

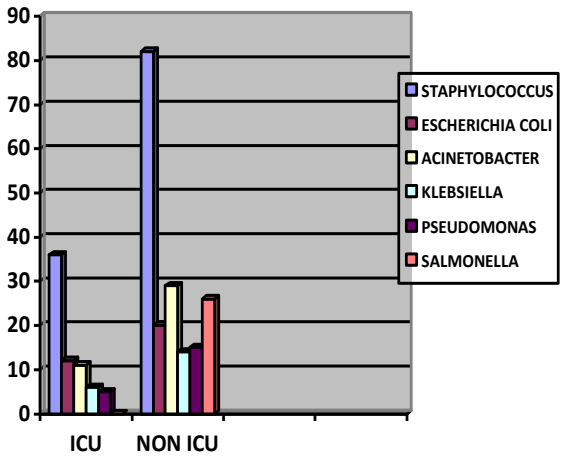

Figure 1: Organisms Isolated In ICU & Non ICUs

In the non ICU settings also *Staphylococcal* isolates 82 (32.4 %) were predominant, followed by *Acinetobacter species* 29 (11.4 %), *Salmonella species* 26 (10.25 %), *E.coli* 20 (7.9 %), *Klebsiella*

14 (5.5%) and *Pseudomonas* 15 (5.9%). Of the 82 *Staphylococcal* isolates 9 (10.97%) were MRSA strains. 7 (24.1%) *Acinetobacter* strains were found pan resistant. Among *Pseudomonas* isolates 6 (40%) were sensitive only to third line drugs. *E.coli* too showed 3 (15%) strains sensitive to third line. 3(21.4 %) *Klebsiella* isolates were sensitive to third line drugs and 2 (14.2 %) were pan resistant. (Figure 1 & 2)

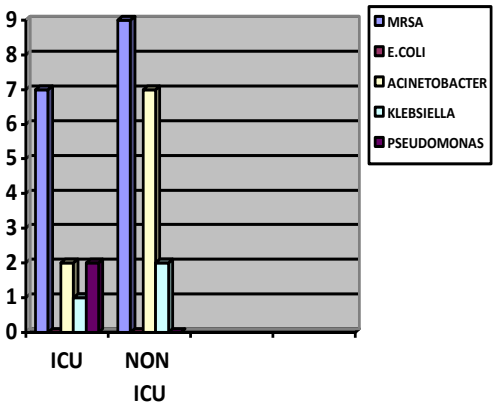

Figure 2: MRSA & Pan Resistance Cases in ICU & Non ICU

All *Staphylococcal* isolates were sensitive to amikacin and cefuroxime. 11.1% strains showed resistance to levofloxacin & ciprofloxacin in both set ups. There was one isolate each of *Burkholderia cepacia* and *Group B Streptococcus* from the ICU. Third line alternatives like piperacillin-tazobactum and cefoperazone-sulbactum combinations along with either imipenem or meropenem exhibited comparable activity against ICU and non ICU isolates of all organisms tested. No resistance was found against vancomycin or linezolid among Gram positive isolates in both settings.

DISCUSSION

Potential risk factors in BSI are patients with cystic fibrosis, neutropenia, iatrogenic immunosuppression or disrupted anatomical barriers that normally prevent bacterial invasion (e.g., skin) are at risk of infection with *Pseudomonas aeruginosa* or *Acinetobacter baumannii.* [3] While a suitable empiric or adequate antibiotic therapy is an important factor for BSI, there are other associated factors like a history of previous hospital stay that may be more important in determining the prognosis among the non-ICU population. [4] Interventions focused on optimizing treatment for non-ICU patients would likely have the greatest benefit in neutropenic and transplant patients, and patients at risk for *Pseudomonas* bacteremia. Bloodstream infections (BSI) are generally discussed as two entities i.e. community acquired (CA) or hospital acquired (HA). A third entity called healthcare-associated (HCA) community onset disease has been increasingly recognized. [5] These infections are also distinctly different based on a number of epidemiologic, microbiologic, and outcome characteristics. [5] Nosocomial or hospital acquired infections begins after admission or are acquired in the hospital. Community-acquired infections are those present or incubating at the time of hospital admission.

As a result of increasingly complex medical services being provided in the community environment patients may present to hospital with infections that closely resemble characteristics with HA infections. [5] An increase in the rate of antimicrobial resistance results in the use of expensive drugs, more prolonged hospitalizations, higher death rates, and health care costs. [6] A number of factors contribute to the emergence of antimicrobial resistance in ICUs including the severity of patient illness, cross-infections, use of invasive devices, mechanical ventilation, prolonged hospital stay and the widespread use of prophylactic and therapeutic antibiotics. [7] The non ICU settings too can be a potential threat as was evident in our study where

intra venous lines, elderly patients with recent hospital admissions and therapies were the predominant associated factors leading to BSI. There were notable differences in the antibiogram of isolates collected from different age and gender groups. A large difference was seen in Imipenem susceptibility, which was higher for the elderly age groups in both settings of our study which was similar to the findings in a study by Wang et al. [8] These threats could probably reflect on the emerging trend of HCA infections.

The most problematic isolates for patients within the ICU were *Enterobacteriaceae* members, non-fermenters like *Pseudomonas aeruginosa, Acinetobacter species, oxacillin-resistant S. aureus* and *vancomycin-resistant enterococci (VRE)* in a study by Aysen Byram et al. [9] In our study too, the most common bacterial blood pathogens encountered in our ICUs were *Staphylococcus aureus, E.coli, Acinetobacter, Klebsiella* & *Pseudomonas species*. Patients in the ICU are more likely than others to be colonized or infected with an antimicrobial-resistant pathogen, leading to higher resistance in patients cared for in the ICU than in non-ICU patients. [9] In recent years *Acinetobacter spp.* has emerged as an important pathogens of ICUs, most of them being resistant to ampicillin, carbenicillin, cefotaxime, chloramphenicol, and gentamicin. [7] On the contrary in our study, non-ICU patients accounted for approximately more than half of the bloodstream infections in the hospital and a large proportion of which were Gram-negative bacteremias as was also an observation by Jonas Marschall. [4] Urinary tract infections were the predominant source of bacteremia in non ICUs and this was in contrast to Gram-negative bacteremia in ICU patients, which frequently were from the respiratory tract.

The rising incidence of ceftazidime-resistant *Klebsiella pneumonia* and *Enterobacter species*, could be attributed to plasmid-mediated extended spectrum-lactamases (ESBLs) and hyperproducers of type 1 chromosomal-lactamases. [4] The most alarming trend detected in a study by Melinda et al [10] was the decreasing activity of ciprofloxacin which was also a similar finding in our study in both setups to *enterobacteriaceae* and non fermenters. The decline in activity of ciprofloxacin correlates with a greater than 2.5-fold increase in use of quinolones (ciprofloxacin, levofloxacin, ofloxacin) popular agents for treating community-acquired pneumonia, urinary tract infections, and skin and soft tissue infections. [4] Ciprofloxacin resistance may be associated with limited treatment options for other classes of agents, as observed in our study and other studies. [11] Despite advances in sanitation, hygiene facilities and newer antimicrobials to tackle nosocomial infections, *Acinetobacter* and *Pseudomonas* infections still remains a threat in critically ill patients with the transmission effected especially by hands of hospital staff. [12]

The resemblance of these pattern of infections and resistance speaks volumes on the unique nature of HCA infections. In our study most of the *Acinetobacter* isolates from both ICUs and non ICUs were resistant to quinolones including levofloxacin, aminoglycosides and third line antibiotics. The resistant rates were comparable to a study by Byram et al., [9] with an exception to *Acinetobacter species* which showed greater pan resistance in non ICU settings during the year under investigation. Carbapenem-resistant isolates

of *Acinetobacter* (isolates resistant to imipenem or meropenem) were more prevalent in the Middle East, Latin America and Asia / Pacific rim than in North America or Europe. Carbapenem-resistant *Acinetobacter* was evenly distributed between gender and age groups but was markedly more common among ICU patients than non-ICU patients [8] in sharp contrast to our findings of a probable health care associated pan resistance.

Acinetobacter however is known to rapidly and effectively acquire or up-regulate mechanisms of drug resistance. [12,13] Our findings were not consistent with findings by Jones et al. in respect to *Acinetobacter* where the current understanding of increased resistance among ICU-based pathogens, as ICUs have played host to the emergence and spread of drug-resistant pathogens globally for several years. [14] *Acinetobacter baumannii* is the third most common pathogen isolated from critical care units in a global study by Hackel et al. [15] The cephalosporins, beta-lactams (with beta-lactamase inhibitors), fluoroquinolones, carbapenems and aminoglycosides are no longer therapeutic options for this difficult to treat pathogen. He also found tigecycline to be the only marketed glycycline available currently as a viable clinical option. [15] In our study colistin was the only option against these pan resistant isolates. Data from a multicentric Intensive Care Unit Surveillance Study (ISS) in the United States demonstrated that resistance to antipseudomonal agents among ICU isolates of *Pseudomonas aeruginosa* especially fluoroquinolones, was increasing. [16] The ICU isolates of *Pseudomonas aeruginosa* in our study too were relatively resistant.

The associated factors in the non ICUs could be attributed to elderly patients and previous contact with a health care system leading to the invariable need for intra venous lines and empirical therapy and urinary catheterization. These could have probably triggered the emergence of greater resistance in the non ICU settings. Our study highlights the concern towards increasing resistance of bacteria especially the non-fermenters *Acinetobacter* and *Pseudomonas species* in these settings in stark contrast to an international study by Wang et al. [8] who noted that the blood derived *Acinetobacter species* ICU isolates showed considerably more resistance than the non ICU counterpart. *A. baumannii* typically colonizes skin and indwelling plastic devices of the hospitalized patients and more than 80 per cent of *Acinetobacter* isolates carry multiple indigenous plasmids of variable molecular size and code for multi drug resistance. [6] Antibiotic practice guidelines or protocols have emerged as a potentially effective means of both avoiding unnecessary antibiotic administration and increasing the effectiveness of prescribed antibiotics. The usage of some empirical antibiotics need to be scrutinized and multidrug-resistant or pan-resistant strains have to be monitored by the hospital infection control committee (HICC) on a routine basis. Protective measures like good hand hygiene, strict contact isolation may be effective to control infection in both ICUs and non ICU set up. [12]

CONCLUSION

The current increase in trend of HCA infections in non ICU settings brings to light the need of setting up strict uniform code of antibiotic stewardship nationwide with an emphasis on the role of continuous monitoring of infection by the HICC in particular to non fermenters which will go a

long way in providing a safe healthy hospital environment for the generations to come.

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