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Original Research Paper

NOSOCOMIAL BACTEREMIA CAUSED BY *PSEUDOMONAS AERUGINOSA*: SENSITIVE TO ANTIBIOTICS AND RISK FACTORS

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ABSTRACT

The present study through transversal analysis reveals the profile of patients' infection in the ICUs of a Tertiary care hospital. It aims at categorizing patients with a focus on the prevalence rates of infection, sites and types of infection, most prevalent bacteria and its antimicrobial resistance patterns, as well as identifying the risk factors for ICU acquired infection. One of the 50 patients admitted to ICU showed bacteremia due to *Pseudomonas aeruginosa*. This isolate might not necessarily have represented the cause of infection nevertheless regarding the isolates reported. The predominance of Gram negative bacilli *P. aeruginosa* was identified. Previous report, showed the predominance of Gram positive cocci *Staphylococcus aureus*, and Gram negative organisms *P. aeruginosa.*

Keywords: Bacteremia, Gram negative, Antibacterial drug resistance, Broad spectrum antibiotics.

INTRODUCTION

The infection is not present in the patient at the time of admission in the hospital. The patient comes in contact with the infective agents, gets contaminated and infected due to altered resistance. This infection is called Nosocomial Infection. Prevention is by cutting the route of transmission and by separating the source of infection from the rest of the hospital. Nosocomial infections are responsible for the morbidity and mortality in hospitalized patients. Various studies highlighted the prevalence of nosocomial infections ranging from 2.8% to 34.6%. Infections in the ICU patients are important problems. The Centre for Disease Control and Prevention defines the Intensive Care Unit (ICU) associated infections as those that occur after 48 hours of ICU admissions or within 48 hours after the transfer of the patients from ICU (Shalini *et al.,* 2010; Steinberg *et al.,* 1996). Blood stream infections associated with severe sepsis (septic shock) are frequently observed and represent major cause of death in patients admitted at ICUs (Jayachandra *et al.,* 2011). Numerous studies have been carried out to assess the implications and the risk factors for the nosocomial bacteremia and several factors including the age of patients, severity of illness, length of ICU stay, presence of invasive catheters and transfusions have been shown to predict mortality independently (Pratham *et al.,* 2011, Khadka *et al.,* 2011). Some studies showed that elderly patients have an increased rate of infections as well as higher prevalence of Bacteremia. Such very frail elderly bacteremic patients are commonly encountered and account for the higher proportion of fatalities in ICUs (Bello *et al.,* 2011, Baghaei *et al.,* 2011; Alberti *et al.,* 2002). With the spread of Multidrug Resistant Bacteria, the treatment of nosocomial bacteremia has become a challenging task. The profile of

nosocomial bacteremia varies between the institutions and also various wards and ICUs of the hospitals (Mathur *et al.,* 2005). Hospital acquired Blood stream infections (BSI) is a serious health care problem worldwide associated with significant morbidity and mortality. In developing countries, 10 – 20 % of Nosocomial Infections are estimated to involve the blood stream (Zorgani *et al.,* 2010; Steinberg *et al.,* 1996).

Appropriate anti-microbial treatment of BSI is critical in decreasing morbidity and mortality due to BSI. Many surveillance studies indicate a trend of increasing anti-microbial resistance among the common pathogens such as *Staphylococcus* species, the most common bacteria reported for BSI among patients in ICUs. The data from the surveillance and control of pathogens of epidemiologic importance (SCOPE) surveillance system in USA hospitals showed that 49.4% of all nosocomial BSI (Lay *et al*., 2010) occurred in the ICU. Risk factors for MRSA blood infections have been extensively described but vary among the institutions and patient population. The frequency of Gram negative sepsis has diminished over the last 20 years. However *Pseudomonas aeruginosa* is considered an important nosocomial blood stream infection (BSI), pathogen with a high mortality. Small numbers of bacteria of low virulence are present from time to time in the blood of normal subjects or in individuals often with minor subclinical lesions. The availability of an ever increasing number of immuno compromised hosts has led to a population where the incidence of bacteremia has increased. Bacteremia is of some importance for whenever they enter the blood, may settle in the body and cause lesions. However, most reports about poly microbial bacteremia are concerned with specific patient populations such as those with malignancies. Nosocomial infections can cause severe RTI and UTI, BI and diseases of other parts of the body (Zorgani *et al.,* 2010; Sabra and Abdel-Fattah, 2012; Arya *et al.,* 2004).

The prevalence of the nosocomial infections is 5 to 10 times higher than other wards. These infections cause higher costs and elongation of patients' ICU stay time. These infections are contagious and may increase the mortality and morbidity in other patients (Alberti *et al*., 2002). National Nosocomial Infections Surveillance system defines a nosocomial infection as a localized or systemic condition that results from adverse reaction to the presence of an infectious agent(s) or its toxin(s) that was not present or incubating at the time of admission to the hospital. As incubation period varies with the type of pathogen and patients underlying condition, each infection must be assessed individually. As incubation period varies with situations in which an infection is considered to be nosocomial (Pratham *et al.,* 2011; Garner *et al.,* 1988; Strausbaugh, 2001).

- Infection that is acquired in the hospital, but does not become evident until hospital discharge.
- Infection in a neonate that results from passage through birth canal.

The source of infection is attributed to various environmental reasons and iatrogenic. Bacteremia is the major problem in the patients who are stayed in the hospitals for more than 3 days in intensive care units and other special wards. Blood culture is planned in this study during August to September 2013. Hence, we studied the nosocomial bacteremia in patients admitted in the ICUs in a hospital in Tiruchirapalli, Tamilnadu, India and traced the source of this pathogen.

MATERIALS AND METHODS

Study Settings and Criteria

The prospective observational study was conducted in Department of Microbiology, Chennai Medical College Hospital and Research Centre, Tiruchirapalli during August to September 2013. After getting approval from institutional ethical committee, informed consent from the participants, the proforma from case sheets were collected. In the present study, microbiological aspects were restricted to bacteriological study only. After explaining the study methodology to the participants/attenders, 50 blood samples were collected from patients admitted in the ICU. Nosocomial or ICU acquired

infection was defined as infection in patients developed after 48 hours of admission (Garner *et al.,* 1988). The adult patients admitted in ICU of both males and females are the inclusion criteria whereas pediatric patients (< 12 years) and HIV positive cases were excluded in this study. For control, samples were collected from ten healthy individuals who are working in hospital.

Sample Collection and Processing

Blood samples were collected under sterile precautions from patients admitted in the ICUs and control subjects. Blood sample of 1 ml was inoculated into Brain Heart Infusion (BHI) broth (1:10 ratio). Bottles were incubated at 37°C for 18-24 hours and subcultured onto MacConkey agar, 5% human blood agar and nutrient agar plates. All plates were incubated at 37°C for 24 to 48 hours (Jayachandra *et al.,* 2011). The isolates bacteria were identified by colony morphology, Gram staining and biochemical tests (Collee *et al*., 1999; Fabiano, 2002).

Antimicrobial Susceptibility Testing

Susceptibility of the bacterial isolates to antimicrobial agents was determined using disc diffusion method as recommended and interpreted according to Clinical and Laboratory Standard Institutes (CLSI). Following antimicrobial agents were used, as standard reference disc with known potency for laboratory use: Imipenam (IPM), Piperacillin/Tozobactam (PIT), Cefotoxime (CTX), Ceftriaxone (CTR), Ceftazidime (CAZ), Cefixime (CFM), Ciprofloxacin (CIP), Amikacin (AK), Azithromycin (AZM), Cefpodoxime (CPD) and Levofloxacin (LE). All tests were performed on plates of Muller Hinton Agar. 0.5 McFarland suspension standardized test bacterial isolates was seeded to the plates and the test antibiotic discs were placed and dried in incubator at 37°C for 15 minutes. Then all agar plates were incubated at 37°C for 18-24 hours. Results were recorded by measuring the inhibition zone in mm and interpreted according to CLSI procedures (Bauer *et al.,* 1966). Data were analyzed using simple descriptive sterility.

RESULTS AND DISCUSSION

Patients' Demography's and Interventions

Among the 50 patients studied 31 (62%) were males and 19 (38%) were females (Figure 1). A total of 9 patients had undergone surgery, 24 hours before admission to ICU of which all are defined as elective surgery patients. All the 50 patients were having IV Catheters. Age wise distribution of patients included in the study is depicted in Figure 2. On the day of study, 8 (16%) patients were under mechanical ventilation, 50 (100%) on central venous catheters, 16 (32%) with urinary catheters and 5 (10%) with Ryles' tube (Figure 3).

Prevalence of Infections

Result of blood culture revealed that positive bacterial blood culture (Bacteremia) was observed in 1 patient (2%) where as all controls showed no growth (Table 1). The comorbid illnesses associated with the patients included in the study are Diabetes mellitus in 21 patients (42%), Hypertension in 9 patients (18%) and both in 1 patient (2%) (Figure 4). Among 50 subjects included, 10 patients (20%) were in unconscious state. The outcome of the hospital stay is an important parameter for determining the type of infections. Thus among the 50 patients, stay in the ICUs ranged from 1-70 days. The detailed description of outcome of ICU stay is shown in (Figure 5).

Antimicrobial Susceptibility

Among the 50 cases included in this analysis, only one patient who underwent surgery was identified to have bacteremia positive and it was a monomicrobial, confirmed as *Pseudomonas aeruginosa.* The antimicrobial susceptibility test showed resistance to Cefixime, Cefpodoxime, intermediate to Ceftrioxone and sensitive to Imepenam, Piperacillin/ Tozobactum, Cefotaxime, Ceftazidime, Ciprofloxacin, Amikacin and Levofloxacin. Three contaminants were grown among 50 blood samples. The detailed interpretation of antimicrobial susceptibility test is depicted in Table 2.

Risk Factors for ICU Acquired Infections

More number of studies suggested and highlighted possibilities of risk factors for

acquiring infections inside the ICU environment. The age group of 50-60 was identified as risk factor. No mortality was recorded. The patients were mainly distributed among the ICUs including post surgical, poisoning, medical, neurological etc. The present study is performed by transversal analysis that reveals the profile of patients' infection in the ICUs of a tertiary care hospital. It aims at categorizing patients with a focus on the prevalence rates of infection, sites and types of infection, most prevalent bacteria and its antimicrobial resistance patterns, as well as identifying the risk factors for ICU acquired infection. *P. aeruginosa* had been reported in the United States by the Centre for Disease Control and Prevention to be the most isolated nosocomial pathogen accounting for 10.1% of all hospital acquired infections, and has been implicated in gastrointestinal infection, primarily in immunocompromised individuals (Jayachandra *et al.,* 2011; Carlos *et al*., 2003, Nadeem *et al*., 2006; Todar, 2004). The results of isolates of the current study are very less compared to other studies showed 10.93% (Pratham *et al.,* 2011), 33.5% (Beaujean *et al.,* 1997) and 16.2% (Richards *et al.,* 1999).

Regarding Bacterial agents, the most prevalent is only one isolate which is *P. aeruginosa*. Concerning resistance patterns for *P. aeruginosa*, Cefixime and Cefpodoxime are ineffective by showing complete resistance, whereas intermediate observation recorded using Ceftriaxone. In general in the Intensive Care Medical environment, possibilities of getting BSIs are high and antibiotic resistant bacteria species were isolated (Carlos *et al*., 2003, Nadeem *et al.,* 2006, Shalini *et al*., 2010). But in this study, isolation of BSI bacteria are very low and it may be attributable to ICU environment due to precautions taken. Normally, empirical treatment schemes are based on knowledge of local microbiota and utilization of wide range of antimicrobials associated are not with others of more specific actions such as Imipenam, Piperacillin/Tozobactum, Ciprofloxacin, Levofloxacin and Amikacin for *P. aeruginosa.* The four major factors which are significantly related to ICU acquired infections are use of catheters and cannulas, post operative status, length of stay in ICUs and age equal to or more than 60 years (reduced immune complex). The maximum age recorded in our study was 59 years concerning with risk factor. This patient had central venous catheters for three days, and the infections may be attributable to central venous catheterization (Carlos *et al.,* 2003, Shalini *et al.,* 2010). According to the literature, Pneumonia was the most frequently observed infection in ICU and Nasogastric intubation represents one of the main risk factors. The usage of drugs that increase gastric pH, facilitate the growth of Gram negative bacteria and raise the risk of pulmonary infections. Post operative patients has a higher propensity for developing infectious complications, since incisions represent gateway for surgery and have a drastic decrease in the immune status due to surgical damage. Early recognition of infections, restricted and short term use of invasive devices and standardized housekeeping practices can therefore, contribute significantly towards decreasing the incidence of nosocomial infections (Pratham *et al.,* 2011).

CONCLUSION

- Only one patient out of 50 studied showed bacteremia with *Pseudomonas aeruginosa*.
- The isolation was sensitive to Imepenam, Piperacillin/ Tozobactum, Cefotaxime, Ceftazidime, Ciprofloxacin, Amikacin and Levofloxacin but resistant to Cefixime and Cefpodoxime.
- Low isolation during the study period may be related to environment, nature of patient treated, immune status of the patient stated.

The limitations of the study are the study is made from single centre, most of the patients were previously exposed to antimicrobials, other sources such as Bone marrow aspirate was not attempted, indirect evidence of bacteremia using biomarkers were not attempted, difficulty in establishing relationships of patient and factors (one cannot predict which factors come first) and

the transversal studies tend to overestimate the long duration of infections and under estimate the short duration infection. Nevertheless this type of transversal analysis has fundamental importance for the knowledge.

SUGGESTIONS

- The integration of clinicians, microbiologists (infection control and housekeeping management) and scientists is very important to achieve the success of Infection control and creating a supportive environment for the patients to recover.
- Regular continuing medical education programs must be conducted to medical and paramedical to maintain proper hygienic environment.
- Invasive procedures may be minimized to reduce the occurrence of bacteremia.
- Anatomical barriers should not be disturbed as much as possible.

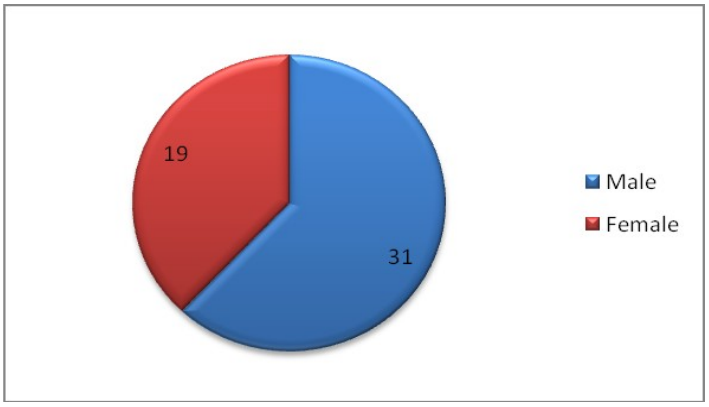

Figure 1: Sex wise distribution of the patients admitted in ICUs

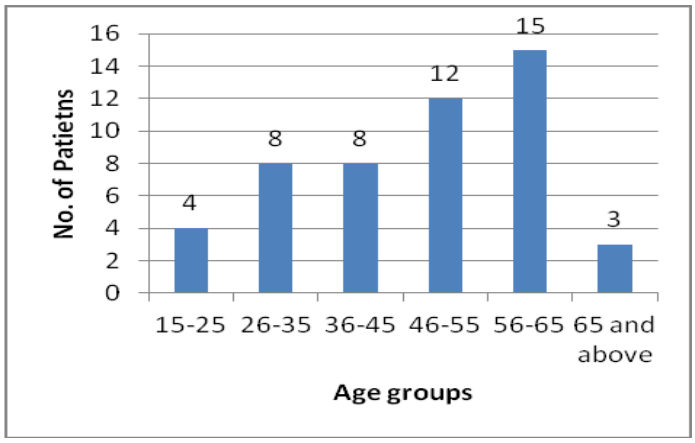

Figure 2: Age wise distribution of patients admitted in ICUs

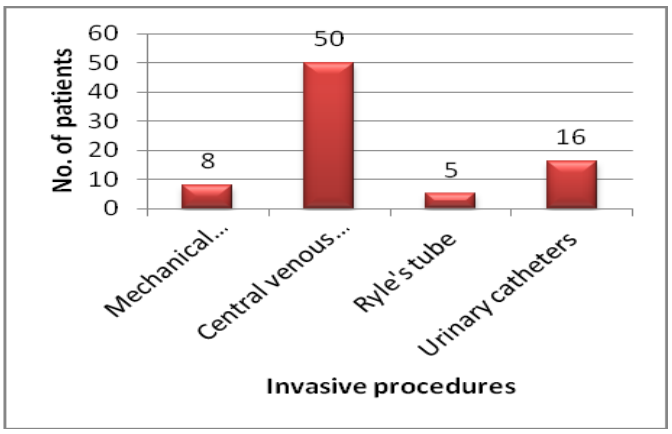

Figure 3: Number of patients with invasive procedures

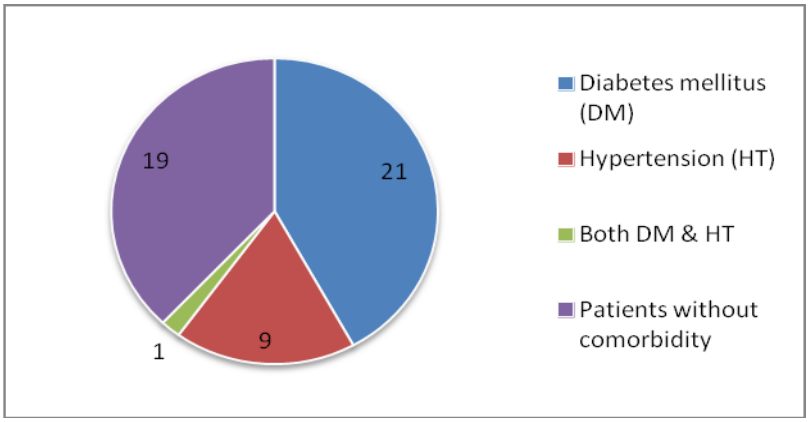

Figure 4: Co-morbid illnesses of the patients admitted in the ICUs

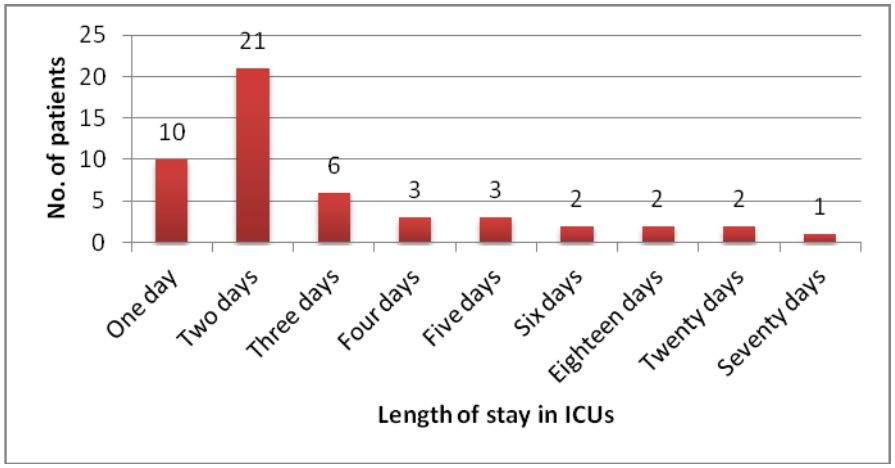

Figure 5: Length of stay of the patients admitted in the ICUs

Table 1: Distribution of Bacteremia among ICU Patients and Control

Patient Group	Total Number	Number of Bacteremia (%)	Number of Non- Bacteremia
Coronary Artery Disease (CAD)	10	0	10 (100%)
Poisoning	3	0	3 (100%)
Fever	3	0	3 (100%)
Obstructive sleep apnea (OSA)	1	0	1 (100%)
Anaphylactic Shock	1	0	1 (100%)
Post Surgery	9	1(11%)	8 (89%)
Rheumatic Heart Disease (RHD)	6	0	6 (100%)
Chronic Liver Disease (CLD)	2	0	2 (100%)
Cerebro vascular Accident (CVA)	13	0	13 (100%)
Diabetic Ketoacidosis (DKA)	2	0	2 (100%)
Total	50	1 (2%)	49 (98%)
Control Subjects	10	0	10 (100%)

Table 2: Interpretation of antimicrobial susceptibility test against *P. aeruginosa*

Antibiotic	Disc Content (mcg)	Standard interpretive criteria (mm)			Results (mm)	Remarks
		Sensitive	Intermediate	Resistant		
Imipenam(IPM)	10	19	16-18	15	39	sensitive
Piperacillin / Tozobactam (PIT)	100/10	21	15-20	14	31	sensitive
Cefotaxime(CTX)	30	23	15-22	14	25	sensitive
Ceftriaxone(CTR)	30	21	14-20	13	20	Intermediate
Ceftazidime(CAZ)	30	18	15-17	14	24	sensitive
Cefixime(CFM)	5	19	16-18	15	13	Resistant
Ciprofloxacin(CIP)	5	21	16-20	15	30	Sensitive
Amikacin(AK)	30	17	15-16	14	27	Sensitive
Cefpodoxime(CPD)	10	17	14-16	13	11	Resistant
Levofloxacin(LE)	5	17	14-16	13	32	Sensitive

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