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A Tertiary Care Hospital Based Study on Antimicrobial Sensitivity Pattern Among Septic Patients

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ABSTRACT

Introduction: Sepsis is a common and highly fatal clinical syndrome that is characterized by systemic inflammatory response syndrome due to infection. It is a final common pathway of many infectious processes, e.g. bacterial, viral, fungal and parasitic infection in critically ill patients. There is a need of study regarding the sensitivity and resistivity pattern of antimicrobials for the proposal or implementation of rational therapy guidelines. This study will also provide the best microbiological information to clinicians to pick the most effective treatment options, positively influencing patient outcomes.

Methodology: A retrospective observational study was conducted among 202 patients at tertiary care teaching hospital during the period from March to November 2018. Patients with sepsis of either gender who are 18 years old or above are included in the study. Non-sepsis adult patient and special populations (pregnant women, psychiatry, HIV) or patients younger than 18 years of age are excluded from the study. Data were collected using validated data collection form. Data were analysed using SPSS 20.0 and Microsoft Excel 2013.

Results: From a total of 202 patients involved in the study, the highest incidence rate was found in the age group >68 years. Gram negative organisms isolated were 81.86%, of these *Klebsiella* species being the most frequent. This isolates showed high rates of sensitivity towards Colistin (96%) Tigecycline (93.3%).

Conclusion: The sensitivity of antibiotics towards species are going down and it is an unpleasant warning of emergence of resistance. From our study it can be anticipated that routine culturing and sensitivity testing should be performed to detect the appearance of resistance

Key Words: Antibiotic, Organisms, Sepsis, Sensitivity

INTRODUCTION

Sepsis is a common and highly fatal clinical syndrome that is characterized by systemic inflammatory response syndrome due to infection^[1]. Sepsis is commonly defined as the presence of infection in association with the systemic inflammatory response to microbial infection which can cause organ damage, shock, and eventual death^[2]. There are typically four progressive stages of sepsis specifically Systemic inflammatory response syndrome, sepsis, septic shock and multi organ dysfunction. Systemic inflammatory response syndrome is stated as the presence of 2 or more of the fol-

lowing: (1) temperature greater than 38°C (100.4°F) or less than 36°C (96.8°F); (2) pulse rate greater than 90 beats/min; (3) respiratory rate greater than 20 breaths/min (or partial pressure of carbon dioxide less than 32); and (4) WBC count greater than 12,000/mm³ or less than 4,000/mm³, or greater than 10% immature band forms^[3]

Age, male gender, black race, and increased burden of chronic health conditions are important risk factors for severe sepsis. It is also more likely to occur in individuals with chronic obstructive pulmonary disease, cancer, chronic renal and liver disease, and diabetes.^[4,5] Other risk factors include

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residence in long-term care facilities, malnutrition, and use of immunosuppressive medications and prosthetic devices. Severe sepsis is more common in colder months, both in the UK (35% higher in winter than in summer) 44 and US (17.7% higher in fall than in summer).^[4] The elderly patient also presents with many symptoms, thus affecting the diagnosis and making it more difficult to make an early diagnosis and to provide therapeutic management^[6].

Although SIRS (Systemic inflammatory response syndrome) often occurs in the setting of infection, non-infectious conditions, such as burns, acute pancreatitis, and trauma, can lead to SIRS. Sepsis was defined as the presence of the SIRS criteria and presumed or proven infection. Severe sepsis was defined as sepsis accompanied by acute organ dysfunction.^[4] The high incidence of sepsis in elderly patients is affected by aging factors that cause the decline in body systems such as metabolism, cardiovascular, visual, genitourinary, immune, nervous system, and drug response.

Worldwide, 31.5 million cases of sepsis occur annually and 5.3 million people have died annually.^[1,7] In 1996, there were 4774 patients admitted to a teaching hospital in Surabaya, Indonesia and 504 patients were diagnosed with sepsis, with a mortality rate of 70.2%. In another study at a teaching hospital in Yogyakarta, Indonesia, there were 631 cases of sepsis in 2007, with a 48.96% mortality rate^[6]. Gram-positive organisms as a cause of sepsis have increased in frequency over time and are now almost as common as gram-negative infections, likely due to greater use of invasive procedures and the increasing proportion of hospital-acquired infection. More frequent use of broad-spectrum antibiotics in increasingly sick patients who remain in the ICU for longer periods of time has likely resulted in an increased bacterial resistance over time. Antibiotic resistance is problematic, prolonging length of stay and duration of mechanical ventilation, although the effect on mortality is uncertain. International variations in the implementation of the two main strategies to control resistance (the more rational use of antibiotics and the prevention of cross-infection between patients) may explain different rates in different countries.^[4]

The discrimination of infection from non-infectious causes of inflammation could also be tough. Biomarkers are prompt to help physicians during this call. There is presently no biochemical technique obtainable that alone permits a speedy and reliable discrimination between infection and non-infectious inflammation. Procalcitonin (PCT) is presently the foremost investigated biomarker for this purpose. C-reactive protein and interleukin 6 perform inferior to PCT in most studies and their value in identification infection is not outlined. All biomarkers together with PCT also are released after various non-infectious inflammatory impacts.

Sepsis is often diagnosed based on simple measurements such as temperature, heart rate and breathing rate. Other tests can help to determine the type of infection and where it is located in body and which body functions have been affected. These include urine or stool samples, wound culture, vaginal secretion, pus or fluid is taken from the affected area for testing, respiratory secretion testing taking a sample of saliva, phlegm or mucous secretion, blood pressure tests, imaging studies such as an X-ray, ultrasound scan or computerised tomography (CT) scan.

A wide spectrum of organisms has been represented that cause blood stream infections and this spectrum is subject to geographical alteration. Increasing antimicrobial resistance is a worldwide concern. The prevalence of resistance of blood borne isolates is increasing and it also varies in accordance with geographical and regional location.

The infection caused by MDR organisms is more likely to prolong the hospital stay, increase the risk of death, and require treatment with more expensive antibiotics. In the majority cases, antimicrobial medical care is initiated through empirical observation before the results of blood culture are available. Keeping in mind the high mortality and morbidity associated with septicaemia, right choice of empiric therapy is of importance.

Therapeutic management of sepsis, severe sepsis, and septic shock requires a systematical approach which combines an accurate diagnosis, rationality of antibiotic use, as well as a rapid and right treatment. Appropriateness in antibiotic use is very important to decrease the mortality and morbidity rate in patients with sepsis. The selection of antibiotics requires information about the location of source infection, the common pathogen that develops into an infection, and the local sensitivity pattern of antibiotics. Aggressive, early antimicrobial therapy is critical in the management of sepsis patients. The regimen selected should be based on the suspected site of infection, likely pathogens, and the local antibiotic susceptibility patterns, whether the organism was acquired from the community or a hospital, and the patient's immune status. Although antibiotic therapy is the cornerstone in the treatment of infections, several studies have questioned that inadequate initial antibiotic treatment of sepsis and bacteraemia is associated with increased mortality.^[8]

One out of four patients in Indian intensive care unit suffer sepsis, a life threatening condition due to bacteria and germs and nearly half of those patients die as a result. An average age of incidence of sepsis in western countries is 57 years and in India 55 years. Economic burden on the patient due to sepsis is very high so the selection of antibiotics should be rational and more appropriate to avoid the burden.

METHODOLOGY

A retrospective observational study was carried out at a multispecialty tertiary care teaching hospital in Mangaluru from November 2017 to March 2018. The study protocol was approved by Institutional Ethics Committee (IEC). Medical records of (male & female) admitted in hospital between November 2016 and November 2018 were obtained from the Medical Records Department of the hospital. A total of 202 cases were collected. Patients with sepsis of either sex who are 18 years old or above were included in the study. Non-septic adult patient and special populations (pregnant women, psychiatry, HIV) and Patients younger than 18 years of age were excluded in the study. The collected data were analysed by using Microsoft Excel 2013 and SPSS 20. The resistivity and sensitivity pattern of antimicrobial agents and prescription pattern were noted and the same were observed and concluded on the basis of prescription to the hospitalized patients in tertiary care hospital

RESULT

Data from 202 patients were collected from the medical record department of tertiary care hospital, out of which 124 (61.4%) were males and 78 (38.6%) were females (Table 1). Out of total population 95 patients had been hospitalized for a duration < 1 week, 68 patients for 1-2 weeks, 28 patients for 2-3 weeks, 8 subjects for 3-4 weeks, 3 patients for > 4 weeks. Most of the patients stayed in hospital for less than one week. Mortality rate of males were 57.25% (N=124) and females, 51.28% (N=78). 77 people were cured during the course of treatment. On analysis we found that out of 78 females and 124 males the percentage of cured population were 41.02% and 36.29% respectively. While 6.93% (14) patients discontinued therapy under LAMA (Leaving Against Medical Advice).

In the present study diabetes mellitus 74(36.6%) is the most common risk factor among patients followed by acute kidney injury 68 (33.6%), bronchopneumonia 47 (23.2%), chronic kidney disease 36 (17.8%), urinary tract infection 18 (8.9%) chronic obstructive pulmonary disorder 15(7.4%), urosepsis 14(6.9%), chronic liver disease 11(5.4%) and acute pulmonary edema 4 (1.9%). We found that 182 culture sensitivity test were conducted out of 202 patients. Out of 182 culture sensitivity tests, gram negative organisms were 149(81.86%) and gram positive organisms were 33(18.14%) (Table 2).

During the study period, 182 culture sensitivity tests were done for 21 organisms out of which *klebsiella* spp. (39, 21.40%) (Figure 1), *Acinetobacter* spp.(33, 18.10%) (Figure 2), *Escherichia coli* (30, 16.40%) (Figure 3) and *Pseudomonas aeruginosa* (18, 09.80%) (Figure 4) were analysed to prescribe antimicrobials.

Table 1: Demographic characteristics of adult sepsis patient

Demographic	Characteristic	Number, %
Gender	Female	78 (38.6%)
	Male	124 (61.4%)
Age	18-28	12 (5.9%)
	29-38	7 (3.5%)
	39-48	27 (13.4%)
	49-58	39 (19.3%)
	59-68	52 (25.7%)
	>68	65 (32.2%)

Table 2: Various organisms identified from sepsis patients

Types	Gram Reaction Percentage N=182	Organism	Number (N%)
Gram positive	33 (18.14%)	<i>Staphylococcus aureus</i>	16 (8.7%)
		<i>Enterococcus faecalis</i>	15 (8.2%)
		<i>Streptococcus agalactae</i>	1 (0.54%)
		<i>Viridans streptococci</i>	1 (0.54%)
		<i>Klebsiella</i> spp	39 (21.4%)
		<i>Escherichia coli</i>	30 (16.4%)
Gram negative	149 (81.86%)	<i>Acinetobacter</i> spp.	33 (18.1%)
		<i>Pseudomonas aeruginosa</i> ,	18 (9.8%)
		<i>Coagulase negative staphylococci</i>	15 (8.2%)
		<i>Enterobacter</i> spp.	3 (1.6%)
		<i>Citrobacter</i>	3 (1.6%)
		<i>Protease vulgaris</i>	2 (1.09%)
		<i>Burkholderia</i> spp.	2 (1.09%)
		<i>Nesseria species</i>	2 (1.09%)
		<i>Chryseobacterium</i> spp.	1 (0.54%)
		<i>Candida</i> spp.	1 (0.54%)

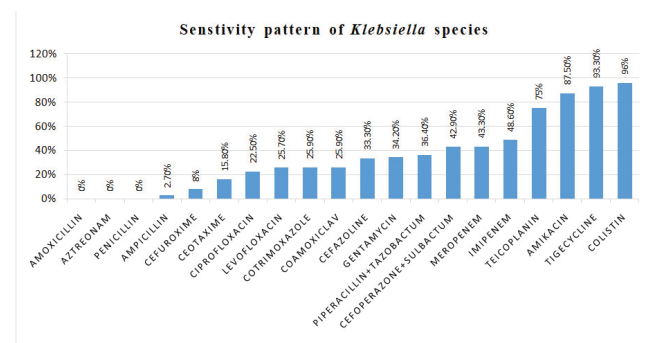


Figure 1: Sensitivity pattern of Klebsiella spp.

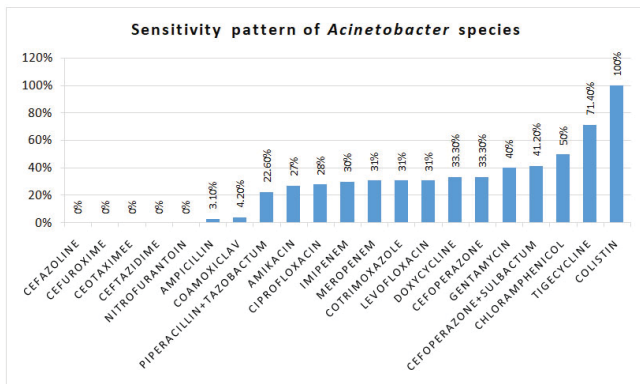


Figure 2: Sensitivity pattern of *Acinetobacter* spp.

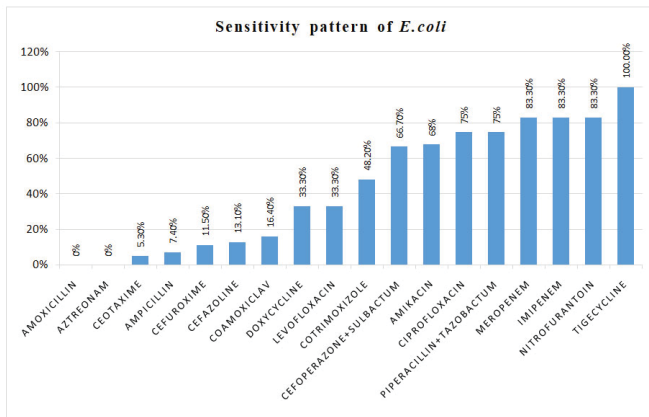


Figure 3: Sensitivity pattern of *E. coli* spp.

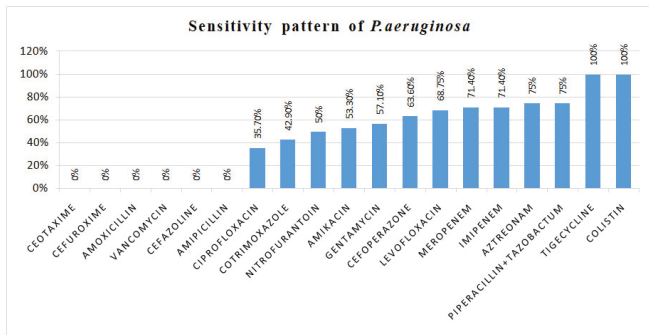


Figure 4: Sensitivity pattern of *P. aeruginosa*.

DISCUSSION

Globally burden of sepsis in healthcare is of considerable importance. Patients with sepsis and no ongoing sign of organ failure at the time of diagnosis have increased chance of death. Patients with severe sepsis or septic shock have the highest mortality rate.

A total of 202 patients, 124 males (61.4%) and 78 females (38.6%) were diagnosed with sepsis. The present study shows that incidence rate of sepsis remains high in males

which was also supported by study done by Angus-DC and Schroder *et al*^[9,10]

Our study found that mortality rate was higher in men than women which was 63.96% and 36.03% respectively, same result was found in study by Schroder, *et al*^[9] Also according to the study conducted by Adrie *et al*, in a group of severe sepsis patients of 50 years of age, women have a lower mortality risk than men.^[11] The differences of incidence and mortality rate between male and female is due to hormonal and non-hormonal factors that influence the immune system. Women have more estrogens production than men, which influences greater activity of the immune system.^[12]

In the present study the highest percentage 32.18% incidence of sepsis is seen in age group above 68 followed by 25.74% fall into age group 59-68 and 31% in age group of 49-58. The highest mortality rate was found in the age group ≥ 68 years. The similar result was found in a study conducted by Ivan pradiptha *et al*. At Bandung private hospital in Indonesia, which showed that highest mortality rate was found in the age group ≥ 65 years.

In critically ill sepsis patients, lacking the quality of antimicrobial therapy at admission to the ICU is associated with a significant attributable mortality. Major among those survivors who did not receive adequate antimicrobial therapy, there is a remarkable increase in ICU and hospital length of stay with the consequences that this implies.

Our study showed that highest risk factor was diabetes mellitus 36.6% which was similar to the result found in the study done by G.C.K.W. Kho *et al*^[13]. The same results were also reported in another study done by Florian B Mayr^[4] that severe sepsis is more likely to occur in individuals with diabetes mellitus, Chronic kidney disease and liver disease.

Among the blood isolated organisms, current study reported that gram positive organisms and gram negative were found as causing sepsis. Organisms isolated were categorized according to their species. Among the blood isolates *Klebsiella* spp. (21.4%) was the predominant cause of sepsis in adults. The second isolated gram negative organism was *Acinetobacter* spp. (18.1%) followed by other organism *E. coli* (16.4%) *Pseudomonas aeruginosa* (9.6%). This finding was similar to other studies reported where Gram negative organism were the common isolated organism than Gram positive such as in Jalandhar (India) (58.46 % and 38.46 %) done by Kumar *et al*.^[14]

In our study imipenem was found to resistant to *Klebsiella* spp. (51.40%). This similar result was found in the study done by Nidhi Pal and Ramamurthy Sujatha that resistance to imipenem seen approximately in 60% with the same organism.^[15]

CONCLUSION

Our study found that gram negative and gram positive bacteria were responsible for adult sepsis while gram negative found to be predominant. Among that, Klebsiella species and Acinetobacter species were found to be common. It was found that the antibiotic Piperacillin/tazobactam was prescribed the most and the same is lacking sensitive to the Acinetobacter species and Klebsiella species. Which gives an alarming conclusion that sensitivity of antibiotics towards the species are going down. From our study it can be anticipated that routine culturing and sensitivity testing should be performed to detect the appearance of resistance.

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