Research Article

Antibiogram for a Teritiary Care Hospital in Kerala

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ABSTRACT

Bacterial sepsis forms a major cause of mortality in the ER ICUs of referral hospitals. This study was performed to propose an antibiogram from a tertiary care centre in south east Asia by tracing out the bacterial spectrum causing sepsis, with special emphasis on body fluid culture sensitivity studies, in the background of presently used empirical antibiotics. One hundred patients with culture positive sepsis, satisfying the inclusion criteria, admitted to the ERICU over a two year period, were selected randomly. Their clinical and demographic profile on admission to the ICU including APACHE II scores, and in vitro culture and antibiotic sensitivity study results were recorded and analyzed. Primary outcome measure was hospital mortality. Out of the 100 sepsis patients admitted in ER ICU, 59 % were under sepsis category, 36% under severe sepsis and 5% under septic shock category. Gram negative bacteria predominated in all cultures. In urine cultures *Escherichia coli* predominated (38.98 %) over *Klebsiella Pneumonia* (18.64%) and *Enterococcus faecalis* (16.95%), blood cultures showed *Escherichia coli* (21.05%), *Klebsiella pneumonia* (18.42%) and *Staphylococcus aureus* (15.78%) as the major organisms. Sputum/ETaspirate/BAL/MiniBAL cultures demonstrated *Klebsiella pneumonia* (33.33%) as the commonest bacteria, followed by *Acinetobacter baumanii* (28.57%). Among the Gram negatives *Klebsiella pneumonia*, and among the Gram positives *Staphylococcus aureus* predominated. Antibiotic sensitivity profile of urosepsis revealed maximum frequency of sensitivity to Nitrofurantoin (12.87%), blood sepsis cases to Amikacin (8.715 %), and lung related sepsis cases to Colistin (10.71%). Amikacin (29.05%) have shown maximum frequency of sensitivity for covering all forms of bacterial sepsis. Gentamicin (21.28%), Cefoperazone sulbactam (19.59%), Piperacillin tazobactam (18.29%), Colistin (17.61%), Levofloxacin (17.1%), Meropenem (16.11%) and Ciprofloxacin (14.54%) also were found to be sensitive.

Keywords: Antibiogram, ERICU (Emergency Room Intensive Care Unit), Culture positive bacterial sepsis, APACHE score (Acute Physiology and Chronic Health Evaluation).

INTRODUCTION

A Systemic Inflammatory Response Syndrome (SIRS) with suspected or proven infection is called sepsis, which is a major cause of mortality and morbidity all over the world, 70% of which are caused by Gram negative bacteria. The unknown nature of incoming pathogens is a major hazard encountered by the Emergency Departments of referral hospitals. Timely identification of sepsis at the entry level, with empirical antibiotic therapy can reduce mortality in the ICUs. The study envisages the identification of probable sepsis causing bacterial pathogens at the entry level taking into account the retrospective and prospective data and to formulate and suggest a suitable empirical antibiotic therapy for future, to reduce mortality in the referral hospital. An antibiogram is *in-vitro* sensitivity of an isolated bacterial strain to different antibiotics. Samples collected from contaminated compartments are analyzed microbiologically and biochemically, following standard protocols. From the culture, an antibiogram is obtained by diffusion (Kirby-Bauer method) or dilution method, and the MIC of a particular bacterial strain is identified. Early empirical broad spectrum antibiotic therapy started parenterally after culture sample withdrawal from the septic patient, ensures improved outcome in septic shock and showed a survival rate of 80% in a retrospective cohort study.[1-3] Each hour of delay in antimicrobial administration over the ensuing 6 hour was associated with an average decrease in survival of 8%.[4]

MATERIALS AND METHODS

Prospective cross sectional study of culture positive sepsis cases, satisfying the inclusion criteria, arriving at Amrita Institute of Medical Sciences (Kochi), during 2012-2014, was reviewed. Sepsis causing bacterial pathogens were identified, and their *in vitro* antibiotic sensitivity studies were conducted. The emergency team managed the patients as per standard protocols.

Once a culture is established, there are two possible ways to get an antibiogram:

Semi-quantitative way based on diffusion (Kirby-Bauer method)

To an agar plate, which is a nutrient-rich environment in which bacteria can grow, drop small discs containing different antibiotics, or impregnated paper discs, in different zones of the culture. A disc of bacterial lysis will become visible when the antibiotic diffuses the area surrounding each tablet. Since the concentration of the antibiotic was the highest at the centre, and the lowest at the edge of this zone, the diameter is suggestive for the Minimum Inhibitory Concentration, or MIC.

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Quantitative way based on dilution

A dilution series of antibiotics is established (this is a series of reaction vials with progressively lower concentrations of antibiotic substance) in which the last vial where no bacteria grow contains the antibiotic at the Minimal Inhibiting Concentration.

Once the MIC is calculated, it can be compared to known values for a given bacterium and antibiotic: e.g. a MIC > 0.06 µg/ml may be interpreted as a penicillin-resistant *Streptococcus pneumoniae*. Such information may be useful to the clinician, who can change the empirical treatment, to a more custom-tailored treatment that is directed only at the causative bacterium.

RESULTS AND DISCUSSION

In our study, culture positive sepsis cases were classified as sepsis, severe sepsis and septic shock categories. Out of the 100 patients admitted with sepsis, 59 % were under sepsis category, 36% of severe sepsis category, and 5% were of the septic shock category (Figure 1).

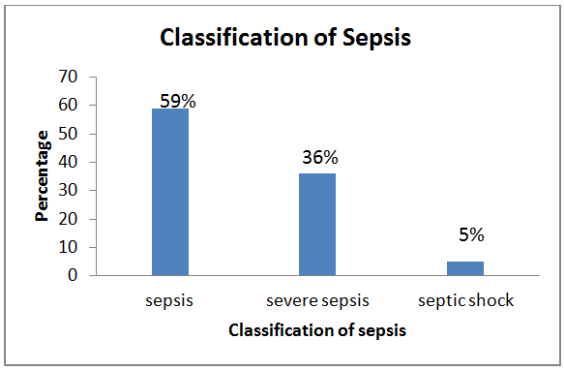

Figure 1: Classification of Sepsis

The Microbiology department of our hospital, adhering to standard techniques and procedures, conducted bacteriological analysis of the urine, blood, sputum/BAL/MiniBAL/ET aspirate samples, that were aseptically collected from the sepsis patients. Out of 100 patients, a total of 120 culture samples (60 urine, 38 blood, 22 sputum/BAL/MiniBAL/ET aspirate) were collected and analysed.

In Figure 2, the Antibiotic sensitivity profile of urine culture positive sepsis cases showed maximum frequency of sensitivity to Nitrofurantoin (12.87%), followed by Amikacin (10.66%), Cefoperazone Sulbactam (8.456%), Meropenem (7.72%), Colistin (5.88%), Gentamicin (5.88%), Piperacillin-Tazobactam (5.88%), Linezolid (5.15%), Levoflox (5.15%) and Cotrimoxazole (5.15%).

In Figure 3, the blood culture positive sepsis cases exhibited maximum frequency of sensitivity to Amikacin (8.715 %), Gentamicin (7.34%), Piperacillin Tazobactam (5.96%) and Cefoperazone Sulbactam (5.5%) and in Figure 4, the Antibiotic sensitivity profile of ET/BAL/MiniBAL culture positive bacterial sepsis cases has shown maximum frequency of sensitivity to Colistin (10.71%) followed by Amikacin (8.67%), Tigecycline (6.63%), Gentamicin (6.63%), Cefoperazone- Sulbactam (6.12%), Piperacillin-Tazobactam (5.61%) and Ciprofloxacin (5.1%), Levoflox (5.1%), Doxycycline (5.1%) and Chloramphenicol (5.1%).

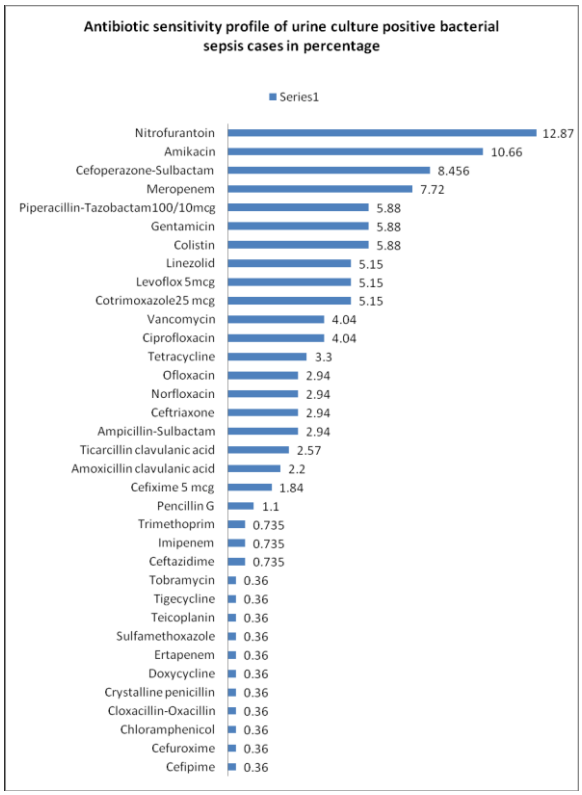

Figure 2: Antibiotic sensitivity profile of urine culture positive bacterial sepsis case

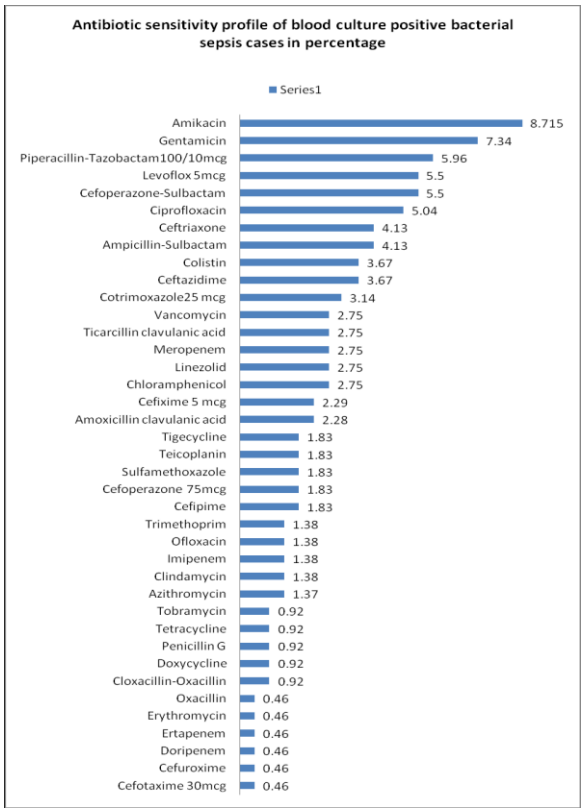

Figure 3: Antibiotic sensitivity profile of blood culture positive bacterial sepsis

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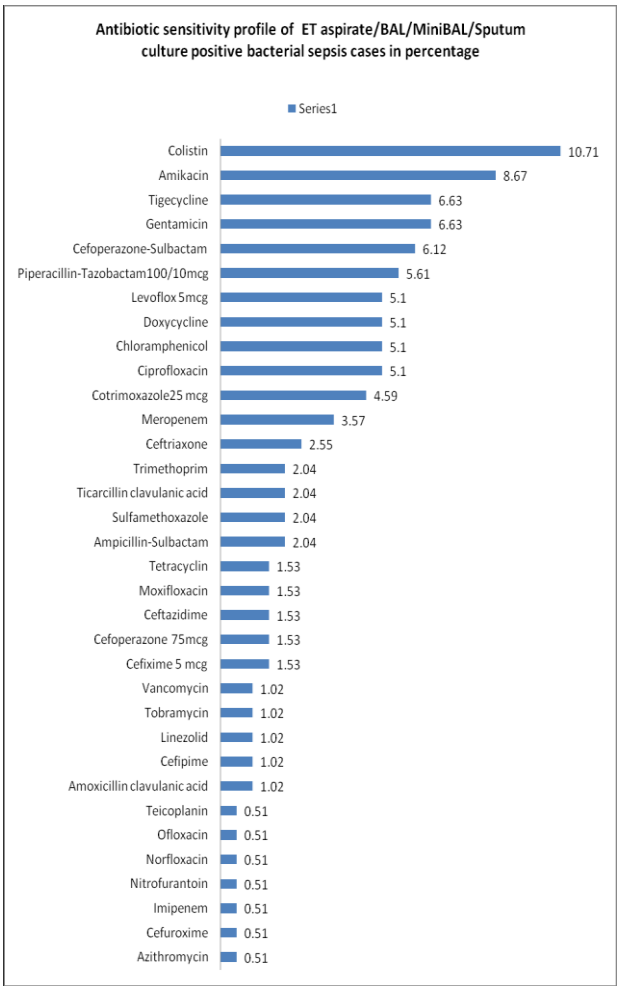

Figure 4: Antibiotic sensitivity profile of ET aspirate/BAL/MiniBAL/Sputum culture positive bacterial sepsis

This study has demonstrated that among the 18 empirical antibiotics administered in urine culture positive bacterial sepsis cases, i.v Piperacillin Tazobactam (25.6 %) was found to be the most prescribed drug, followed by Ceftriaxone (15.85 %), Cefoperazone Sulbactam (14.63 %) and Amoxicillin Clavulanic acid (7.32%). Among the 15 empirical antibiotics administered in blood culture positive bacterial sepsis cases, i.v Piperacillin Tazobactam (21.15%) was the most prescribed drug, and Ceftriaxone (15.38%), Cefoperazone Sulbactam (13.46%), Meropenem (11.54%), Levoflox (9.61%), and Metronidazole (7.69%) followed suit. Fifteen empirical antibiotics were administered in sputum/BAL/MiniBAL/ET aspirate culture positive bacterial sepsis cases. i.v Piperacillin Tazobactam (29.31%) was the most prescribed drug, followed by Meropenem (12.06%), Cefoperazone sulbactam (10.34%), Clindamycin (8.62%), Levoflox (6.89%), and Amoxicillin Clavulanic acid (6.89%).

Out of a total of 100 patients admitted with sepsis, 72% survived and 28 % expired.UK ICNARC studies showed a hospital mortality of 36% from severe sepsis, and the Surviving Sepsis Campaign reported a mortality of 34.8%.[5]

DISCUSSION

In this study, data of 100 culture positive sepsis cases admitted via ER were collected, of which 59 belonged to sepsis category, 36 of severe sepsis category and 5 belonged to septic shock category. From these patients, a total of 120 samples were collected, analysed and the causative bacterial pathogens were identified and studied. Out of the 100 sepsis cases, 60 belongs to urine culture positivity with sepsis, 38 belongs to blood culture positivity with sepsis and 22 belongs to sputum/BAL/MiniBAL/ET culture positivity with sepsis. The results of urine, blood and sputum/BAL/MiniBAL/ET aspirate bacterial sepsis were compared, to identify the pathogens common to all. This study has shown that out of all the gram+ve sepsis cases, Staphylococcus aureus constituted the majority, followed by Enterococcus faecium and Enterococcus faecalis.

Spread of *Staphylococcus aureus* (including MRSA) and faecal contamination indicator organisms can be prevented by maintenance of personal hygiene and disinfection measures. Carriers of resistant strains may be subjected to “eradication therapy”, as per standard protocol.

Among the gram negatives, Klebsiella pneumonia exhibited predominance over Escherichia coli and Acinetobacter baumanii. Hence, specific antibiotic therapy against these bacteria is suggested. Piperacillin Tazobactam, Cefoperazone Sulbactam, Ceftriaxone and Meropenem were the most commonly administered empirical antibiotics. The repeated usage of antibiotics can cause increased bacterial resistance in the community, and hence not advocated, unless indicated.

Based on the available data collected from the microbiological reports, amikacin was found having maximum frequency of sensitivity for covering bacterial sepsis in urine, blood as well as in lungs. Other drugs found sensitive were Piperacillin Tazobactam, Levofloxacin, Ciprofloxacin, Gentamicin, Cefoperazone Sulbactam, Colistin and Cotrimoxazole. The evolution of bacterial resistance to repeated doses of Piperacillin Tazobactam, and the rising sensitivity profile of the sparingly used Amikacin, should lead the ER physicians to try alternative empirical drugs to decrease bacterial resistance. To overcome the resistance the combination therapy of Piperacillin tazobactam with amikacin/tobramycin is preferred.

The maximum prescribed drug as per our study was Piperacillin Tazobactam. The urosepsis cases referred to our hospital showed more sensitivity to Nitrofurantoin, Amikacin, Cefoperazone-Sulbactam and Meropenem. The blood sepsis cases showed more or less equal sensitivity to Amikacin, Gentamicin, Piperacillin Tazobactam and lung related sepsis showed fairly equal sensitivity to Amikacin, Gentamicin, Colistin, Levofloxacin, Piperacillin Tazobactam and Meropenem. The drawback in this observation could be that, all the isolated bacteria were

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not tested for sensitivity with all the available empirical antibiotics. This could have brought certain bias in our study. The minimum inhibitory concentration for every drug has to be measured, and every bacterial culture has to be tested with all the listed empirical antibiotics, to accurately comment on the efficacy of a particular antibiotic. Further studies involving larger groups, and testing of all the empirical antibiotics for sensitivity, are urgently warranted, to clearly suggest a reliable antibiotic formulation to combat sepsis, in the Emergency Department.

CONCLUSION

Bacterial sepsis is caused by gram positive and gram negative bacteria, the latter constituting the predominant group. The former comprised of *Staphylococcus aureus and Enterococcus faecium*, and the latter included *Klebsiella pneumonia and Escherichia coli indole*.

Escherichia coli, Klebsiella pneumonia and *Enterococcus faecalis* constituted the major bacterial pathogens in urosepsis.

Klebsiella pneumonia, Acinetobacter baumanii and *Pseudomonas aeruginosa* constituted the major bacterial lung pathogens.

Escherichia coli, Klebsiella pneumonia and *Staphylococcus aureus* constituted the major bacterial pathogens in blood culture positive sepsis cases.

Since all the antibiotics presently administered for empirical therapy were not tested for MIC values and sensitivity; further studies involving a larger group of referred sepsis patients have to be undertaken, before arriving at a suitable empirical antibiotic selection profile to combat sepsis. It was observed that for gram negative bacteria piperacillin tazobactam with amikacin combination was effective, piperacillin tazobactam with tobramycin combination is also a good alternative, but it is slightly costlier than the previous one.

For gram positive bacteria cefoperazone sulbactam with amikacin combination was effective, and cefoperazone sulbactam with tobramycin/gentamycin combination also equally effective alternative.

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