Pattern of Antibiotic Sensitivity and Resistance in Various Cases of Sepsis in a Mixed Intensive Care Unit set up in a Tertiary Hospital

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ABSTRACT

Introduction: Sepsis has been shown to be one of the critical reasons for Intensive Care Unit admissions of patients for which early and empirical use of antibiotics have been used. Antibiotics resistance is becoming a matter of serious concern, especially in developing countries like ours. In this study, all the cases those were diagnosed with sepsis and had culture positive results for bacteria have been evaluated. **Aims:** To find out the common organisms responsible for sepsis in patients admitted to the Intensive Care Unit and to know the antibiotic sensitivity/resistance patterns. **Methods:** The study was done from May 2022 to April 2023 in mixed Intensive Care Units on the clinical isolates from blood, urine, sputum, endotracheal tube aspirate, central venous catheter tips and wound swabs and those were sent to microbiology department for culture and sensitivity. All the organisms were identified morphologically and biochemically and antibiotic susceptibility pattern was determined by standard laboratory procedure. **Results:** We took a total of 102 samples in which organisms were isolated. The most frequently isolated bacteria were Klebsiella (24.91%) followed by Staphylococcus aureus (24.5%), both were sensitive to Doxycycline and Tazobactam-piperacillin in most cases. Other organisms isolated were Escherichia coli (15.69%), Streptococcus (9.8%), Pseudomonas (8.82%), Acinetobacter (6.86%), Enterobacter species (3.92%) and Proteus (0.98%). Azithromycin was found to be the most resistant drug followed by Amoxycillin/clavulanic acid and Levofloxacin. **Conclusion:** Klebsiella was found to be the most prevalent cause of sepsis in ICU. Most of the frequently isolated pathogens were resistant to Beta lactamase inhibitors, Cephalosporins and Quinolones. Regular surveillance of antibiotic susceptibility pattern is very important for setting a guideline to the clinician in choosing an appropriate therapy for patients with sepsis.

Keywords: Antibiotic Sensitivity, Bacterial resistance, Infection, Intensive care unit, Tertiary Hospital

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INTRODUCTION

Antibiotics have been extensively used in hospital settings, especially in intensive care unit (ICU). There are many sources of infections prevalent in ICU and these are related to blood stream, urinary catheterization, central venous catheterization, wounds, nosocomial infection etc. These infections can turn out to be the cause of life-threatening sepsis which requires prompt and aggressive management with antimicrobial agents.[1] As soon as sepsis is diagnosed, empirical use of antibiotics is started before the results of blood cultures are available. Inappropriate use of antibiotics in treatment of sepsis increases the mortality of patients and increases the risk of emergence of drug resistant strains which is a major public health concern in the present day.[2] Thus, regular surveillance of antibiotics use is mandatory as the infection caused by multi-drug resistant (MDR) organisms is more likely to prolong the hospital stay, increase the risk of death, and require treatment

with more expensive antibiotics.[3]

Nepalgunj Medical College Teaching Hospital (NGMCTH) receives majority of its patients from Western parts of Nepal, including Banke, Dang, Salyan, Pyuthan, Rukum, Kailali and Kanchanpur districts, with high volume of patient flow. Studies on different types of antibiotics used, their resistance pattern in different types of infections have not been studied in recent past in our ICU Setup. Hence, we have carried out this study in order to ascertain better care of the patients with the designed antibiotic policy after knowing the profile of prevalent strains along with their antimicrobial resistance pattern.

METHODS

We conducted a, descriptive, cross-sectional study for a period of one year (May 2022 to April 2023) at NGMCTH, a tertiary care centre in Banke district. Ethical approval was taken from the Institutional Review Board. Irrespective of intubation status, those patients who were admitted to the mixed ICU set up and had positive bacterial culture reports were included in the study. All those cases which failed to meet the SOFA criteria for sepsis were excluded in the study.

Sepsis is defined as a life threatening organ dysfunction caused by a dysregulated host response to infection. Clinical criteria for sepsis include suspected or documented infection and an acute increase of two or more sequential organ failure assessment (SOFA- altered mental status, respiratory rate ≥ 22 breaths/minute, systolic Blood pressure ≤ 100 mm of Hg).[14]

A total of 102 samples of sepsis cases which yielded pathogenic bacteria from sputum, pus, urine, blood, wound swabs, central venous catheter (CVC) tips and endotracheal tube were obtained. Following strict aseptic precautions, all the samples were collected. All the organisms were identified morphologically and biochemically by standard laboratory procedure.

The samples were received in the microbiology laboratory for culture and sensitivity and inoculated on to blood and MacConkey agar. Urine specimens were inoculated onto cysteine lactose electrolyte deficient medium (CLED) and incubated at 37°C for 24 hours. Growths obtained on solid media after 24 hours of aerobic incubation were processed for identification and antimicrobial susceptibility. Using the colony characteristics, the morphology of growth, Gram's stain, and different biochemical tests, organisms were identified as per standard guidelines.

Antibiotic susceptibility testing was done for the most predominant Bacteria (Klebsiella, Staphylococcus aureus, Escherichia coli, Streptococcus), using Muller Hinton agar method by Kirby Bauer disc diffusion method.[4] The following antibiotics (Hi–media disc) that were tested include amoxicillin/clavulanic acid, tazobactam-piperacillin, ceftriaxone, amikacin, nitrofurantoin, levofloxacin, imipenem, doxycycline, ofloxacin and azithromycin.

RESULTS

Of the 102 samples which yielded growth of bacteria in culture, 67(66%) were gram negative and 35(34%) were gram positive bacteria.

The two most common organisms responsible for sepsis were found to be Klebsiella (n=30, 29.41%) and Staphylococcus aureus (n=25, 24.50%), followed by E. coli, Streptococcus, Pseudomonas, Acinetobacter, Enterobacter and Proteus respectively.

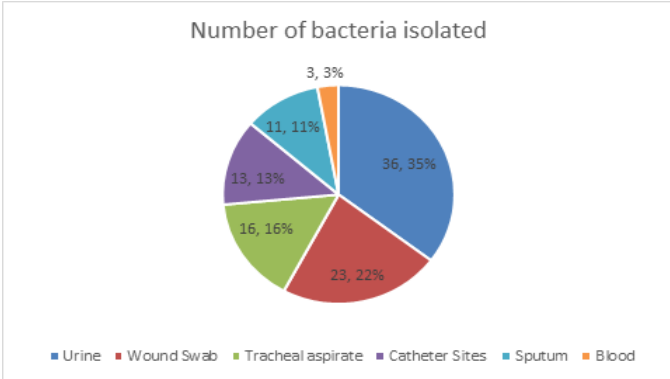

Figure 1: Distribution of organism based on types of specimen

The highest percentage of organism was isolated from urine sample (35%) followed by wound swab (22%), then tracheal aspirate (16%) and CVC tip (13%) as shown in figure 1.

Microorganism		TA	Sputum	Blood	Urine	CVC tip	WS
Klebsiella	Count	6	5	2	5	5	7
	% in sample type	37.5%	45.45%	66.66%	13.88%	38.46%	30.43%
	%within Klebsiella	20%	16.66%	6.66%	16.66%	16.66%	23.33%
	%within total	5.88%	4.90%	1.96%	4.90%	4.90%	6.86%
Streptococcus	Count	5	3	1	1	0	0
	% in sample type	31.25%	27.27%	33.33%	2.77%	0%	0%
	%within strepto	50%	30%	10%	10%	0%	0%
	% within total	4.90%	2.94%	0.98%	0.98%	0%	0%
Staph. aureus	Count	1	1	0	14	5	4
	% in sample type	6.25%	9.09%	0%	38.88%	38.46%	17.39%
	%within Staph	4%	4%	0%	56%	20%	16%
	% within total	0.98	0.98	0%	13.72%	4.90%	3.92%
Enterobacter species	Count	1	0	0	2	0	1
	% in sample type	6.25%	0%	0%	5.55%	0%	4.34%
	% in Entero-bacter	25%	0%	0%	50%	0%	25%
	% within total	0.98%	0%	0%	1.96%	0%	0.98%

Pseudomonas	Count	1	2	0	1	1	4
	% in sample type	6.25%	18.18%	0%	5.55%	7.69%	17.39%
	% in Pseudomonas	11.11%	0%	0%	11.11%	11.11%	44.44%
	% within total	0.98%	1.96%	0%	0.98%	0.98%	3.92%
E.coli	Count	0	0	0	11	0	5
	% in sample type	0%	0%	0%	30.55%	0%	21.73%
	% in E. coli	0%	0%	0%	68.75%	0%	31.25%
	% within total	0%	0%	0%	10.78%	0%	4.90%
Acinetobacter	Count	2	0	0	2	2	1
	% in sample type	12.5%	0%	0%	5.55%	15.38%	4.34%
	% in Acinetobacter	28.57%	0%	0%	28.57%	28.57%	14.28%
	% within total	1.96%	0%	0%	1.96%	1.96%	0.98%
Proteus vulgaris	Count	0	0	0	0	0	0
	% in sample type	0%	0%	0%	0%	0%	0%
	% in Proteus	0%	0%	0%	0%	0%	0%
	% within total	0%	0%	0%	0%	0%	0%

TA- Tracheal Aspirates, CVC- Central Venous Catheter, WS- Wound Swabs

Table I: Distribution of bacterial isolates in the clinical samples and overall bacterial isolates

In the clinical samples of tracheal aspirate, sputum, blood, catheter site and wound swab, the predominant bacteria isolated was found to be Klebsiella (29.411%), which was highest isolate in tracheal aspirate (37.5%) whereas, Staphylococcus was the most common organism for urinary infection (n=14, 38.88%) and CVC tip infection (n=5, 38.46%). (Table I) E coli was isolated as second most common organism causing Urinary infection (n=11, 30.55%)

Antibiotics	Klebsiella Gram Negative		Staph. aureus Gram Positive		E.coli Gram Negative		Streptococcus Gram Positive	
	Sensitive	Resistance	Sensitive	Resistance	Sensitive	Resistance	Sensitive	Resistance
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Doxycycline	25 (83.34)	5(16.66)	21 (84)	4 (16)	14 (87.5)	2 (12.5)	8 (80)	2 (20)
Tazobactam+ Piperacillin	16 (53.33)	14 (46.66)	18 (72)	7 (28)	12 (75)	4 (25)	7 (70)	3 (30)
Amikacin	12 (40)	18 (60)	13 (52)	12 (48)	8 (50)	8 (50)	2 (20)	8(80)
Ofloxacin	15(50)	15(50)	13 (52)	12 (48)	8 (50)	8 (50)	5 (50)	5(50)
Amoxicillin+ Clavulanate	2 (6.66)	28 (93.34)	5 (20)	20 (80)	6 (37.5)	10 (62.5)	6 (60)	4 (40)
Levofloxacin	7 (23.34)	23 (76.66)	9 (36)	16 (64)	8 (50)	8 (50)	5 (50)	5 (50)
Ceftriaxone	5 (16.66)	25 (83.34)	12 (48)	13 (52)	7 (43.75)	9 (56.25)	7 (70)	3 (30)
Imipenem	18 (60)	12 (40)	14 (56)	11 (44)	10 (62.5)	6 (37.5)	7 (70)	3 (30)
Azithromycin	4 (13.33)	26 (86.67)	2 (8)	23 (92)	2 (12.5)	14 (87.5)	5 (50)	5 (50)

Table II: Antibiotic sensitivity and resistance pattern of predominant bacteria isolates

The antibiotic sensitivity testing was done for the four major common bacterial isolates.

Doxycycline was found to be the most sensitive antibiotic (66.66%) to both gram positive and gram negative bacteria responsible for ICU infections in our setting, closely followed by Tazobactam+ Piperacillin and Imipenem at 51.9% and 48.8% respectively. Azithromycin was found to be the most resistant drug overall for the bacterial isolates in our ICU setting at 67.9%, along with Amoxycillin/clavulanic acid and Levofloxacin at 61.9% and 49.9% respectively.

For the most commonly isolated bacteria (Klebsiella), the most sensitive and most resistant antibiotics were found to be Doxycycline(83.34%) and Amoxycillin+Clavulanate(93.34%) respectively, as compared to the other antibiotics.

DISCUSSION

Though infections can be both primary and secondary, it is found that secondary infection is found to be more common in ICU than primary.5 Infection among ICU patients may be due to Community acquired (bacterial meningitis / encephalitis, pneumonia, intra –visceral abscesses, urinary tract infection) or hospital and health care associated infection like surgical site infections, hospital acquired pneumonia, central venous catheter related blood stream infections and catheter associated UTI.[6] Our study revealed that infection rate was highest in urinary tract (35.29%) followed by wound infection (22.54%), which is similarly to the finding of Patwardhan et al.[1]

Our study showed Staphylococcus aureus as the most common bacterial isolated from the urine sample followed by E coli. Most of the studies have shown E coli being the most frequent isolate from urinary samples. However, study from Nigeria done by Onanuga A et al has suggested the increasing prevalence of Staph aureus in UTI.[12] Study done by Akortha E et al has shown Staph. aureus as the most common isolate from urine sample ahead of E coli.[13]

The key goal for any ICU should be to reduce antimicrobial resistance. This will improve treatment outcome and consequently decrease the length of ICU stay leading to reduced hospital costs.[7] Therefore, appropriate knowledge of bacterial profile and antibiogram is imperative while treating patients in the ICU. In the present study, Klebsiella, a gram negative, facultative anaerobic rod-shaped bacteria, is the most common organism (29.41%) followed by Staphylococcus (24.5%), E coli

(15.69%) and Streptococcus (9.8%) in our ICUs, which is similar to the study conducted by Pawar and Steth et al,[2,3] showing gram negative bacteria to be the most frequently isolated bacteria, among which Klebsiella was the most common.

Doxycycline has been shown to have good activity against many organisms, including gram-positive, gram-negative and atypical bacteria. In addition, it appears to have some potentially clinically useful anti-inflammatory properties while reviewing the safety and efficacy.[4] Our study revealed that doxycycline followed by tazobactam+piperacillin proved to be most sensitive to both gram positive and negative organisms which is in concordance with the study done by Singh A et al and Chaturvedi et al.[5,6]

Overall, majority of resistance was observed to azithromycin (67.9%). Antimicrobials such as azithromycin, amoxycillin/clavulanic acid, levofloxacin and ceftriaxone showed > 50% of resistance. This might be due to the widespread use of macrolides and cephalosporins. Similar findings with higher percentage of resistance was observed in a study by Sanjana et al.[8]

The resistance of Klebsiella to cephalosporins is usually due to breakdown of the drug by extended spectrum beta-lactamases (ESBL) as seen in study done by Sheth et al.[3] Infection with ESBL organisms is associated with increased hospital stay and increased cost of management. In our study, Klebsiella was most resistant to amoxicillin+clavulante, azithromycin and ceftriaxone. Our findings are similar to those of the study conducted by Keyal et al, where Klebsiella showed high rate of resistance to azithromycin (93%), amoxicillin+clavulanate(82%), and ceftriaxone (60%).[9]

Staphylococcus and E coli, both were found to be resistant to Azithromycin (>80%) followed by amoxicillin+clavulante and Levofloxacin. Our study findings are similar to those seen in study done by RK Sanjana et al.[8] High resistance rate to cephalosporins and quinolone antibiotics to these frequently isolated pathogens were also noted.[10] In our study, Streptococcus was found to be resistant to Amikacin, an aminoglycoside (80%), followed by Ofloxacin, Levofloxacin and Azithromycin. This finding is comparable to those seen in study done by Patwardhan RB et al.[1]

All these studies reassure that indiscriminate use of antibiotic, without institutional policy, contributes to the emergence of antimicrobial resistance in gram positive as well as gram negative bacteria which could result in treatment threat.[10,11]

CONCLUSION

Antibiotic resistance is an increasing problem because of its excessive use in clinical practice. Gram-negative pathogens made up the majority of the infections agent in our ICU setting. Klebsiella and E. coli were the most predominant pathogens isolated. Among the gram positive organism, Staphylococcus aureus was the most predominant. Most of bacteria were sensitive to doxycycline and resistant to amoxicillin+clavulante, ceftriaxone, azithromycin and levofloxacin in our study. Therefore, antibiotics need to be prescribed based on the antibiogram of individual pathogens in order to diminish antibiotic resistance. In addition, antibiotic stewardship program ought to be followed in each hospital.

LIMITATIONS

The most important limitation of our study is the small sample size. Not all antibiotic discs were available throughout the study period in the Department of Microbiology. Same antibiotic discs could not be used for the isolated organism in each isolates. So those samples could not be included in the study. Also the range of antibiotics used for the sensitivity testing was also guarded due to limited availability.

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