ORIGINAL ARTICLE

Trends in Bloodstream Infection in Tertiary Care Hospital: A Retrospective Cross-sectional Study

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ABSTRACT

Introduction: Bloodstream Infection is one of the leading causes of mortality and morbidity among various groups of patients in a developing country like Nepal. Identification of the bacteria and their susceptibility to commonly used antibiotics is very essential for the treatment of the patients. **Aims:** This study aims to analyze current trends in bloodstream infection by accessing their bacteriological profile and antibiotic susceptibility. **Methods**: This is a hospital-based retrospective analysis of blood cultures of patients suspected with bloodstream infection. We conducted a three years (January 2018 to January 2021) retrospective analysis of blood culture reports from patients suspected with bloodstream infection. Data of the laboratory reports were used to determine bloodstream infection, blood culture contamination, pathogen profile and antimicrobial resistance patterns. **Results:** Out of 12811 blood samples that were sent to microbiology laboratory for culture, 438 were positive cultures. The most common etiological agent causing Bloodstream Infection was found to be Salmonella Typhi with129 isolates (29.6%) followed by Escherichia coli (21.9%). There was a significant rise in resistance to most of the frequently used antibiotics. **Conclusion**: Salmonella Typhi is the most frequent bacteria to be isolated in Bloodstream Infection. Resistance towards different etiological agents of Bloodstream Infection is alarmingly increasing every year. Resistance to frequently prescribed drugs should be of concern to the clinicians prescribing the drugs.

Keywords: Blood, Drug Resistance, Salmonella Typhi

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INTRODUCTION

Blood is a sterile body fluid. Presence of any kind of micro-organism in blood due to various reasons might lead to Bloodstream Infection (BSI). BSI is a major cause of morbidity and mortality despite the availability of broad-spectrum antimicrobials and major advances of supportive care.[1] According to World Health Organization (WHO), around 20% of all global deaths is due to sepsis- which is a complication of BSI.[2] Bacterial bloodstream infections are defined as presence of viable bacteria in bloodstream that can elicit immune response.[1] Bacteria may enter the sterile parts of the body through bloodstream and the spread of toxins produced by these bacteria cause life-threatening consequences.[4] Wide range of bacterial species cause BSI. Gram-positive bacteria Staphylococcus aureus, Coagulase-negative Staphylococci (CoNS), Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, and Enterococcus faecium and Gram-negative bacteria Escherichia coli, Pseudomonas aeruginosa and Klebsiella species are the common species of bacteria found to cause BSI.[5,6] Emergence of MDR has created much hindrance in the treatment of patients with sepsis and infection caused by MDR organisms are leading to inadequate/ delayed treatment, resulting in adverse outcome of the patient being treated.[7] The etiology of bloodstream infection has been poorly characterized in Nepal, which is mainly due to lack of required diagnostic tools.[8] This study aims to find out current trend in etiologies of BSI and their antibiotic susceptibility patterns which will be very useful for proper empirical therapy of patients in future.

METHODS

This is a hospital-based retrospective study of blood cultures

over three years period from January 2018 to January 2021 at Dhulikhel Hospital. All the blood culture reports from patients attending different OPDs and admitted patients during above mentioned study period were collected from the Bacteriology unit of Department of Microbiology, Dhulikhel Hospital. Ethical clearance was obtained from Ethical Review Committee (IRC) of Kathmandu University School of Medical Sciences (KUSMS).

Inclusion criteria: All the blood culture reports from January 2018 to January 2021.

Exclusion criteria: Reports from timeframe other than the mentioned one and all the cultures except blood cultures

Procedure: Standard microbiological techniques were followed for the collection of blood samples and were placed in Bactec bottle (BD BactecPlus Aerobic/F Culture Vials for Adult BD BactecPeds Plus/F Culture Vials for children) and incubated at 37°C in BD Bactec FX40 Blood culture System. If there was growth on Bactec bottle on the second day, then it wassubcultured on Blood Agar (BA), Mc-Conkey's agar (MA) and Chocolate agar plates (HiMedia/Oxoid). BA and CA were kept on candle jars and all BA, CA and MA incubated at 37°C for 18 to 24 hours. Periodic subculture was done after overnight incubation for up to five days. The obtained growth was identified by colony characteristics, gram staining and biochemical tests.[9] Susceptibility of the isolates to different antibiotics were evaluated by using Kirby-Bauer disk diffusion method. Zone-sizes were measured and interpretation was done according to Clinical and Laboratory Standards Institute (CLSI) guidelines.[10]

The culture reports were reviewed and stored in a computerized database (SPSS 16). Inconclusive results were excluded. Patient demography, bacterial isolates and their antimicrobial susceptibility patterns were included in the extracted data. Organisms like micrococcus species, Bacillus species and Polymicrobial organisms were considered contaminants.

RESULTS

During the period of three years, there were total of 12811 blood samples suspected cases of BSI, among which 438 showed growths after culture. Gram-negative bacteria accounted for 355/438 (81.05%) of BSI pathogens and gram-positive bacteria was found in 73/438 (16.66%) of total BSI pathogens. The most common etiological agent was found to be Salmonella Typhi (29.6% of all the positive cultures) followed by Escherichia coli (21.9%). Majority of gram-negative bacteria belonged to Salmonella Typhi and gram-positive bacteria belonged to Staphylococcus aureus. (Table I). Female dominance was seen with male: female ratio of 53:47. (Table I I). Children of age group 2-15 years and adults of age group 16-65 years were found to be most affected (21.77% and 53.65% respectively) (Table III)

Trends in Organism isolation and antibiotic susceptibility patterns:

We looked through antibiotic resistance pattern over 3 years for significant trends. There was significant rise in resistance to all the antibiotics except Azithromycin and Cotrimoxazole. We observed a trend towards increasing frequency of resistance to all the antibiotics except Azithromycin and Cotrimoxazole (Table IV, Table V, Figure I). Another figure shows MDR of commonly isolated organisms from 2018 to 2021(Figure II). Organism wise, there is a trend towards increasing number of Escherichia coli and Enterococcus spp. No other organism isolates varied growth years.

Organisms	Numbers	Percentage (%)
GRAM-NEGATIVE BACTERIA		
Salmonella Typhi	130	29.68
Salmonella Paratyphi	41	8.81
Escherichia coli	96	21.91
Klebsiellapneumoniae	69	10.75
Klebsiellaoxytoca	4	0.91
Enterobacter spp	6	1.36
Acinetobacter spp.	6	1.36
Pseudomonas aeruginosa	3	0.64
GRAM-POSITIVE BACTERIA		
Staphylococcus aureus	23	5.25
Streptococcus pneumonia	15	3.42
Streptococcus species	3	0.68
Enterococcus species	15	3.42
CoNS	7	1.59
MRSA	6	1.36
MR CoNS	3	0.64
Alpha-hemolytic streptococcus	1	0.22
Total	**438**	**100**

Table I: Frequency of blood culture isolates

Gender	Numbers	Percentage (%)
Male	207	47
Female	231	53
Total	**438**	**100**

Table II. Distribution among gender

Age-group	Number	Percentage (%)
0-1	57	14.01
2-15	91	21.77
16-65	235	53.65
>65	45	10.57
Total	**438**	**100**

Table III: Age-wise distribution

	Acinetobacterspp	Enterobacter spp.	E.coli	K. oxytoca	K. pneumoniae	P. aeruginosa	S. typhi	S. paratyphi
AMP	50	66.66	74.35	100	94.5	NT	3.6	05.40
AK	33.33	50	33.33	33.33	14.5	0	0	0
AMC	0	25.0	69.2	33.3	64	NT	33.3	33.3
AZT	0	NT	40	0	NT	NT	8.2	28.5
CIP	25	20	53.4	100	49.1	NT	56.7	28.6
CTX	66.6	50	75	66.6	68.7	100	37.5	33.3
COT	0	NT	0	NT	NT	NT	2.7	0
CFX	66.6	0	55.1	0	68	NT	5.3	2.6
CTZ	0	0	0	NT	100	0	NT	NT
CTR	66.6	40	50	100	64.4	NT	3.3	2.56
CFU	100	0	76	100	96.96	NT	0	0
GEN	33.3	15.6	32.4	33.3	45.8	0	3.2	0
IMI	100	0	NT	0	22.2	0	0	0
MERO	100	0	20.4	0	25	NT	0	0
NA	100	NT	75	NT	NT	NT	90.5	91.8
PTZ	25	0	NT	100	28.5	0	0	0

Table IV: Percentage resistance among gram-negative organisms

	A-hemolytic Streptococcus	CONS	Enterococcus spp.	MR CoNS	MRSA	S. aureus	S. pneumoniae	Streptococcus spp
AZT	NT	NT	50	0	100	0	0	NT
AMP	0	NT	76.9	0	0	50	0	100
GEN	NT	0	100	NT	25	0	100	NT
CLD	NT	0	100	NT	100	20	NT	NT
VA	0	NT	8.3	0	0	NT	0	50
ERY	NT	0	NT	NT	100	40	100	NT
PTZ	NT	NT	69.2	NT	NT	0	0	0
CTX	NT	NT	100	NT	100	25	NT	NT
COT	0	NT	0	0	20	25	100	0
CIP	NT	0	90.9	0	50	42.8	0	0

Table V: Percentage resistance among gram-positive organisms

AMP= Ampicillin, AMC= Amoxyclav, AK= Amikacin, AZT=Azithromycin, CIP=Ciprofloxacin, CTX= Cefotaxime, COT= Cottrimoxazole, CFX=Cefixime, CTZ=Ceftazidime, CTR= Ceftriaxone, CFU=Cefuroxime, GEN= Gentamicin, IMI=Imipenem, MERO=Meropenem, NA=Nalidixic Acid, PTZ=Piperacillin-Tazobactam, CLD=Clindamycin, VA=Vancomycin, ERY= Erythromycin.

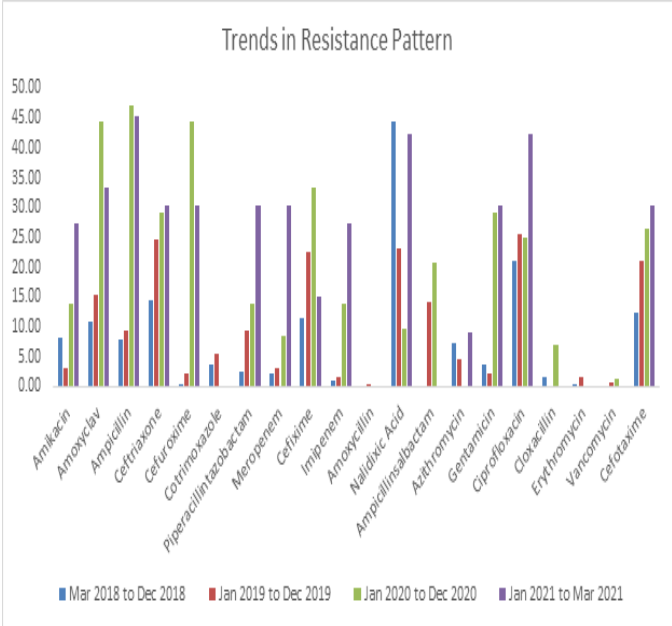

Figure1: Trends of Antibiotic resistance pattern over 3 years (%)

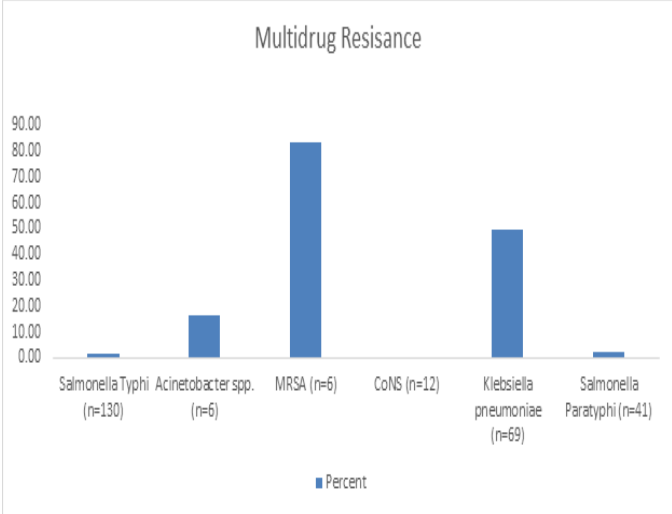

Figure 2 : Multidrug Resistance in commonly isolated organisms (%)

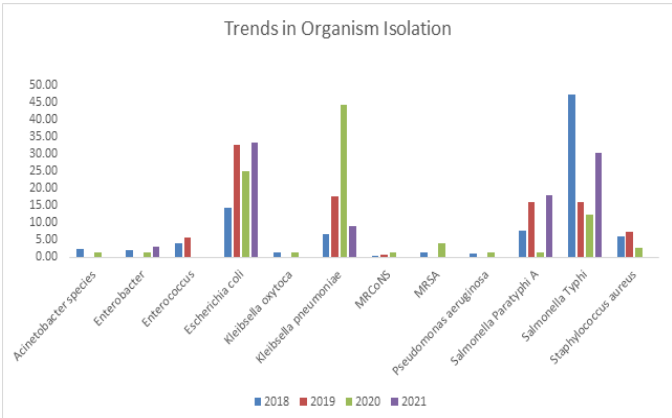

Figure 3 : Trends in organism isolation over a period of 3 years (%)

DISCUSSION

Our study has shown bloodstream infections accounted for 3.41 % of total blood cultures. Similar study conducted in Western Nepal has reported 6% of culture positivity[8] and 13.3% in a teaching hospital of Nepal, a year later.[15] Other studies have shown much higher rates of BSI.[5,11,12]

The incidence of BSI varied significantly among different age groups, where adults of age group 16-65 years were mostly affected followed by 2-15 years. Most of the studies on sepsis have shown infants as more susceptible[11-14] which is not in accordance with our study. Among the organisms responsible for BSI, 83.21% were caused by gram negative and 16.06% by gram-positive organisms. This is comparable to other studies where infection caused by gram-negative organisms have predominated the study.[5,8,11,15] In contrast to majority of studies, in a study done in Ghana, gram-positive organisms have accounted for most of the positive cultures.

Salmonella Typhi was the most frequent organism to be isolated in our study (30.9%) which indicates enteric fever as a rising health problem in Nepal. Other bacterial isolates belonging to Enterobacteriaceae were Salmonella Paratyphi (9.8%), Escherichia coli (23.3%) and Klebsiella pneumoniae (16.5%). Similar high incidence of Enterobacteriaceae has been reported in a study done in Nepal and India.[8,16] Lower percentage of isolation Enterobacteriaceae has been reported in previous studies done in Nepal.[13,15] Isolation of organisms with high resistance to antibiotics like Acinetobacter spp. (1.4%) was also observed. These organisms are found to be associated with hospital acquired infections[17,19] and high degree of resistance to wide range of antibiotics.[17-19] Very high resistance of Nalidixic Acid-a type of Quinolone, to Salmonella Typhi and Salmonella Paratyphi (90.5% and 91.8%) has been observed in this study. Also, drugs belonging to Fluoroquinolone like Ciprofloxacin has shown 56.8% of resistance in our study, which is quite alarming because Quinolone and Fluoroquinolone were once effective drugs for Salmonella Typhi and Salmonella Paratyphi before the emergence of NARST (Nalidixic Acid resistant Salmonella Typhi).[24-27]

An alarming observation in our study is the increasing trend towards resistance to most of the frequently used antibiotics over 3 years review period. This resistance may be due to haphazard use of antibiotics through self-medication from over-the-counter drugs, which is very common in Nepal. More than 95% of typhoid bacilli are susceptible to Aminoglycosides, Cotrimoxazole and Cephalosporins (table) which is similar to a study done in a peri-urban area of Nepal.[15] Number of CoNS in our study was 7(1.7%). Although small in number, CoNS is considered to be an emerging pathogen in BSI and CoNS when isolated in blood culture needs to be evaluated as it is one of the most common nosocomial BSI.[20-22] As CoNS is also a skin commensal, it is very important to distinguish between contaminant and possible pathogen.[23] Patients with prosthetic devices like pacemakers, orthopedic implants, prosthetic heart valves, IV catheters etc. are at risk for CoNS infection.[20] Hence, only one isolate was further proceeded for AST during this time period and the isolate was sensitive to all the antibiotics that were tested.

LIMITATIONS

This study was conducted in one hospital setting; it would have been more informative if it covered other areas of the country as well. Also, a more detailed study in multidrug resistance could not be performed because this was a retrospective study and samples had already been discarded.

CONCLUSION

Salmonella Typhi is the most frequent bacteria to be isolated in BSI. Considering the findings, it can be concluded that antibiotic resistance towards different etiological agents of BSI is alarmingly increasing every year. Resistance to frequently prescribed drugs like cephalosporins, aminoglycosides and fluoroquinolones should be of concern to the clinicians prescribing the drugs. We recommend medical personnel involved in prescribing antimicrobial drugs to consider current effective antibiotics.

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