ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

BACTERIOLOGICAL PROFILE, ANTIBIOTIC SENSITIVITY AND RESISTANCE PATTERN OF BLOODSTREAM NOSOCOMIAL INFECTION IN CHILDREN ADMITTED IN PICU OF A TERTIARY CARE HOSPITAL

Dr. Nitika Singh[1], Dr. Anita Mehta[2*], Dr. Maunil Tomar[3], Dr. Nishant Kumar Singh[4], Dr. Kamaldeep Singh Sethi[5], Dr. Mohd. Saeed[6]

1.Junior Resident, Department of Pediatrics, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh-273013, India
2.Professor Department of Pediatrics, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh-273013, India
3.Senior Resident, Department of Gastrosurgery, Mahatma Gandhi Medical College, Rajasthan-302022
4.Senior Resident, Department of Orthopedics, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh-273013, India
5.Junior Resident, Department of Pediatrics, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh-273013, India
6.Junior Resident, Department of Pediatrics, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh-273013, India

***Corresponding author:**
Dr. Anita Mehta, Professor Department of Pediatrics, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh-273013, India

INTRODUCTION

Background: Nosocomial infection (NI) is the one which usually comes in notice after 48 hours of hospital admission. This study includes bloodstream nosocomial infection. Incidence of nosocomial infections in previous studies were 6-8%.

Aim And Objectives: To study bloodstream nosocomial infection and its antibiotics sensitivity and resistance pattern in Paediatrics Intensive Care Unit (PICU). To find out the common organisms leading to bloodstream nosocomial infection and assess the mortality in patients affected by organisms.

Material and Methods: This is an observational study conducted in PICU of tertiary care centre. After ethical clearance and proper consent from parents of patients of age of >1 month and <18 years with complain of fever after 48 hour of hospitalization or with new onset of symptom for a period of 1 year (1 Aug 2021-31 July 2022). All patients qualifying the study criteria during data collection period were included in the study (n=86). Blood culture samples were taken for the patients who developed signs of nosocomial infection after 48 hours of hospital admission.

Results: The most common organism isolated from blood culture is gram negative bacteria Klebsiella pneumoniae. The sensitivity is observed with carbapenums, fluoroquinolones, polymixins and sulfonamide group of drugs. The resistance pattern of organisms isolated with maximum resistance to cephalosporin, macrolides, glycopeptide and tetracycline group of drugs.

Conclusion: The causative agent of bloodstream NI were predominantly gram negatives 12 (70.1%) out of 17 (19.7%) with most common to be Klebsiella pneumoniae 5 (29%) followed

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

by Acinetobacter 4 (23.5%). The maximum mortality pattern was observed among patients who were mechanically ventilated 8 (22%) or placed with central line 5 (20%).

Keywords: blood culture, nosocomial infection, mechanically ventilated, antibiotic sensitivity

1. Introduction

Nosocomial infection(s)/hospital acquired infection are infection(s) are the main adverse event acquired during the process of receiving health care that was not present during the time of admission. This usually comes in notice after 48 hours of hospital admission. The incidence of nosocomial infection in developed countries is about 11.5% [1]
NI include bloodstream infection, ventilator associated, non-ventilator-associated hospital-acquired pneumonia (NV-HAP), gastrointestinal infections (including clostridioides difficile), other primary bloodstream infections—not associated with central catheter use, and other urinary tract infections—not associated with catheter use.
Hence the present study was carried out with the aim to study bloodstream nosocomial infection and its antibiotic sensitivity and resistance pattern in PICU in our tertiary care centre.

2. Materials and Methods

Study setting –Pediatrics intensive care unit (PICU), Department of Pediatrics, Baba Raghav Das Medical College, Gorakhpur.
Study sample – Patients of age > 1 month and <18 years with complain of fever after 48 hour of hospitalization or with new onset of symptom.
Study design- Observational study
Study duration- 1 year (1 Aug 2021-31 July 2022)
Sample Size- All patients qualifying the study criteria during data collection period were included in the study (86)
Study subjects - All the patient fulfilling inclusion criteria and exclusion criteria during a period of 1 year were enrolled.
Data entry & analysis- Data entry and analysis was done using appropriate statistical test.
Study Procedure: All the patients with defined inclusion criteria admitted in PICU were enrolled for the study.
INCLUSION CRITERIA
All the patients between 1 month to 18 years of age after 48 hours of admission to the pediatric intensive care unit if they had-
(i) Unexplained fever >38 degree C, leucopenia <4000 WBC/mm3 or leukocytosis >12,000 WBC/mm3;
(ii) New infiltrates on chest X-ray, persistent tracheal aspirates or secretions;
(iii) Turbid urine, suprapubic tenderness, dysuria, burning micturition;
(iv) Thrombophlebitis or cloudy effluent containing more than 100 neutrophils/ mm3 were enrolled in our study.

EXCLUSION CRITERIA
Following patients were excluded from study-
1) Those having fever prior to admission to the intensive care unit, or any other clinical features of infection secondarily acquired in the wards prior to transfer to the intensive care unit

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

2) Patient who left against medical advice or expired before 24 hours of PICU stay.
3) Patient not willing to give consent.

NOSOCOMIAL INFECTION DEFINED AS- These infections usually appear 48 hours or more after hospital admission or within 30 days after discharge (Benenson, 1995).[1]

SAMPLES REQUIRED-

1) Blood culture and sensitivity in all patient's

Method.

This study was conducted in Paediatric department of BRD medical college Gorakhpur, Uttar Pradesh, India, over a period of 12 months. All the consecutive children from in patient's department, fulfilling the inclusion criteria were enrolled for the study after taking proper consent from the parents.

History of illness: A detailed epidemiological and clinical history of patient was taken including fever after 48 hours of admission, burning micturition, cough, new onset infiltrates in chest X-Ray etc. Onset and duration of clinical symptoms was recorded. Nutritional status was assessed in every child. Patients were managed according to antibiotic sensitivity and resistance pattern of organisms.

Daily monitoring was done to record the improvement in the patient, deterioration or development of complications.

Lab Investigations:

Routine investigations

1. Hematological, CBC, CRP, ESR was done as per standard protocol and according to severity of patient.
2. Blood culture and sensitivity or
3. X -Ray chest was advised in selected patient. Chest X-ray findings can be hyperinflation, peri bronchial cuffing, interstitial infiltrates, patchy opacity, lobar consolidation, collapse, effusion, pneumothorax, pneumatocele and lung abscess or
4. X- Ray neck and CT-scan of chest was done whenever needed.

Sample collection and transportation:

For detection of bacterial pathogen samples was collected from equal number of consecutive patients with infection in different transport medium, after labelling and transported at the earliest to the laboratory. The samples were transported to the laboratory (ICMR-Regional Medical Research centre) situated in premises of BRD MC Gorakhpur.

For the isolation of bacterial pathogens patients, sample were collected and put on chocolate agar medium for bacterial culture.

Antibiotic Susceptibility Testing

Antibiotic susceptibility testing (AST) specifies effective antibiotic dosage and formulates a profile of empirical therapy for the proper management of an individual patient's health against deadly infections.

Disk Diffusion Technique: - The disk diffusion method is the gold standard for confirming the susceptibility of bacteria.

The following antibiotic disk was mainly used for gram positive organisms Ampicillin-Sulbactum, Vancomycin, Gentamycin, Ciprofloxacin, linezolid, Co-Trimoxazole, Clindamycin, cefotaxime.

For Gram negative organisms, the followings antibiotics was mainly used – Amoxicillin, ofloxacin, meropenem, ciprofloxacin, Ceftriaxone, Gentamycin, Colistin, Piperacillin/Tazobactam, Co-trimaxazole.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

Broth micro dilution method: - It was used because of its accuracy and clears results. Minimal inhibitory concentrations (MICs) for the antibiotics were determined by a micro dilution method.
E test: -Epsilometer testing (E test) was another significant development for the routine analysis of widespread antibiotic resistance in bacteria.
Children of age 1 month to 18 years with new onset symptoms after 48 hours of hospital admission.
Data entry & analysis
Data entry and analysis were done using SPSS. Data was analysed using Chi square/independent sample t-test. Descriptive statistics were represented by frequency and percentages. Inferential statistics were done using Chi square test, fisher's exact test and wilcoxan test for bivariate analysis. The significance level was decided as 95% and P value was considered significant.

TABLE:1 Pattern of organisms isolated from culture positive samples based on gram staining status

Gram staining status	Organism	Number (N=17)	Percentage
Gram positive bacteria	S. aureus	4	23.5%
	Streptococcus	1	5.88%
Gram negative bacteria	E. coli	3	17.6%
	Acinetobacter	4	23.5%
	Klebsiella	5	29%

Table 1 shows that out of 86 patient's 17(19.7%) patients came to be culture positive and the most common organism isolated is gram negative bacteria Klebsiella pneumoniae 5 (29%) followed by Acinetobacter baumanii 4 (23.5%) followed by gram positive bacteria staphylococcus aureus 4 (23.5%) followed by Escherichia coli 3 (17.6%) followed by Streptococcus 1 (5.88%) were responsible for causing culture positive bloodstream nosocomial infection.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

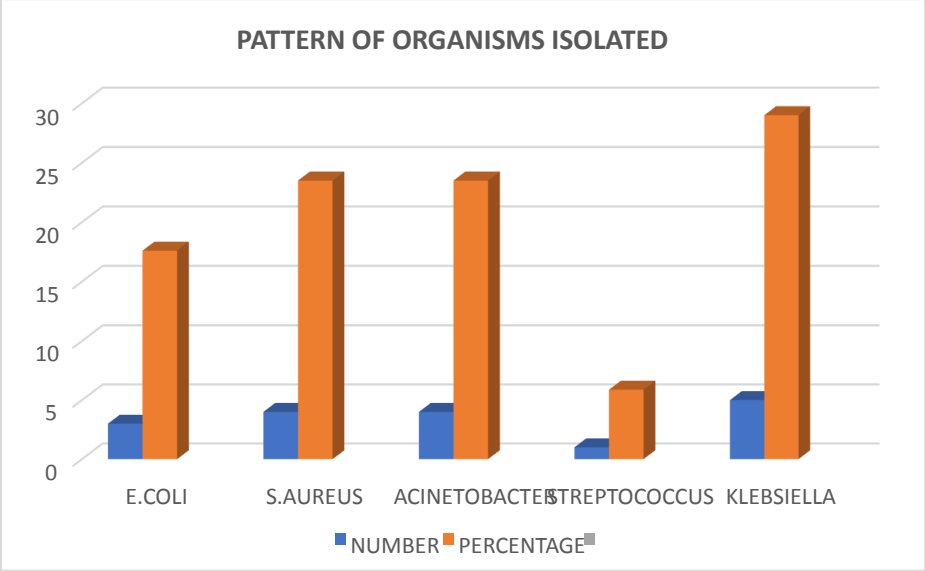
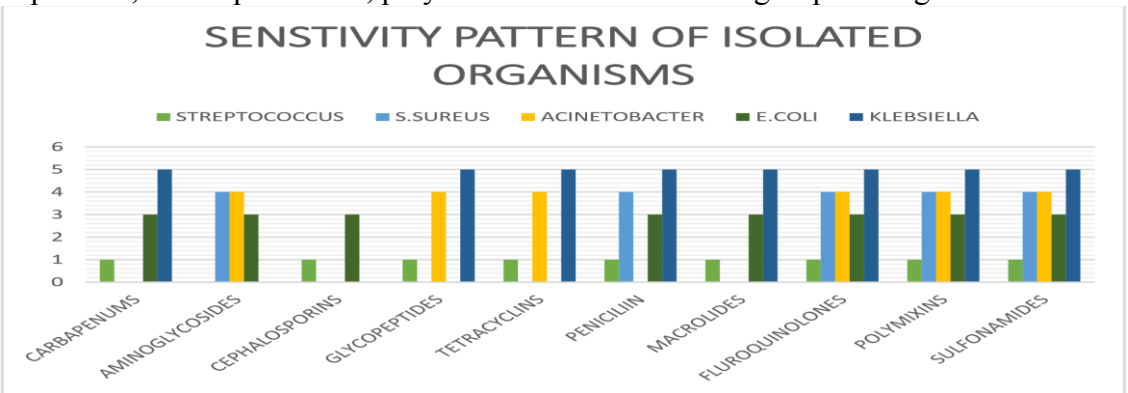


TABLE:2 Sensitivity pattern of culture positive organisms for different antibiotics

	Gram Positive Bacteria		**Gram Negative Bacteria**			
Antibiotics	Steptococcus	S.Aureus	Acinetobacter	E.Coli	Klebsiella	Total
Carbapenums	1	4	4	3	5	17
Aminoglycosides	-	4	4	3	-	11
Cephalosporins	1	-	-	3	-	4
Glycopeptides	1	-	4	-	5	10
Tetracyclins	1	-	4	-	5	10
Penicillin	1	4	-	3	5	13
Macrolides	1	-	-	3	5	9
Fluroquinolones	1	4	4	3	5	17
Polymixins	1	4	4	3	5	17
Sulfonamides	1	4	4	3	5	17

Table 2 shows sensitivity pattern of isolated organisms with maximum sensitivity to carbapenums, fluoroquinolones, polymixins and sulfonamide group of drugs.



ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

TABLE:3 -Resistance pattern of culture positive organisms for different antibiotics

	Gram Positive Bacteria		Gram Negative Bacteria			
Antibiotics	Streptococcus	S.Aureus	Acinetobacter	E.Coli	Klebsiella	Total
Carbapenums	-	-	-	-	-	0
Aminoglycosides	1	-	-	-	5	6
Cephalosporins	-	4	4	-	5	13
Glycopeptides	-	4	-	3	-	7
Tetracyclines	-	4	-	3	-	7
Penicillin	-	-	4	-	-	4
Macrolides	-	4	4	-	-	8
Fluroquinolones	-	-	-	-	-	0
Polymixins	-	-	-	-	-	0
Sulfonamides	-	-	-	-	-	0

Table 3 shows resistance pattern of organisms isolated with maximum resistance to cephalosporin macrolides, glycopeptide and tetracycline group of drugs.

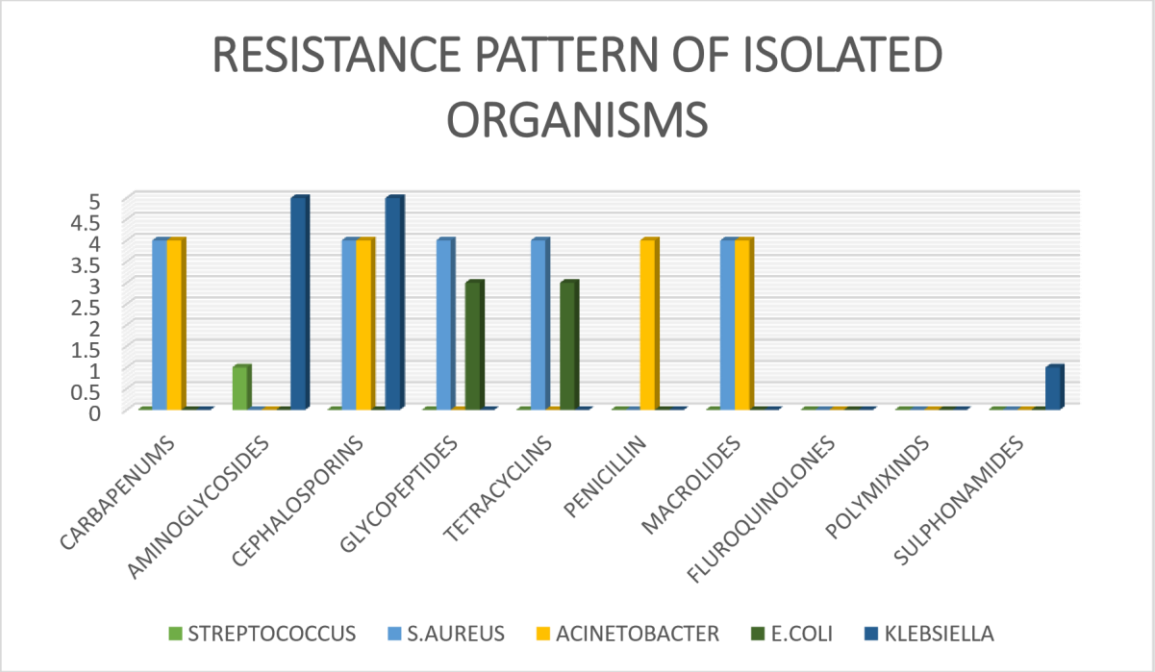


TABLE:5 Association between use of central line and mortality of bloodstream nosocomial infected patients

Central line (n=86)	**Discharge (n=78)**	**Death (n=8)**	**Chi square**	**P value**
Yes (25,29%)	20(80%)	5(20%)	Fisher exact	0.04
No (61,71%)	58(95%)	3(5%)		

Table 5 shows that out of 25 (29%) patients admitted to PICU who were intervened by central venous catheterization 20 (80%) were discharged and 5 (20%) died. Out of 61 (71%) patients admitted to PICU who were not intervened by central venous catheter 58 (95%) patients were discharged and 3 (5%) patient's died significant p value of 0.04

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

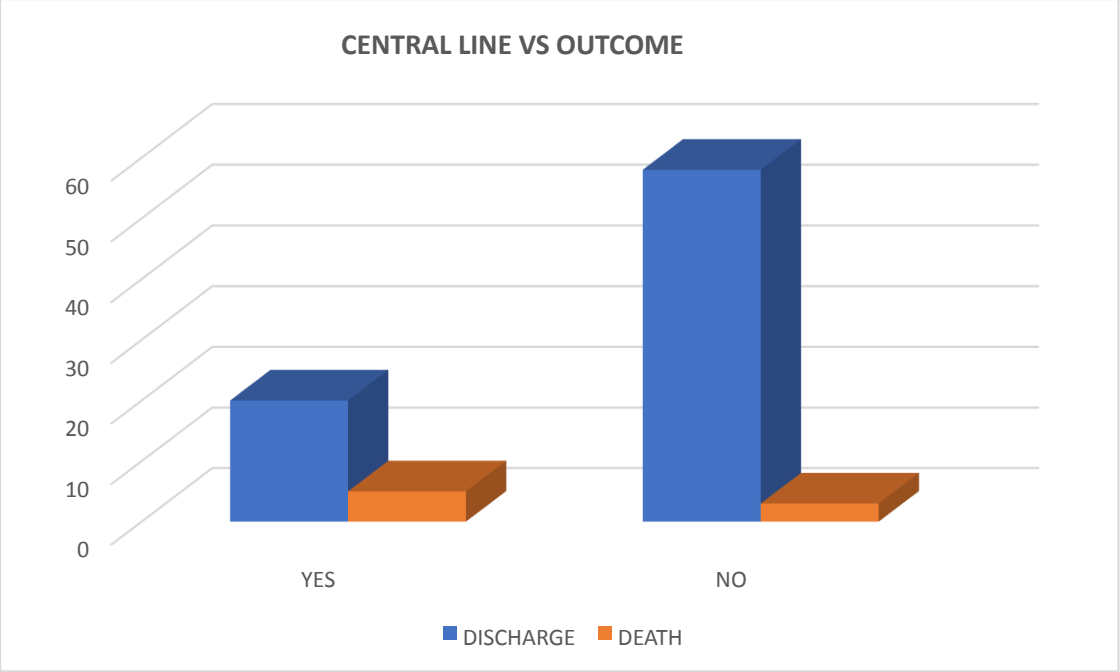
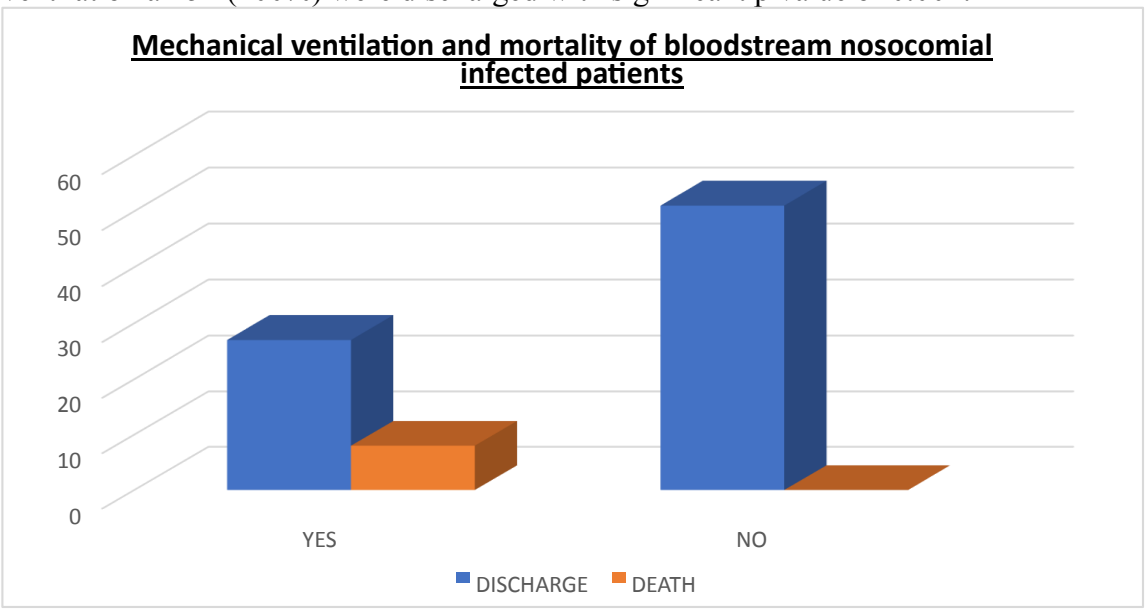


Table:6 Association between use of mechanical ventilation and mortality of bloodstream nosocomial infected patients

Mechanical Ventilation (n=86)	**Discharge (n=78)**	**Death (n=8)**	**Chi square**	**P value**
Yes (35,40.7%)	27(77.1%)	8(22.9%)	Fisher exact	<0.001
No (51,59.3%)	51(100%)	0(0%)		

Table 6 shows that out of 35 (40.7%) patients who were mechanically ventilated 27 (77.1%) were discharged and 8 (22.9%) of them died, 51 (59.3%) patients were not on invasive mode of ventilation all 51 (100%) were discharged with significant p value of 0.001.



ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

3. Discussion

This is a hospital based observational study conducted in PICU of BRD Medical College Gorakhpur, a tertiary care teaching institute over a period of one year from August 2021 to July 2022. Total 86 children were included in this observational study who were admitted to PICU and were suspected to develop bloodstream nosocomial infection. Risk factors, comorbid factors, bacteriological profile, antibiotic sensitivity and resistance pattern were studied and all parameters were compared.

Out of 19.7% of admitted patients developed bloodstream NI. The prevalence of bloodstream NI in this study (19.7%) was higher than in studies done in Pakistan (4.7%), Lithuania (13.6%), Egypt (15.6%), American study (11.9%), Rwanda (12.1%) and Peru (20%) (Hansa haftu et al 2019, Amanuel hadgu et al 2020)[3,4,5,6,7,8] but it was lower than studies done in Egypt (27.7%), Serbia (32.7%), Nigeria (45%) and consistent with the study done in India (27.3-30.5%)[8,9,10,11,12] (Mohammed mustefa et al 2019). This study differs as we only assessed the focus, and it does not differentiate the type of infection, including whether it was ventilator-associated or not, urinary infection, and other modes of infection. The differences in the prevalence of NI in developing countries may be due to the disparities in quality of care, strong infection prevention mechanism implementation, the study design we used, and the study area (we used only PICU, but in others, adult ICU and General ICU were included) and the type of patients where NI was assessed. According to our findings, the main focus of infection was the bloodstream which was consistent with a study done in Peru [4] (Maria R Becerra et al 2010), but in other studies, respiratory infection was more prevalent than bloodstream infection like in Lithuania and Egypt (58.8%) [3] (Jolanta Asembergiene et al 2009, Rimantas Kevalas et al 2009).

Despite the differences between studies with regard to causative organisms, Gram-Negatives showed the most common pathogens identified in this study, which is consistent with other studies (Deep A et al 2004, Kandian S et al 2004, Despotovic A 2020, Dharmawati I et al 2019) [8,9,12,13] as in our current study we have observed that among bloodstream culture analysis, 5 isolates of organisms were found, of which Gram-Negatives accounted

70.1% and the rest 29.9% were Gram-Positives. Klebsiella pneumonia 5 (29%) was the leading bacterial etiology of NI, followed by Acinetobacter baumannii 4(23.5%) then staphylococcus aureus 4(23.5%) then Escherichia coli 3(17.6%). This is parallel to the study reported in the literature (Chang J et al 2011) [3,4,14] This may be due to differences in the site of infection (chest vs BSI), sampling site, demographic differences, and the degree of infection prevention implementations. Klebsiella (33.33%) was the most common isolate with maximum sensitivity to amikacin (Akashdeep et al 2004) [2]. Gram negative bacteria (66.01%) were the most common organisms causing bloodstream infection, various literatures from the world are showed these phenomena such as; (Gupta et.al 2010), (Haeusler et.al 2009), and (Kirsty et.al 2019) showed gram negative organisms' predominant pathogen for bloodstream infection. [4,5,15] Their study has gained commonest gram negative bacteria species as B. cepacea(11.26%).

B. cepacea has emerged as a serious human pathogen in the last two decades, causing fatal necrotizing pneumonia and bacteremia. B. cepacea has been associated without breaks involving infections of the bloodstream,

respiratory tract, and urinary tract in intensive care unit setting. [4,5,15] (Antony et.al 2007) stated that the intensive care unit bloodstream infections in tertiary hospital often caused by B. cepacea infections.[16]

According to our findings, statistically significant predictors which increase the risk of nosocomial infection were females, younger age (under one year). This could be attributed to young age groups' immature immune Systems [9,11,13,14], prolonged duration of

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

mechanical ventilation (more than 7 days), presence of central venous catheter, patients being started empirical antimicrobial therapy at admission and long duration of hospital stay (more than two weeks). Some of these findings were compatible with that of previous studies like duration of hospital stay [3] (Valinteliene R et al 2009), mechanical ventilation, presence of central venous catheter [11] (Bendary S et al 2012), preceding use of antibiotics [9] (Oladele RO et al 2016), and using the medical device [14] (Li Y- C et al 2011)

In the present study we have found the pattern of sensitivity for antibiotics group such as carbapenums, polymixins, fluroquinolones and sulphonamides. The sensitivity pattern is consistent with study done by (Wayan putra et al 2019) who also revealed that the isolates are sensitive to commonly used antibiotic such as cefoperazone-sulbactam, vancomycin and carbapenum group. Antibiotic susceptibility pattern of gram-negative bacteria isolates in their study finding were resistant to three or more groups antimicrobial agents and therefore consider multidrug resistant (MDR), almost all of the isolate are resistant to; penicillin, cephalosporin, tetracycline, chloram-phenicol, sulfa and quinolones groups. In our present study multidrug resistance was observed for cephalosporins, macrolides, glycopeptides and tetracyclins group of drugs. The development of antibiotic resistant in their hospital might be caused by unnecessary, inappropriate, or suboptimal prescribed antibiotic therapy from community before, previous healthcare and hospital itself. Previous study similar that, find very high level of resistance penicillin derivate, approximately one-half isolate in infants and young children [17] (Downie L 2013) Other study in Africa 75% isolate is MDR to ampicillin, chloramphenicol and cotrimoxazole [18] (Phoba M F et al 2014) WHO in 2014 report that five out of the six WHO regions had more than 50% resistant to third generation of cephalosporin and fluoroquinolones in hospital setting [19,20]. In our present study we have observed multidrug resistance to penicillin, cephalosporins, tetracyclins, sulphonamides group of drugs

4. References

1. Masur H, Brooks JT, Benson CA, Holmes KK, Pau AK, Kaplan JE. Prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Updated Guidelines from the Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America. Clinical infectious diseases. 2014 May 1;58(9):1308-11.
2. Hormozi SF, Saeedi AA, Aminianfar M, Alishah MS, Darvishi M. Studying the frequency of nosocomial infection and its relative factors in the intensive care unit of hospitals based upon NNI system. Eurasian Journal Of Analytical Chemistry. 2018 Jan 1;13(3):p-em16.
3. Ašembergienė J, Gurskis V, Kėvalas R, Valintėlienė R. Nosocomial infections in the pediatric intensive care units in Lithuania. Medicina. 2009 Jan;45(1):29.
4. Becerra MR, Tantaleán JA, Suárez VJ, Alvarado MC, Candela JL, Urcia FC. Epidemiologic surveillance of nosocomial infections in a Pediatric Intensive Care Unit of a developing country. BMC pediatrics.
5. Haque A, Bano S. Clinical profile and outcome in a paediatric intensive care unit in Pakistan. Journal of the College of Physicians and Surgeons Pakistan. 2009;19(8):534.2010 Dec;10:1-9.
6. Ananthanarayan R. Ananthanarayan and Paniker's textbook of microbiology. Orient Blackswan; 2006.
7. El-Sahrigy SA, Shouman MG, Ibrahim HM, Rahman AM, Habib SA, Khattab AA, Gomaa HE, Helmy NA. Prevalence and anti-microbial susceptibility of hospital acquired infections in two pediatric intensive care units in Egypt. Open access Macedonian journal of medical sciences. 2019 Jun 6;7(11):1744.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 06, 2023

8. Deep A, Ghildiyal R, Kandian S, Shinkre N. Clinical and microbiological profile of nosocomial infections in the pediatric intensive care unit (PICU). Indian Pediatr. 2004 Dec 1;41(12):1238-46.
9. Iwuafor AA, Ogunsola FT, Oladele RO, Oduyebo OO, Desalu I, Egwuatu CC, Nnachi AU, Akujobi CN, Ita IO, Ogban GI. Incidence, clinical outcome and risk factors of intensive care unit infections in the Lagos University Teaching Hospital (LUTH), Lagos, Nigeria. PloS one. 2016 Oct 24;11(10):e0165242.
10. Lukas S, Hogan U, Muhirwa V, Davis C, Nyiligira J, Ogbuagu O, Wong R. Establishment of a hospital-acquired infection surveillance system in a teaching hospital in Rwanda. International Journal of Infection Control. 2016 Sep 2;12(3).
11. Mansour MG, Bendary S. Hospital-acquired pneumonia in critically ill children: Incidence, risk factors, outcome and diagnosis with insight on the novel diagnostic technique of multiplex polymerase chain reaction. Egyptian Journal of Medical Human Genetics. 2012 Feb 1;13(1):99105.
12. Despotovic A, Milosevic B, Milosevic I, Mitrovic N, Cirkovic A, Jovanovic S, Stevanovic G. Hospital-acquired infections in the adult intensive care unit—Epidemiology, antimicrobial resistance patterns, and risk factors for acquisition and mortality. American journal of infection control. 2020 Oct 1;48(10):1211-5.
13. Putra IW, Setyaningtyas A, Puspitasari D, Wahyu AD, Dharmawati I, Azis AL. Microbial pattern and antibiotic susceptibility in pediatric intensive care unit Dr. Soetomo hospital, Surabaya. Indonesian Journal of Tropical and Infectious Disease. 2019;7(5):122-30.
14. Chang YJ, Yeh ML, Li YC, Hsu CY, Lin CC, Hsu MS, Chiu WT. Predicting hospital-acquired infections by scoring system with simple parameters. PloS one. 2011 Aug 24;6(8):e23137.
15. El-Sahrigy SA, Shouman MG, Ibrahim HM, Rahman AM, Habib SA, Khattab AA, Gomaa HE, Helmy NA. Prevalence and anti-microbial susceptibility of hospital acquired infections in two pediatric intensive care units in Egypt. Open access Macedonian journal of medical sciences. 2019 Jun 6;7(11):1744.
16. Patra PK, Jayashree M, Singhi S, Ray P, Saxena AK. Nosocomial pneumonia in a pediatric intensive care unit. Indian Pediatrics. 2007 Jul 1;44(7):511.
17. Downie L, Armiento R, Subhi R, Kelly J, Clifford V, Duke T. Community-acquired neonatal and infant sepsis in developing countries: efficacy of WHO's currently recommended antibiotics— systematic review and meta-analysis. Archives of disease in childhood. 2013 Feb 1;98(2):146-54.
18. Ombelet S, Ronat JB, Walsh T, Yansouni CP, Cox J, Vlieghe E, Martiny D, Semret M, Vandenberg O, Jacobs J, Lunguya O. Clinical bacteriology in low-resource settings: today's solutions. The Lancet Infectious Diseases. 2018 Aug 1;18(8):e248-58.
19. Founou RC, Founou LL, Essack SY. Clinical and economic impact of antibiotic resistance in developing countries: A systematic review and meta-analysis. PloS one. 2017 Dec 21;12(12):e0189621.
20. Sarangi KK, Pattnaik D, Mishra SN, Nayak MK, Jena J. Bacteriological profile and antibiogram of blood culture isolates done by automated culture and sensitivity method in a neonatal intensive care unit in a tertiary care hospital in Odisha, India. Int j adv med. 2015 Oct;2(4):387-92