International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Changing Pattern of Antibiotic Profile of Gram Negative Blood Stream Infections in NICU in a Tertiary Care Hospital

Dr. Gurpreet Kaur[1], Dr. Kamaldeep Singh[2*], Dr. Loveena Oberoi[3], Dr. Tavishi Oberoi[4]

[1]Senior Resident

[2]***Corresponding Author,** Assistant Professor

[3]Professor

Abstract: ***Introduction: Blood stream infection is a key determinant of clinical outcomes among patients in neonatal intensive care units. Studies on infections in NICU have reported that Blood Stream Infections, Urinary Tract Infections and Soft Tissue Infections are the common infections in NICU. These infections are commonly caused by Gram negative isolates. These organisms are highly resistant to antibiotics. Early recognition of bacteria and appropriate antimicrobial therapy are essential for controlling infection and preventing the morbidity and mortality. Objectives: To study the profile of Gram negative bacteria causing blood stream infection in patients admitted in neonatal intensive care unit. To know the antibiotic susceptibility pattern of these isolates. Materials and Methods: A total of 2766 blood cultures samples received from Neonatal Intensive Care Unit (NICU) in the hospital, were analyzed. The organisms were identified by Gram staining, cultural characteristics and a battery of biochemical tests. Drug susceptibility was performed on the isolates by Kirby Bauer's disk diffusion method. Results: Of the 2766 samples, 660 (23.8%) blood cultures were positive. Among 660 positive samples 510 (77.2%) were the Gram negative isolates and 150 were Gram positive (22.8%). The most common isolate was Klebsiella pnuemoniae (45.5%), followed by Pseudomonas aerogenosa (25.9%), Escherichia coli (14.1%), Acinetobacter baumani (12.3%), Citrobacter fruendi (1.4%) and others (Salmonellatyphi & proteus spp). Among Gram negative bacilli low resistance was observed against Imipenem 10 (2. %) followed by Piperacillin - Tazobactam 219 (43%) and Amikacin 189 (37%). High resistance was against Ampicillin 501 (98 %) and Cefipime 364 (71.3%) Conclusion: 1) Appropriate antibiotic utilization in Intensive Care Units is crucial not only in ensuring an optimal outcome but also in preventing multidrug resistant bacteria. 2) De-escalation of the high-end antimicrobials once the sensitivity pattern of the isolate is known is suggested to reduce the antimicrobial pressure. 3) Formulation of hospital antibiotic policy and compliance with existing guidelines will go long way in reducing multi-drug resistance in pathogens.***

Keywords: NICU, Gram Negative bacteria, Antibiotic susceptibility pattern

1. Introduction

High morbidity and mortality resulting from neonatal septicemia is due to deficient host defense mechanisms in newborn, particularly when preterm, lack of specific and sensitive tests to diagnose sepsis early and little use of host defense modulating therapies in neonatal septicemia. Early manifestations of infection are often subtle and nonspecific such as inability to tolerate feed, irritability or lethargy. Many organs and tissues alone or in combination may become infected from hematogenous spread.1

Infections caused by multidrug resistant bacteria constitute a serious problem for intensive care patients throughout the world. Prevalent pathogens and their antimicrobial resistance pattern may vary in different intensive care units (ICUs) depending upon the antibiotic usage in that healthcare facility. Invasion of the bloodstream by microorganisms constitutes one of the most serious situations in infectious disease. Bacteremia ranges from self-limiting infections to life- threatening septicemia that requires rapid and aggressive antimicrobial treatment. Septicemia leads to a significant morbidity and mortality. The mortality rate ranges from 20% to 50% in cases of bacteremia. It is among the most common health-care associated infections. In recent years, there has been an increase in the incidence of bacteremia caused by the members of *Enterobacteriaceae* and other Gram-negative bacilli. Sensitive bacterial strains are now being replaced by multi-drug resistant (MDR) strains of *Klebsiella*, *Pseudomonas*, *Acinetobacter*, and *Citrobacter* species. This increasing antimicrobial resistance is a worldwide concern andis subjected to regional variation. Awareness of the baseline microbial resistance pattern specific to a hospital prevents irrational use of antibiotics in that hospital, thus helps progress a step forward in the prevention of spread of antibiotic resistance. Thus, regular surveillance of blood stream etiology is important in monitoring the spectrum of bacterial pathogens and their sensitivity pattern in a particular area. The application of hospital-wide antibiogram to guide clinicians in the initial choice of antimicrobials is the usual approach adopted. If more resistant organisms are isolated from ICU patients, this important information would be masked by the use of hospital-wide antibiogram. Hence the present study was conducted to analyze the prevalent microorganisms causing Blood Stream Infection (BSI) and their antimicrobial resistance pattern as seen among the ICU patients in a tertiary care centre[2].

2. Materials and Methods:

This retrospective study was conducted from January 2021 to June 2022 among cases admitted in NICU in a tertiary care Hospital. All neonates admitted in NICU of GNDH

hospital, who had clinical features suggestive of neonatal septicemia such as refusal to feed, dullness, fever, seizure, respiratory distress, excessive irritability, vomiting, abdominal distension, jaundice, bleeding or shock were included in the study after 48 hrs of admission. A total of 2766 blood cultures samples received from Neonatal Intensive Care Unit (NICU) in the hospital, were analyzed.

1 to 2 mL of blood sample was collected and was inoculated immediately into BHI blood culture bottles under complete aseptic conditions and was incubated at 37°C for 48 hrs and sub cultures were done on Blood agar and MacConkeyAgar till 5 days.

The growth obtained was identified by colony morphology, Gram stain of the isolated colonies, biochemical identification tests done as per the standard protocol followed in ourlaboratory[3].

The antibiotic susceptibility pattern of the isolated organisms was performed by Kirby-Bauer disc diffusion method on Mueller-Hinton Agar plates, and the results were recorded as per the Clinical and Laboratory Standards Institute 2020 guidelines[4]. The antibiotic discs that were used to identify the susceptibility pattern of the Gramnegative pathogens were Ciprofloxacin (15µg), Ceftazidime (30µg)), Ceftriaxone (30µg), Piperacillin / Tazobactum (100/10µg)), Cefipime (30µg)), Ampicillin (10µg)), Imipenem (10µg)), Amikacin (30µg)). (HiMedia Laboratories, Mumbai) and results were interpreted as per Clinical Laboratory Standards Institute (CLSI) guidelines.

3. Results and Observations

A total of 660 (23.8%) blood cultures were positive from 2766 blood cultures received from the NICU in probable neonatalsepsis cases.

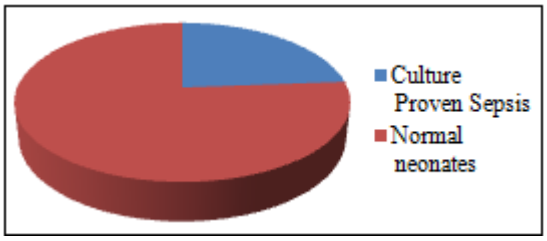


Figure 1: Neonatal Sepsis

Among 660 positive samples 510 (77.2%) were the Gram negative isolates and 150 were Gram positive (22.8%). Microbial profile of isolated Gram Negative Organisms is as shown in Table 1

Table 1: Bacteriological profile of Gram negative organisms isolated from NICU

Organisms	No.	Percentage (%)
Klebsiella pnuemoniae	232	45.5%
Pseudomonas aeroginosa	132	25.9%
Escherichia coli	72	14.1%
Acinetobacter baumanii	63	12.3%
Citrobacterfreundi	7	1.4%
Others (*Salmonella typhi and Proteus* spp)	4	0.8%
Total	510	100%

Table 2: Antimicrobial resistance pattern of Gram negative bacilli

GNBs (n)	Ampicillin (%) (n)	Ceftriaxone (%) (n)	Ceftazidime (%) (n)	Cefipime (%) (n)	Piperacillin / Tazobactum (%) (n)	Amikacin (%) (n)	Ciporfloxacin (%) (n)	Imepenem (%)
Klebsiella *pnuemoniae (*232)	98 (227)	88 (204)	-	84 (195)	39 (90)	39 (90)	91 (208)	2 (5)
Pseudomonas aeroginosa (132)	100 (132)	-	33 (44)	33 (44)	30 (40)	22.4 (30)	20.4 (27)	1.2 (2)
Escherichia coli (72)	100 (72)	95 (68)	-	94 (68)	40 (29)	39 (28)	95.6 (69)	1 (1)
Acinetobacter baumanii (63)	100 (63)	93 (59)	-	84 (53)	90 (57)	62 (39)	87.5 (55)	3 (1)
Citrobacter freundi (7)	100 (7)	67 (5)	-	60 (4)	47 (3)	27 (2)	27 (2)	3.2 (1)

Among Gram negative bacilli maximum resistance was seen against Ampicillin 501 (98. %) and Third Generation Cephalosporins (85%). Minimum resistance was seen against Imipenem 10 (2. %) followed by Piperacillin - Tazobactam 219 (43%) and Amikacin 189 (37%).

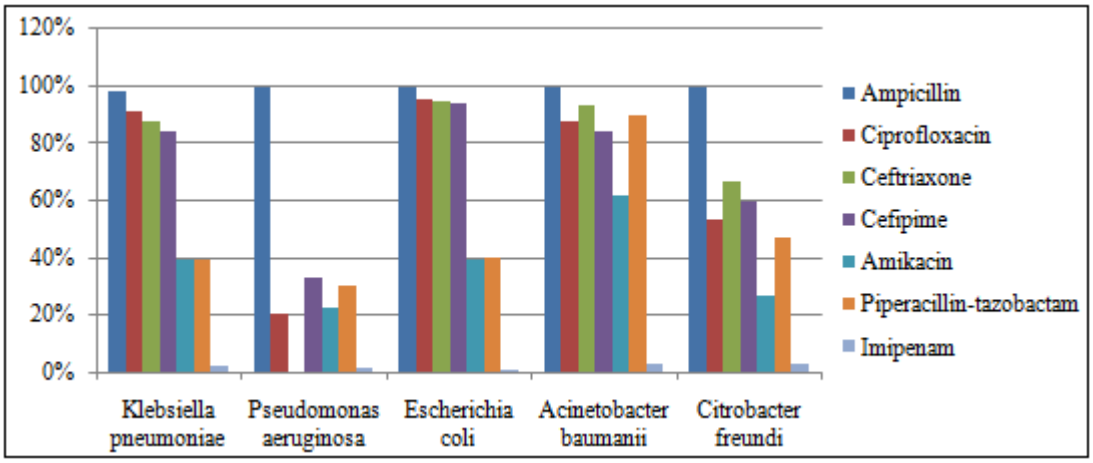
For *Klebsiella* pneumoniae species (232) maximum resistance was seen against Ampicillin 227 (98%), Ciprofloxacin 208 (91%) followed by Ceftriaxone 204 (88%) and Cefipime 195 (84%) and minimum resistance was seen against Amikacin followed by Piperacillin - Tazobactam 90 (39%) and Imipenem 5 (2%).

For *Pseudomonas aeroginosa* species maximum resistance was seen against Ampicillin100 (100%), Ceftazidime and Cefipime 44 (33%) and minimum resistance was seen against Piperacillin-Tazobactam 40 (30%) followed by Amikacin 30 (22.4%) and Ciprofloxacin 27 (20.4%) and Imipenem 2 (1.2%).

For *Escherichia coli (72)* isolates maximum resistance was seen against Ampicillin 72 (100%) followed by Ciprofloxacin 69 (95.6%) and Ceftriaxone 68 (95%). Minimum resistance was seen against Piperacillin - Tazobactam 29 (40%) and Amikacin 28 (39%), followed by Imipenem 1 (1%).

For *Acinetobacter baumanii* species maximum resistance was seen against Ampicillin 63 (100%) Ceftriaxone 59 (93%) followed by Piperacillin-Tazobactum 57 (90%) Ciprofloxacin 55 (87.5%) and Cefipime 53 (84%). Minimum resistance was seen against Amikacin 39 (62%) followed by Imipenem 1 (3%).

For *Citrobacterfreundi* species maximum resistance was seen against Ampicillin 7 (100%) followed by Ceftriaxone 5 (67%) and Cefipime 4 (60%). Ciprofloxacin 4 (53%). Minimum resistance was seen against Piperacillin-Tazobactum 3 (47%) Amikacin 2 (27%) followed by Imipenem 1 (3%)



AMR pattern of Gram negative bacilli as depicted in table 2

4. Discussion

Blood stream infections (BSIs) is a challenging problem, and sometimes, it may be life threatening; therefore, timely detection, identification, and antimicrobial susceptibility testing of blood-born epathogens are one of the most important function of diagnostic microbiology laboratory[5]. The present study provides information on the distribution of bacterial isolates causing blood stream infections along with their antibiotic susceptibility pattern that plays a crucial role ineffective management of septicemia cases. The blood culture positivity rate in NICU found in our study was 23.8%, which was comparable to study (22%) conducted in tertiary care hospital at Gangtok, Sikkim and in study conducted at Government Medical College and Hospital Chandigarh. [6, 7]. In contrast, low culture positivity ranging from 5.6% to 8.39% whereas high culture positivity ranging from 33.9% to 52.10%were reported by various other authors from time to time[8, 9]. Such variation in blood culture positivity can be explained by various factors such as volume or the number of blood culture samples taken for study as explained by Lee et al., 2007. [10]. The low isolation rate in our study could also be explained by the fact that quite a few numbers of patients already undergo some kind of primary treatment at peripheral health centers before reaching a tertiary care hospital. Self medication is also common due to over-the-counter availability of the medicines.

In most of the studies, Gram-negative bacteria were found to be predominant over Gram-positive organisms, especially in ICUs settings. In the present study also, Gram-negative isolates were predominant over Gram-positive isolates as observed in various other studies too.9, [11] Among Enterobacteriaceae, *E. coli* and *Klebsiella species* were the predominant isolates (56.6%) similar to findings reported in earlier studies.1[2, 13]. A high prevalence of non fermenters; *Pseudomonas species (*25.9%) and *Acinetobacter species (*12.3%); was found in our study as similar to as reported by

Gupta and Vanithaet al[14]

This study documents the extent of drug resistance among the frequently isolated Gram negative isolates from neonatal intensive care patients. An interesting observation of this analysis is the comparatively moderate to high sensitivity of aminoglycoside against the majority of GNB. Similar observations of moderate aminoglycoside sensitivity (30-40%) were observed by other authors as well[15]. High resistance to cephalosporin's and beta lactamase combinations observed in our study might be due tothe selective influence of extensive usage of these antimicrobials as compared to aminoglycoside. Our results show a low prevalence of carbapenem resistance among non-fermenters, 1% both in *Acinetobacter spp* and *Pseudomonas aeruginosa*. Carbapenem resistance observed in *Acinetobacter spp.* Isolates was much low compared to some recent studies in ICUs where the resistance is reported to be 16-17%[16, 17]. An increase in the prevalence of non-fermenters might have led to an increase in the usage of second-line antibiotics such as β-lactam/inhibitor combinations and carbapenems which may lead to increase incidence of resistance with time. Colistin alone or in combination with Carbapenems or Aminoglycosides appear to be the remaining treatment options for such Gram negative infections.

5. Conclusion

De-escalation of the high-end antimicrobials once the sensitivity pattern of the isolate is known is suggested to reduce the antimicrobial pressure. More aggressive measures such as routine screening cultures to identify and isolate carriers and the various environmental sources are also recommended, as well as periodical antibacterial sensitivity assessment in ICUs because of the continuous changes in the antibacterial susceptibility patterns. Routine surveillance of baseline resistance, formulation of hospital antibiotic policy and compliance with existing guidelines will go long way in reducing multi drug resistance in pathogens.

References

[1] TayalM, Sharma AK, Sharma R. Incidence of culture proven neonatal sepsis, pattern of antibiotic sensitivity and clinical course in neonatal intensive care unit in tertiary care center in North India. Int J Contemp Pediatr 2019; 6: 2419-27.

[2] Kirti Nirmal, Stuti Kansra Arora, Anuradha Shulania, Arvind Achra & Nandini Duggal. Ecology of Blood Stream Infection and Antibiotic Resistance in Intensive Care Unit At A Tertiary Care Hospital in Central

Delhi: International Journal of current medical and applied sciences; 2020, 28 (3), 16-20.
[3] Collee JG, Fraser AG, Marmion BP, Simmons A. Tests for identification of Bacteria. In: Mackie and McCartney Practical Medical Microbiology. 14th ed. London: Churchill Livingstone; 1996. p. 131-149.
[4] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing. Twenty-second Informational Supplement. Wayne, PA, USA: Clinical and Laboratory Standards Institute; 2012. p. M100-S22.
[5] Vasudeva N, Nirwan PS, Shrivastava P. Bloodstream infections and antimicrobial sensitivity patterns in atertiary care hospital of India. TherAdv Infect Dis 2016; 3: 119-27.
[6] Tsering DC, Chanchal L, Pal R, Kar S. Bacteriological Profile of septicaemia and the risk factors in neonates and infants in Sikkim. J Glob Infect Dis. 2011; 3 (1): 42-5.
[7] Agnihotri N, Kaistha N, Gupta V. Antimicrobial susceptibility of isolates from Neonatal Septicemia. Jpn J Infect Dis. 2004; 57 (6): 273-5.
[8] Vanitha RN, Kannan G, Venkata NM, Vishwakanth D, Nagesh VR, Yogitha M, et al. A retrospective study on blood stream infections and antibiotic susceptibility patterns in a tertiary care teaching hospital. Int J Pharm PharmSci 2012; 4: 543-8.
[9] Ndugulile F, Jureen R, Harthug S, UrassaW, Langeland N. Extended spectrum -lactamases among gram-negative bacteria of nosocomial origin from an intensive care unit of a tertiary health facility inTanzania. BMC Infect Dis 2005; 5: 86.
[10] Lee A, Mirrett S, Reller LB, Weinstein MP. Detection of bloodstream infections in adults: How many blood cultures are needed? J ClinMicrobiol 2007; 45: 3546-8.
[11] Garg A, Anupurba S, Garg J, Goyal RK, Sen MR. Bacteriological profile and antimicrobial resistance of blood culture isolates from a university hospital. J Indian AcadClin Med 2007; 8: 139-43.
[12] Kumar Y, Qunibi M, Neal TJ, et al. Time to positivity of neonatal blood cultures. Arch Dis Child Fetal Neonatal Ed.2001; 85: 182-6.
[13] Gohel K, Jojera A, Soni S, Gang S, Sabnis R, Desai M. Bacteriological profile & drug resistance patterns of blood culture isolates in a tertiary care nephrourology teaching institute. Biomed Res Int 2014; 2014: 153747.
[14] Chhina D, Gupta V. Bacteriological profile and antimicrobial susceptibility pattern of Blood isolates from a tertiary care hospital in North India. IJPRBS 2013; 2: 24-35.
[15] Jafari NJ, Ranjbar R, Haghi-Ashtiani MT, Abedini M, Izadi M. The study of prevalence & antimicrobial susceptibility of tracheal bacterial strains isolated from pediatric patients. PakJBiol Sci. 2009; 12: 455-8.34.
[16] Wroblewska MM, Rudnicka J, Marchel H, etal. Multidrug-resistant bacteria isolated from patients hospitalized in intensive care units. Int J Antimicrob Agents.2006; 27: 285-9.35.
[17] Japoni A, Vazin A, Hamedi M, et al. Multidrug resistant bacteria isolated from intensive-care-unit patient samples. Braz J Infect Dis. 2009; 13: 118-22.9.