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ORIGINAL ARTICLE

Causative Organisms in Neonatal Sepsis and Their Antibiotic Sensitivity and Resistance Pattern

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ABSTRACT

Objective: To determine different causative organisms confirmed through blood culture in babies presenting with neonatal sepsis and their antibiotic sensitivity and resistance pattern.

Methodology: This cross sectional observational study was conducted at The Department of Neonatology, Holy Family Hospital, Rawalpindi from Jan 2020 to Jan 2021. During the study period, a total of 241 neonates with positive blood culture were included. After following aseptic measures blood sample of 2.5ml was taken from neonate with features of sepsis. Samples were sent to microbiology sector while organism grown on culture media was noted and their sensitivity was checked for commonly used antibiotics.

Results: There were 110(45.64%) female and 131(54.36%) male. Most common organism was staphylococcus aureus i.e. 29.88% (72/241) followed by klebsiella pneumonia and pseudomonas in 17.43% each, salmonella typhi 14.52% Acinetobacter 8.3%, E.coli 7.475 and enterococcus 4.98%. Drug sensitivity was assessed and found that drug Sulzone was 80% to 100% sensitive for pseudomonas, salmonella typhi and Acinetobacter organisms and 71.4% sensitive for klebsiella pneumonia negative organism while ciprofloxacin and Imipenem was sensitive for E.coli

Conclusion: The most common causative organism of neonatal sepsis was staphylococcus aurues followed by klebsiella pneumonia and pseudomonas. Sulzone (cefoperazone/sulbactum) was found to be the most sensitive drug.

Keywords: Blood culture and, klebsiella pneumonia, neonatal sepsis, staphylococcus aureus.

INTRODUCTION

Septicemia is the 3rd most frequent cause of neonatal mortality following prematurity and birth asphyxia.[1,2] The incidence of neonatal sepsis is calculated to be between 1 to 10 deaths per 1, live-births while the incidence is about 3-fold among developing parts of the world. Neonatal sepsis is accounted for 5 million deaths annually whereas 40% of those deaths occur within first 7 days of life. Only 2% of these deaths occur in the developed world rest all in developing countries. Low birth weight babies are more prone to neonatal sepsis.[3] Neonates surviving neonatal sepsis are more prone to short as well as long term neurodevelopmental morbidities.[3, 4]

Among cases of early-onset neonatal sepsis (EONS), prematurity, low birth weight, lack of skilled birth attendants, inadequate antenatal care, maternal malnutrition and high incidence of infection are some of the major risk factors.[3,4] Maternal chorioamnionitis is also knows to be an established risk factor for EONS.[5,6] Late-onset neonatal sepsis (LONS) usually occurs following a vertical transmission that results in the initial colonization evolving later. In horizontal transmission, LONS is thought to be due to the contact with the healthcare provider or the environmental factors.[7-9].

A predominance of Gram-positive bacteria has been revealed in the developed countries while Gram-negative agents are more common among developing countries. Last few decades have witnessed increasing trends in antibiotic resistance patterns which could be due the mutant forms of the most prevalent bacteria, misuse/overuse/underuse of the broad spectrum antimicrobial drugs.[9] It is therefore necessary to gather local patterns of the most commonly involved pathogens and their antimicrobial susceptibilities. We aimed this research to determine different causative organisms confirmed through blood culture in babies presenting with neonatal sepsis and their antibiotic sensitivity and resistance pattern. The findings of this study are thought to provide local epidemiological data about the neonatal sepsis and antibiotic sensitivity/resistance patterns so that local guidelines and management protocol can be updated to include better choice of empirical antibiotics.

METHODOLOGY

This cross-sectional observational study was conducted in Department of Neonatology, Holy Family Hospital, Rawalpindi from Jan 2018 to Jan 2019. Sample size was calculated using WHO sample size calculator by taking Confidence level = 95%, anticipated population proportion = 6%, absolute precision required = 3% and minimally required sample size = 241.[10] Sampling Technique used was non-probability consecutive sampling technique. Neonates admitted with positive blood culture of either gender were included. Patients who had taken prior treatment with antibiotics, syndromic babies, patients with congenital heart disease, endocrine disease, metabolic disorder and babies with jaundice were excluded from the study. Neonatal sepsis was described as a positive blood culture report. Permission was taken from Institutional Forum of RMC. Informed consent was taken from parents/guardians.

After following aseptic measures, blood sample of 2.5ml was taken from neonate with features of sepsis. Samples were sent to Microbiology Sector, Department of Pathology, Holy Family Hospital, Rawalpindi. Organisms that grew on culture media were noted and their sensitivity were checked for commonly used antibiotics. All information was recorded in a structured proforma. Culture was done on agar plates used as growth media. Agar plate was spread with blood sample of patient containing pathological organism, then paper disks of antibiotics was added to the plate. Microorganisms were allowed to grow on the agar media and then was observed and identified under microscopic examination. The amount of space around each antibiotic space was indicated lethality of the antibiotic on specific microorganism.

The data collected was entered and analyzed in the SPSS version 26.0. All the categorical variables (gender, Gram positivity/negativity, type of microorganism, sensitivity, resistance), mode of delivery and residence was presented as frequencies and percentages. The continuous variables like, age in days was presented as mean and standard deviation. Effect modifiers like age, gender, gestational age, Mode of delivery, residence was controlled by stratification. Chi-square test was employed considering $p \leq 0.05$ as significant.

RESULTS

In a total of 241 neonates with positive blood culture, mean age was 7.28±2.74 days. There were 110 (45.64%) female and 131 (54.36%) male. Babies delivered by spontaneous vaginal delivery (SVD) were 162 (67.2%) and 79 (32.8%) by cesarean section.

Out of 241 neonates, gram-positive organisms were found in 84 (34.9%) cases and gram-negative organisms in 157 (65.1%) cases. Most common organism was staphylococcus aureus i.e. 29.88% (72/241) followed by klebsiella pneumonia and pseudomonas in 17.43% each, salmonella typhi 14.52%, acinetobacter 8.3%, E.coli 7.475 and enterococcus 4.98%.

In our study, drug Sulzone was 80% to 100% sensitive for pseudomonas, salmonella typhi and Acinetobacter organisms and 71.4% sensitive for klebsiella pneumonia while ciprofloxacin and Imipenem was sensitive for E.coli. Regarding positive organism, Vancomycin was sensitive for enterococcus and staphylococcus aureus. The overall resistance pattern highlighted 74% organisms to be resistant to ampicillin, cefotaxime (52%), ceftazidime (72%), ceftriaxone (60%), amikacin (42%), imipenem (14%), ofloxacin (42%) and aztreonam (56%).

Comparison of different causative organisms in babies presenting with neonatal sepsis with respect to age groups, gender, gestational age, mode of delivery and residential status are shown in table 1 to 3.

Table 1: Comparison Of Different Causative Organisms in Babies with Neonatal Sepsis With respect to Age Groups and Gender

Organism	Age Groups (Days)			P-Value	Gender		P-Value
	1-5 (n=100)	6-10 (n=120)	11-15 (n=21)		Male (n=110)	Female (n=131)	
E. coli	18(18%)	0(0%)	0(0%)	0.001	6(5.5%)	12(9.2%)	0.276
Klebsiella Pneumoniae	30(30%)	11(9.2%)	1(4.8%)	0.001	12(10.9%)	30(22.9%)	0.015
Pseudomonas	24(24%)	10(8.3%)	8(38.1%)	0.001	24(21.8%)	18(13.7%)	0.100
Salmonella Typhi	10(10%)	22(18.3%)	3(14.3%)	0.217	10(9.1%)	25(19.1%)	0.028
Acinetobacter	0(0%)	18(15%)	2(9.5%)	0.001	10(9.1%)	10(7.6%)	0.68
Enterococcus	6(6%)	5(4.2%)	1(4.8%)	0.823	6(5.5%)	6(4.6%)	0.756
Staphylococcus aureus	12(12%)	54(45%)	6(28.6%)	0.001	42(38.2%)	30(22.9%)	0.010

Table 2: Comparison of Different Causative Organisms in Neonatal Sepsis With Respect To Gestational Age and Mode of Delivery

Organisms	Gestational Age		P-Value			
	≤137 n=135	>137 n=106		Normal n=162	C-Section n=79	P-Value
E. coli	12 (8.9%)	6 (5.7%)	0.344	18(11.1%)	0(0%)	0.002
Klebsiella Pneumoniae	18(13.3%)	24(22.6%)	0.059	30(18.5%)	12(15.2%)	0.523
Pseudomonas	6(4.4%)	36(34%)	0.0005	42(25.9%)	0(0%)	0.001
Salmonella Typhi	30(22.2%)	5(4.7%)	0.0005	15(9.3%)	20(25.3%)	0.001
Acinetobacter	15(11.1%)	5(4.7%)	0.074	15(9.3%)	5(6.3%)	0.439
Enterococcus	6(4.4%)	6(5.7%)	0.677	12(7.4%)	0(0%)	0.013
Staphylococcus aureus	48(35.6%)	24(22.6%)	0.030	30(18.5%)	42(53.2%)	0.001

Table 3: Comparison of Different Causative Organisms in Neonatal Sepsis With Respect To Residential Status

Organisms	Resident Status		P-Value
	Rural (n=54)	Urban (n=187)	
E.coli	0(0%)	18(9.6%)	0.018
Klebsiella Pneumoniae	12(22.2%)	30(16%)	0.292
Pseudomonas	6(11.1%)	36(19.3%)	0.165
Salmonella Typhi	20(37%)	15(8%)	0.001
Acinetobacter	10(18.5%)	10(5.3%)	0.002
Enterococcus	0(0%)	12(6.4%)	0.056
Staphylococcus aureus	6(11.1%)	66(35.3%)	0.001

DISCUSSION

Recent decades have seen lots of improvements in the diagnosis and treatment of bacterial infections, yet, blood culture remains the mainstay investigation about the causative agents in neonatal sepsis.[1,3,11]

In present study the average age of the neonate was 7.28±2.74 days. There were 110(45.64%) female and 131(54.36%) male. Similar result was also reported in Vijayvergia et al study.[12] There were 59.3% male representing male-to-female ratio of 1.45:1. We noted staphylococcus aureus to be the commonest bacteria i.e. 29.9% followed by klebsiella pneumonia and pseudomonas in 17.4% each, salmonella typhi 14.5% ancinetobactor 8.3%, E.coli 7.5% and enterococcus 5.0%. Liaqat et al[10] in 2015 analyzed that predominant microorganisms isolated were Gram-negative (84%), with Enterobacter as the most common organism (48%) followed by E.coli (16%), Klebsiella (14%) and Pseudomonas (6%). In terms of gram-positive bacteria, S. aureus was the commonest (10%) while streptococcus pneumonia reported in 6%.

In this research, we noted relatively higher overall resistance patterns for some of the most commonly used antibiotics like ampicillin (74%), cefotaxime (52%), ceftazidime (72%), ceftriaxone (60%), amikacin (42%), ofloxacin (42%) and aztreonam (56%). Local data by Mustafa MA analyzing neonatal infections found higher resistance rates of gram-negative microorganisms to ampicillin (79%), cefotaxime (55%), ceftazidime (71%) and amikacin (22%) which is quite similar to the present findings.[13] Thaver D described high resistance rates of E. coli with ampicillin (72%), cotrimoxazole (78%) and 3rd generation cephalosporins (19%).[14] They also highlighted that almost all cases of Klebsiella species were resistant to ampicillin, cotrimoxazole (45%), and 3rd generation cephalosporins (66%). Resistance to gentamicin was lower among E.coli (13%), but higher among Klebsiella species (60%).[14] Hasvold et al found ampicillin and gentamicin resistance to be emerging among neonates having E. coli infections.[15]

Finding out trends in the prevalence of causative agents and their sensitivity/resistance patterns to commonly used antibiotics is vital for the effective infections control in a given geography. It is also known that causative agents of neontatal sepsis vary from one place to another while same goes for their resistance and sensitivity patterns. Some of the reasons behind these differences are thought to be geographical, social, economic and seasonal factors whereas trends in usage of various antimicrobial drugs also influence antibiotic resistance patterns.[13,16] The developed world has reported “coagulase-negative staphylococcus (CoNS)” and “group-B streptococcus (GBS)” to the most commonly found bacteria responsible for neonatal sepsis while data from developing countries predominantly shows E. coli, klebsiella and S. aureas to be the most commonly found bacterial agents.[17,18] As antibiotic resistance is rising all over the globe, a broad and multifactorial global approach is needed to handle this issue. Frequent microbiological surveillance programs, infection control and strict aseptic protocols can help in minimizing the overall burden of emergeing antibiotic resistance.

Our study had some limitations as well. As this was a single center study, our findings cannot be generalized and further research involving multiple centers and different sets of neonatal

population are necessary to further establish our findings. We were unable to record outcomes of neonatal sepsis.

CONCLUSION

The most common causative organism of neonatal sepsis was staphylococcus aurues followed by klebsiella pneumonia and pseudomonas. Sulzone (cefoperazone/sulbactum) was found to be the most sensitive drug. There is a need to review the antibiotics policy. As bacteriological organisms of neonatal sepsis vary from time to time, future studies are also required to know the changing bacteriological spectrum.

REFERENCES

1. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2017;390(10104):1770-80.
2. Zaman S, Shah SA, Mehmood S, Shahzad S, Munir M. Diagnosis and outcome of birth asphyxia in resource constrained health care set up. Pak Armed Forces Med J. 2017;67(6):971-75.
3. Woldu MA, Guta MB, Lenjisa JL, Tegegne GT, Tesafye G, Dinsa H. Assessment of the incidence of neonatal sepsis, its risk factors, antimicrobials use and clinical outcomes in Bishoftu General Hospital, neonatal intensive care unit, Debrezeit-Ethiopia. Int J Contemp Pediatr. 2017;1(3):135-41.
4. Pek JH, Yap BJ, Gan MY, Seethor ST, Greenberg R, Hornik CP, Tan B, Lee JH, Chong SL. Neurocognitive impairment after neonatal sepsis: protocol for a systematic review and meta-analysis. BMJ open. 2020;10(6):e038816.
5. Murthy S, Godinho MA, Guddattu V, Lewis LE, Nair NS. Risk factors of neonatal sepsis in India: A systematic review and meta-analysis. PloS one. 2019;14(4):e0215683.
6. Jehanzeb K, Shah SA, Zaman S, Haq ZU, Lodhi MA, Ashraf N. A comparison of morbidity and mortality among early, moderate and extreme premature infants reporting in Gilgit. Pak Armed Forces Med J. 2020;70(2):503-07.
7. Gowda H, Norton R, White A, Kandasamy Y. Late-onset neonatal sepsis—a 10-year review from North Queensland, Australia. Pediatr Infect Dis J. 2017;36(9):883-8.
8. Nour I, Eldegla HE, Nasef N, Shouman B, Abdel-Hady H, Shabaan AE. Risk factors and clinical outcomes for carbapenem-resistant Gram-negative late-onset sepsis in a neonatal intensive care unit. J Hosp Infect. 2017;97(1):52-8.
9. Al-Matary A, Heena H, AlSarheed AS, Ouda W, AlShahrani DA, Wani TA, et al. Characteristics of neonatal Sepsis at a tertiary care hospital in Saudi Arabia. J Infect Public Health. 2019;12(5):666-72.
10. Liaqat I, Khan SN, Naveed A. Bacteriological Spectrum of Neonatal Sepsis. J Rawalpindi Med Coll. 2015:19(1):29-32
11. Gomaa HH, Udo EE, Rajaram U. Neonatal septicemia in Al-Jahra Hospital, Kuwait: etiologic agents and antibiotic sensitivity patterns. Med Princ Pract. 2001;10(3):145-50.
12. Vijayvergia V, Gupta S, Goyal J. Neonatal septicemia - bacteriological spectrum and antibiogram-a study from a tertiary care center of north India. Int J Curr Microbiol App Sc.i 2016; 5(11):741-50
13. Mustufa MA, Korejo R, Shahid A, Nasim S. Infection remains a leading cause of neonatal mortality among infants delivered at a tertiary hospital. J Infect Dev Ctries. 2014;8(11):1470-75.
14. Thaver D, Ali SA, Zaidi AK. Antimicrobial resistance among neonatal pathogens in developing countries. Pediatr Infect Dis J. 2009 ;28(1):19-21.
15. Hasvold J, Bradford L, Nelson C,Harrison C, Attar M. Gentamycin resistance among Escherichia coli strains isolated in neonatal sepsis. J Neonatal Perinatal Med. 2013;6(2):173-77.
16. Haque KN, Khan MA, Kerry S, Stephenson J, Woods G. Pattern of culture-proven neonatal sepsis in a district general hospital in the United Kingdom. Infect Control Hosp Epidemiol. 2004;25(9):759-64.
17. Waheed M, Laeeq A, Maqbool S. The etiology of neonatal sepsis and patterns of antibiotic resistance. J Coll Physicians Surg Pak. 2003;13(8):449-52.
18. Aftab RU, Iqbal I. Bacteriological agents of neonatal sepsis in NICU at Nishtar Hospital Multan. J Coll Physicians Surg Pak. 2006;16(3):216-19.