ORIGINAL ARTICLE

ANTIMICROBIAL SUSCEPTIBILITY PATTERN OF NEONATAL SEPSIS IN NEONATAL INTENSIVE CARE UNIT

Hafsa Waseem[1], Rabia Sadaf[2], Abdul Jalil Khan[3], Afnan Naeem[4], Sakhawat Ali[5], Javaid Usman[6]

Authors' Affiliation

[1]Department of Pathology, Al-Nafees Medical College and Hospital Islamabad

[2]Department of Pathology, Rawal Medical College Islamabad

[3]Department of Public Health & Social Sciences, Khyber Medical University Peshawar

[4,5,6]Department of Pathology, Army Medical College Rawalpindi

Corresponding Author

Dr. Hafsa Waseem

Assistant Professor, Department of Pathology, Al-Nafees Medical College and Hospital Islamabad

Email:drhafsaalishah@gmail.com

ABSTRACT

Objective: To determine the antimicrobial susceptibility pattern of neonatal sepsis in the neonatal intensive care unit.

Material & Methods: A cross-sectional study was conducted from January to July 2018 at the department of microbiology, Army medical college Rawalpindi. Blood and MacConkey agar were used for colony identification and pigment production, Gram stain was done to identify Gram-positive and Gram-negative bacteria, Rapid tests like catalase, coagulase, motility, and oxidase were performed, and API 10S and 20 E were used to identify at genus and species level. For sensitivity testing of antimicrobials modified Kirby- Bauer Disk Diffusion method was used. Data was analyzed in SPSS.

Results: Out of the total of 470 samples 137(29%) were positive. Gram-positive were 43(31.3%) and Gram-negative were 94(68.6%). Maximum organisms were Stenotrophomonas maltophilia and Serratia marscenes which were 26 (19%) each followed by Klebsiella pneumoniae 18 (13.1%) and others. Pathogens showed 100% resistance to ampicillin and were maximum sensitive to colistin. However, Gram-positive were 100% sensitive to minocycline and linezolid and Gram-negative showed maximum sensitivity towards tigycycline which is 75.4%.

Conclusion: Minocycline or linezolid in combination with tigycycline is the drug of choice for the management of neonatal sepsis.

Key Words: Antibiotics, Bacteria, Neonates, Sepsis.

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INTRODUCTION

In developing countries like Pakistan neonatal sepsis is the foremost important reason of neonatal mortality. WHO estimates that about 40% of children deaths are due to neonatal sepsis and highest burden occurs in middle and lower income countries.[1,2] It may manifest as a subclinical infection or might end up with severe focal or systemic disease. For the neonatal sepsis to develop, acquiring the infections from intrauterine or maternal flora.[3-5]

Multiple risk factors both in the neonates and the mother involves in the development of sepsis in the neonatal period, most important of which include premature birth and low birth weight.[6-8] Inadequate antenatal care, unhygenic birth and careless umbilical cord care practices associated with high rate of births conducted at home along with late recognition of conditions that pose a risk in mother or baby are major problems faced in third world countries.[9] In addition to the neonatal factors conditions like Chorioamnionitis and premature rupture of membranes are major maternal risk factors.[10]

Neonates might acquire infections in-utero or postnatal from the community or the hospitals. In NICU premature neonates are more prone to infections due to invasive procedures and their prolonged stays in neonatal intensive care unit.

For the diagnosis of sepsis, blood culture is gold standard. Neonatal sepsis is treatable with good supportive care and appropriate use of antibiotics. Causative pathogens vary from hospital to hospital and it also varies from time to time in the same hospital. So neonatologist must know the suspected pathogen and its susceptibility pattern before starting empirical therapy.[8] Another major problem associated with the neonatal infections is the prompt and proper identification of the infected infant, while making sure not to overlook the identification of a noninfected infant. It is definitely desirable to administer appropriate therapy as early as possible to the infant who is suffering from infection and still equally important is to make sure not to administer antibiotics to an infection free neonate.[11]

MATERIAL AND METHODS

A cross sectional study was performed from 31st January 2018 to 31st July 2018 at the department of Microbiology, Army Medical College Rawalpindi. Non probability consecutive sampling technique was used. All the samples received from Neonatal intensive care unit (NICU) of Pak Emirates Military Hospital Rawalpindi during the study period were included in the study.

As per routine blood agar, MacConkey agar was used for aerobic culture and incubated at 35°C ± 2°C for 24 hours. After 24 hours' bacteria was identified according to colony morphology and pigment production. Then Gram staining procedure was performed to identify Gram positive and Gram-negative bacteria. After that rapid test performed like for Gram positive catalase and coagulase tests were performed. For Gram negative oxidase test and motility tests were performed. To identify organism up to genus and species level API 10S and 20E (Biomerieux, France) were used and antibiotic susceptibility testing was performed by using Modified Kirby- Bauer Disk Diffusion on Mueller Hinton agar according to CLSI 2018 guidelines. After incubation of 24 hours' susceptibility pattern of all drugs were noted and data was analyzed in SPSS version 22.

RESULTS

Total 470 blood samples were received in microbiology department for blood culture. Out of these 470, only 137 (29%) were positive, and out of these positive, 43 (31%) were Gram positive and 94 (68.6%) were Gram negative. In this study a total of 137 patients were enrolled to assess the pathogen type and its susceptibility. Out of the total 137 cases, the majority of the patients 94 (68.6%) had gram negative pathogens whereas 43 (31.4%) patients had gram positive bacterial pathogens in this study. Stenotrophomonas maltophilia 26(19.0%) and Serratia marcescens 26(19.0%) were the main organisms isolated in this study. Klebsiella pneumoniae 18(13.1%), Coagulase negative Staphylococcus (MRSE) 17(12.4%), and Enterococcus faecalis 11(8.0%) were the other common pathogens. Moreover, 7(5.1%) patients each had Klebsiella oxytoca, Staphylococcus aureus and Acinetobacter baumannii followed by Staphylococcus aureus (MRSA) in 5(3.6%) cases. Rest all organisms noted are less than 3%. Pathogens showed highest rate of resistance towards Ampicillin 92(100.0%), amoxi-clavulanate30 (93.3%) and penicillin 37(88.1%). Pathogens also showed high resistance towards aztreonam (77.6%), ceftriaxone (70.3%), erythromycin (59.5%) gentamycin (58.5%), meropenam (52.1%), ciprofloxacin (51.1%).

On the other hand, pathogen showed maximum sensitivity towards Linezolid (100%), vancomycin (93.0%), chloramphenicol (92.9%), clindamycin (87.5%) and tigycycline (75.4%) as shown in **(Table 1)**.

The sensitivity pattern of different antimicrobials was assessed according to Gram positive and Gram-negative classification of pathogens. Moreover, the antimicrobials showed maximum sensitivity towards Gram positive pathogens were Minocycline (100.0%), Linezolid (100%), Vancomycin (93.0%), Chlorompheniсol (92.9%), Clindamycin (87.5%) and Cefoperazone-sulbactum (71.1%). Even many Gram-negative pathogens were highly resistant to many routine drugs. Perperacilin-tazabactum and Amoxi-clavulanate were 100% resistant. Other drugs with low sensitivity against these pathogens were penicillin (11.9%), Ciprofloxacin (26.2%), Cloxacillin (31.2%), Erythromycin (40.5%) and Gentamycin (40.5%). Similarly, comparatively most of the drugs also had low sensitivity against Gram negative pathogens when compared with Gram positive pathogens.

For Gram negative pathogens the most sensitive drugs were Tigecycline (75.4%), Minocycline (67.0%), Peperacilin-tazobactum (61.4%), Cotrimoxazole (60.0%), Cipfloxacin (59.6%) and Colistin (100%). Even the fourth generation and life-saving drugs had quite low sensitivity against gram negative bacterial pathogens. Amoxi-clavulanate (10.5%), Ampicillin-sulbactum (12.5%), Ceftriazone (33.7%), Amikacin (45.7%) and Meropenam (47.9%) had quite low and average level of sensitivity against Gram negative pathogens in this study.

Table 1: Susceptibility of various drugs

	Resistant	**Sensitive**
Chloromphenicol (n=42)	3 (7.1%)	39 (92.9%)
Ciprofloxacin (n=137)	70 (51.1%)	67 (48.9%)
Clindamycin (n=32)	4 (12.5%)	28 (87.5%)
Cloxacillin (n=32)	22 (68.8%)	10 (31.2%)
Cotrimoxazole (n=122)	52 (42.6%)	70 (57.4%)
Erythromycin (n=42)	25 (59.5%)	17 (40.5%)
Fucidic acid (n=32)	16 (50.0%)	16 (50.0%)
Gentamycin (n=135)	79 (58.5%)	56 (41.5%)
Linezolid (n=43)	0 (0%)	43 (100%)
Minocycline (n=119)	29 (24.4%)	90 (75.6%)
Penicillin (n=42)	37 (88.1%)	5 (11.9%)
Tetracycline (n=42)	18 (42.9%)	24 (57.1%)
Vancomycin (n=43)	3 (7.0%)	40 (93.0%)
Amikacin (n-94)	51 (54.3%)	43 (45.7%)
Ampicillin (n=92)	92 (100.0%)	0 (0.0%)
Ampicillin-sulbactum (n=73)	64 (87.7%)	9 (12.3%)
Aztreonam (n=67)	52 (77.6%)	15 (22.4%)
Cefoperazone-sulbactum (n=90)	26 (28.9%)	64 (71.1%)
Ceftriaxone (n=101)	71 (70.3%)	30 (29.7%)
Colistin (n=66)	0 (0%)	66 (100%)
Meropenam (n=94)	49 (52.1%)	45 (47.9%)
Peperacilin-tazobactum (n=77)	34 (44.2%)	43 (55.8%)
Tigecycline (n=57)	14 (24.6%)	43 (75.4%)
Amoxi-clavulanate (n=30)	28 (93.3%)	2 (6.7%)

DISCUSSION

The incidence of sepsis is highest in children and neonates.[12] Neonatal sepsis is a major health problem of neonates. it is of more concern in developing countries.[13] In the present study, the total number of blood samples of neonates received from the neonatal intensive care unit were 470, out of which the positivity ratio was 29% which indicates towards the magnitude of the problem and is way higher than a study conducted in a children hospital in Kathmandu Nepal in the year 2018.[14] Which showed a positivity rate of 16.9%, indicating a much higher magnitude of problem in our set up. Still in another study conducted by Sharma et al in the year 2013 in India showed a positivity ratio of 37.63%.[15]

Among positive cases in our study, the bacteriological profile showed 68.6% of the organisms to be Gram negative whereas only 31% were identified as Gram positive. This finding was similar to the results obtained in a study conducted by Yadav et al who reported their bacteriological profile to be mainly showing the Gram negative bacilli being isolated as the major organisms as the cause of neonatal sepsis in their study i.e. 46% were Gram-positive cocci and 54% were Gram-negative rods. Yadav et al. reported in their study the highest number of pathogen isolated were Staphylococcus aureus (35.6%) followed by Klebsiella pneumoniae (15.3%) followed by others, whereas the bacteriological profile in our study showed Stenotrophomonas maltophilia (19.0%) and Serratia marcescens (19.0%) to be the main organisms isolated.

Strenotrophomonas was reported as the rare cause of neonatal sepsis in a case report published in the year 2018.[16] whereas in our study it is reported to be the most frequent organism amogst the Gram negative organisms, which is an alarming situation based on the extensive degree antibiotic resistance associated with this organism.

The bacteriological profile as reported in a study also reported Gram-negative organisms to be most commonly isolated in their study conducted in August, 2020 by Jatsho et.al, as were the findings in our study. They reported Klebsiella pneumoniae to be the most frequently reported organism which in our study was Strenotrophomonas maltophilia.[17] Still another study conducted by Pokhrel et.al, in the year 2018 in Nepal, reported the same bacteriological profile with overall prevalence of Gram negative organisms as reported in our study.[18]

The antiobiotic susceptibility pattern as reported in as seen in our study showed Strenotrophomonas, Serratia followed by Klebsiella species.

The antibiotics to which most of the Gram positive pathogens were found to be sensitive included Minocycline and linezolid showing 100% sensitivity followed by Vancomycin, Chloramphenicol and Clindamycin, whereas the profile of antimicrobial susceptibility against Gram negative organisms yielded maximum sensitivity against Colistin, Tigecycline and Minocycline.

Based on the findings in our study implementation of effective and efficient preventive strategies to fight against the emerging antibiotic resistance is urgently required.

CONCLUSION

Minocycline or linezolid in combination with tigycycline is the drug of choice for empirical treatment of neonatal sepsis, for the decision of empirical treatment periodical studies for the antibiotic resistance pattern should be done in neonatal intensive care unit as pathogens changes their antibiotic resistance pattern quickly.

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