Original Article

Bacterial Resistance in Neonates With Sepsis, Not Responding to First Line Antibiotics

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ABSTRACT

Objective: To determine the bacterial resistance in neonates with sepsis not responding to first line antibiotics, at Neonatal Intensive Care Unit, Nazeer Hussain Medical Complex Hyderabad

Study Design: Descriptive / cross sectional study.

Place and duration of study: This study was conducted at the Neonatal Intensive Care, Nazeer Hussain Medical Complex Hyderabad from July to December 2016

Materials and Methods: A total of 63 neonates admitted to NICU, Nazeer Hussain Medical Complex Hyderabad with suspected neonatal sepsis and fulfilling the inclusion criteria were included.

After taking blood culture second line broad spectrum antibiotics (Meropenem, Vancomycin) started and blood culture followed for the presence of bacteria and its sensitivity to various antibiotics, antibiotics resistance to first line antibiotics (Amikin, Cefotaxime, Ampicillin) was also followed.

Results: Most common age of presentation was <5 days ie 76.2%, having the male predominance 85.7% and most neonates were between 2 to 3 Kg ie 85.7%. Most neonates were born at term 61.9%. Most common organism was Staphylococcus Aureus 24 (38%). Death occurred in 9 (14.3%) neonates. Blood Culture was negative in 24 (38.09%) neonates. Klebsiella Pneumonia was the most common organism isolated and it was sensitive to Colistin and Meropenem in 100% cases, while it was resistant to Amikacin and Ampicillin in 100% cases.

Conclusion: Proper Blood Culture and Judicious use of antibiotics in neonatal sepsis can reduce the mortality, even in neonates who did not respond to first line antibiotics. Care should be taken, while using second line antibiotics, because resistance to second line antibiotics is emerging, hence there is need of vigilance and Blood Culture follow up to know the bacterial sensitivity and proper antibiotic coverage.

Key Words: Neonatal Sepsis, Blood Culture, Antibiotics Resistance

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INTRODUCTION

Sepsis is most common etiology of neonatal mortality in developing countries. Neonatal sepsis has no specific feature that can help in diagnosis, but it can present with drowsiness, feeding difficulties, tachycardia or tachypnea [1]. In previous studies neonates with moderate sepsis presented with drowsiness, grunting, tachypnea or nasal flaring, while neonates with severe sepsis presented with unconsciousness, cyanosis, pallor or feeding problems [2].

Blood Culture yield in neonatal sepsis is between 25 to 54%. Though acute phase reactants like C-Reactive Proteins (CRP) may help in the diagnosis of neonatal sepsis but it lacks sensitivity and specificity. It also cannot detect specific organism and availability of these investigations are issues in developing countries.

Gold standard investigation for neonatal sepsis is Blood Culture but the results are not available immediately thus needs to start empiric treatment in suspected neonatal sepsis [3]. Aminoglycosides and Penicillin are used as first line empiric treatment for neonatal sepsis for last decades in developed countries and this was based on culture and sensitivity results of various research studies. As there is increased resistance of gram negative rods to aminoglycosides and Penicillin all over the world and antibiotic sensitivity vary between different hospitals and region, so we need local data to treat infections confidently [4].

As a part of developing country and problems of cost and availability of Blood Culture facilities, most of the Neonatal Units in our area are not performing the Blood Culture in suspected Neonatal Sepsis and just starts recommended first line antibiotics i.e. Ampicillin and Cefotaxime or Amikacin. If the neonate dose not responds to first line antibiotics and becomes worse, then they shift the neonates to Neonatal Intensive Care Units having the facility of Ventilators and well equipped laboratory.

As our hospital is among one of the hospital that receives the major bulk of serious neonates with Severe Sepsis, so this study is performed to know the Bacterial yield and their sensitivity pattern, hence to make a local

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protocol to start empirically second line antibiotics, if first line antibiotics fails to respond.

MATERIALS AND METHODS

It was a Cross sectional study carried out by Non-probability consecutive sampling over 63 neonates, from July to December 2016 at Neonatal Intensive care of Nazeer Hussain Medical Complex Hyderabad. This study was approved by Ethical review committee of institute. All neonates admitting to Neonatal Intensive Care fulfilling inclusion criteria (aged less than one month of either sex shifted from another Neonatal Unit with Neonatal Sepsis not responding to Injection Ampicillin, Cefotaxime, and Amikin with clinical features suggestive of Sepsis ie. Fever, unable to feed, convulsions, respiratory distress, lethargic was enrolled in the study after taking informed consent from Parents. Patients with Neonatal Sepsis but already taking second line antibiotics ie, Injection Vancomycin, Meropenem were excluded from the study.

After history taking and detailed examination, Blood Culture was taken from the vein over the dorsum of hands in sterile bottle provided by laboratory and was sent to certified recognized microbiology laboratory. Bacteriological examination of Blood sample was carried out according to standard procedure. All specimens inoculated on following media: Mac conkey agar, Blood agar. Plates were allowed to warm to room temperature prior to use and inoculated within 30 minutes of specimen collection.

Antimicrobial susceptibility testing was performed in cases of positive culture by microbiologist having at least five years of experience in microbiology. Kirby-Basuer disc-diffusion method used for challenge for selected antibiotics with all pertinent isolates. McFarland 0.5 standardized bacteria suspension is swabbed over the Mueller-Hinton agar plate and allows it to dry for about 5-15 minutes. Paper disks containing single concentration of each antimicrobial agent were placed into the inoculated surface. After overnight incubation at 37^0C, cut-off diameters of resultant inhibition zones were measured.

The data collection proforma was filled separately for each patient by researcher. Data was entered and analyzed in SPSS v 22.0. Descriptive statistics i.e. mean + standard deviation was calculated for quantitative variables like age and duration of Sepsis. Frequency and percentage was reported for qualitative variables such as gender, bacterial pathogens isolated from blood samples, for drug resistance and for drug sensitivity.

Operational Definitions: Neonates: Age ≤ 28 days

Sepsis: Systemic inflammatory response syndrome secondary to infection**.**

RESULTS

Table No. 1: Demographic Data

Characteristics	No. of Patients	%
Age		
3 -5 days	48	76.2
6- 10 days	12	19.0
> 10 days	3	4.8
Gender		
Male	54	85.7
Female	9	14.3
Weight		
< 2kg	3	4.8
≥2 - 3	54	85.7
> 3 K	6	9.5
Gestational Age		
<37 Weeks	24	38.1
> 37 weeks	39	61.9

Table No.2: Blood Culture Results

Blood culture		%
K. Pneumonae	12	19.04
Staphylococcus species	3	4.76
Acinobacter	3	4.76
Burkholderia cepacia	9	14.28
Enterobacter	3	4.76
Serratia species	9	14.28
No Growth	24	38.09

Table No.3: Neonatal Outcome

Outcome		%
Improved	54	85.7
Death	9	14.3

Table No.4: Bacterial Culture Sensitivity and Resistance

Bacteria	Meropenem		Amikacin		Vancomycin		Cotrimoxazole		Colistin		Ampicillin		Levofloxacin		Fosfomycin	
	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S
K.Pneumonia	0	12 (100%)	12 (100%	0	12 (100%)	0	_	_	0	12 (100%)	12 (100%)	0	_	_	_	_
Acinobacter	3 (100%)	0	3 (100%)	0	_	_	_	_	0	3 (100%)	_	_	_	_	_	_
Burkholderia Cepacia	0	9 (100%)	_	_	_	_	0	9 (100%)	_	_	_	_	9 (100%)	0	_	_
Enterobacter	0	3 (100%)	0	3 (100%)	_	_	_	_	_	_	3 (100%)	0	_	_	_	_
Serratia Species	9 (100%)	0	9 (100%)	0	_	_	_	_	_	_	9 (100%)	0	_	_	0	9 (100%)
Staphylococcus Species	_	_	0	3 (100%)	0	3 (100%)	_	_	_	_	3 (100%)	0	_	_	_	_

Most common age of presentation was <5 days i.e. 76.2% (Table 1), having the male predominance 85.7% (Table 1) and most neonates were between 2 to 3 Kg ie 85.7% (Table 1). Most neonates were born at term 61.9% (Table 1). Most common organism was Staphylococcus Aureus 24 (38%) (Table 2). Death occurred in 9 (14.3%) neonates (Table 3). Blood Culture was negative in 24 (38.09%) neonates (Table 2). Klebsiella Pneumonia was the most common organism isolated and it was sensitive to Colistin and Meropenem in 100% cases, while it was resistant to Amikacin and Ampicillin in 100% cases (Table 4).

DISCUSSION

In our study out of 63 neonates, 39 neonates (61.9%) had positive Blood Culture. Most common bacteria were K.Pneumonia, while least common bacteria were Staphylococcus, Acinobacter and Enterobacter.

A different local study from Peshawar showed 59.8% positive blood culture and this difference in high positive bacterial yield may be due to no antibiotic use prior to Blood Culture. Escherichia coli (E. coli) was the commonest organism causing (54; 80.5%) followed by Pseudomonas (6; 8.9%), Klebsiella (5; 7.4%) and Staphylococcus aureus (11; 16.4%) respectively, while in our study most common organism was K. Pneumonia, this shows the importance of different organism in different regions. The gram-negative organisms showed high degree of resistance to commonly used antibiotics, ampicillin (79.3%), cefotaxime (55.2%) and comparatively low resistance to gentamicin (43.2%), tobramycin (34.3%), imipenem (23.6%), amikacin (22.3%), and ciprofloxacin (11.9%) respectively, while in our study these organism were 100% resistant to Ampicillin and Amikacin and most of the gram negative organism were sensitive to Meropenem (100) but Serratia Species were 100 resistant to Meropenem. Staphylococcus aureus showed almost the same resistance to ampicillin, 75%, and comparatively low resistance to the rest of the antibiotics as compared to the gram-negative organisms, while in our study Staphylococcus was 100% sensitive to Amikacin and Vancomycin while 100% resistant to Ampicillin [5].

An international study from America showed GBS (43%) and E coli (29 %,) were most frequently isolated. 16% of infected infants died, most commonly with E coli infection (33%), while in our study we did not found any GBS or E.Coli.[6] This shows the variation in organisms presence in different countries. The death rate was lower in our study that may be due more severity of E.Coli or GBS in international study.

In another different local study Staphylococcus Aureus (64.1%) was the most common organism [7]. Gram positive organisms were mostly sensitive to Vancomycin, amikacin and amoxicillin, while gram negative organisms were mostly sensitive to amikacin and imipenem. Ampicillin was found to be resistant to both gram positive and gram negative organism. While in our study Staphylococcus Aureus was the least common organism (4.76%), Gram positive organism were sensitive to Amikacin and Vancomycin, while resistant to Ampicillin.

In another international study Positive blood culture was found in 47.1%. Deaths occurred in 19% of neonates. K. Pneumonia was resistant to Ampicillin in 100% cases, while resistant to Amikacin in 67% cases[8], while in our study 62% cases were Blood Culture positive and death ratio was in 9% cases.

In another local study the predominant microorganisms were Enterobacter and Staphylococcus aureus. The antibiotic sensitivity pattern revealed Ampicillin (74% resistance [9]. While in our study K.Pneumonia was the most common organism and Enterobacter was the least common organism.

In another different study from India, Gram positive bacteria showed high resistance to Ampicillin (13.6%) and Amikacin-66%. They were highly susceptible to Vancomycin (95%). Among the Gram negative bacteria, many of them were resistant to ampicillin (7.5%), They were highly susceptible to Colistin (100%) and Meropenem (100%) [10]. While our study showed 100% resistance to Ampicillin.

CONCLUSION

Proper Blood Culture and Judicious use of antibiotics in neonatal sepsis can reduce the mortality, even in neonates who did not respond to first line antibiotics. Care should be taken, while using second line antibiotics, because resistance to second line antibiotics is emerging, hence there is need of vigilance and Blood Culture follow up to know the bacterial sensitivity and proper antibiotic coverage.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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