Neonatal Sepsis: Frequency and Antibiogram Profiling of Bacterial Isolates in a Tertiary Teaching Hospital Lahore, Pakistan

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ABSTRACT

Introduction: Neonatal sepsis is one of the most common cause of neonatal morbidity and mortality in Pakistan and worldwide so the present study was aimed to evaluate frequency and antibiotic sensitivity pattern of bacteria associated with neonatal sepsis in Paediatric Intensive Care Unit of a teaching hospital in Lahore, Pakistan.

Material and methods: It was an observational, cross-sectional study conducted at Paediatric Intensive Care Unit, Department of Paediatrics, Arif Memorial Hospital, Lahore from 1st July 2018 till 31st December 2018. Total 166 Neonates (1 – 28 days of life) with neonatal sepsis were included in this study. Neonates with gross congenital malformation or those who had already received any antibiotic were excluded from the study. All those neonates who met the inclusion criteria were further investigated in laboratory (complete blood count, prothrombin time, and blood cultures). Positive Blood cultures were checked for their sensitivity to various antibiotics.

Results: The mean age of cases was 17.3±7 days. Gender distribution was 90 (54.2%) males and 76 (45.8%) females. Out of total 166 cases, 100 (60.2%) had early onset neonatal sepsis and 66 (39.8%) had late onset sepsis. History of Preterm Premature rupture of membrane was present in 24.6%. The most common organism isolated on blood culture was Klebsiella pneumoniae (38.29%) followed by Escherichia coli (23.40%) and Staphylococcus aureus (17.02%). Klebsiella was sensitive to Amikacin, Gentamycin and Ciprofloxacin in 100% cases, while it was resistant to Ampicillin in 100% cases.

Conclusion: It is concluded from our study that Klebsiella pneumoniae is the most common organism for neonatal sepsis and it is sensitive to common antibiotics.

Keywords: Bacterial Sensitivity Pattern, Neonatal Sepsis.

INTRODUCTION

Neonatal sepsis is one of the leading causes of neonatal morbidity and mortality.[1] Clinical manifestations may be vary from a subclinical infection to some severe focal or a systemic disease. Pathogens responsible for sepsis may arise from intrauterine infection, maternal flora, or may be acquired postnatally from the hospital or surroundings.[2] In the recent years, there is a significant decrease in neonatal mortality around the world.[3] Clinically diagnosed sepsis is present in 49170 per 1000 live births in developing countries, while culture-proven sepsis is present in 16 per 1000 live births.[4] According to a study, early-onset sepsis is caused by Group B Streptococcus (GBS) isolated in 50% cases, followed by Escherichia coli isolated 25% of cases.[5] Similarly late onset sepsis is caused by Coagulase Negative Staphylococci (CoNS) in 50% of cases, while other important agents are E. coli, Klebsiella and Candida. Pathogens responsible for late onset sepsis are more resistant to antibiotics as compared to those causing early-onset sepsis.[6] Neonatal sepsis must be treated by keeping in mind, the most common pathogens and their antibiotic sensitivity patterns.[7] In the last 10 years, ampicillin and aminoglycosides have remained sensitive to almost 90% of pathogens, therefore it must be considered the first line therapy for suspected cases of early-onset sepsis.[8-10] This study was conducted to determine the prevelance of micro organisms among various prenatal risk factors. It will help in planning a risk-based strategy for the management of early onset neonatal sepsis (EONS), through focused antibiotic therapy rather than to initiate empiric treatment which also poses the risk of antibiotic resistance. Although this study is done in a neonatal unit of a tertiary care teaching hospital, further studies should be done in various hospitals to check the most common organisms and their antibiotic sensitivity patterns, because the organisms and their sensitivity pattern may vary in different countries and areas, hence local data of a particular community is very important for selection of empiric therapy in suspected cases of neonatal sepsis.

MATERIAL AND METHODS

This observational cross sectional study was carried out at Neonatal Unit, Department of Paediatrics, Arif Memorial Teaching Hospital, Lahore from 1st July 2018 to 31st December 2018. A total number of 166 neonates were included in this study. Sample size was calculated with 95% Confidence Interval, 4% bound on error and based on least frequent proportion of presumed sepsis with culture proven

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in Pakistan, 32% by the statistical formula. Approval was taken from ethical review committee of the institute.

Inclusion criteria

1. Neonate's age within 28 days,
2. Full term or preterm baby
3. Having clinical symptoms and signs of sepsis
4. Certain high risk groups like +ve history of prom (prolong rupture of membrane) > 18 hours.
5. Neonates aged less than 28 days of life having the history of sepsis like, Poor temperature control, Refuse to feed or poor sucking, Inactivity or irritability or Seizure and patients who were meeting the inclusion criteria were also enrolled in the study.

Exclusion criteria

1. Neonates having the history of antibiotic administration 48 hours prior to admission
2. Neonates having Gross congenital anomalies.

The purpose of the study was explained to every patient's parents and an informed consent was taken. Blood was drawn using aseptic precautions and inoculated into Trypticase Soya Broth to isolate aerobic bacteria. Since anaerobic bacteria are less frequently involved in neonatal sepsis, for that reason its isolation was not included in the study. After inoculation, the blood culture bottles were incubated at 37˚C and sub-cultured on solid media like Blood agar, Mac-Conkey agar and Chocolate agar after 24-48hrs and on 7th day of incubation. The isolated bacteria were identified by Gram staining and routine biochemical methods. After identification, the isolates were tested for their susceptibility against ten most commonly used antibiotics. The method employed was disk diffusion method and the zones of inhibition were measured. The calibrated inoculums of bacterial pathogens at 0.5 McFarland concentration was inoculated into Muller Hinton media and the antibiotic disks were placed on the surface of plates. Inhibition zones were determined after incubation at 37˚C for 24 hrs. We recorded the positive blood culture cases in a separate record file. The cases were classified as:

1. Early onset sepsis, if presented at the hospital in less than 7 days of life and
2. late onset sepsis, if presented at or after 7 days of life.

STATISTICAL ANALYSIS

All the data were recorded on pre-designed proforma. Data were entered and analyzed in statistical program SPSS version 20.0. Qualitative data such as gender, sepsis, microorganisms and drug sensitivity etc were calculated by simple frequencies and percentages. For comparison between the proportions of early and late onset sepsis we applied Chi square test. Mean ± Standard Deviation was calculated for numerical variables like age (in years) and t' test (2 tailed) was applied. Data was calculated on 95% Confidence Interval. Any p value <0.05 was considered as statistically significant.

RESULTS

A total of 166 patients were enrolled for this study. Among these 166 patients, the mean age was 17.3±7 days (Table I), 91 (54.8%) were male and 75 (45.2%) were females. The male to female ratio was approximately 1.2:1 (Table I), 100 (60.24%) cases were of early onset neonatal sepsis and 66 (39.75%) were of late onset sepsis (Table 1). The most common presentation was poor feeding, lethargy and respiratory distress (Table 2). 29.78% hospital born neonates had sepsis and among them 70.2% were resistant to Ampicillin / Gentamycin, while 82.53% home born neonates has sepsis and among them 42.42% were resistant to Ampicillin / Gentamycin (Table 3). History of Premature rupture of membrane was present in 24.69% (Table I). Blood Culture was positive in 47 (28.31%) neonates. Klebsiella pneumoniae was the most common organism isolated from blood 38.29% cases followed by E. coli 23.40% and Staphylococcus aureus in 17.02% cases (Table 4). Antibiotic sensitivity is summarized in Table 5.

DISCUSSION

This study was done in 116 neonates with suspected neonatal sepsis, among them 60.24% were < 7 days old (Early onset

	Number	Percentage %
Age		
< 7 days	100	60.24
>7 days	66	39.75
Sex		
Male	91	54.8
Female	75	45.2
Sepsis Onset		
Early onset neonatal sepsis	100	60.24
Late onset sepsis	66	39.75
Antenatal Status		
Antenatal Checkup	46	27.7
No antenatal Checkup	120	72.28
Socioeconomic Status		
Good	21	12.65
Low	145	87.34
Weight		
>2.5 Kg	47	28.31
1.5 - 2.5 Kg	84	50.60
1 - 1.49 Kg	35	21.08
< 1 Kg	0	0
PROM	41	24.69
Mean age: 17.3±7 days, Male to Female ratio: 1.2:1		

Table-1: General status (n=166)

Features	Number	Percentage%
Poor Feeding	146	87.95
Lethargy	130	78.31
Respiratory distress	111	66.86
Jaundice	19	11.44
Fever	37	22.28
Vomiting	27	16.26
Apnea	07	4.21
Hypothermia	11	6.62
Convulsions	24	14.45

Table-2: Clinical features

Birth Place	Number (%)	Positive Blood Culture (n=47)	Birth weight	Mode of delivery	Bacterial sensitivity to ampicillin/gentamycin
Hospital Born	29 (17.46)	14 (29.78%)	>2.5 Kg=18 (62.06%) 1.5-2.5Kg=10(34.48%) 1-1.49 Kg=1(3.44%)	C/Section=19 (65.51%) Spontaneous=10 (34.49%)	Sensitive = 3 (21.14%) Resistant= 11 (78.57%
Home Born	137(82.53)	33 (70.2%)	>2.5 Kg=28(20.43%) 1.5-2.6 Kg=74(54.01%) 1-1.49 Kg=35(25.54%)	C/Section= 0 Spontaneous=137(100%)	Sensitive = 19 (59.37%) Resistant= 14(42.42%)

Table-3: Comparison between hospital versus home born neonates with sepsis (n=166)

Pathogen	Number	Percentage%
Blood Culture Positive	47	28.31
Blood Culture Negative	119	71.68
Klebsiella Pneumoniae	18	38.29
E.coli	11	23.40
Staphylococcus aureus	8	17.02
Pseudomonas	3	6.38
Proteus	2	4.25
Listeria	1	2.12
Streptococcal viridians	2	4.25
Streptococcal pneumonia	2	4.25

Table-4: Frequency of pathogens isolated from blood (n=47)

	Amp	Gent	Amk	Cefta	Vanc	Mero	Ceftria	Cipro	Cefur
E.coli(11)	R	S	S	S	S	S	S	S	S
Listeria(1)	S	S	S	S	S	I	I	S	S
Klebsiella sp(18)	R	S	S	S	S	-	S	S	R
Staph aureus(8)	S	R	R	R	S	S	I	I	S
Streptococcal viridians (2)	S	R	R	R	S	S	S	I	S
Streptococcal pneumonia (2)	S	S	R	R	R	S	I	S	S
Pseudomonas (3)	R	R	S	S	S	S	R	S	R
Proteus sp (2)	R	S	S	S	S	S	S	S	S

Amp-Ampicillin, Gent-Gentamycin, Amk-Amikacin, cefta-cefotaxime, Vanc-Vancomycin, Mero-Meronium, ceftria -ceftriaxcin, cipro-cipraftoxcin, cefur-cefurcxim R= Resistant, S=Sensitive, I=Intermediate

Table-5: Frequency of antimicrobial sensitivity patterns (n=47)

neonatal sepsis), while 39.75% were > 7 days old (Late onset sepsis). In our study male neonates were 54.8% and female neonates were 45.2%. Weight of the neonates at the time of admission was <2.5 Kg in 71.68% and >2.5Kg 28.31% cases. In an unsimilar study Late Onset Sepsis was present in 139 (78.53%) neonates and 38 (21.46%) had early onset sepsis (EOS)[11], while in a similar study among the 140 cases of culture proven sepsis, 86 (61.4%) presented as early onset sepsis and 54 (38.6%)as late onset sepsis.[13] Regarding sex of neonates with neonatal sepsis, a similar study had 309 (70.2%) males and 131 (29.8%) were females. Mean age of patients was 8.93±8.70 days.[14] In our study 27.7% mothers had the history of antenatal checkup, while 72.28% mothers had no antenatal checkup. 12.65% women belonged to good socioeconomic background and 87.34% belonged to low socioeconomic families. In present study 87.95% neonates presented with poor feeding, 78.31% with lethargy, 66.86% with fast breathing, 11.44% with Jaundice, 22.28% with fever, 16.26 with Vomiting, 4.21% with Apnea, 6.62% with Hypothermia and 14.45% neonates with Convulsions. In an unsimilar study the most common clinical signs of neonate were: hyperthermia, somnolence and hypotonia.[16] About 24.69% mothers had the history of prolonged rupture of membrane, 17.46% neonates born at Hospital and 82.53% born at home. Our data is consistent with a similar study in which, 95 (47.0%) were inborn and 107 (53.0%) out born, with M: F ratio of 1.3:119. In current study out of 116 neonates, Blood Culture was positive in 47 (28.31%) neonates. Klebsiella Pneumoniae was the most frequent pathogen 38.29%, E coli was present in 23.40% neonates, Staphylococcus aureus in 17.02%, Pseudomonas in 6.38%, Proteus in4.25%, Listeria in 2.12%, Streptococcus viridians in 4.25% and Streptococcal pneumonia in 4.25% neonates. Our results were different to a study which showed, Staphylococcus epidermidis the most frequent agent (37.9%), followed by Staphylococcus aureus (12.9%).[11] In another unsimilar study, Escherichia coli (44.3%) was the commonest organism followed by Staphylococcus aureus (26.3%), Klebsiella (18.6%) and Pseudomonas (12.1%). Most of the organisms were resistant to Ampicillin.[13] In another study the predominant isolated strain was Gram positive Streptococcus, which accounted for 60% (50/84) of cases.[15] In another different study, Eighty-five (10.29%) neonates showed positive results and Coagulase-negative

Staphylococci were the predominant organism (41.18%).[17] The similar results were from a different study showing Coagulase-negative Staphylococci (CONS), Staphylococcus aureus and Klebsiella pneumoniae the most common pathogens.[18] These unsimilar studies signify the presence of different organisms in different areas. Results of a similar study showed Klebsiella pneumonia in 25%, Enterobacter in 12.5%, Group B Streptococcus in 12.5% neonates.[12] In another study from Pakistan, E coli was the dominant pathogen seen in 811 (52.8%), Staphylococcus aureus in 300 (19.5%), Pseudomonas in 199 (13%), Klebsiella in 102 (6.7%), Proteus in 87 (5.7%), Staphylococcus epidermidis in 28(1.8%) and Salmonella in 7 (0.5%) neonates.[20] In present study Klebsiella (most common pathogen) was sensitive to commonly used antibiotics like Amikacin, Gentamycin, Cefotaxime and Ciprofloxacin while it was resistant to Ampicillin and Cefuroxime. E Coli was also sensitive to commonly used antibiotics like Amikacin, Gentamycin Ciprofloxacin and Cefuroxime, while it was resistant to Ampicillin. Staphylococcus aureus was sensitive to Ampicillin and Cefuroxime, while it was resistant to Amikacin and Gentamycin. Listeria was sensitive to all commonly used drugs like Ampicillin, Amikacin, Gentamycin and Ciprofloxacin. In another study, Gram positive organisms were mostly sensitive to Vancomycin, Imepenem, Cefotaxime, Amikacin and Amoxicillin, while gram negative organisms were mostly sensitive to Amikacin and Imepenem.[14] In some other study the most common isolate was Staphylococcus aureus (52%). All the isolates except Staphylococcus aureus were susceptible to ampicillin.[19] In current study neonates born at hospital versus home had blood culture positive among birth weight > 2. 5 Kg Blood in 18 (62.06%) versus 28 (20.43%) neonates, among birth weight ranging from 1.5 to 2.5 Kg it was positive in 10 (34.48%) versus 74 (54.01%), while it was positive in 1 (3.44%) versus 35 (25.54%) neonates having birth weight between 1 to 1.4 kg respectively. A different study from Pakistan showed more positive blood cultures (58.3%) in low birth weight neonates, this difference may be due to their inclusion criteria that all neonates in their study were hospital born so increasing the risk of infection[20], while a similar study from Indonesia showed 62.6% positive blood Cultures in normal weight neonates.[24] Hospital born Neonates who were born by Cesarean Section had 38 (64.4%) positive blood cultures, while it was positive in 64 (23.4%) neonates born at home by Spontaneous vaginal delivery. The neonates who were born at hospital were sensitive to first line antibiotics (Ampicillin and gentamicin) in 07 (24.1%) cases while it was sensitive in 39 (59.3%) cases born at home. In an unsimilar study bacterial sensitivity to gentamycin was high (50%) to all organism, showing the difference in sensitivity pattern at various regions.[21] Other different studies showed 100% resistance of all organisms to Ampicillin.[22,23]

CONCLUSION

It is concluded that Klebsiella pneumonia was the most common organism for neonatal sepsis and it was sensitive to commonly used antibiotics.

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