



NEONATAL SEPSIS; COMMON BACTERIAL ISOLATES AND THEIR ANTIMICROBIAL SUSCEPTIBILITY PATTERNS IN NEONATAL INTENSIVE CARE UNIT, ISLAMABAD

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Article received on:

06/05/2017

Accepted for publication:

15/08/2017

Received after proof reading:

06/10/2017

ABSTRACT... Introduction: Neonatal sepsis is a systemic condition characterized by bacteremia that occurs in the first month of life. It is a fatal condition and need to be treated promptly. Bacterial isolates include both gram positive and negative bacteria and the cure of condition is highly dependent on antimicrobial drug sensitivity and resistant patterns. It is there for utmost important to known commonly occurring bacteria in neonatal septic states and their drug sensitivity patterns. **Objectives:** To determine the frequency of the bacterial isolates in blood and their sensitivity patterns to commonly used antibiotics in neonatal sepsis. **Setting:** Neonatal intensive care unit(NICU), Department of Shifa International Hospital. (SIH), Islamabad. **Study Design:** Cross sectional. **Duration:** This study was conducted between 6^{1st} June 2013 to 30th November 2013. **Subject and Methods:** A total of 180 neonates, admitted in NICU with evidence of clinical sepsis i.e. with signs and symptoms suggestive of septicemia (fever, lethargy, reluctance to feed, seizures, and irritability) were included in this study. The samples for blood cultures were taken. Identification of bacterial isolates was carried out by the standard bacteriological techniques, which include gram staining and bacterial cultures and antimicrobial sensitivity patterns which was performed by modified Kirby and Bauer disc diffuse method as per CLSI (Clinical and Laboratory StandardsInstitute)guidelines.A predesigned Performa was filled. **Results:** Culture revealed bacterial growth in 7.2% samples. Gram negative organisms were observed in 6.67% and only 1 were gram positive. In this study, 50% and 100% of E-coli were sensitive to ampicillin, meropenem and amikacin, gentamycin respectively. Sixty to 100% of pseudomonas was sensitive to ceftazidime, tazobactam, meropenem and 100% of enterococcus was sensitive to ampicillin and vancomycin. **Conclusion:** Antimicrobial drug resistance and constantly changing resistance patterns is emerging issues in various groups of infections and septic states, especially for routinely used antibiotics as found in our study. Thus by prescribing rational use of antimicrobial as per bactriogram, It'll be easier totreat sepsis effectively and economically and reduce the mortality and morbidity related to neonatal sepsis.

Key words: Neonatal Sepsis, Blood Culture, Gram Positive and Negative Organisms, Sensitivity Pattern.

Article Citation: Abbasi NB, Jabeen N, Khatoon S. Neonatal sepsis; common bacterial isolates and their antimicrobial susceptibility patterns in neonatal Intensive Care Unit, Islamabad. Professional Med J 2017;24(10):1455-1460.

DOI:10.17957/TPMJ/17.3914

INTRODUCTION

Septicemia is a systemic condition characterized by bacteremia and when it affects neonates in first month of life is called as neonatal sepsis. It is fatal condition and need to be treated by means of sensitive and effective antimicrobial agents. Clinical signs and symptoms of neonatal sepsis include fever, lethargy, reluctance to feed, seizures, tachypnea, tachycardia etc.¹ It is mainly divided in to two groups depending on time period and peri partum pathogenesis. Early onset sepsis that occurs at any time from birth to 7th days of

lifeand late onset sepsis that occurs from day 7th till one month of life. In developed countries the incidence of the neonatal sepsis is much less i-e 1-4 per 1000 live births because a septic deliveries and improved neonatal care² while it'sthe leading cause of mortality and morbidity in the developing countries.³ The neonatal mortality rate ofPakistan is 49/1000 live births.⁴

In neonatalsepsisthecommonestbacterialisolates are gram positive bacterial agents in developed countries² and according to a study conducted at

a tertiary care hospital of Australia, staphylococcal sepsis is the most common bacterial isolate among gram positive bacteria.⁵ Similarly, group B Streptococcus is considered as one of the most common pathogens in the early onset sepsis⁶ but is relatively uncommon in countries like Pakistan.⁷ One of the studies conducted in Bhavnagar, India reported that the commonest isolate in neonatal sepsis was Klebsiella and E. coli. Similarly antimicrobial susceptibility pattern of bacteria also varies in developed and under develop countries.⁸ According to an study conducted at Sheikh Zaid hospital, Lahore on 150 cases of suspected neonatal sepsis, it was found that the most common organisms detected were gram negative bacteria (86%), which include E.coli (20%), Klebsiella (13%). Only 14% were gram positive and out of which staph aureus was only 8%. Most of these organisms were resistant to ampicillin, gentamycin and cefotaxime.⁹ Only 10% and 26% of E.coli was sensitive to ampicillin and gentamycin respectively. Sensitivity of Klebsiella and Staph aureus to gentamycin was 23% and 25% to respectively. Sensitivity of Amikacin was 57% for E.coli, 61% for Klebsiella and 50% for Staph aureus.⁹ The rationale of my study is to find out the most common pathogens responsible for neonatal sepsis and their antimicrobial sensitivity patterns to various antibiotics. Knowing bacteriogram will limit the unnecessary use of the antibiotics and the emergence of multidrug resistant organisms. It will also be helpful to review the commonly used empirical treatment regimens, judicious use of antibiotics and their cost effectiveness. This can reduce the overall mortality and morbidity related to neonatal sepsis.

Study Design

This is a Cross sectional, observational study

Study Settings

Conducted at Shifa International Hospital, NICU Islamabad

Duration of Study

Comprised of 6 months study starting from 1st June, 2013 to 3rd November, 2013

Sample Size

By using WHO sample size calculator, the sample size is collected, the values taken as Confidence level 95%, anticipated population proportion 8%¹² and absolute precision required is 4%. With these values sample size calculated was 180 patients.

Sample Technique

The technique used was, Consecutive, Nonprobability

Inclusion Criteria

Study population included neonates aged 0-1 month, admitted in NICU with clinical suspicion of septicemia. (fever, lethargy, reluctance to feed, seizures, irritability etc)

Exclusion Criteria

All the neonates with congenital anomalies like dysmorphism, congenital heart disease, renal and Gastrointestinal abnormalities were excluded from study

Neonates already received antibiotics prior to admission were also excluded from study.

Data Collection Procedure

This study was conducted in SIH, NICU, Islamabad. Neonates fulfilling the above mentioned criteria were included in this study. The blood cultures were taken and sent in culture bottles to the department of Microbiology. Becton Dickinson cultures bottles was inoculated with specimen and incubated in Bactec 9240 Blood culture system. Identification of isolates was carried out by the standard bacteriological techniques, which include gram stain and culture sensitivity, which was performed by modified Kirby and Bauer disc diffuse methods according to per guidelines. Inhibition zone sizes were interpreted as per CLSI guidelines. Culture report was reported by the Department of Microbiology within 5 days. A predesigned Performa was filled by the researcher itself.

Data Analysis Procedure

The statistical analysis was performed using SPSS 16. Frequency and percentages were calculated for categorical values like gender,

blood isolates and their sensitivity patterns. Mean and Standard deviation were calculated for the quantitative variables like age. Chi-square test was applied and p value less than 0.05 considered as significant.

RESULTS

A total of 180 neonates, admitted in NICU with evidence of clinical sepsis were included in this study. There were 121(67.22%) were male and 59(32.78%) were female as shown in Figure-1.

Out of 180 suspected sepsis, culture growth was observed in 13(7.2%) neonate and culture bacteria growth was not observed in 167(92.7%) neonates as in figure 2. Gram negative organisms were observed in 6.67% (12/180), which include 2(1.1%) acinetobacter, 2(1.1%) e.coli, 5(2.8%) klebsiella and 3(1.6%) pseudomonas. Only 1 were gram positive that is enterococcus as presented in Figure-2 and Table-I. These organisms with respect to age of neonate were presented in Table-II.

In this study, 50% of Acinetobacter was sensitive to amikacin, gentamycin and meropenem. 50% and 100% of E-coli were sensitive to ampicillin, meropenem and amikacin, gentamycin respectively. Twenty percent of klebsiella was sensitive to meropenem and tazobactam. Sixty to 100% of pseudomonas was sensitive to ceftazidime, tazobactam, meropenem while 33.3% of pseudomonas was sensitive to amikacin and gentamycin. 100% of enterococcus was sensitive to ampicillin and vancomycin.

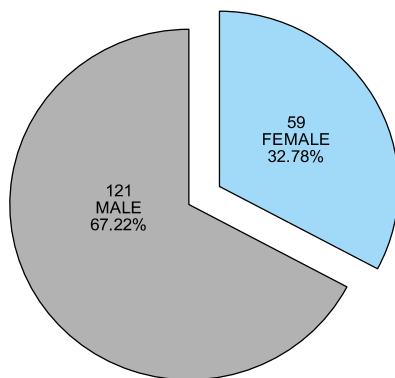


Figure-1. Sex distribution of the children (n=180)

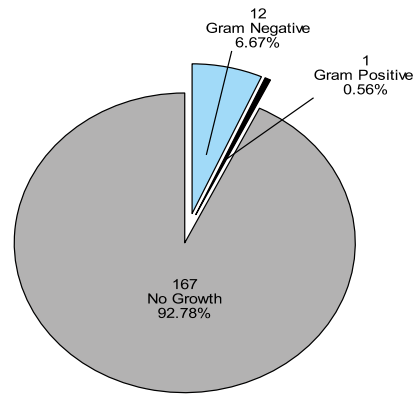


Figure-2. Micro organisms isolated (n=180)

Organisms	organisms	Frequency	Percentage
Acinetobacter	Negative	2	1.1%
E.coli	Negative	2	1.1%
Klebsiella	Negative	5	2.8%
Pseudomonas	Negative	3	1.6%
Enterococcus	Positive	1	0.56%
No Growth		167	92.8%

Table-I. Frequency of the bacterial isolates in blood (n=180)

Organisms	Age Groups	
	1 to 15 days	16 to 30 days
Acinetobacter	2(1.3%)	0(0%)
E.coli	2(1.3%)	0(0%)
Klebsiella	3(2%)	2(6.9%)
Pseudomonas	3(2%)	0(0%)
Enterococcus	1(1.3%)	0(0%)
No Growth	140(92.7%)	27(93.1%)

Table-II. Distribution of bacterial isolates according to age of neonates
Chi-Square= 3.64 p=0.601

DISCUSSION

Neonatal sepsis is a common health problem especially in developed countries. Poor socio economic factors, illiteracy, lack of health education, poor maternal health, poor compliance to antenatal visits and non-professional handling of deliveries all these factors are directly or indirectly related to increased rate of neonatal infection rate. According to a consensus 75-90% of Spontaneous Vaginal deliveries are being carried out homes by a relatively untrained birth attendant in developed countries.¹⁰

Sensitivity Pattern	Acinetobacter n=2	E.coli n=2	Klebsiella n=5	Pseudomonas n=3	Enterococcus n=1
Ampicillin	0(0%)	1(50%)	0(0%)	0(0%)	1(100%)
Amikacin	1(50%)	2(100%)	0(0%)	1(33.3%)	0(0%)
Gentamycin	1(50%)	2(100%)	0(0%)	1(33.3%)	0(0%)
Cefotaxime	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Ceftazidime	0(0%)	0(0%)	0(0%)	2(66.6%)	0(0%)
Cloxacillin	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
Meropenem	1(50%)	1(50%)	1(20%)	3(100%)	0(0%)
Tazobactam	0(0%)	0(0%)	1(20%)	2(66.6%)	0(0%)
Vancomycin	0(0%)	0(0%)	0(0%)	0(0%)	1(100%)

Table-III. Frequency of the bacterial isolates in blood and their sensitivity to commonly used antimicrobials

In developed countries situations much better due to relatively better socioeconomic factors, education and health awareness status, properly trained health attendants (Obstetrician and pediatrician), a septic handling and better neonatal health. Factors which contribute to neonatal sepsis include premature deliveries, premature rupture of membranes, septic handling of delivery, frequent manipulation of the baby with un hygienic means etc. As per data from India 50-60% of neonatal sepsis occur in premature babies and low birth weight.¹¹ These scenarios are changing with progressive improvement in health care facilities, provision of more potent broad spectrum antibiotics and improved knowledge about microorganisms susceptibility patterns, that's why in developed countries the rates of perinatal infection has declined from 50-60% that was twenty years ago to 20-30%.¹²

The commonest gram negative organisms involved in neonatal sepsis are Klebsiella, E coli, pseudomonas and salmonella while the commonest gram positive organisms isolated are staphylococcus aureus, coagulase negative staphylococci (CONS), pneumococcus and streptococcus pyogenes. Drug sensitivity patterns shows that 5-50% staphylococcus including coagulase negative & streptococcus have developed resistance against third generation cephalosporin.^{13,14}

In our study gram negative organism was observed in 6.67% (12/180), which include 2(1.1%) acinetobacter, 2(1.1%) E.coli, 5(2.8%) klebsiella and 3 (1.6%) pseudomonas. Only 1

were gram positive that is enterococcus. An observational study conducted at Sheikh Zayed hospital, Lahore reported that out of 150 cases of suspected sepsis, most common were gram negative (86%), which include E.coli (20%), Klebsiella (13%). Only 14% were gram positive and out of which staphy aureus is only 8%. Most of the organisms were resistant to ampicillin, gentacin and cefotaxime.⁹

The frequency of bacterial isolates in Khan et al study was as¹⁵, Escherichia coli in 36(40.91%) cases, Klebsiella spp. in 17(19.32%) cases, Staphylococcus aureus in 14(15.91%) cases, Pseudomonas aeruginosa in 12(13.63%) cases and Staphylococcus epidermidis in 9(10.23%) cases.

In our study, 50% of Acinetobacter was sensitive to amikacin, gentamycin and meropenem. 50% and 100% of E-coli were sensitive to ampicillin, meropenem and amikacin, gentamycin respectively. Twenty percent of klebsiella was sensitive to meropenem and tazobactam. Sixty to 100% of pseudomonas was sensitive to ceftazidime, tazobactam, meropenem while 33.3% of pseudomonas was sensitive to amikacin and gentamycin. 100% of enterococcus was sensitive to ampicillin and vancomycin. In Ahmad et al study only 10% and 26% of E.coli was sensitive to ampicillin and gentamycin respectively. Similarly isolated Klebsiella was 23% sensitive to gentamycin, while sensitivity of Staph aureus was 25% to gentamycin. Amikacin sensitivity was 57%, 61% and 50% for E. coli, Klebsiella and Staph aureus respectively.⁹

Antimicrobial sensitivity patterns are given in Waheed et al study.¹⁶ according to that study cefotaxime was the most effective drug and covers most of bacterias as; 80% to Klebsiella, 70% staphylococcus aureus and 65% Escherichia coli. Ceftazidime showed similar effectiveness. 80% klebsilla was sensitive to Amikacin but it was less sensitive for other organisms. No encouraging or impressiveresults were shown for ciprofloxacin sensitivity. In another study i-e Anwar et al¹⁷ amikacin was found as the most effective antibacterial agent and it had 90-100% effectiveness, cefotaxime was the second most effective agent with sensitivity of 84-89% and sensitivity to Ampicillin was less than 20%. An other study Ellabib et al revealed that the most common bacterial isolate in neonatal sepsis was Enterobacteriaceae, (Serratia, Klebsiella and Enterobacter spp.) others were staphylococci both coagulase negative and positive. Antimicrobial sensitivity patterns showed imipenem, ciprofloxacin and piperacillin/tazobactam as effective agents while almost all the staphylococci were sensitive to vancomycin.¹⁸

One of study from Bangladeshi showed that the most common bacterial isolate in neonatal sepsis was Ecoli (30%) while in Indian study the most common isolate was klebsiella (55%).¹² Antimicrobial sensitive patterns for those bacteria was imipenem, ciprofloxacin, gentamycin and cotrimoxazole. Imipenem was relatively costly medicine and inadequate safety data was present for ciprofloxacin. Because of frequent and sometimes irrational use of antibiotics, bacterias are showing resistance patterns to previously sensitive antibiotics. These patterns are different in different places and its constantly changing.¹⁹ it is there for necessary to identify common bacterial isolates and their common sensitivity patterns so that judicious use of antibiotics can be ensured to attain maximum response rate and thus cure of infection.

CONCLUSION

A gram negative organism was observed the most common pathogens locally and its sensitivity, limit the unnecessary use of the antibiotics and the emergence of multidrug resistant organisms.

Drug resistance is an import hindrance in infections management especially for routinely used antibiotics as found in our study. By knowing the common bacterial isolates and their drug sensitivity patterns it would be possible to cure neonatal sepsismore effectively.

Recommendations

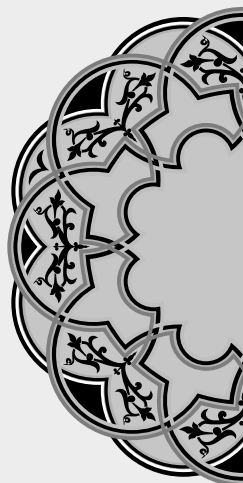
Every Hospital should arrange studies to find bacteriogram to determine common bacterial isolates in their locality and their Antimicrobial sensitivity patterns in order to designed better and effective empirical treatment (Antimicrobial) regimens, avoid unnecessary use of antibiotics and emergence of drug resistance. In this way sepsis related mortality and mortality can be reduced and treatment can be made relatively cost effective.

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“Don't hate what you don't understand.”

Unknown

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
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2	Nighat Jabeen	Concept, and data analysis	
3	Shafat Khatoon	Intellectual concept, Study design, Analysis, Discussion	