CAUSATIVE ORGANISMS AND THEIR SENSITIVITY PATTERN IN NEONATAL SEPSIS

Jahanzeb Khan Afridi, Salman Mastan, Rahida Karim, Ahmad Saud Dar

ABSTRACT

Introduction: Neonatal sepsis is a serious disease, with high rate of morbidity and mortality in developing countries. The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region. Therefore continued surveillance is mandatory to identify the organisms involved in neonatal sepsis and to select an appropriate empirical therapy according to sensitivity patterns, to reduce neonatal mortality and morbidity.

Objectives: The objectives of my study were to:

1. Identify the micro-organisms causing neonatal sepsis in a tertiary care hospital.

2. Determine the drug sensitivity pattern of the micro-organisms causing neonatal sepsis.

Study Design: It was a descriptive study.

Duration: The duration of the study was one year from 1st of September 2013 to 31st of August 2014.

Setting: The study was carried out in the Department of Pediatrics, Post Graduate Medical Institute, Hayatabad Medical Complex, Peshawar, a tertiary health care facility.

Materials And Methods: One hundred and forty patients were collected on non-probability convenient sampling. Neonates having signs and symptoms suggestive of neonatal sepsis with positive blood, urine or cerebrospinal fluid cultures were included in the study. Cultures were taken before administration of antibiotics.

Results: Among the 140 cases of culture proven sepsis, 86 (61.4%) presented as early onset sepsis and 54 (38.6%) as late onset sepsis. Among the bacteriological isolates, gram-negative organisms were more common in neonatal sepsis (75%). Among the organisms isolated, Eschereichia coli (44.3%) were the commonest organism followed by Staphylococcus aureus (26.3%), Klebsiella (18.6%) and Pseudomonas (12.1%). Most of the organisms were resistant to Ampicillin. There was significant degree of resistance to Cefotaxime too. Eschereichia coli were mostly sensitive to Ciprofloxacin (93.5%), Cefipime (83.9%) and Amikacin (74.2%). Staphylococcus aureus were also mostly sensitive to Ciprofloxacin (81.8%), Cefipime (75.8%) and Amikacin (66.7%).

Conclusion: Eschereichia coli and Staphylococcus aureus are the most common organisms causing neonatal sepsis and there is a high degree of resistance to Ampicillin and Cefotaxime.

Key Words: Neonatal sepsis, Septicemia, Eschereichia coli, Antibiotic sensitivity, Resistance.

INTRODUCTION

Neonatal sepsis is a common cause of morbidity and mortality. The incidence of neonatal sepsis is 1-10/1000 live births in the developed countries, where as it is roughly three time more in the developing countries like Pakistan[1]. This high incidence is mainly due to poor antenatal care and lack of trained staff to conduct deliveries[2]. There is a strong association between maternal urinary tract infection (UTI), vaginal discharge, pyrexia and septic technique while performing vaginal examination during labor, and early onset neonatal sepsis (EONNS)[3, 4].

In our setup, there is lack of proper antenatal care. Inadequate antenatal visits by mothers have been shown to be highly associated with neonatal sepsis, neonatal morbidity and mortality[5]. Furthermore, the high percentage (up to 25%) of low birth weight (LBW) deliveries in our country increases the risk of development of sepsis in these neonates[6].

Because of the above mentioned risk factors, neonatal sepsis and related mortality can significantly be reduced by controlling maternal infections, maintaining asepsis during labor, avoiding unclean vaginal examination and by administering appropriate antibiotics to treat the babies who develop sepsis[7].

Clinical diagnosis of neonatal sepsis is not easy because signs and symptoms of neonatal sepsis are non-specific. There is no laboratory test which has 100%

Department of Paeds, HMC, Peshawar

Address for correspondence:
Dr. Jahanzeb Khan Afridi
Senior Registrar
Peads B Unit, HMC, Peshawar
Ph No. 0321-9090107
0346-9090107
E-mail: zarakbehram@yahoo.com

specificity and sensitivity for neonatal sepsis In spite of some rapid indicators of neonatal sepsis like C-reactive protein, absolute neutrophil counts and thrombocytopenia; isolation of the micro-organism is the "gold standard" for the diagnosis of neonatal sepsis[8,9].

The spectrum of organisms that cause neonatal sepsis changes over time and varies from region to region. Gram-negative organisms had been the most common cause of neonatal sepsis in the developed countries in 1960s[10]. But over a period of time, now gram-positive organisms are more common as a cause of neonatal sepsis in the developed countries[11]. At present, gram-negative organisms are the most common cause of neonatal sepsis in the developing countries[12,13].

As the first antibiotic became available for clinical use, the problem of bacterial antibiotic resistance emerged. Over the last two decades, micro-organisms involved in neonatal sepsis have developed resistance to multiple drugs[14]. The reasons for this resistance are indiscriminate and irrational use of antibiotics, over the counter sale of antibiotics and ineffective infection control in maternity centers[15].

In our country, the pre-existing data on both EONNS and late onset neonatal sepsis (LONNS) shows great diversity in the changing pattern of micro-organism and their sensitivity patterns[16]. Continued surveillance is mandatory to detect these changes in the spectrum and sensitivity of organisms causing neonatal sepsis, which will help in treating neonates with sepsis adequately and thus decreasing morbidity and mortality[2].

MATERIAL & METHODS

Setting: The study was carried out in the Department of Pediatrics, Post Graduate Medical Institute, Hayatabad Medical Complex, Peshawar.

Hayatabad Medical Complex is approximately 600 bedded, tertiary care health facility, located in the posh locality of Hayatabad Township. The latter is an area where people of high income group and belonging to various districts of the province are residing. A good number of Afghan families also live here.

Pediatric unit of Hayatabad Medical Complex has a daily OPD of around 200 children including neonates. Afghan children make almost half of the outpatient attendance.

DURATION:

The duration of the study was one year from 1st of September 2008 to 31st of august 2009.

SAMPLE SIZE

Minimum of 140 neonates with neonatal sepsis, confirmed by blood, urine or CSF cultures were collected. Sample size was calculated using WHO sample size calculator where, Confidence level= 95%

Anticipated population proportion (p) = 0.1

Absolute precision (d) =0.05

Formula $n= z^2 p (1-p)/ d^2$

SAMPLE TECHNIQUE

Sample technique was Convenience (Non-probability).

STUDY DESIGN Descriptive study.

DATA COLLECTION PROCEDURE

Neonate with signs and symptoms suggestive of neonatal sepsis, from all incoming sources to nursery like out patient department, emergency, labor room and referred from private clinics, were admitted in the newborn nursery of Hayatabad Medical Complex, Peshawar. Permission was taken from local hospital ethical committee prior to initiation of study. An informed written consent was taken from the attendants of the patient and they were told that the data of the patient was to be used for research and publication keeping his/her identity confidential. A thorough history and physical examination was performed. Blood was sent to the laboratory for cultures and sensitivity under aseptic conditions. Blood was placed in Brain Heart Infusion media and was incubated with in 30 minutes. Subcultures were plated daily up to 7 days on Blood Chocolate agar and Mc-Conkey agar. Pure colonies were identified by Gram stain and biochemical tests. Sensitivity of the bacterial isolates to different antibiotics was determined using Standard Disc Diffusion method. The patients were started on antibiotics empirically after sending the blood and urine for cultures and sensitivity. Regarding CSF routine examination and culture, it was done only if indicated (excessive irritability, seizures, bulging fontenalle etc). Other investigations including total leukocyte count, differential leukocyte count, hemoglobin levels, platelet count, CXR, urinalysis, serum electrolytes, renal function test, random blood sugar etc were done as required.

DATA ANALYSIS PROCEDURE

The data was analyzed on computer using SPSS version 14 .Variables of the study will include age, gender, gestational age .Mean+/-standard deviation was calculated for measurable/continuous/ quantitative variables (for example age, gestational age etc) .Frequency/percentage was calculated for qualitative variables (for example gender, blood culture, urine culture, CSF culture etc). The sensitivity of different drugs to micro-organisms was presented as percentage.

RESULTS

Among the clinically suspected cases of neonatal sepsis, 140 had a positive culture. EONNS was present

Table 1: Distribution of bacteria isolated, on the basis of gram staining

Bacteria isolated from cultures	Number of Patients (n=140)	Percentage
Gram-positive bacteria	35	25%
Gram-negative bacteria	105	75%

Table 2: Distribution of Micro-organisms involved in neonatal sepsis

Micro-organism	Number of Patients (n=140)	Percentage
Eschereichia coli	62	44.3%
Staphylococcus aureus	33	23.6%
Klebsiella	26	18.6%
Pseudomonas	17	12.1%
Streptococcus pneumoniae	2	1.4%

Table 3: Distribution of Micro-organism according to onset of sepsis

Micro-organism	Early onset sepsis (n=86)	Late onset sepsis (n=54)
Eschereichia coli	36 (41.9%)	26 (48.2%)
Staphylococcus aureus	21 (24.4%)	12 (22.2%)
Klebsiella	20 (23.2%)	6 (11.1%)
Pseudomonas	9 (10.5%)	8 (14.8%)
Streptococcus pneumoniae	0 (0%)	2 (3.7%)

Table 4: Sensitivity pattern of Eschereichia coli

Antibiotic	Eschereichia coli (n=62)			
	Sensitive		Resistant	
	No. of patients	Percentage	No. of patients	Percentage
Ampicillin	3	4.8%	59	95.2%
Amikacin	46	74.2%	16	25.8%
Cefotaxime	23	37.1%	39	62.9%
Ceftazidime	39	62.9%	23	37.1%
Cefipime	52	83.9%	10	16.1%
Ciprofloxacin	58	93.5%	4	6.5%

Table 5: Sensitivity pattern of Staphylococcus aureus

Antibiotic	Staphylococcus aureus (n=33)			
	Sensitive		Resistant	
	No. of patients	Percentage	No. of patients	Percentage
Ampicillin	3	9%	30	91%
Amikacin	22	66.7%	11	33.3%
Cefotaxime	15	45.5%	18	54.5%
Ceftazidime	20	60.6%	13	39.4%
Cefipime	25	75.8%	8	24.2%
Ciprofloxacin	27	81.8%	6	18.2%

Table 6: Sensitivity pattern of Klebsiella

Antibiotic	Klebsiella (n=26)			
	Sensitive		Resistant	
	No. of patients	Percentage	No. of patients	Percentage
Ampicillin	4	15.4%	22	84.6%
Amikacin	20	76.9%	6	23.1%
Cefotaxime	12	46.2%	14	53.8%
Ceftazidime	17	65.4%	9	34.6%
Cefipime	14	53.8%	12	46.2%
Ciprofloxacin	22	84.6%	4	15.4%

Table 7: Sensitivity pattern of Pseudomonas

Antibiotic	Pseudomonas (n=17)			
	Sensitive		Resistant	
	No. of patients	Percentage	No. of patients	Percentage
Ampicillin	2	11.8%	15	88.2%
Amikacin	14	82.4%	3	17.6%
Cefotaxime	10	58.8%	7	41.2%
Ceftazidime	10	58.8%	7	41.2%
Cefipime	8	47%	9	53%
Ciprofloxacin	9	53%	8	47%

Table 8: Sensitivity pattern of Streptococcus pneumoniae

Antibiotic	Streptococcus pneumoniae (n=2)			
	Sensitive		Resistant	
	No. of patients	Percentage	No. of patients	Percentage
Ampicillin	0	0%	2	100%
Amikacin	1	50%	1	50%
Cefotaxime	2	100%	0	0%
Ceftazidime	2	100%	0	0%
Cefipime	2	100%	0	0%
Ciprofloxacin	1	50%	1	50%

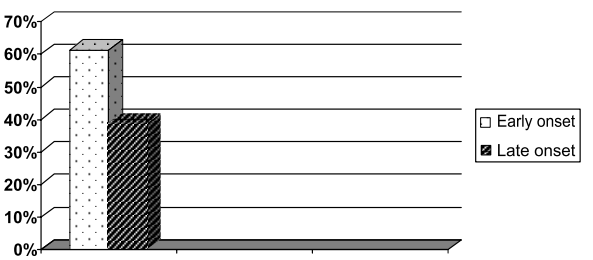

Figure1: Percentage distribution of onset of sepsis

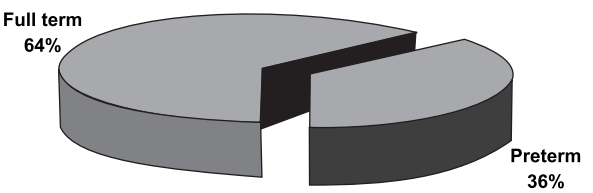

Figure 2: Percentage distribution of Gestational age of babies with sepsis.

in 86 babies (61.4%) and LONNS was present in 54 babies (38.6%) [Figure 1]. Male to female ratio was 1.5: 1. The minimum and maximum age at the time of presentation of babies with sepsis was 1 day and 28 days respectively, with a mean age of 7.42.

Regarding the gestational age of the neonates having sepsis, 89 (63.6%) babies were full-term. On the other hand, 51 (36.4%) babies were preterm [Figure 2]. 83(59.3%) babies with sepsis had blood culture positive while 57(40.7%) babies had urine culture positive. In this study, no baby with sepsis had positive CSF culture.

Of the 140 positive cultures, 105(75%) were gram-negative micro-organisms and only 35(25%) were gram-positive micro-organisms [Table 1]. Among the gram-negative micro-organisms, Eschereichia coli was the most common pathogen followed by Klebsiella and

Pseudomonas. Eschereichia coli was found in 44.3% of the total cases while Klebsiella was found in 18.6% and Pseudomonas in 12.1%. Among the gram-positive organisms, Staphylococcus aureus was the most common bacteria followed by Streptococcus pneumoniae. Out of 140, 33 patients (23.6%) had cultures positive for Staphylococcus aureus while only 2 patients (1.4%) had cultures positive for Streptococcus pneumoniae [Table 2].

In EONNS, the most common organism isolated was Eschereichia coli (41.9%) followed by staphylococcus aureus (24.4%), Klebsiella (23.2%) and pseudomonas (10.5%). No streptococcus pneumoniae was found in EONNS. In LONNS, again Eschereichia coli (48.2%) was the most common organism followed by staphylococcus aureus (22.2%), pseudomonas (14.8%) and Klebsiella (11.1%). Streptococcus pneumoniae was found in 2 (3.7%) cases of late onset sepsis [Table 3].

Regarding the antibiotic sensitivity patterns of the bacteria isolated, Eschereichia coli was mostly sensitive to Ciprofloxacin (93.5%), Cefipime (83.9%) and Amikacin (74.2%) [Table 4]. Similarly, Staphylococcus aureus was sensitive to Ciprofloxacin (81.8%), Cefipime (75.8%) and Amikacin (66.7%) [Table 5]. Klebsiella was sensitive mostly to Ciprofloxacin (84.6%) and Amikacin (76.9%) [Table 6].Pseudomonas was sensitive particularly to Amikacin (82.4%) [Table 7]. Streptococcus pneumoniae was sensitive to Cefotaxime (100%), Ceftazidime (100%) and Cefipime (100%) [Table 10]. Most of the bacteria had developed significant resistance to Ampicillin and Cefotaxime.

DISCUSSION

Neonatal sepsis is one of the major health problems in both developing and developed countries. Neonatal septicemia is responsible for 1.5 to 2.0 million deaths per year or 4000 to 5000 deaths per day in the less developed countries of the world[17]. It is a common cause for admission to NICU. The spectrum of organisms that causes neonatal sepsis changes over time and varies from region to region. Therefore continued surveillance is mandatory to identify the organism involved in neonatal sepsis and to select an appropriate empirical therapy according to sensitivity patterns, to reduce neonatal mortality and morbidity.

In this study 140 cases of culture proven sepsis were identified. EONNS constituted 61.4%. This high frequency for EONNS is comparable with many studies conducted earlier[18, 19]. However, one study conducted in Nishtar hospital Multan showed LONNS to be more common[20]. This high proportion of EONNS in my study may be because we have scanty facilities for antenatal and natal care in our community. Moreover, education regarding antenatal care and its importance is very low in our society.

In this study, male babies were more often involved in neonatal sepsis than the females. Similar finding is present in data from previously conducted studies[21, 22]. This may be because we live in male dominant society and parents bring male neonates more often to hospitals than the females.

Preterm neonates are more vulnerable to develop sepsis as they are innately immunocompromised as a result of premature birth. Regarding the gestational age, in this study full-term babies were more commonly having sepsis than the preterm babies (63.6 vs36.4%). This finding is comparable with the studies conducted by Waheed[21] and Rushda [20]. This contrast of full-term babies being more involved in sepsis than the preterm neonates (which are at a greater risk to develop sepsis) may be because of the high mortality of preterm babies before arriving to the hospital.

Gram-negative organisms are the most common pathogens causing neonatal sepsis in developing countries. In this study, gram-negative organisms were more frequently involved in neonatal sepsis (75%). This conforms to many studies conducted in Pakistan [22] and India[23, 24]. There are very few studies in Pakistan which shows gram-positive organisms to be the main cause of neonatal sepsis[19].

In this study, Amikacin and Ceftazidime have shown reasonably good sensitivity to both gram-negative and gram-positive organisms. Previous data from Lahore[2], Peshawar[25] and Multan[20] conform to this pattern. Study from Gaza also showed Amikacin to have good sensitivity to different organisms[26].

In this study, Ciprofloxacin (a quinolone) and cefipime (a fourth generation cephalosporin) showed good sensitivity patterns to different pathogens with the exception of Pseudomonas. 93.5% of Eschereichia coli, 81.8% of Staphylococcus aureus and 84.6% of Klebsiella were sensitive to ciprofloxacin. Rushda[20] reported that 75% of Eschereichia coli and 100% of Klebsiella were sensitive to ciprofloxacin. Study from Gaza city hospitals[26] also showed reasonably good sensitivity pattern of ciprofloxacin to different drugs.

In this study, Pseudomonas showed a significant resistance to most of the drugs with the exception of Amikacin to which its sensitivity was 82.4%.

CONCLUSION

Neonatal sepsis is a life threatening emergency that demands urgent diagnosis and treatment. The organisms causing neonatal sepsis vary from time to time and from region to region. Principally, gram-negative organisms cause neonatal sepsis in our country. These organisms are highly resistant to the commonly used antibiotics including Ampicillin and Cefotaxime. The organisms have good sensitivity to Amikacin, Ciprofloxacin and Cefipime.

RECOMMENDATIONS

Neonatal sepsis is a life threatening emergency that demands urgent diagnosis and management. Any neonate, who has signs and symptoms suggestive of neonatal sepsis, should be admitted in NICU. Blood should be sent for culture and sensitivity, before starting empirical antibiotic therapy. Empirical antibiotic therapy should be such that it covers the organisms commonly involved in causing neonatal sepsis in a particular unit.

Resistance of organisms to commonly used antibiotics is increasing. Therefore, steps should be taken to address this problem promptly and quickly. These steps should include improving antenatal care and also improving infection control in maternity centers. Over the counter sale and indiscriminate use of antibiotics should be discouraged.

As the spectrum of organisms causing neonatal sepsis changes over time and varies from place to place, studies should be performed on regular basis in respective units to identify these changing spectrums of organisms, which will help in treating neonates with sepsis adequately and thus decreasing morbidity and mortality.

REFERENCES

1. Neonatology. In: Haneef SM, Maqbool S, Arif MA. Text book of paediatrics.edi.Lahore: Pak Paediatr Assoc. 2000: 165-248.
2. Waseem R, Khan M, Izhar TS, Qureshi AW. Neonatal sepsis. Professional Med J 2005; 12(4):451-6.
3. Jamal M, Khan N. Neonatal Morbidity and Mortality in high risk pregnancies. J Coll Physicians Surg Pak 2002; 12(11):657-61.
4. Bhutta ZA, Yusuf K. Early onset neonatal sepsis in Pakistan. A case control study of birth cohort. Am J Perinatology 1997; 14(a):557-81.
5. Tasnim N, Muhammad G, Arif MS. Impact of reduced prenatal visits frequency on obstetric outcome in low risk mothers. J Coll Physicians Surg Pak 2005; 15(1):26-9.
6. Butt MA, Malik BA, Sheikh S, Shamoon M. Proffesional Med J 2004; 11(4):394-9.
7. Schuchat A, Zywichi S, Dinsmoor MJ, Mereer B, Sulliran MJ. Risk factors and oppurtunities for prevention of early onset neonatal sepsis: A multi center case control study. Paediatrics 2000; 105:21-6.
8. Anwar S, Mustafa S. Rapid identification of Neonatal Sepsis. J Pak Med Assoc. 2000; 50(3):94-8.
9. Bhutta ZA. Epidemiology of Neonatal Sepsis in Pakistan. An analysis of available evidence and implication for care. J Coll Physicians Surg Pak 1996; (6):12-7.
10. Freedman RM Ingram DL, Gross I, et al. A half century of neonatal sepsis at Yale. Am J Dis Child 1981; 135:140-4.
11. Stoll BJ, Hansen N. Infections In VLBW Infants: Studies From The NICHD Neonatal Research Network. Semin Perinatol. 2003; 27: 293-301.
12. Anwer SK, Mustafa S, Pariyani S, Ashraf S, Taufiq KM. Neonatal sepsis: an etiological study. J Pak Med Assoc. 2000; 50:91-4.
13. Akhtar R, Haider A, Raza R. Neonatal sepsis in NICU: bacterial isolates and their sensitivity pattern. J Surg Pak 2005; 10(4):18-21.
14. Friedman S, Shah V, Ohlsson A, Matlow AG. Neonatal Escherichia coli infections: concern regarding resistance to current therapy. Acta Pediatr 2000; 89:686-9.
15. Haque KN. Update on management of neonatal sepsis. Proceedings of 10th National Annual Paediatrics Conference: Bhurban/Muree, Lahore: April 20-22, 2001, Pak Paediatr Assoc. 2001:19.
16. Malik MA, Hussain w, Izhar M, et al.Ten year surveillance of bacterial isolates from blood cultures of neonate. Pak Ped J 2002; 26(3):113-8.
17. Stoll BJ. The global impact of neonatal infection. Clin Perinatol 1997; 24:1–21.
18. Rasul CH, Hassan MA, Ullah MH.Neonatal sepsis and use of antibiotic in a tertiary care hospital. Pak J Med Sci 2007; 23(1): 78-81.
19. Anwer S, Mustafa S, Pariyani S, Ashraf S, Taufiq K. Neonatal sepsis: an etiological study. J Pak Med Assoc 2000; 50(3): 91-4.
20. Aftab R, Iqbal I. Bacteriological agents of neonatal sepsis in NICU at Nishtar Hospital Multan. J Coll Physicians Surg Pak 2006; 16:216-9.
21. Waheed-M, Laeeq-A, Maqbood-S. The etiology of neonatal sepsis and patterns of antibiotic resistance. J Coll Physicians Surg Pak 2003; 13(8): 449-452.
22. Batool A, Akram DS, Arif F. Changing antibiotic sensitivity of organisms causing neonatal sepsis: a hospital based study. Pak Paed J 2005; 29(2):57-61.
23. Joshi SJ, Ghole VS, Niphadkar KB. Neonatal gram negative bacteremia. Indian J Pediatr 2000; 67; 27-32.
24. Gupta A. Hospital acquired infections in the neonatal intensive care unit- Klebsiella Pneumoniae. Semin Perinatol 2002; 26: 340-5.
25. Aurangzeb B, Hameed A. Neonatal sepsis in hospital-born babies: bacterial isolates and antibiotic susceptibility patterns. J Coll Physicians Surg Pak 2003; 13:629-32.
26. El-Jadba AHE, El-Yazji MS. Neonatal Septicemia in Gaza City Hospitals. Pak J Med Sci 2009; 25(2):226-231.