

NEONATAL SEPSIS AND USE OF ANTIBIOTIC IN A TERTIARY CARE HOSPITAL

Choudhury Habibur Rasul¹, M. Abul Hassan², M. Habibullah³

ABSTRACT

Background: Neonatal infections currently cause 1.6 million deaths in developing countries. Resistance to commonly used drug is emerging as the most important problem globally. Therefore rational use of antibiotic is a priority to reduce the burden of treatment failure.

Objective: To evaluate the magnitude of neonatal infections in the neonatal ward of a medical institution and pattern of antibiotic use in these cases.

Methodology: This was a cross sectional retrospective study. All the cases of neonatal infections admitted between October 2003 to September 2005 were included in the study. Relevant informations like age, sex, birth weight, investigations, diagnosis, antibiotic use and outcome were noted in the predesigned proforma. Infection within first week of birth was regarded as the early onset infections and infections thereafter were considered as late onset infections.

Results: Eleven hundred and ninety six cases got admitted in the neonatal ward during the 24 months of study period. Three hundred and thirty four neonates with sepsis constituted 27.8% of the total cases. Majority of these cases were early onset infections (70.7%). Septicemia was the commonest (34.6%) major infections followed by pneumonia (19.5%). The dominant minor infections were umbilical sepsis (10.5%) and pyoderma (6.9%). The most frequently used antimicrobial agent was third generation cephalosporin (36.2%) and next in order was the combination of ampicillin and gentamycin (18.9%). Regarding outcome 78.1% cases recovered well. Among the rest of the cases with unsatisfactory progress, 12.3% died in the hospital.

Conclusion: Neonatal sepsis constituted nearly one third of the health problem in neonatal ward and majority of them are early onset infections. Septicemia is the most frequently encountered infections and costly third generation cephalosporin topped the list of antibiotic use.

KEY WORDS: Neonatal sepsis, Antibiotic, Rational use.

Pak J Med Sci January - March 2007 Vol. 23 No. 1 78-81

INTRODUCTION

World Health Organization estimates that globally there are about 5 million neonatal death a year. Ninety eight percent of them are occurring in developing countries in first week of life. Death rate varies in developing countries between 11-68/1000 live birth in Asia, Africa and Latin America. It is generally

assumed that neonatal mortality in developing countries is underreported by at least 20%.¹

Advances in neonatal management have considerable improvement in survival of the newborn including the low birth weight group. In both term and preterm infants, early warning signs and symptoms are often minimal, subtle, nonspecific and can be easily misinterpreted as being due to transient tachypnea of the newborn, apnea of prematurity, bronchopulmonary dysplasia and environment induced temperature fluctuation.²

The most common causes of death in neonatal period are infections (32%) including septicemia, meningitis, pneumonia, diarrhoea and neonatal tetanus followed by birth asphyxia (29%) and prematurity (24%).³ In Bangladesh infant mortality rate and neonatal mortality rate are 56 and 42 per 1000 live birth and leading cause of these death are perinatal asphyxia,

1. Dr. Choudhury Habibur Rasul,
Professor of Paediatrics
 2. Dr. M. Abul Hassan,
Assistant Professor of Paediatrics
 3. Dr. M. Habibullah,
Honorary Trainee Doctor
- 1-3: Khulna Medical College & Hospital,
Khulna-9000, Bangladesh.

Correspondence:

Dr. Choudhury Habibur Rasul
E-mail: chrasul@bttb.net.bd

* Received for Publication: March 15, 2006

* Accepted: August 25, 2006

neonatal infection and premature birth.⁴ Factors related to neonatal sepsis are suboptimal antenatal care and unhygienic home delivery. Incidence of perinatal sepsis in Bangladesh is 20-30/1000 & mortality varies from 15-25%.⁵

Children differ significantly from adults in the way they absorb, metabolize and excrete drugs. These parameter also vary from birth to adolescence. The importance of pediatric medication safety has been gaining increasing attention in the developed world in the past decades. Rational use of drugs is the first priority now.⁶ It is estimated that 25-75% of antibiotic prescription in teaching hospitals are inappropriate and half of the world's 15 billion injection are unsafe.⁷

In developing countries, use of antibiotic is mostly a guess work and mostly irrational.⁸ Since there is no universal diagnostic marker, and also because of poor investigation facilities, physicians prescribe antibiotic on clinical suspicion. Many of them are broad spectrum blanket antibiotic as the organism and sensitivity pattern are mostly unknown. So this study was done to evaluate the magnitude of neonatal infection in a medical institute & the frequency of antibiotic use in those infections.

PATIENTS AND METHODS

This was a retrospective cross sectional study in Khulna Medical College Hospital, Bangladesh between the period of October 2003 to September 2005. All the admitted patients in the neonatal ward of KMCH were noted on the basis of diagnosis. Thereafter the case histories of neonatal infection were isolated and all the relevant points were noted in predesigned proforma. The important features were age, sex, clinical diagnosis, antibiotic use and outcome of treatment.

Table-I: Disease profile in neonatal ward

Disease	Normal birth weight	Low birth weight	No. (%)
Perinatal asphyxia	236	207	443(37.1)
Neo infection	183	151	334 (27.8)
Neo jaundice	80	86	166 (13.9)
Neo convulsion	41	61	102 (8.5)
Others	81	70	151 (12.7)
Total (%)	621 (51.9)	575 (48.1)	1196 (100)

Table-II: Infections depending on onset

	Early infections	Late infections	Total (%)
Major infections	161	68	229 (68.6)
Minor infections	75	30	105 (31.4)
Total (%)	236 (70.7)	98 (29.3)	334 (100)

To avoid confusing information case files were reviewed along with the patient register book of neonatal ward. Infection in the first week was considered as early onset infection (EOS) and beyond that period was considered as late onset infection (LOS). Diagnosis was mostly clinical. Supportive findings in routine or special investigations were taken into account. Data after collection were analyzed with the help of statistical software (SPSS-10).

RESULTS

A total of 1196 patients got admitted in neonatal ward during the period of 24 months. Among them majority (37%) suffered from perinatal asphyxia and next common was neonatal infection (27.8%). Low birth weight babies constitutes 48.1% of total admitted cases (Table-I).

Among all the cases of sepsis (334); early onset infection was 70.7% and the rest was late onset infection and again highest share (68.6%) was taken by major infections (Table-II). Major infection includes septicemia, pneumonia, diarrhoea and meningitis and infections like umbilical sepsis, pyoderma, oral candidiasis and conjunctivitis were considered under minor infections. Septicemia (34.6%) was the commonest major infection (Table-III). Besides routine investigations, CSF examination was done for suspected meningitis and blood culture was done only in 4 cases of septicemia without any positivity. Pattern of antibiotic use has been shown in Table-IV. Third generation cephalosporin (cefotaxime, ceftriaxone, ceftazidime) were frequently (36.2%) used for different infections. Combination drugs like ampicillin & gentamycin was second in frequency (18.9%) of use. Drugs like pivmicellinium, nystatin and tobramycin were grouped under other drugs and used in specific infections of bloody

Table-III: Use of antibiotic in neonatal sepsis

<i>Infections</i>	<i>Total (%)</i>	<i>Clox</i>	<i>Erythr</i>	<i>Cephra</i>	<i>TGC</i>	<i>Amp+ Clox</i>	<i>Amp+Genta</i>	<i>Ampi+Ceftri</i>	<i>Others</i>
Septicemia	115 (34.6)	–	–	–	66	–	34	15	–
Pneumonia	66(19.5)	–	–	06	11	12	15	22	–
Diarrhoea	27(8.1)	–	08	–	09	–	–	–	10
Meningitis	21(6.3)	–	–	–	15	–	04	02	–
Umb sepsis	35(10.5)	–	–	14	13	–	08	–	–
Pyoderma	23(6.9)	11	08	–	–	04	–	–	–
Others	47(14.1)	–	–	03	07	–	02	–	35
Total %	334(100)	11(3.3)	16(4.8)	23(6.9)	121(36.2)	16(4.7)	63(18.9)	39(11.7)	45(13.5)

diarrhea, oral candidiasis and conjunctivitis respectively.

DISCUSSION

In the developing countries, most (75-90%) of deliveries occur at home with the help of traditional birth attendant.⁵ The situation in developed countries is quite different and almost all deliveries occur in hospital or clinic by skilled attendant with aseptic precaution. The majority of neonates with septicemia have one or more risk factors. These are premature rupture of membrane (PROM >24hours), prematurity, septic delivery, frequent manipulation of the baby. Study from Bangladesh shows 29.2% of septicemia is contributed by PROM.⁹ Reports from India showed 50-60% of septic babies are premature babies and VLBW are more vulnerable.³ In our cases 48.1% were LBW babies.

The availability of more potent broad spectrum antibiotic and changing pattern of micro-organism has changed the scenario of perinatal infection. The high incidence of perinatal infection which was 50-60% twenty years ago has come down to 20-30% in many developing countries.¹⁰ Epidemiological studies regarding incidence are not sufficient in the developing countries and the available data are mostly hospital based. In India, different studies have shown that the incidence varies from 10-20/1000 lives.^{3,11}

Clinical predictors of infection are reluctant to feed, Jaundice, lethargy, respiratory distress, fever, vomiting, apneic spell, hypothermia

etc.¹² Approximately 8.5% of infants younger than 90 days and having a temperature >38°C will have serious bacterial infections. The remaining infants are presumed to have viral infection. Therefore majority of them if confirmed to have no bacteria can be treated outside and without antibiotic.¹³

There is no consensus about timing of EOS & LOS. Early onset varies from 2-7 days.¹⁰ The bacteriological profile differs in EOS and LOS and it also differs in developing and developed countries. In developed countries gram (+)ve organism is predominant in both EOS and LOS but GBS is found more in EOS. In developing countries gram (-)ve organism are predominant in EOS & LOS but E. coli is predominant in EOS.^{5,10} Since the first 7 days was considered as early onset the EOS in our series was quite high (70.7%).

Early onset sepsis are indistinguishable from that of perinatal asphyxia and respiratory distress syndrome, on the other hand late onset sepsis is indistinguishable from metabolic acidosis and hypoglycemia. A number of screening procedures like micro ESR, C reactive protein, serum IgM, absolute neutrophil count and the relation of immature to total cell are helpful for diagnosis of neonatal sepsis.¹⁴ Most of these investigations could not be done in our cases and diagnosis was mostly clinical.

CRP, Cytokines and surface markers are promising for diagnosis but the cost and complexity of test are deterrent for suitability of its applications.¹⁴ Blood culture remains the mainstay of investigation and treatment of potential sepsis in infants despite recent advances in the molecular diagnosis of infection. Success of getting isolates depends upon suitable skin preparation, volume of blood drawn, blood culture technique and time of culture.¹⁵

Table-IV: Outcome of treatment

<i>Status</i>	<i>Male</i>	<i>Female</i>	<i>Total (%)</i>
Improved	147	114	261(78.1)
Borderline	18	14	32 (9.6)
Expired	23	18	41 (12.3)
Total (%)	188 (56.2)	146 (43.8)	334 (100)

Favorable outcome in perinatal septicemia results from prescribing correct antibiotic and at an early stage. The choice of antibiotic must be based on bacterial profile and its susceptibility pattern in the locality. In the past ampicillin-gentamycin was the primary choice of antibiotic but most of the organisms developed resistance probably because of indiscriminate use of antibiotic. Survival of VLBW babies gives rise to nosocomial infection.¹¹ So a third generation cephalosporin is the preferred drug but at times it is combined with gentamycin or ampicillin depending on the suspected organism.¹⁶ The frequent use of costly cephalosporin in this study is consistent with other observations.^{6,16}

As a whole gram negative organisms are more common such as Klebsiella, E coli, pseudomonas and salmonella and the gram positive organisms are staph aureus, coagulase negative staphylococci (CONS), pneumococcus and streptococcus pyogenes. Third generation cephalosporin was also becoming ineffective (5-50%) to staphs & streptococcus.¹⁷ Most CONS is resistant to this and vancomycin should be a choice.¹⁸ Handwashing, barrier nursing, clean delivery, exclusive breast feeding and restricted antibiotic use should be possible strategies in neonatal ward.

In a Bangladeshi study E coli was shown as the leading organism (30%) however klebsiella was the dominant organism (55%) in Indian study.^{10,11} Study report from Dhaka Shishu Hospital revealed that principal organisms are klebsiella, acinetobacter, E coli, coagulase negative staphylococci and staph aureus.⁹ Maximum sensitive drugs are imipenem, ciprofloxacin, gentamycin and cotrimoxazole. Imipenem is costly and ciprofloxacin has inadequate safety data. Bacterial isolates are becoming resistant to different generation of cephalosporin

In developed countries 10-20% of all neonates are treated for suspected sepsis but serious sepsis occurs in 1-10/1000 live birth.¹⁹ The pattern of bacterial organism are constantly changing with time and place. Previously sensitive organism are rapidly becoming resistant to commonly used antibiotic due to indiscrimi-

nate use thus making the treatment difficult and costly.²⁰

In conclusion, septicemia is the dominant infections and third generation cephalosporin is the frequently used antibiotic in neonatal ward. The uncertainty regarding the choice of antibiotic can be minimized by periodic survey of aetiological agent and their antibiotic susceptibility pattern.

REFERENCES

1. WHO. Perinatal mortality. Report No. WHO/ FRH/MSM/ 967. Geneva. WHO 1996.
2. Ng PC. Diagnostic markers of infection in neonate. Arch Dis Child Fetal Neonatal 2004;89: F229 – 35.
3. Bang AJ, Bang RA, Baitale B. Burden of morbidities and unmet need for healthcare in rural Indian neonate. Ind Pediatr 2001;38:952-65.
4. Bangladesh Demographic & Health survey. Report on Health statistics 2004.
5. Islam MN. Neonatal infections in developing countries. Workshop on improving neonatal survival in developing countries. Dhaka 2-3 Nov 2001.
6. Begg SA, Cranswick NE, Reed MD. Improving drug use for children of the developing world. Arch Dis Child 2005;90:1091-3.
7. WHO. The world Health Report 2002: Reducing the risk and promoting healthy life. Geneva. World Health Organization 2002.
8. Stoll BH. Early onset sepsis in very low birth weight neonates. J Pediatr 1996;129: 72-80.
9. Hossain MM, Afroza S, Shirin M, Chowdhury NA, Saha SK. Bacterial aetiology of neonatal sepsis in a tertiary care hospital in Bangladesh. Bang J Child Health 2004;28: 81-5.
10. Ahmed ASMNU, Chowdhury MAK, Hoque M, Damstadt GL. Clinical & Bacteriological profile of neonatal septicemia in tertiary level pediatric hospital in Bangladesh. Ind Pediatr 2002;39:1034-9.
11. Malik A, Hasani SE, Khan HM, Ahmed AJ. Nosocomial infections in newborn. Ind Pediatr 2001;38:68-71.
12. Broner CW, Polk CA, Sherman JM. Febrile infants less than 8 weeks old- Predictors of infection. Clin Pediatr 1990;29:438-43.
13. Byington CL, Enriquez R, Hoff C, Tuohy R. Serious bacterial infection in febrile infants upto 90 days old with or without viral infection. Pediatr 2004; 113: 1662-5
14. Weinschenk NP, Farina A, Bianchi DW. Premature infant's respond to early and late onset sepsis with leukocyte activation. J Pediatr 2000;137:345-50.
15. Hurst MK, Yoder BA. Detection of bacteremia in young infants. Pediatric Infect Dis J 1995;14:711-3.
16. Heath PT, Yusoff NKN, Baker CJ. Neonatal meningitis. Arch Dis Child Fetal Neonatal 2003;88:F173-8.
17. Vernango S, Sharland M, Kazembe P, Mwansambo C, Heath PT. Neonatal sepsis: An international perspective. Arch Dis Child Fetal Neonatal 2005;90:F220-4.
18. Gandy G, Reunie J. Antibiotic treatment for suspected neonatal meningitis. Arch Dis Child 1990;65:1-2.
19. Sacs D. Rationing antibiotic use in neonatal units. Arch Dis Child Fetal Neonatal 2000;82:F1-2.
20. Deman P, Verhoeven BA, Verburgh HA. An antibiotic policy to prevent emergence of resistance bacilli. Lancet 2000;355:973-8.