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Original Research Article

Predisposing factors for pneumonia in the neonatal period and acute phase reactants as a prognostic marker-a study in a tertiary care hospital of eastern India

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ABSTRACT

Background: Respiratory distress is the most common cause for NICU admission and pneumonia accounts for more than 50% of cases. There are different predisposing factors for occurrence of neonatal pneumonia. This study aimed to find out different predisposing factors leading to occurrence of pneumonia in neonates and also to study CRP and mESR as acute phase reactants to determine prognosis as these two markers are most widely used marker in clinical practice.
Methods: A total 250 neonates who presented with features of pneumonia were included in the study. All the predisposing factors were corroborated with the clinical findings of the neonates and prognosis were assessed by serial acute phase reactants assay.
Results: Most of the patients (57%) diagnosed with neonatal pneumonia have early onset neonatal sepsis. 66% of them had history of premature rupture of membrane >24 hours ($p<0.001$). The mean period of gestation is 32.9 weeks, so majority of them are preterm ($p<0.001$). 30% of them had history of birth asphyxia ($p<0.001$). The mean Downe's score comes out to be 3.74 and score >4 had worst outcome ($p<0.05$). Blood culture become positive in 36% of the cases who carried adverse prognosis ($p<0.001$). CRP ($p<0.0001$) has a definite valuable role to determine the prognosis but micro ESR ($p=0.2267$) found to be non-significant in this study.
Conclusions: Premature rupture of membrane, premature birth, birth asphyxia, Downe's score >4 and blood culture positivity found to be risk factor for pneumonia in neonates and serial CRP may be done to determine the prognosis.

INTRODUCTION

Pneumonia is a major cause of mortality in the neonatal period worldwide. So, this is an extremely important topic for scientific study among researchers. Globally, nearly 5 million children aged under 5 years died in 2016; regionally, South Asia contributed nearly a quarter (24.8%) of the global burden of under 5 mortalities with almost a million deaths occurring in India alone, the largest of any nation.[1] Throughout childhood, the greatest risk of death from pneumonia is in the neonatal period. More than 96% of all neonatal deaths occur in developing countries and pneumonia accounts for a significant proportion of these.[2] In a field trial of community based management of childhood pneumonia in India, more than half of all child deaths from pneumonia occurred among neonates.[3] About one third of neonatal mortality in India is due to infectious disease, comprising pneumonia (16%), sepsis (15%) and diarrhea (2%).[4] About 15% of term neonate and 29% of late preterm neonates admitted to the neonatal intensive care unit develop significant respiratory morbidity.[5] The causes of respiratory distress in a newborn are diverse and multisystemic. Pulmonary causes may be related to alteration during normal lung development or transition to extrauterine life. The

common causes of respiratory distress like TTN, RDS, neonatal pneumonia, MAS, PPHN etc. are results of complications during prenatal and postnatal transition period. Pneumonia is among the most common respiratory disorders in neonates. Its prevalence is more in developing countries. Pneumonia is defined as invasion of lung by an infectious agent which may start an inflammatory response and ensuring damage which may involve airways, alveoli, connective tissue, visceral pleura and vascular structures. Neonatal pneumonia can be arbitrarily classified as early and late onset. Some of the authors have used 48hrs as cut off, others have suggested 7 days.[2] The infection may occur either due to aspiration into lungs or through bloodstream. The infant may aspirate contaminated liquor in-utero if he makes gasping efforts due to foetal hypoxia or aspiration may occur during his passage through birth canal or subsequently. Pneumonia can occur during the course of septicaemia any time in the neonatal period. Neonates with life threatening non infective respiratory and cardiac problems (hyaline membrane disease, congestive heart failure) may develop superadded bacterial infection leading to pneumonia. Infants requiring endotracheal intubation and assisted ventilation are also at risk to develop secondary pneumonia. In most of the cases gram negative bacteria predominate in the first week and gram-positive bacteria predominate after that. The important risk factors may be the following: Premature rupture of membranes, i.e., more than 18 hours interval between the rupture of membranes and birth of baby, unclean vaginal examinations after the rupture of membranes, Foul smelling liquor amnii, febrile maternal illness during peripartal period, foetal hypoxia, prolonged or difficult delivery.[8] Respiratory infection in newborn may be bacterial, viral, fungal, protozoan or spirochetal in origin. Infants may acquire pneumonia trans placentally through infected amniotic fluid. Perinatal pneumonia is the most common form of pneumonia and is acquired at birth.[9] *Klebsiella*, *E. Coli*, *Enterobacter*, *Pseudomonus aeruginosa*, *Staphylococcus aureus*, and albus are common etiologic agents.[7] Group B *Streptococcus* (GBS) is the most common organism that affects term neonates.[6] Congenital pneumonia occurs when causative organism is passed trans placentally to foetus. CRP and micro ESR as a sole are not recommended as indicator of pneumonia but may be used as a part of workup or a serial study may be done which can help us to assess the response to antibiotic, duration of therapy/identify a relapse.[11]

METHODS

The study was done to find out different predisposing factors that can aggravate the outcome in neonates suffering from pneumonia and to study the prognosis in relation to acute phase reactants.

Study design

The study design was of an observational prospective single centre study.

Place of study and study period

The study conducted at SNCU and NICU of department of paediatric medicine, North Bengal medical college and hospitals, Darjeeling from May 2020 to April 2021.

Study population

All newborn with respiratory distress who is diagnosed with pneumonia on basis of radiological finding. i.e., nodular/ coarse patchy infiltrate, diffuse haziness/ granularity, air bronchogram, lobar/ segmental consolidation.

Sample size

From the records and other studies, it is found that frequency of pneumonia in hospitalised neonates (There are approximately 8000 admissions in each year in our SNCU and NICU) are about 16% to 20%. Taking a mean of 17%, confidence level as 95% and acceptable error 5%, by calculation the sample size is estimated as 212. So, sample size taken of approximately 250.

Exclusion criteria

Patients are excluded if 1. Neonates with congenital anomalies, more importantly congenital heart disease or lung anomalies. 2. Neonates with RDS. 3. Neonates with meconium aspiration syndrome. 4. Neonates who are put on mechanical ventilation. Because the course may be altered due to ventilator associated pneumonia. 5. Neonates who have acute complication of pneumonia e.g., pnumothorax, empyema, pneumatocele etc. 6. Parents not consenting for the study.

To diagnose a case of neonatal pneumonia 2 things are to be done: 1. Chest radiograph-diffuse parenchymal infiltrate or air bronchogram or lobar consolidation and 2. The sepsis work up-as it is a part of generalised sepsis.

The work up includes CBC, DC, blood and CSF culture and CSF examination. A sepsis screen should be appropriate which include:

Table 1: Lab tests.

Components	Abnormal value
TLC	Less than 5000/cmm
Absolute neutrophil count	Low count as per Monroe chart for term and Mouzinhoe's chart for pre term
Immature/ total neutrophil	≥0.2
Micro ESR	≥15 mm in 1st hour
CRP	≥1 mg/DL

Although some authors recommend to do a CSF study for only those who have culture positive sepsis because of low incidence of meningitis in a culture negative sepsis.

Blood picture may indicate sepsis in various ways like: 1. Reduced platelet count in the 1st 10 days of life, 2. Reduced WBC count; although it is non-specific and has low positive predictive value, 3. I/T neutrophil ratio is a more specific indicator, 4. C reactive protein is elevated in about 50-90% of neonates with bacterial infection. Serial CRP may be used to assess response to antibiotic and determine duration of therapy and 5. Blood culture-this is the most sensitive and specific test.

Statistical analysis

Standardized forms (case record form) are to be used to record the relevant demographic, historical, clinical, laboratory data for each neonate before uploading to a data base maintained to track the clinicopathological progress of the babies. Records kept will be confidential. MS excel and SPSS will be used where appropriate for analysis. For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. and Graph Pad Prism version 5. $p \leq 0.05$ was considered statistically significant.

RESULTS

In this study of 250 neonates the mean age (mean ± SD) of patients was 4.1440 ± 2.9486 days with range 1-14 days and the median was 3 days out of which 119 (47.6%) patients was female and 131 (52.4%) patients was male.

Table 2: Distribution of H/O PROM.

H/O PROM	Frequency	Percentage (%)
No	83	33.2
Yes	167	66.8
Total	250	100

In this study 83 (33.2%) patients had no H/O PROM and 167 (66.8%) patients had H/O PROM. P<0.001. This table shows history of premature rupture of membrane >24 hours. It shows majority of the patients i.e 66.8% had history of PROM. In all the studies regarding neonatal sepsis PROM has been identified as one of the important risk factors. Here in this case is found that majority of the patients who have pneumonia had H/O PROM.

The mean Downe's score (mean ± SD) of patients was 3.7400±2.3077 with range 0-8 and the median was 3. P<0.05%. This table shows that the mean Downe's score of the patients admitted with pneumonia. The mean value comes out to be 3.74. Downe's score >4 represents clinical respiratory distress and >7 represents impending respiratory failure. sOnly 4% of the cases have score >6.

The mean period of gestation (mean ± SD) of patients was 32.9000±2.4581 weeks with range 30-42 weeks and the median was 32 weeks. P<0.001. Here distribution of mean period of gestation showned. The mean value is 32.9 weeks with standard deviation of 2.45 weeks. It is denoting the fact that premature babies are more prone in developing pneumonia. In all the studies prematurity has been established as an important risk factor which is also reflecting in this study.

175 (70.0%) patients had cried at birth and 30% did not cried at birth. P<0.001. So, it is about another risk factor of sepsis which is birth asphyxia. It is found in this study that in all the patients admitted with pneumonia 70% cried spontaneously after birth whether the remaining 30% did not cried spontaneously and needed some resuscitative measures. It is also reflecting the fact that birth asphyxia is a risk factor for sepsis.

89 (35.6%) patients had positive blood culture on D1 (p<0.001). Incidence of blood culture becoming positive in the study cases. It shows the blood culture became positive in 35.6% of the patients within 48 hours of incubation. The other cases which are about 65% yield no growth after 48 hours of incubation. It means 65% of cases have evidence of pneumonia in X ray but no growth is there in blood culture. but those having blood culture positivity all of them found significant patches radiologically.

At day 1, the mean CRP (mean ± SD) of patients was 10.3412±6.9612 mg/L with range 3.2000-34.0000 mg/L and the median was 6.9000 mg/L. At day 3, the mean CRP (mean ± SD) of patients was 8.9248±6.4137 mg/L with range 3.2000-35.4000 mg/L and the median was 6.4000 mg/L. At day 7, the mean CRP (mean ± SD) of patients was 7.7200±5.5667 mg/L with range 3.2000-36.1000 mg/L and the median was 5.6000 mg/L. Association of CRP in three-day investigation was statistically significant (p<0.0001).

Table 3: Distribution of mean Downe's score.

Variable	Number	Mean	SD	Minimum	Maximum	Median
Downe's score	250	3.7400	2.3077	0	8	3

Table 4: Distribution of mean period of gestation.

Variable	Number	Mean	SD	Minimum	Maximum	Median
Period of gestation	250	32.9000	2.4581	30	42	32

Table 5: Distribution of neonates at birth.

Cried at birth	Frequency	Percentage (%)
No	75	30
Yes	175	70
Total	250	100

Table 6: Distribution of blood culture positivity.

Blood culture D1	Frequency	Percentage (%)
No	161	64.4
Yes	89	35.6
Total	250	100

Table 7: Distribution of mean CRP in three days of investigation.

CRP	Number	Mean	SD	Minimum	Maximum	Median	P value
Day 1	250	10.3412	6.9612	3.2000	34.0000	6.9000	
Day 3	250	8.9248	6.4137	3.2000	35.4000	6.4000	<0.0001
Day 7	250	7.7200	5.5667	3.2000	36.1000	5.6000	

Table 8: Distribution of mean mESR in three days of investigation.

mESR	Number	Mean	SD	Minimum	Maximum	Median	P value
Day 1	250	5.8280	5.7041	1.0000	20.0000	3.5000	
Day 3	250	5.0160	5.2526	1.0000	20.0000	2.0000	0.2267
Day 7	250	5.6960	5.9681	1.0000	20.0000	2.0000	

The mean mESR on D1 (mean ± SD) of patients was 5.8280±5.7041 with range 1.0000-20.0000 and the median was 3.5000. At day 3, the mean mESR (mean ± SD) of patients was 5.0160±5.2526 with range 1.0000-20.0000 and the median was 2.0000. At day 7, the mean mESR (mean ± SD) of patients was 5.6960±5.9681 with range 1.0000- 20.0000 and the median was 2.0000. Association of mESR in three-day investigation was not statistically significant (p=0.2267).

DISCUSSION

In this study it is found that there are important predisposing factors which will lead to occurrence of pneumonia in the neonates. History of premature rupture of membrane >24 hours is an important predisposing factor found in this study (Table 1). It shows majority of the patients i.e., 66.8% had history of PROM. In most of the studies regarding neonatal sepsis PROM has been identified as one of the important risk factors.[2] Here in this study it was found that majority of the patients who have pneumonia had history of PROM (p<0.001). The study done by Choudhury et al also supports the finding found in this study.[15] Downe's score >4 at presentation is an important risk factor for neonatal pneumonia. The mean value comes out to be 3.74. Downe's score >4 represents clinical respiratory distress and >7 represents impending respiratory failure. The mean score of 3.74 with standard deviation of 2.3 denotes the patients are identified well in advance in the course of the disease (Table 2). Prematurity is an important predispoing factor for pneumonia in neontes found in this study (p<0.001). The mean value is 32.9 weeks with standard deviation of 2.45 weeks (Table 3). It is denoting the fact that premature babies are more succeptable to pneumonia. In all the studies prematurity has been established as an important risk factor which is also reflecting in this study.[2,4] Asphyxiated babies are also more prone to develop pneumonia found in this study (p<0.001). Among all the patients admitted with pneumonia 70% cried spontaneously after birth whether the remaining 30% did not cried spontaneously and needed some resuscitative measures (Table 4). It is also reflecting the fact that birth asphyxia is a risk factor for neonatal pneumonia. This finding is supportive by the study done by Nair et al.[16] Blood culture positivity has a definite role for occurrence of the disease. These findings are corroborative of findings in different studies.[17,18] During follow up of the patient's prognosis was assessed by serial acute phase reactants study (Table 6 and 7). It has been noted that CRP has a definite role (p<0.0001) for determination prognosis but mESR has a limited role (p=0.2267) in this study. This finding is corroborative with the study done by Hawk.[11] So, according to results of this study antenatal care should be regularize and neonatal resuscitation should be strengthened up. Prognosis of neonates with pneumonia can be assessed by serial CRP evaluation so that need for repeated X-ray radiation can be minimised.

Some limitations are also there in this study. Only the cases admitted in a tertiary care hospital are evaluated, so the large community scenario may be different. This

study has been done in a tertiary care hospital with 250 samples with ages between 1 to 14 days and gestational age between 28 weeks to 42 weeks. This study should be followed up and should be performed on a larger cohort to determine predisposing factors related to pneumonia in neonates and determination of prognosis.

CONCLUSION

Predisposing factors should be kept in mind so that pneumonia in neonates can be prevented by proper antenatal and intranatal measures and serial CRP to be done during management to determine the treatment accuracy.

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REFERENCES

1. Bennett D, Bisanzio D, Deribew A. Global, regional and national under-5 mortality, adult mortality, age-specific mortality and life expency,1970-2016: a systemic analysis for the Global Burden of Disease study. 2016,2017.
2. Duke T. Neonatal pneumonia in developing countries. Arch Dis Child Fetal Neonatal Ed. 2005;90:F211-9.
3. Bang AT, Bang RA, Tale O. Reduction in pneumonia mortality and total childhood mortality by means of community-based intervention trial in Gadchiroli, India. Lancet 1993;336:201-6.
4. World Health Organisation (WHO). Neonatal and Child Health profile, India. Department of Maternal Newborn Child and Adolescent Health 2013. Available at: hptt://www.who.int/maternal-child-adolescent/epidemiology/profiles/neonatal-child/ind.pdf. Accessed on 10 Feb 2020.
5. Gouyon JB, Ribakovsky C, Ferdynus C, Quantin C, Sagot P, Gouyon B. Burgundy Perinatal Network. Severe respiratory disorders in term neonates. Paediatr Perinat Epidemiol. 2008;22(1):22-30.
6. Verani JR, McGee L, Schrag SJ. Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention. Prevention of perinatal group B *Streptococcal* disease: revised guidelines from CDC, 2010. MMWR Recomm Rep. 2010;59(RR-10):1-36.
7. Misra S, Bhakoo ON, Ayyagiri A. Clinical and bacteriological profile of neonatal pneumonia. Indian J Med Res. 1991;93:366-70.
8. Williams O, Hutchings G, Hubinont C, Debauche C, Greenough A. Pulmonary effects of prolonged oligohydramnios following midtrimester rupture of the membranes-antenatal and postnatal management. Neonatology. 2012;101(2):83-90.
9. Warren JB, Anderson JM. Newborn respiratory disorders. Pediatr Rev. 2010;31(12):487-95.
10. Magder S. Bench-to-bedside review: ventilatory abnormalities in sepsis. Crit Care. 2009;13(1):202.
11. Hawk M. C reactive protein in neonatal sepsis. Neonatal Netw. 2008;27(2):11720.
12. West JB. Respiratory Physiology: The Essentials. Baltimore, MD: Williams and Wilkins. 2012.
13. Davis RP, Mychaliska GB. Neonatal pulmonary physiology. Semin Pediatr Surg. 2013;22(4):179-84.
14. Wilmott RW, Boat TF, Bush A, Chernick V, Deterding RR. Kendig and Chernick's Disorders of the Respiratory Tract in Children. Philadelphia, PA: Elsevier Saunders. 2012.
15. Choudhury AM, Nargis S, Mollah AH, Kabir M, Sarkar RN. Determination of risk factors of neonatal pneumonia. Mymensingh Med J. 2010;19(3):323-9.
16. Nair S, Lewis LE, Godinho MA, Murthy S, Lakiang T, Venkatesh BT. Factors associated with neonatal pneumonia in India: Protocol for a systematic review and planned meta-analysis. BMJ Open. 2018;8:e018790.
17. Hibbard JU, Wilkins I, Sun L. Consortium on Safe Labor. Respiratory morbidity in late preterm births. JAMA. 2010;304(4):419-25.
18. Bhat R, Vidyasagar D. Delivery room management of meconium-stained infant. Clin Perinatol. 2012;39(4):817-31.

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