Original Research Article

Clinical profile and outcomes among neonatal pneumonia patients admitted in a tertiary care hospital, Gujarat, India

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ABSTRACT

Background: Neonates are highly vulnerable to infection due to factors like immaturity, immunologic deficiencies at time of birth and in-utero maternal infection. Neonatal pneumonia continues to remain important cause of mortality and morbidity in developing countries like India. The aim of this study was to study the clinical profile and outcome of neonatal pneumonia.
Methods: This descriptive observational study was carried out at NICU of tertiary care hospital with level III nursery during August-October 2012. A total of 200 neonates admitted in NICU during the study period were included as per inclusion criteria. All neonates were observed on day of admission, on day of deterioration and day of discharge. Clinical parameters, investigation profile, probable aetiology, intervention required and outcome was noted.
Results: Out of 200 neonates admitted during study period, 64 neonates were having neonatal pneumonia, making incidence of 32%. All symptomatic patients having respiratory distress were evaluated by taking blood samples for blood culture with antibiotic sensitivity, C-reactive protein, sepsis screen and X-ray chest. Onset of pneumonia was decided on basis of appearance of symptoms like early onset (<72hours) or late onset (>72 hours). Half of the patients had shown improvement after intervention but 16% deteriorated which required ventilatory support. Mortality was 32.81% and it was more in early onset (40%) than late onset (28.2%).
Conclusions: There was no single parameter which can be used for diagnosis of neonatal pneumonia. Clinical features with chest X-ray with sepsis markers have to be considered in diagnosing pneumonia.

Keywords: Neonatal pneumonia, ARI, Outcome, Investigation

INTRODUCTION

Infections are a frequent and important cause of neonatal and infant morbidity and mortality. As many as 2% of fetuses are infected in utero and up to 10% of infants have infections in the 1st month of life. Neonatal infections are unique. Infectious agents can be transmitted from the mother to the fetus or newborn infant by diverse modes.[1]

The clinical manifestations of newborn infections vary and include subclinical infection, mild to severe manifestations of focal or systemic infection and rarely, congenital syndromes resulting from in utero infection. The timing of exposure, inoculum size, immune status and virulence of the etiologic agent influence the expression of disease. Maternal infection that is the source of transplacental fetal infection is often undiagnosed during pregnancy because the mother was either asymptomatic or had nonspecific signs and symptoms at the time of acute infection.

A wide variety of etiologic agents infect the newborn, including bacteria, viruses, fungi, protozoa and

mycoplasmas. Immature, very low birth weight (VLBW) newborns have improved survival but remain in the hospital for a long time in an environment that puts them at continuous risk for acquired infections.[1]

The risk of dying during the neonatal period is highest closest to birth and decreases over the subsequent days and weeks; up to 50% of neonatal deaths occur within the first 24 hours of life and about 75% during the first week of life.[2]

Neonatal mortality has been declining worldwide. The number of deaths among babies 0-28 days of life decreased from 4.4 million in 1990 to 3.1 million in 2010. There was also a 28% reduction in neonatal mortality rates (NMRs) over the same period of time, from an estimated 32 deaths per 1000 live births to 23 deaths per 1000 live births-a slow progress. While some advancement has been in place and NMRs have declined in all WHO regions of the world, progress is unequally distributed.[2]

More than three-fifths of all 2.3 million child deaths in India in 2005 were from five causes; pneumonia, prematurity and low birth weight, diarrheal diseases, prematurity and low birth weight diarrheal diseases, neonatal infections and birth asphyxia and birth trauma. Concern has been raised that neonatal death rates in India are not falling fast enough.[3,4]

The objective of this study was to assess clinical profile and outcome of neonatal pneumonia and to evaluate maternal and neonatal risk factors in early and late onset pneumonia.

METHODS

This descriptive observational study enrolled 200 neonates admitted to NICU and delivered at new civil hospital, Surat (NCHS) a tertiary care hospital in Gujarat were evaluated over period of stay at NICU. The study was conducted during month of August-October in 2012. Neonates were observed on day of admission, on day of deterioration and on day of discharge from NICU.

Neonates in NICU evaluated for clinical profile of pneumonia and for maternal and neonatal risk factors for pneumonia. Neonates also searched for aetiology of pneumonia. We have also observed for intervention required at the time of deterioration. We have divided patients with pneumonia in two groups early onset and late onset as who develops pneumonia in first 72 hours of life early onset and who develops after 72 hours of life as late onset. We have observed for aetiology, clinical profiles and outcome in each group.

Inclusion criteria

All neonates included in study were admitted in NICU at NCHS and whose guardian gave written consent were included in this study. Asymptomatic high risk patients such as having history of PROM, foul smelling liquor, meconium stained liquor, maternal fever, LBW, preterm neonates. Symptomatic high risk patients such as having symptoms of respiratory distress (difficult, noisy, rapid breathing), RR >60/min, sub costal retractions, grunting, cyanosis, other signs of infections like poor feeding, poor reflexes, temperature disturbances, other clinical non-specific features were included in study.

Exclusion criteria

Neonates having congenital/severe life threatening anomalies, neonates whose parents have taken DAMA (discharge against medical advice), neonates who had taken treatment outside NCHS and born to other hospital were excluded from the study.

Investigations

Chest X-rays PA view of neonate taken at NICU or radiology department NCHS and reporting of chest X-ray were done by consultants of radiology not knowing clinical profile of patients.

The diagnosis of neonatal pneumonia was established using clinical presentation and septic screen markers like total blood count, platelet count, CRP. As per inclusion criteria all symptomatic patients were immediately evaluated with X-ray chest and blood investigations whereas asymptomatic high risks were screened clinically. In case of deterioration those group were immediately investigated as per protocol. The criterion for early-onset neonatal pneumonia was when neonates present within first 72 hours of life and late-onset neonatal pneumonia when neonates present after 72 hours of life.[5] We have considered a pneumonia case in our study as a neonate with respiratory distress (any of rapid noisy or difficult breathing, respiratory rate >60/min, chest retraction, grunting) who has a positive blood culture or any two or more of the following: predisposing factors (any one or more) like maternal fever (>38°C), foul smelling liquor, prolonged rupture of membranes (>18 hours); clinical picture of sepsis (any one or more) like poor feeding, lethargy, poor reflexes, hypothermia or hyperthermia; radiograph suggestive of pneumonia (nodular or coarse patchy infiltrate, lobar or segmental consolidation) not resolved within 48 hours and positive sepsis screen (any one or more) like raised CRP, leucocytosis (TLC >20000) or leucopenia (TLC <5000) or platelet count <150000.[5]

Statistical analysis

Data was entered in microsoft excel worksheet. Descriptive statistics have been presented as frequencies (percentage). Chi-square test was applied to find factors associated with pneumonia. A p value of <0.05 was considered to be statistically significant.

RESULTS

In our study out of 200 neonates, total 64 patients classified as a pneumonia patients as per definition criteria mentioned in methodology section. Hence incidence of pneumonia in our study was 32%. In clinical features wise difficult breathing, RR >60/min, sub costal retractions and poor feeding were significantly present in patients of pneumonia. Above 4 clinical features found statistically significant in pneumonia patients (p=0.003) (Table 1).

Table 1: Distribution of clinical features between pneumonia and non-pneumonia patients (n=200).

Clinical features	Pneumonia (n=64) (%)	Non pneumonia (n=136) (%)
Difficult or labored breathing	44 (68.75)	40 (29.45)
RR >60/min	48 (75)	32 (23.53)
Cyanosis	28 (43.8)	28 (20.6)
SCR	39 (60.64)	35 (25.58)
Grunting	28 (43.75)	20 (14.71)
Lethargy	28 (43.75)	32 (23.53)
Poor feeding	48 (75)	52 (38.24)
Poor reflexes	20 (31.25)	32 (23.53)
Temp disturbances	4 (6.25)	16 (11.76)
Other non-specific	8 (12.5)	23 (16.71)

Out of 64 patients with neonatal pneumonia, 25 were classified as early onset and 39 classified as late onset taking 72 hours of life. Among all pneumonia patients 36 (56.3%) were male and 26 (43.8%) were female neonates. Regarding gestational age, 40 (62.5%) neonates were full term and 24 (37.5%) were preterm. Majority of patients were vaginally delivered, as in our study all patients were intramural.

In birth weight wise distribution of patients with pneumonia, 6 were extremely low birth weight (<1.0 kg), 9 were very low birth weight (between 1.0 to 1.5 kg), 13 were low birth weight (between 1.5 to 2.5 kg), 37 were >2.5 kg. LBW (BW <2.5 kg) neonates found to have pneumonia significantly as compared to non-pneumonia patients (p=0.001). Hence low birth weight was one of the risk factor for development of pneumonia.

Among various risk factors only PROM (premature rupture of membrane >18 hours) were found significant (p=0.0001), other risk factors FSL (foul smelling liquor) p value 0.14, MF (>38°C), p value 0.3, MSL, p value 0.29, HMC (high maternal count) p value 0.4, so none was found statistically significant in our study. All sepsis markers (total leukocyte count, CRP, platelet count) were evaluated on day of deterioration in all patients of pneumonia. Platelet count <150000 and positive CRP >20000 were statistically significant in pneumonia patients. But leucopenia (TLC <5000) was not found in significant numbers. Among pneumonia patients 31 patients shows changes on X-ray, X-ray positivity were more in late onset. Changes of pneumonia on chest X-rays include consolidation 13% bilateral paracardiac, 31.25% RT UZ, 6% LT UZ, 13% LT MZ, 12.50% RT MZ and LZ, 15% diffuse haziness, 6.25% RT sided collapse, 3% LT sided collapse were present.

Table 2: Clinical profile, risk factors, investigations and outcome among patients with neonatal pneumonia (n=64).

Variables	Number	Percentage (%)
Onset		
Early onset	25	39.06
Late onset	39	60.93
Maturity		
FT	40	62.50
PT	24	37.50
Mode of delivery		
Vaginal	48	75.0
Forceps	4	6.25
C.S.	12	18.75
Birth weight		
<1 kg	6	9.37
1-1.49 kg	9	14.06
1.5-2.49 kg	13	20.31
≥ 2.5 kg	36	57.81
Maternal risk factors		
Foul smelling liquor	12	18.75
Maternal fever (>38°C)	10	15.63
Meconium stained liquor	12	18.75
PROM	19	26.69
High maternal count	4	6.25
Etiology		
Aspiration	9	14.06
Congenital	4	7.8
MAS	13	23.43
Sepsis	31	43.75
Vent ASSO sepsis	7	10.93
Average days of stay in NICU in pneumonia patients: 7.3 (mean) days. Mean of day of deterioration: 4th day		
Investigations		
TLC <5000	4	6.25
TLC >20000	20	31.25
PLT <150000	34	53.12
CRP positivity	28	43.75
Chest X-ray suggestive	31	48.43
Outcome		
Recovered	43	67.19
Died	21	32.81

Table 3: Comparison of clinical factors between early and late onset of pneumonia among study population (n=64).

Variable	Early onset (n=25) (%)	Late onset (n=39) (%)
Maternal risk factors		
Maternal fever	3 (14)	2 (5.6)
Foul smelling liquor	5 (17.9)	2 (5.6)
PROM	6 (25)	5 (13.9)
High maternal count	4 (17.9)	9 (22.2)
Meconium stained liquor	3 (10.7)	6 (16.7)
Etiology		
Aspiration	2 (8)	7 (17.94)
Congenital	4 (16)	0
MAS	7 (28)	6 (15.38)
Sepsis	9 (36)	22 (56.4)
Vent ASSO sepsis	2 (8)	5 (12.8)
Investigations		
TLC<5000	0	5 (11.76)
TLC>20000	7 (26.94)	13 (33.34)
PLT<150000	19 (76)	19 (48.75)
CRP positivity	6 (23)	23 (58)
Chest X-ray suggestive	10 (40)	21 (53.84)
Outcome		
Died	10 (40)	11 (28.20)
Recovered	15 (60)	28 (71.80)
Cause of death		
Septicemia	6 (60)	6 (54.54)
Pneumothorax	2 (20)	4 (36.37)

Probable aetiology included aspiration, meconium, sepsis, congenital and ventilator associated infection. Average days of stay in NICU in pneumonia patients was 7.3 days and mean of day of deterioration was 4th day. In our study mortality was 32.81% (Table 2).

In early and late onset distribution of risk factors was almost similar, only PROM was more in early onset which was significant (p value 0.0002) and high maternal count was in late onset but was not significant but MSL which is found in late onset more was statistically significant (p value 0.0001). In early and late onset there was no significant difference in distribution of clinical features. In early onset RR >60/min, poor feeding, sub costal retractions, grunting. In late onset similar distribution was found. Whereas investigation profile indicates that in early and late onset PLT <150000 were found in both in high percentage, CRP positivity more in late onset. TLC was almost same in distribution. But blood culture positivity was more in late onset on day of deterioration. In early onset only 4 patients showed growth on blood culture while 11 patients in late onset showed growth on blood culture. Sepsis was common in both early and late onset and also most common cause. After sepsis meconium was more common in early onset while aspiration was more common in late onset.

Ventilator associated sepsis also more in late onset. In our study mortality was 32.81%, 40% in early onset and 28.20% in late onset. Major cause of death was septicemia followed by pneumothorax and DIC. Incidence of pneumothorax in cause of death was more in late onset pneumonia (Table 3).

DISCUSSION

It has been difficult in defining case of neonatal pneumonia and identification of its related causes. The diagnosis of neonatal pneumonia is difficult and though there is much information from necropsy reports there is little from clinical and laboratory studies of surviving babies.[4]

Moreover, there are many challenges in implementation of any programme for reducing burden of neonatal pneumonia in terms of morbidity and mortality. In India, pneumonia is the single most important cause of death among children in the post neonatal period, contributing as much as 27.5% of total under-five mortality according to one estimate.[6]

The overall incidence of neonatal pneumonia in present study is 32% compared to other studies which ranges from 12.7% to 15%.[7,8] Many studies have reported less incidence of pneumonia less than 5%.[9-11]

Incidence of early and late onset pneumonia was 39.06% and 60.93% respectively. In study of Weber 1990 incidence of early and late onset were 46% and 54% respectively but cut off for early and late was 48 hours of birth.[4]

A male preponderance is noted in almost all the studies of neonatal sepsis.[12] The male preponderance in neonatal septicemia may be linked to the X-linked immunoregulatory gene factor contributing to the host's susceptibility to infections in males.[13]

62.50% were full term and 37.50 % were preterm in Mathur et al distribution were 62.8% term and 76.6% preterm.[8] Such difference was due in this study most of newborn were delivered at home and in present study all neonates were delivered in hospital.

As prematurity is one of predisposing factor for developing sepsis, preterm infants have a 3-10 fold higher incidence of infection than full-term infants. Premature babies have less immunogenic ability to resist and combat infections, also require prolonged intravenous access and other invasive procedures that impair barrier and clearance mechanisms, so they are at highest risk of acquiring sepsis.[1,14] However, in present study development of pneumonia is more in full term because major admissions in NICU were due to birth asphyxia which is more in full term so due to more numbers of asphyxia patient present study showed more incidence in pneumonia.

The presenting complaints in neonates with pneumonia included rapid breathing (75%), poor feeding (75%) and difficult breathing (68.75%), SCR (60.64%). These findings are similar to an earlier series.[14,15] In primary neonatal care rapid breathing, poor feeding and difficult breathing are useful symptoms suggestive of respiratory distress. The clinical diagnosis of pneumonia remains subjective and unreliable for a scientific study. We therefore thought it necessary to use an objective tool such as chest radiography for the diagnosis. The difficulty, inconsistency and large interobserver difference in eliciting chest findings among physicians and occurrence of pneumonia in the absence of classic signs such as fever, cough, and rales are well documented. Moreover, radiological evidence of pneumonia may be absent in many young infants with any combination of pulmonary findings such as tachypnoea, crepitations, or decreased breath sounds.

In investigations TLC >20000 was 31.25% no major difference in early and late onset. In study at medical university of Warsaw, Poland, it was only 3.9% and 33.9% in study at Mathur et al.[7,8] In contradictory leucopenia which is more sensitive in detecting sepsis was found 6.25% which is very less. Hoque et al in 2010 has showed 86% CRP positivity, 81% thrombocytopenia (platelet <1,00,000) and 53% leucopenia (TLC <5000) in septicemia cases.[15] The differences in the results of parameter in different studies may be due to variations in the blood sampling time, the severity of infection, the diagnostic criteria followed, the age of neonates, the time of onset of infection (criteria for early and late onset) and different methods used for testing of these parameters. Thrombocytopenia was noted as a significant septic screen marker in the neonates with septicemia in present study.

CRP positive in 43.75% in total pneumonia patients which is more in late onset 58%, compare to study at medical university of Warsaw, Poland it was 38.2% and in Mathur et al study 54.3% in pneumonia patients.[7,8]

CXR positive patients were 48.53% in present study, early onset patient showing changes of pneumonia 40% and 53.84% were late onset. In study of Mathur et al chest X-ray positivity in pneumonia patients 47.6% which is similar to present study.[8] But in study of medical university of Warsaw, Poland only 12.7% was positive for CXR.[7] The appearance of pneumonia on X-ray varies, depending upon the duration of infection at the time the X-ray is obtained, the etiology of the pneumonia, the presence of other respiratory disease, such as respiratory distress syndrome or bronchopulmonary dysplasia.

Probable aetiology in present study aspiration 14.06%, meconium 23.43%, sepsis 43.75%, congenital 7.8%, ventilator associated infection were in 10.93%. Sepsis was common in both early and late onset and also most common cause. After sepsis meconium was more common in early onset while aspiration was more common in late onset. Ventilator associated sepsis also

more in late onset. These findings were comparable with other studies.[9-11]

Overall mortality in our study 32.81% which was similar to studies conducted by Mishra et al 32% and Mathur et al 31%.[8,9] Mortality in neonatal pneumonia has been reported to be 60% in low birth weight babies as compared to 20% in normal birth weight group. Again mortality among the first week onset pneumonia has been reported to be 74% as compared to 26% started during second to fourth week of life. And cause of mortality in most patients was sepsis, following that pneumothorax and rest died due to pulmonary hemorrhage.

There were several limitations in this study. Being a cross-sectional study, we could not establish temporal association between exposure and outcome variables. Multiple factors are required for diagnosis of neonatal pneumonia but we are unable to comment on sensitivity and specificity of the investigation procedure. There were many confounders in this study like gestational age, birth weight of newborn, maternal risk factors which were difficult to control.

CONCLUSION

Neonatal pneumonia was more common in males and low birth weight neonate. Late onset pneumonia was more common which can be minimized by early diagnosis, prevention of cross infection and early interventions. Only few maternal risk factors were helpful in predicting pneumonia in neonates like PROM and meconium stained liquor are most important. Though clinical features of pneumonia are non-specific but respiratory symptoms and poor feeding should arise suspicion of pneumonia. No single parameter is diagnostic in pneumonia in neonates like clinical features with chest X-ray with sepsis markers should include in defining pneumonia.

Recommendations

There is a need of more surveillance and multicentric studies are required in forming uniform and generalized definition of neonatal pneumonia. Gastric aspirates cytology is preferred for congenital pneumonia but in absence of it chest skiagram should be most recommended noninvasive bedside investigation for all sick neonates. All high risk neonates must screen with chest skiagram especially at clinical deterioration. Each NICU should have their protocol defining pneumonia and treatment protocol as per organism prevalence and antibiotics sensitivity pattern. Importance of antenatal health check-up and intuitional deliveries of newborn should be promoted.

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