Discussion
The present study was conducted on 50 neonates, admitted in NICU of the Department of Pediatrics, M.L.B. Medical College, Jhansi from November 2003 to September 2004, with respiratory distress. The present study was undertaken with the following aims:

1. To find the causes of respiratory distress in neonates brought to our Neonatal Intensive Care unit with symptoms suggestive of respiratory disorder.

2. To evaluate clinical signs like cough, difficulty in feeding, cyanosis, respiratory rate, chest retractions, flaring of alae nasi and adventitious sounds for diagnosis of neonatal pneumonia.

3. Determine bacterial etiology of neonatal pneumonia.

4. To study the sensitivity pattern of the prevalent bacteria in neonatal intensive care unit.

Incidence of spectrum of Respiratory distress disorders

It was our endeavor to explore the spectrum of respiratory distress in neonates encompassing four disorders namely: Pneumonia, HMD, MAS and TTNB. In our study, pneumonia was the leading cause of respiratory distress with incidence 46%, followed by HMD 42%, MAS 8%, and TTNB 4% respectively. Respiratory distress
forms 30% of all the admissions to our NICU. Studies in the past by Shaffer et al, had found RDS as the leading cause in premature and massive aspiration in full term with pneumonia as second. Cunnigham and Smith attributed the respiratory distress as belonging to RDS 75% and massive aspiration as 23%. SP Khatua (1979), reported highest incidence of aspiration syndrome (57.1%), followed by pneumonia 9.35% and RDS 8.8%. S.Thomas et al, found pneumonia in 44% of cases as a leading disorder with TTNB in 19.2%, MAS in 12.2% and HMD in 8.6%. Mathur et al (2002), also found in his study that pneumonia was the most common cause of respiratory distress in neonates. He reported the incidence to be 68.7%, other disorders were as follows – HMD (4%), MAS (4%), TTNB (7.33%).

The admission figures are in close similarity to the study by NB Mathur et al, where they are 29.2% of all admissions.

In our study the male : female ratio of neonates developing respiratory distress was 2.3 : 1. Males were 1.6 times more predisposed than the females in hyaline membrane disease. Pneumonia and MAS affected approximately 3 males for every female in our study. Driscoll and Smith (1962), found the male : female ratio as 2:1. S.P. Khatua found that the male : female ratio was 1.94 : 1.
Birth weights and gestational ages of neonates in various study groups

It is evident from table 4 that 40% of neonates with pneumonia were low birth weight, and one was small for gestational age. 7 neonates did not complete 37 weeks of gestation and were born prematurely. So, 14 (60%) of our cases developing pneumonia were fullterm, while nine (40%) were preterms in this study.

While, in HMD 100% neonates were low birth weight, 85.8% were < 2000 gms and all the 21 cases of HMD were premature (< 34 weeks). In MAS and TTNB none of the babies were of low birth weight or premature.

The mean birth weight for neonates developing pneumonia was 2.2 Kg, 1.4 Kg for HMD, 3.02 Kg for MAS and 2.6 Kgs for TTNB.


In the study by SP Khatua et al (1979), 30.45% cases with respiratory distress were premature and 53.7% were fullterm. In the study by S. Thomas et al (1981), they found a higher percentage of preterms developing respiratory distress. In their study they found that
out of 51 cases of pneumonia 26 were preterm. In the study by NB Mathur et al (2002), 48% of neonates with pneumonia were preterm.

**Clinical signs and symptoms**

Most of the neonates in our study were admitted with signs of respiratory distress, but we found few signs more specific for one disease and few signs more sensitive for the others. Table 5 of our study compares the number and percentage occurrence of various signs and symptoms in the study group. RR > 60 / minute difficulty in feeding, flaring of alae nasi and chest retractions had maximum incidence in all the four groups, while cyanosis and cough were most specific for pneumonia only. Adventitious sound on chest auscultation were found in maximum number (34.8%) in the cases belonging to pneumonia.

In our study we found cough, adventitious sounds & cyanosis had high specificity (100%), (88.8%) and (85%) respectively in diagnosing neonatal pneumonia. Difficulty in feeding, RR > 60 , flaring of alae nasi and chest retractions had high sensitivity (95.6%), (91.3%), (100%) and (86.9%) respectively for diagnosing pneumonia (Table 6). In the study by NB Mathur et al, cough, adventitious sounds, and flaring of alae nasi had high specificity which were (100%), (91.4%) and (70.2%) respectively. Chest retractions, difficulty
in feeding and RR > 60 / minute had high sensitivity (> 88%) for diagnosis of pneumonia in neonates.

In our study, of 23 cases of pneumonia, we found two cases with RR < 60 (8.7%), both of them had gestational age < 34 weeks and weight < 2 Kg, but the mortality was 100%. Thus, 100% mortality in non-tachypnoeic babies in our study was basically correlated to low birth weight and prematurity.

It was first pointed out by Mishra et al (1985), that the mortality in non-tachypnoeic as compared to tachypnoeic cases was significant. He found that out of 12 non-tachypnoeic babies, 7 died which was 58.3% mortality, while only 7 out of 32 with tachypnoea expired (21.31%). Further, he discovered one of the important correlate of low birth weight with non-tachypnoeic neonates. This was further substantiated by Mathur et al, who found 11.6% neonates had respiratory rate < 60/minute and found that the mortality increased even more (57.1%) when the RR was less than 50. In his study, out of 12 neonates having RR < 60/minute 5 expired, 7 had gestational age < 34 weeks and birth weight < 1800 gms.

**Antenatal history**

In our study, (Table 11) 11 mothers had factors like history of PRM (10), maternal fever (2), leaking per vaginum predisposing to
pneumonia. These factors like the study by Mathur et al had high specificity (> 80%) and positive predictive value. In his study on the spectrum of respiratory distress disorders in neonates, SP Khatua (1979), took similar parameters to aid antenatal diagnosis of pneumonia like the ones in our study. According to him out of 17 cases of pneumonia, 2 had history of prolonged rupture membranes (PRM) in mothers. In the study by S Thomas et al (1981), out of 40 infants of pneumonia, 17 mothers had history of PRM for > 24 hours and 2 had history of PRM for < 24 hours. In a study by NB Mathur (2002), out of 103 cases of pneumonia 35 mothers had prolonged rupture of membranes. In the same study, 21 mothers had history of recent febrile illness around labour. All in all the study by Mathur et al, 42 mothers had predisposing factors for pneumonia.

None of the factors like maternal fever, prolonged rupture membranes, leaking per vagina or foul smelling liquor was found to have any association at all with transient tachypnoea of newborn (TTNB).

Except for a history of fetal distress, none of the factors enumerated in antenatal history like PRM, maternal fever, LPV had any association at all with meconium aspiration syndrome (MAS) (Table 12).
Fetal distress had a high specificity and negative predictive value for MAS.

SP Khatua et al (1979), found the highest incidence of aspiration syndrome in their study and in retrospect found that such mothers had poor antenatal check-up history and history of fetal distress (n = 64) too.

S Thomas et al (1981), like in our study could not find any association between PRM and MAS.

The most unprecedented finding while calculating for observations (Table 13) for ANH (antenatal history) in diagnosing neonates with HMD was the high incidence of prolonged rupture membranes (PRM) and leaking per vaginum (L P/V) in mothers of such neonates. No earlier study has ever mentioned these findings, so no comparison was available. In our study, 5 mothers of neonates with HMD had PRM and 5 had L P/V. Probable explanation could be that these factors were indirectly also responsible for preterm labour and birth.

Natal history

In our study (Table 14), we found that prolonged labour was the only natal factor which was found to have a high specificity (88.8%) for neonates having pneumonia. Other factors like precipitate / traumatic
labour or a history of poor cry failed to show any association at all in our study regarding pneumonia.

SP Khatua et al, found that 15 out of 17 cases of pneumonia in his study also had a history of prolonged labour. NB Mathur et al, had not done any study regarding the natal study of pneumonia. Bhakoo et al in their study on septicemia had given a high risk score of 2 for septicemia if it had a history of PRM, but had not mentioned any cases.

Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with TTNB in our study.

In the present study, prolonged labour and a history of poor cry or resuscitation in newborn have a high specificity (91.3%) and (100%) respectively for MAS (Table 15). History of poor cry in natal history had a 100% positive predictive value (PPV) for neonates developing respiratory distress due to MAS. This study is substantiated by the study of SP Khatua et al (1979), who found that out of 104 cases of aspiration syndrome, 64 infants had abnormal delivery due to fetal distress, prolonged labour, failed medical induction or obstetrical accidents.
Prolonged / precipitate / traumatic labour or a history of poor cry failed to show any association at all in neonates with HMD in our study.

**Mode and Method of delivery**

In our study (Table 16, 17) 28% of all neonates with respiratory distress were delivered at home, while 43.5% of all cases with pneumonia were delivered outside by Dais or P/V in hospitals by untrained staff having meager facilities. We also found that 3 out of 4 neonates (75%) having MAS were delivered by emergency LSCS, the indication was prolonged labour in all three of them. Both the neonates with TTNB in our study were delivered in the hospital by emergency LSCS. 18 cases of HMD were delivered in hospital, because most of them had to be delivered by emergency LSCS. There were 5 twins in our study, which was in itself a high risk delivery.

S. Thomas et al (1981), found that there was no significant correlation between the mode of delivery and the development of pneumonia. He also found that most of the babies with MAS were born by emergency LSCS, for which the indication was fetal distress or MSAF. In his study of 22 babies having TTNB 14 were delivered vaginally and 4 by 8 by emergency LSCS. In the same study, 10
neonates with HMD were born equally by emergency LSCS and spontaneous vaginally. However, NB Mathur commented in his study, that 51% of the neonates with respiratory distress were delivered at home, which shows that the mode of delivery had been underplayed by most previous authors.

SP Khatua et al (1979), found that out of 104 cases of aspiration syndrome, 64 were delivered abnormally due to fetal distress, prolonged labour, failed medical induction. In the same study, he found 6 cases of TTNB, out of which 4 were born by normal delivery and 2 by emergency LSCS.

Studies by SP Khatua (1979), PK Mishra (1987) and P Kumar (1999) comprised neonates which were exclusively inborn delivered by trained personnel, so the real incidence of pneumonia in out patient deliveries could not be ascertained.

Post natal history

In our present study (Table 18) we found that a history of difficulty in feeding in the post natal period with fever had a high specificity for diagnosing pneumonia. Fever post maturity also had a high specificity, but (0%) sensitivity, in the case of post maturity. 47.8% of cases had an onset of respiratory distress within 15 hours of birth and were later diagnosed as pneumonia.
In the study by SP Khatua, out of 104 cases of aspiration syndrome 41 had history of meconium staining of amniotic fluid (MSAF) with or without staining of cord, skin or nails. Out of 104 cases, 14 neonates were preterm, 87 were term and 3 were post term.

In our study (Table 19) meconium staining of cord, liquor and nails had a 100% sensitivity, specificity and predictive value for MAS. Post maturity (n=2 out of 4) also had a 100% specificity and positive predictive value in cases diagnosed as MAS.

In our study 75% of neonates with meconium aspiration syndrome developed respiratory distress within 8 hours of birth.

In the study by Thomas et al, out of 14 cases with MAS, 4 were preterm and rest were term. Most of the babies were born by emergency LSCS and indication was MSAF (8 out of 14).

In our study (Table 20), all the 21 neonates with HMD had a gestational age < 34 weeks. Both weight and gestational age had the highest sensitivity (89.6%) (93.1%) and negative predictive value (89.6%) (100%) respectively for diagnosing HMD. 71.4% neonates with HMD developed respiratory distress within 6 hours of birth. In a study by SP Khatua, out of 16 neonates with HMD, 15 were premature, while in a study by Thomas et al, all the ten infants with HMD were preterms.
Apart from a difficulty in feeding (50%), none of the other postnatal factor could be associated with TTNB. 100% cases later diagnosed as TTNB presented with respiratory distress within 4 hours of birth (Table 21).

Investigations

It was our endeavor to identify cases of pneumonia responsible for respiratory distress in neonates, for which we had to resort to certain investigations enumerated in various texts by different authors. CRP was one such test whose high specificity has been proved in studies by NB Mathur et al (2002), and Mathai et al (2004) in diagnosing infections in neonates. In the study conducted by us (Table 23), we found the values for sensitivity (60%), specificity (92.6%), PPV (87.5%) and NPV (73.5%) for CRP. In comparison to other indicators of infection CRP is the single best indicator after blood culture in diagnosing early onset sepsis (EOS) (Table 24). According to Mathai et al, sensitivity, specificity and positive and negative predictive values of CRP estimation at 24 hours of age for diagnosis of early onset of sepsis using > 6 mg/L as cut off were 80%, 60%, 7.7% and 98.6% respectively. NB Mathur et al, got sensitivity and specificity of CRP as 54.3 and 90% respectively. CRP earns its respect in being a quick indicator which increases its utility. Although, its sensitivity in our study
was low (60%), if utilized with caution this test can help in reducing indiscriminate antimicrobial use in the newborn.

Studies by S Thomas et al (1979), Mishra et al (1991) and NB Mathur et al (2002) have mentioned utility of micro-ESR band cells and blood culture sensitivity in identifying EOS. But apart from NB Mathur, none of them have discussed their specificity and predictive values in detail. In our study (Table 23), specificity for Micro-ESR was 100% and sensitivity was 26%. In the study by Mathur et al, micro-ESR had a specificity of > 90% but a very low sensitivity 32%. We had a different experience with band cells and toxic granules, our specificity was close to the studies by NB Mathur i.e. > 90% but sensitivity was very low 13%, in contrast with 52.4% in the study by NB Mathur et al.

Several authors have stressed the utility of blood culture positivity in identifying cases of pneumonia, to mention a few Bhakoo (1979), Mishra et al (1991), Shakuntala et al (1978), NB Mathur et al (2002).

In the present study (Table 21), the percentage of definitive pneumonia (based on isolation of bacteria) and probable pneumonia (blood culture negative) were 39.1 and 34.8% respectively. This was close to that found in the study by Mathur et al, where definitive pneumonia was 37.9% and probable pneumonia 47.6%. This was
identical to that observed by Webber et al (1990). In our study (Table 28), the bacterial isolation percentage 56.5%, which is slightly higher than that reported by earlier authors. This could be due to the promptness in sending the blood culture samples before administration of antibiotics.


In a study by Mishra et al (1991), a bacterial etiology of pneumonia was found in 36.4% cases, Shakuntala et al (1978), found it to be 44%. In the study by NB Mathur et al (2002) the percentage of bacterial etiology of pneumonia was established in 47.5% neonates.

8.7% cases in our study (Table 21), had only sepsis screen positive. In the cases studied by Mathur (2002), 4.8% neonates had only sepsis screen positive. No earlier study has stated detailed diagnostic criteria for pneumonia in neonates utilizing blood culture or sepsis screen positivity.

Amongst 17 x-ray chest positive cases in pneumonia in our study, 11 cases showed alevolar infiltrates (47.8%), 4 cases showed diffuse haziness (17.3%), 2 cases showed lobar consolidation (8.6%), while 6 cases had chest x-ray clear (26.1%).
Chest x-ray and clinical signs (Table 21) alone would have missed the diagnosis of pneumonia in 26% cases and these had to corroborated with sepsis screen and blood culture. Mathur et al, found this data to be 15%, no other study was available for comparison.

In the present study, X-ray chest was positive in 50% cases of TTNB. Chest x-ray showed changes pertaining to MAS in 50% cases. In HMD, only 33.3% cases turned out to be chest x-ray positive. Rest other investigations were negative in all these three diseases i.e. HMD, TTNB, MAS and diagnosis was aided by clinical history and examination. No study was available for the comparison of chest x-ray positivity in the above disorders.

**Bacterial isolation**

The bacterial isolates in our study (Table 28) are consistent with the earlier studies which suggest an increasing trend of Klebsiella (61.5%, in our study). In the present study Staph aureus was found only in 2 cases (15.4%), while E.coli was responsible for pneumonia in 3 cases (23.1%). Other studies in the past which had hinted an increasing incidence of Klebsiella are S. Thomas et al (1979), ON Bhakoo (1980) (20.5%), JN Mishra et al (1985), S Mishra et al (1991) (11.3%), M Singh (1991), Mathur et al (2002) (57.9%). No cases of streptococcus pneumoniae were found as compared to Mishra et al
(1991), who found it in 10 cases (22.4%) and Shakuntala (1978) (20%). Bhakoo et al (1979) and Jeffery et al (1979) had shown higher incidence of Gram negative septicemia in neonates having early onset sepsis. This is again proved by our study, which shows a higher incidence of Klebsiella, which is a Gram negative bacteria.

No study so far had evaluated usefulness of ciprofloxacin in combating serious infections. It was our endeavor to find the antibiotic sensitivity of the bacterial isolate from our cases of pneumonia. The best coverage in our study (Table 29), has been shown by ciprofloxacin (84.62% cases) followed by ofloxacin and chloramphenicol 76.92% and 61.5% respectively. Amikacin was effective in only 23.08% cases.

Study by JN Mishra et al (1985), found all Gram negative bacteria sensitive to Amikacin, and staph aureus sensitive to methicillin / cloxacillin. We share the experience of Amikacin sensitivity to Gram negative bacteria (E.coli) in our cases too. S Mishra et al (1991), stated that gentamycin + chloramphenicol gave the best coverage 87%, followed by cloxacillin + gentamycin (76%). Similarly, cloxacillin and erythromycin showed 95% and 60% efficacy against staphylococcus pyogenes.
Fatality

In our study, respiratory distress was responsible for 28.7% of all the fatalities in the NICU. This was similar to the data found in the study by NB Mathur et al, where it was 32% of all mortality. The mortality figures were 52% for HMD in our study and 75% for MAS. The mortality figures were 81.2% for HMD in studies by SP Khatua and 100% by NB Mathur. The mortality rate for MAS is 30% by SP Khatua and 50% by Mathur et al. Mortality figures for various disorders found by S Thomas et al were pneumonia (22.4%), MAS (14.3%) and HMD (100%).

In the study by SP Khatua, the incidence of morbidity and mortality of respiratory distress amongst various birth weights was

<table>
<thead>
<tr>
<th>Weight</th>
<th>No. of cases</th>
<th>%</th>
<th>No. expired (%)</th>
</tr>
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<tbody>
<tr>
<td>1.6 – 2 Kg</td>
<td>44</td>
<td>24%</td>
<td>32 (72%)</td>
</tr>
<tr>
<td>2.1 – 2.5 Kg</td>
<td>55</td>
<td>30.3%</td>
<td>13 (23.7%)</td>
</tr>
</tbody>
</table>

We also have similar data in our study, these are 39% low birth weights (< 2.5 Kg) in pneumonia with 57.1% mortality rate. Since, there were 2 neonates with birth weight less than 2 Kg having pneumonia and both of them expired the mortality rate was 100%. In our study, 100% of low birth weight neonates with HMD expired because of their disease.