NEONATAL APNOEA- AN OBSERVATIONAL STUDY

Debasis Kr. Samanta1, Shubhra Datta2, Shyamali Datta3

1Senior Resident, Department of Paediatrics, IPGMER & SSKM Hospital, Kolkata.
2Senior Resident, Department of General Surgery, IPGMER & SSKM Hospital, Kolkata.
3Associate Professor, Department of Paediatrics, MGM Medical College & LSK Hospital, Kishanganj, Bihar

ABSTRACT

BACKGROUND
Apnoea is a pathological cessation of breathing that results in hemodynamic disturbances & hence merits treatment. This is an important cause of mortality & brain damage in immature babies especially those with a gestation of less than 32 weeks. Inspite of its common incidence, its aetio-pathogenesis have not been systematically studied. This study was aimed to estimate the frequency of apnoea in new born, at different gestational age and birth weight and establish different etiological factors of apnoea in newborn and their outcome.

MATERIALS AND METHODS
The present study was conducted on neonates admitted in Sick Neonatal Care Unit, Department of Neonatology, IPGMER & SSKM Hospital, Kolkata between September, 2014 to August, 2016. All neonates at risk of apnoea (<32 weeks gestation) were monitored for at least the first week of life. Only neonates who developed apnoea were included in this study.

RESULTS
Out of 1270 new borns admitted in sick neonatal care unit, 634 were preterm and 96 newborns were diagnosed as having apnoea-94 were preterm and 2 were term. The frequency of apnoea in babies ≤30 weeks was 45.91 per 100 live births. It gradually decreased to 13.45, 5.30 and 0.31 per 100 live births in newborn aged 31-32 weeks, 33-36 weeks and ≥37 weeks respectively (statistically significant, p value <0.001). The survival rate in babies with apnoea of prematurity was 72.41% (p<0.001) as compared to 32% (P<0.001) in apnoea due to infection group. The percentage of survival in <1000 gm, 1000-1499 gm, 1500-2499 gm and 2500 gm was 22.85,55,60 and 100 percent respectively (p value <0.001).

CONCLUSION
Infection (Sepsis, pneumonia, meningitis) and apnoea of prematurity are common causes of apnoea in newborn. All babies ≤32 weeks gestation needs to be closely monitored for apnoea. Apnoea spells occurring in infants at or near term are always abnormal and are nearly always associated with serious causes. Apnoea due to sepsis carries a poor prognosis.

KEYWORDS
Apnoea, Apnoea of Prematurity, Neonatal Sepsis, Low Birth Weight, Preterm.


BACKGROUND
Apnoea of prematurity is often defined as a cessation of respiration usually 20 seconds or more or any cessation of respiration of any duration followed by bradycardia <100 bpm & or cyanosis. Apnoea is commonly seen in preterm babies with a periodic breathing pattern characterized by three or more respiratory pauses of >20 seconds duration. After 20 secs of apnoea baby developed bradycardia, if it’s persists for 30 secs then developed cyanosis & may become unresponsive to stimulation. This is an important cause of mortality & brain damage in immature babies especially those with a gestation of less than 32 weeks.

Aetiology
i. Immaturity
ii. Pulmonary conditions- pneumonia, respiratory distress syndrome etc.
iii. Cardiac malformations- Fallot’s tetralogy, pulmonary atresia etc.
iv. Neurological disorders- birth trauma with or without intra cranial bleeding, maternal sedation.
v. Infections- sepsicaemia, meningitis etc.
vi. Metabolic causes- hypoglycaemia, hyperbilirubinemia, hypocalcaemia, acidosis etc.

Neonates who are born at a gestational age <29 weeks or birth weight <1000 gm mostly experience apnoea of prematurity. Although the pathophysiology of AOP is poorly understood, it is often attributed to immature respiratory control mechanisms. In preterm infants, hypoxia results in transient hyperventilation, followed by hypoventilation and causing apnoea. Hypoxia makes the premature infant less responsive to increased level of carbon dioxide. This shows that immaturity of peripheral chemoreceptor may be involved in the pathogenesis of apnoea. The spell generally begins at 1-2 days of life but common within first 7 days of life. Sepsis is also an important cause of neonatal apnoea. Sepsis is more common in preterm infants and low birth weight infants and has high incidence rates of apnoea.
MATERIALS AND METHODS
The present study was conducted on neonates admitted in Sick Neonatal Care Unit, Department of Neonatology, IPGME & SSKM Hospital, Kolkata between September, 2014 to August, 2016.

The gestational age and birth weight of all neonates were recorded. All neonates at risk of apnoea were monitored for at least the first week of life. Only neonates who developed apnoea were included in this study. After emergency treatment and stabilization, all the babies with apnoea were examined for the history, birth weight and sex, approximate gestational age (Modified Ballard score), evidence of birth asphyxia, evidence of respiratory distress and features of neonatal sepsis. Detailed clinical examination of all neonates with apnoea, was done with attention to temperature instability, jaundice, pallor, cardiac murmur, poor perfusion, seizures, jitteriness and neurological examination. Investigations like septic screen, Chest X-ray, blood glucose level, serum calcium and sodium, CSF examination, Urine examination and culture, CBC, arterial blood gas, USG head, ECG/Echocardiography were done to rule out common causes of secondary apnoea.

Apnoea of prematurity is a diagnosis of exclusion. Monitoring was done for respiratory activity, heart rate and oxygen saturation by advanced apnoea monitor integrated with pulse oximeter. The day of onset of apnoea and number of apnoeic episodes were recorded for each baby. General measures like tactile stimulation, avoidance of vigorous suctioning of oropharynx, blood transfusion if haematocrit was <30%, treatment of underlying cause and specific measures for apnoea like caffeine and nasal CPAP were the treatment given.

A loading dose of caffeine citrate in a dose of 20 mg/kg was administered intravenously over 30 mins with maintenance dose of 5-10 mg/kg/day IV once daily. Caffeine was continued till 34 weeks corrected gestational age and stopped thereafter if no episodes of apnoea have occurred in the last 7 days.

RESULTS
Out of 1270 newborns admitted in Sick Neonatal Care Unit, 634 were preterm and 96 newborns were diagnosed as having apnoea- 94 were preterm (15.07%) and 2 were term. The frequency of apnoea in babies ≤30 weeks was 45.91 per 100 live births. It gradually decreased to 13.45, 5.30 and 0.31 per 100 live births in newborn aged 31-32 weeks, 33-36 weeks and ≥37 weeks respectively. (Statistically significant, p value <0.001).

<table>
<thead>
<tr>
<th>Days</th>
<th>Frequency of APNOEA</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Day 2-7</td>
<td>74</td>
<td>77.55 (p value &lt;0.001)</td>
</tr>
<tr>
<td>Day&gt;7</td>
<td>02</td>
<td>2.04</td>
</tr>
</tbody>
</table>

Table 1. Onset of apnoea

The frequency of apnoea in babies whose weight was less than 1000 gm, between 1000-1499 gm, 1500-2499 gm and ≥2500 gm was 38.88, 15.09, 6.45 and 0.49 per 100 live births respectively. (Statistically significant, p value <0.001).

Out of 96 babies developed apnoea, 20 babies developed apnoea on day one, 74 babies on day 2-7 and 2 babies developed apnoea after 7 days (Table 1).

All the cases of apnoea of prematurity developed apnoea on day 2-7. Out of 96 newborns having apnoea, 63.54% had ≥3 episodes, (p <0.001) (Table 2).

In our study, commonest causes of apnoea were infection (51.02%) and apnoea of prematurity (29.59%), the mean birth weight and gestation were 1434.34 gm and 31.6 weeks for the infection group and 1117.41 gm and 30.34 weeks for the apnoea of prematurity group in our study.

The survival rate in babies with apnoea of prematurity was 72.41% (p <0.001) as compared to 32% (P <0.001) in apnoea due to infection group (Table 3).

The percentage of survival in <1000 gm, 1000-1499 gm, 1500-2499 gm and 2500 gm was 22.85, 57.89, 60 and 100 percent respectively (p value <0.001) (Table 4).

The percentage of survival in 30 weeks, 31-32 weeks, 33-36 weeks and 37 week was 27.27, 55.56, 78.57 and 100 percent respectively (P<0.0001) (Table 5).

DISCUSSION
This study had several unique features which were designed to estimate the frequency of apnoea in newborn, at different gestational age and birth weight and establish different etiological factors of apnoea in newborn and their outcome.

In our study, we found that the frequency of apnoea in babies ≤30 weeks was 45.91. It gradually decreased to 13.45,
5.30 and 0.31 per 100 live births in newborn aged 31-32 weeks, 33-36 weeks and ≥37 weeks respectively. (This proportion is statistically significant, <0.001), which were comparable to earlier studies. In our study total number of low birth weight babies was 634 out of which 96 developed apnoea, the frequency being 15.14 per 100 live births. The frequency of apnoea in babies whose weight was less than 1000 gm, between 1000-1499 gm, 1500-2499 gm and ≥2500 gm was 38.88, 15.09, 6.45 and 0.49 per 100 live births respectively which was statistically significant. The result was close to study by Narang A et al, but was lower as compared to study by Smart H et al.9 The lower incidence of apnoeic spells in our babies may be due to decreased survival of more immature babies and less admission. Santin RL et al, stated that apnoea may occur during the postnatal period in 25% of neonates who weigh less than 2500 gm at birth and in 84% of neonates who weigh less than 1000 gms.10 The lower incidence of apnoea in very low birth weight babies at our hospital in comparison to Santin RL et al. may be due to less survival and less admission of very low birth weight infants.10

In one study, as many as 25% of all premature infants weigh less than 1800 gm (About 34 weeks gestational age) have at least one apnoeic episode.10

The apnoea of prematurity presents after 1-2 days of life and within the first 7 days. Apnoea presenting within the first 24 hours or after 7 days of age is unlikely to be apnoea of prematurity.11 Most of the apnoea episodes in apnoea of prematurity in our study had occurred on day 2-7, which was similar to various investigators.12-14

In this study, we found that 64.28% of newborns having apnoea had ≥3 episodes. This finding correlates with observations done by Narang A et al, in whose study 37.7% newborns had only 1-2 episodes of apnoea whereas 62.3% had three or more episodes.8

In this study commonest causes of apnoea was infection (51.02%) and apnoea of prematurity (29.59%), rest of the apnoeic episodes were caused by other diseases like birth asphyxia, hyaline membrane diseases, intraventricular haemorrhage, hypoglycaemia, seizures and hypocalcaemia, which were responsible for 5.10%, 2.04%, 3.06%, 5.10%, 2.04% and 2.40% respectively which are very similar to the study done by Narang A et al 22% of infants with bacterial sepsis presented with apnoea in a study on clinical signs of bacterial sepsis in 455 newborn infants studied at four medical centers.8,15

Similarly, in a study, the presenting features of first episode of sepsicaemia was apnoea/bradycardia in 55% of total neonates with sepsis.16 These findings can be correlated with statement that "it is imperative that infection be definitively ruled out or diagnosed and treated in all cases of recurrent apnoea events. This is an important part of clinical practice with premature infants".8

With standard treatment (Treatment of secondary causes, caffeine, bag and mask ventilation and/or nasal CPAP) the survival rate in babies with apnoea of prematurity was 72.4% (p <0.001) as compared to 32% (P<0.001) in apnoea due to infection group. The above finding were close to the study by Narang A et al where survival rate for babies in infection group and apnoea of prematurity were 23.1% and 69.3% respectively.8 Better survival rate in apnoea of prematurity can be explained by the fact that unless severe, recurrent and refractory to therapy, apnoea of prematurity does not alter an infant's prognosis.8,9 As associated problems of intraventricular haemorrhage, BPD and retinopathy of prematurity are critical determining the prognosis for apnoea infants.12,13

Clinical manifestations of hypocalcaemia include apnoea, seizures, jitteriness, increased extensor tone, clonus, hyperreflexia, and stridor. Prognosis of neonatal tetany per se is good, most cases making full recovery without sequelae.18,19 In our study hypocalcaemia was associated with 2.04% of apnoea and survival rate was 100%.

The survival of babies increased with increasing birth weight. The percentage of survival in <1000 gm, 1000-1499 gm, 1500-2499 gm and < 2500 gm was 22.85, 56.41, 63.15 and 100 percent respectively (P <0.001). In a study, 13.3, 73.6, 88.7, 97.5 percent survival in newborn weighing <1000 gm, 1000-1500 gm, 1500-1999 gm and 2000-2500 gm respectively.20 The mortality in <1000 gm in our study was comparable with this study. The high mortality in our study in newborn >1000 gm may be due to associated comorbidity.

Similarly, as gestational age increases the survival rate also increased. The percentage of survival in ≤30 weeks, 31-32 weeks, 33-36 weeks and ≥37 weeks was 27.27, 55.56, 70.57 and 100 percent respectively (P <0.0001). In a study 0, 60, 63.2, 87.1 percent survival was observed in newborn aged <28, 29-30, 31-32, 33-34 weeks respectively.21 The findings in our study are comparable in newborn ≤32 weeks with the above study. A higher mortality in newborn >32 weeks may be due to associated comorbidity.

CONCLUSION
As the maturity increases (increasing gestational age), the frequency of apnoea decreases. The same is true for birth weight. Most of the apnoea occurred on day 2-7. Infection was the most common cause of apnoea; apnoea of prematurity was second most common cause of apnoea in newborn. Other important cause of apnoea in newborn was birth asphyxia, hyaline membrane disease, intraventricular haemorrhage, hypoglycaemia, seizure and hypocalcaemia. Survival rate increased as the gestational age of newborn increased. As birth weight decreases, survival rate of newborn decreased. The survival rate for babies in apnoea of prematurity group (72.41%) was better than babies with infection (32%).

It is concluded that all babies ≥32 weeks gestation need to be closely monitored for apnoea. Apnoeic spells occurring in infants at or near term are always abnormal and are nearly always associated with serious, identifiable causes. Infection is the most common cause of apnoea and carries a poor prognosis. Apnoea of prematurity which constitutes the second most common cause of apnoea does not alter the outcome. So, infection must be ruled out or diagnosed and treated in all cases of recurrent apnoea. As apnoea may be a manifestation of severe sepsis, any delay in diagnosis and initiation of treatment may result in death of the infant.

REFERENCES


