

## TO STUDY THE OUTCOME OF PRETERM INFANTS WITH RESPIRATORY DISTRESS ON CPAP

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### Abstract

**Background:** This study was conducted to study the outcome of preterm infants with respiratory distress on CPAP.

**Material and methods:** The period of gestation was calculated on the basis of first day of LMP and date of delivery and was confirmed by New Ballard Scoring System in case of any disparity. Preterm babies born  $\geq 28$  weeks and  $< 37$  weeks with moderate respiratory distress were started on nasal CPAP soon after birth. Babies were grouped according to gestational age and birth weight. Routine Investigations and Chest Xray was done. Predesigned proforma was used for investigations, monitoring and outcome. Outcome was studied in the form of recovery (weaning off from CPAP), shifting to the mechanical ventilation and mortality. All the results were recorded in Microsoft excel sheet and were analyzed by SPSS software. Chi- square test was used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

**Results:** In the present study, a total of 100 neonates were analyzed. Mean gestational age was found to be 32.13 weeks. Gestational age was 30 weeks, 31 weeks, 32 weeks and 33 weeks in 13 percent, 14 percent, 11 percent and 12 percent of the patients respectively. 57 percent of the neonates of the present study were males while the remaining were females. Mode of delivery among 68 percent of the neonates was cesarean while among the remaining 32 percent of the neonates was vaginal. 35 percent and 33 percent of the neonates had weight between 100 to 1499 gram and between 1500 to 1999 gram respectively. 19 percent of the neonates had weight between 2000 to 2500 gram. Apgar score at 1 minute was more than 7 in 33 percent of the patients, while it was 0 to 3 and between 4 to 5 in 13 percent and 23 percent of the patients respectively.

**Conclusion:** CPAP is an effective way of improving oxygenation of preterm LBW babies with respiratory distress due to various causes. CPAP use can reduce hospital stay and the need for mechanical ventilation.

**Keywords:** neonates, gestational age, preterm birth, CPAP

## Introduction

Preterm birth is defined as birth before 37 completed weeks gestation, and it is estimated that each day, across the world over 41,000 infants are born before this gestational age. The risk of adverse consequences of premature birth declines with increasing gestational age.<sup>1</sup>

Premature birth is a significant cause of infant and child morbidity and mortality. In the United States, the premature birth rate, which had steadily increased during the 1990s and early 2000s, has decreased annually for four years and is now approximately 11.5%. Babies born at 23-24 weeks of gestation in developing countries, stand a chance of 50% survival. Infant girls, on average, have better outcomes than infant boys.<sup>2</sup>

Despite technological advances and efforts of child health experts during the last generation, the extremely premature infant (less than 28 weeks gestation) and extremely low birth weight infant (ELBW) (< 1000 grams) remain at high risk for death and disability with 30–50% mortality and, in survivors, at least 20–50% risk of morbidity.<sup>2</sup>

Respiratory complications of preterm birth are an important cause of infant mortality and morbidity. Respiratory distress syndrome of prematurity is a major cause of morbidity and mortality in preterm infants. Primarily, respiratory distress syndrome is caused by deficiency of pulmonary surfactant. Surfactant is a complex mixture of phospholipids and proteins that reduces alveolar surface tension and maintains alveolar stability. As most alveolar surfactant is produced after about 30-32 weeks' gestation, preterm infants born before then will probably develop respiratory distress syndrome. In addition to short gestation, several other clinical risk factors have been identified.<sup>2-4</sup>

Preterm infants with respiratory distress syndrome present immediately or soon after birth with worsening respiratory distress. The presenting features include tachypnoea (respiratory rate > 60 breaths per minute); intercostal, subcostal, and sternal recession; expiratory grunting; cyanosis; and diminished breath sounds.<sup>5</sup>

If untreated, infants may become fatigued, apnoeic, and hypoxic. They may progress to respiratory failure and will need assisted ventilation. High airway pressures may be required to ventilate the stiff, non-compliant lungs, thereby increasing the risk of acute respiratory complications, such as pneumothorax, pneumomediastinum, and pulmonary interstitial emphysema.<sup>6</sup>

Respiratory disease may result from developmental abnormalities that occur before or after birth. Early developmental malformations include tracheoesophageal fistula, bronchopulmonary sequestration (abnormal mass of pulmonary tissue not connected to the tracheobronchial tree), and bronchogenic cysts (abnormal branching of the tracheobronchial tree). Later in gestation, parenchymal lung malformations, including congenital cystic adenomatoid malformation or pulmonary hypoplasia from congenital diaphragmatic hernia or severe oligohydramnios, may develop. More common respiratory diseases, such as TTN, RDS, neonatal pneumonia, MAS, and persistent pulmonary hypertension of the newborn (PPHN), result from complications during the prenatal to postnatal transition period. Although mature alveoli are present at 36 weeks' gestation, a great deal of alveolar septation and microvascular maturation occur postnatally. The lungs are not fully developed until ages 2 to 5 years. Therefore, developmental lung disease can also occur after birth.<sup>3-6</sup>

Over the past 20-30 years, two major advances in perinatal management—the use of antenatal corticosteroids and exogenous surfactant replacement—have greatly improved clinical outcomes for preterm infants with respiratory distress syndrome.<sup>7</sup>

The simplest and least invasive type of ventilator provides nasal continuous positive airway pressure (CPAP). These ventilators provide a constant end distending pressure to maintain alveolar recruitment, prevent atelectasis, and improve gas exchange.<sup>8</sup>

Positive pressure therapy was first used by Poulton, and Oxan in 1936 who used facemask to treat acute ventilatory insufficiency. Harrison was the first to recognize the use of an increased alveolar pressure during expiration in infants with RDS. He observed that grunt appears in cases of RDS, which increases progressively with increasing severity of disease and abolition of this grunt by use of endotracheal tube led to decrease in partial arterial pressure of oxygen (PaO<sub>2</sub>) and further worsening of the disease. In early 70s, first methods of delivery of CPAP were described for treatment of RDS: through endotracheal tube and by pressure chamber around infant's head. Subsequently facemask and nasopharyngeal tube have been used. Currently, the

most commonly used method is delivery of CPAP by nasal prongs. Infants with mild RDS can often be managed on CPAP alone, without surfactant treatment.<sup>6-9</sup>

CPAP is effective in preventing failure of extubation in preterm infants. Cohort studies have also showed that early use of CPAP in preterm infants with respiratory distress syndrome may reduce the need for endotracheal intubation for positive pressure ventilation.<sup>8-10</sup>

Benefits of CPAP include:

- Non-invasive
- Reduction of respiratory failure,
- Reduced complications,
- Reduced mortality

A concern in the universal application of CPAP to preterm infants is that those with significant respiratory distress syndrome (RDS) will be inadequately supported by CPAP, ultimately require intubation, and receive exogenous surfactant at a later than ideal time. The American Academy of Paediatrics statement concluded that management with early CPAP alone does not confer an increased risk of adverse outcome if treatment with surfactant were delayed or not given.

However, none of the RCTs examined outcomes differentially for infants succeeding or failing on initial CPAP support. Data from several hospital-based cohort studies strongly suggest that CPAP failure is primarily caused by untreated surfactant deficiency, and is associated with adverse outcomes, including increased risk of mortality as well as morbidities, including air leak, bronchopulmonary dysplasia (BPD), and intraventricular haemorrhage (IVH).<sup>9-11</sup>

Reported studies of CPAP failure have involved relatively small cohorts of infants managed at 1 or 2 centres. Examination of the effects of initial CPAP support and CPAP failure within large-scale neonatal databases has been hampered by difficulty in identifying the exact sequence of respiratory management in early life within the reported data. Population-based data on the incidence of, and outcomes after, CPAP failure would give clarity on the magnitude of the problem, both overall and within gestation strata. The confounding of adverse outcomes by factors overrepresented among infants with CPAP failure (e.g. low birth weight, male sex, and incomplete antenatal steroid exposure) could also be dealt with more effectively. Finally, the potential impact of CPAP failure on duration of mechanical respiratory support and/or length of stay could be determined.<sup>12-14</sup>

Hence, under the light of above-mentioned data, the present study was undertaken for assessing whether the introduction of continuous positive airway pressure (CPAP) results in improved respiratory outcomes in preterm neonates <37 weeks of gestation with respiratory distress.

## **Material and methods**

### **Study design**

Hospital Based Prospective Observational study setting: Department of Pediatrics, Government Medical College and Rajindra Hospital, Patiala, located in Patiala, Punjab.

In this study PHOENIX BUBBLE CPAPs were used which are available at Neonatology Section of Rajindra Hospital Patiala.

### **Study population**

Preterm babies with gestational age  $\geq 28$  weeks and <37 weeks delivered in Obstetrics and Gynecology Department and admitted to the Neonatology section of Department of Pediatrics, Government Medical College and Rajindra Hospital, Patiala.

### **Inclusion criteria**

Babies born at  $\geq 28$  weeks and <37 weeks of gestational age having respiratory distress with Downe's score 4 to 7.

### **Exclusion criteria**

1. Babies born <28 weeks of gestation
2. Babies born  $\geq 37$  weeks of gestation
3. Babies with congenital anomalies
  - choanal atresia
  - any mass in the neck
  - tracheo-esophageal fistula
  - adenomatoid malformations of lung
  - congenital diaphragmatic hernia
  - major cardiovascular abnormalities

- central nervous system abnormalities
  - neuro-muscular abnormalities,
4. Babies needing intubation at birth (Downe's score >7),
  5. Recurrent apnea
  6. Shock.

### Methodology

The period of gestation was calculated on the basis of first day of LMP and date of delivery and was confirmed by New Ballard Scoring System in case of any disparity.

Classification of Newborns by weight and Gestational Age:

SGA: Babies with birth weight less than 10<sup>th</sup> percentile of weight for that gestational age.

AGA: Babies with birth weight between 10<sup>th</sup> to 90<sup>th</sup> percentiles of weight for that gestational age.

LGA: Babies with birth weight beyond 90<sup>th</sup> percentile for weight for that gestational age.

Classification of newborns based on gestational age:<sup>[25]</sup> Preterm: less than 37 completed weeks (259 days) Term: 37 to 41 (6/7 weeks) (260-294 days).

Post term: >42 weeks (294 days or more)

### Sample size

A total of 100 eligible preterm infants were included in the study. The sample size was calculated utilizing the proportion (p) of CPAP recovery without mechanical ventilator as 0.78 (Sunil B et al<sup>5</sup>) at 10% margin of error and 95% confidence level taking the finite population as 500 considering the previous year 2016 admission rate of preterm infants with respiratory distress in the Neonatology section of Department of Pediatrics, Government Medical College and Rajindra Hospital, Patiala using the formula:

$n = N * X / [X + (N - 1)]$ , (Finite Population Correction) where,

$X = Z^2 * p * (1-p) / e^2$  OR

$1.96 * 1.96 * p * (1-p) / e^2$

and  $Z_{\alpha/2}$  is 1.96,  $e$  is the margin of error(10%),  $p$  is the sample proportion(0.78), and  $N$  is the population size (500).

Using the formula above, the derived sample size was 63. Considering a non response rate of 10%, the calculated sample size was 70. So, overall, a sample size of 100 was taken for the purpose of the above study.

### Study procedure

Preterm babies born  $\geq 28$  weeks and  $< 37$  weeks with moderate respiratory distress were started on nasal CPAP soon after birth. Babies were grouped according to gestational age and birth weight. Routine Investigations and Chest Xray was done. Predesigned proforma was used for investigations, monitoring and outcome. Outcome was studied in the form of recovery (weaning off from CPAP), shifting to the mechanical ventilation and mortality.

### CPAP failure is defined as

- SpO<sub>2</sub>  $< 88\%$  on FiO<sub>2</sub>  $> 60\%$  for  $> 30$  minutes (with requirement of CPAP  $> 8$  cms of H<sub>2</sub>O)
- Pathologic apnea
- Increasing Retractions

### Statistical analysis

All the results were recorded in Microsoft excel sheet and were analysed by SPSS software. Chi-square test was used for assessment of level of significance. P- value of less than 0.05 was taken as significant.

### Results

**Table 1: Distribution of patients according to gestational age**

Gestational age (weeks)	Number of patients	Percentage of patients
28 weeks	8	8
29 weeks	9	9
30 weeks	13	13
31 weeks	14	14
32 weeks	11	11

33 weeks	12	12
34 weeks	10	10
35 weeks	12	12
36 weeks	11	11
Total	100	100
Mean $\pm$ SD weeks	32.13 $\pm$ 2.48	

In the present study, a total of 100 neonates were analyzed. Mean gestational age was found to be 32.13 weeks. Gestational age was 30 weeks, 31 weeks, 32 weeks and 33 weeks in 13 percent, 14 percent, 11 percent and 12 percent of the patients respectively.



**Table 2: Gender-wise distribution of patients**

<b>Gender</b>	<b>Number of patients</b>	<b>Percentage of patients</b>
Males	57	57
Females	43	43
Total	100	100

57 percent of the neonates of the present study were males while the remaining were females.

**Table 3: Distribution of patients according to mode of delivery**

<b>Mode of delivery</b>	<b>Number of patients</b>	<b>Percentage of patients</b>
Cesarean	68	68
Vaginal	32	32
Total	100	100

Mode of delivery among 68 percent of the neonates was cesarean while among the remaining 32 percent of the neonates was vaginal.

**Table 4: Distribution of patients according to birth weight**

<b>Weight (gm)</b>	<b>Number of patients</b>	<b>Percentage of patients</b>
Less than 1000	7	7
1000-1499	35	35
1500-1999	33	33
2000-2500	19	19
More than 2500	6	6
Total	100	100

35 percent and 33 percent of the neonates had weight between 100 to 1499 gram and between 1500 to 1999 gram respectively. 19 percent of the neonates had weight between 2000 to 2500 gram.

**Table 5: Distribution of patients according to Apgar score at 1 minute**

<b>Apgar score</b>	<b>Number of patients</b>	<b>Percentage of patients</b>
0 to 3	13	13
4 to 5	23	23
6 to 7	31	31
More than 7	33	33
Total	100	100

Apgar score at 1 minute was more than 7 in 33 percent of the patients, while it was 0 to 3 and between 4 to 5 in 13 percent and 23 percent of the patients respectively.

**Table 6: Distribution of patients according to Apgar score at 5 minute**

<b>Apgar score</b>	<b>Number of patients</b>	<b>Percentage of patients</b>
0 to 3	3	3
4 to 5	22	22
6 to 7	26	26
More than 7	49	49
Total	100	100

Apgar score at 5 minutes was more than 7 in 49 percent of the patients while it was less than 6 in 25 percent of the patients.

**Table 7: Distribution of patients according to Outcome**

Outcome		Number of patients	Percentage of patients	p-value
CPAP success	Recovery (weaning off from CPAP)	76	76	0.012
CPAP failure	Recovered after shifting to mechanical ventilation	11	11	
	Mortality	13	13	
	Total	100	100	

Out of 100 patients, CPAP success as characterized by complete recovery was seen in 76 percent of the patients. Among the remaining 24 patients, mortality occurred in 13 patients, while recovery after shifting to mechanical ventilation occurred in 11 percent of the patients.

**Table 8: Distribution of patients on the basis of CPAP outcome in relation to gestation age**

Gestational age (weeks)	Total		CPAP success		CPAP failure				p-value
	n	%	Recovery		Recovery after shifting to ventilation		Mortality		
			n	%	n	%	N	%	
28 weeks	9	100	5	55.6	1	11.1	3	33.3	0.809
29 weeks	9	100	6	66.7	1	11.1	2	22.2	
30 weeks	13	100	8	61.5	2	15.4	3	23.1	
31 weeks	14	100	12	85.8	1	7.1	1	7.1	
32 weeks	11	100	9	81.8	1	9.1	1	9.1	
33 weeks	12	100	9	75	1	8.3	2	16.7	
34 weeks	10	100	8	80	1	10	1	10	
35 weeks	12	100	11	91.7	1	8.3	0	0	
36 weeks	11	100	9	81.8	2	18.2	0	0	
Total	100	100	76	76	11	11	13	13	

5 patients (55.6 percent of the patients) while CPAP failure occurred in 4 patients (44.4 percent of the patients). Out of 9 patients with gestational age of 29 weeks, CPAP success occurred in 6 patients (66.7 percent of the patients) while CPAP failure occurred in 3 patients (33.3 percent of the patients). Out of 13 patients with gestational age of 30 weeks, CPAP success occurred in 8 patients (61.5 percent of the patients) while CPAP failure occurred in 5 patients (38.5 percent of the patients). Out of 12 patients with gestational age of 36 weeks, CPAP success occurred in 9 patients (81.8

percent of the patients) while CPAP failure occurred in 2 patients (18.2 percent of the patients). While correlating the outcome of the patients on CPAP with gestational age, non-significant results were obtained.



**Table 9: Distribution of patients on the basis of CPAP outcome in relation to weight**

Weight (gm)	Total		CPAP success		CPAP failure				p-value
	n	%	Recovery		Recovery after shifting to ventilation		Mortality		
			n	%	n	%	n	%	
Less than 1000	7	100	3	42.8	1	14.4	3	42.8	0.002
1000-1499	35	100	30	85.7	2	5.7	3	8.6	
1500-1999	33	100	25	75.8	4	12.1	4	12.1	
2000-2500	19	100	14	73.7	3	15.8	2	10.5	
>2500	6	100	4	66.6	1	16.7	1	16.7	
Total	100	100	76	76	11	11	13	13	

Out of 7 patients with weight of less than 1000 grams, CPAP success occurred in 3 patients (42.8 percent of the patients) while CPAP failure occurred in 4 patients (57.2 percent of the patients). Out of 35 patients with weight between 1000 gram to 1499 gram, CPAP occurred in 30 patients (85.7 percent of the patients) while CPAP failure occurred in 5 patients (14.3 percent of the patients). Out of 6 patients with weight more than 2500 gram, CPAP success occurred in 4 patients (66.6 percent of the patients) while CPAP failure occurred in 2 patients (33.3 percent of the patients). While correlating the outcome of the patients on CPAP with birth weight, significant results were obtained.

**Table 10: Distribution of patients according to duration of CPAP in recovered cases**

Duration	Number of patients	Percentage of patients
Less than 24 hours (1 day)	3	3.95
1 to 3 days	25	32.89
3 to 5 days	22	28.95
5 to 7 days	19	25.00
More than 7 days	7	9.21
Total	76	100

Duration of CPAP in CPAP success was more than 7 days in 9.21 percent of the patients, while 3 to 5 days and 1 to 3 days in 28.95 percent and 32.89 percent of the patients.

### Discussion

The respiratory management of preterm infants with or at risk for respiratory distress syndrome (RDS) has evolved dramatically in neonatal intensive care units (NICUs) over the past decade. Results from several randomized trials have suggested that early use of continuous positive airway pressure (CPAP) offers potential benefits over endotracheal intubation (ETI) and mechanical ventilation (MV) with or without administration of surfactant for preterm infants. This has led to practice guidelines and recommendations by the American Academy of Pediatrics (AAP) and other agencies to utilize CPAP as the primary mode of respiratory support even in the most premature neonates. A recent meta-analysis suggested that avoiding ETI and MV significantly reduces the incidence of death or bronchopulmonary dysplasia (BPD) in premature infants less than 30 weeks gestational age (GA). Furthermore, the procedure of ETI can result in complications, and primary intubation as well as re-intubation has been recognized as risk factors for death and other morbidities in preterm infants. Despite the AAP guidelines recommending CPAP as the primary mode of respiratory support even in the most premature neonates, frequently, preterm infants are intubated in the labour room (LR) for resuscitative maneuvers and delivery of surfactant.

Continuous positive airway pressure (CPAP), which refers to the application of continuous distending pressure in a spontaneously breathing neonate, increases the functional residual capacity of the lung resulting in better gas exchange. CPAP has been shown to reduce the risk of mortality by 48% and the need for surfactant and mechanical ventilation by about 50%.

B-CPAP differs from conventional CPAP in that in B-CPAP the expiratory limb is placed under water and oscillatory vibrations transmitted into the chest resulting in wave forms similar to those produced by high frequency ventilation CPAP, often thought to be the missing link between supplemental oxygen and mechanical ventilation and is gaining immense popularity in neonatal intensive care units. Being technically simple, in expensive and effective, it has become the primary modality of respiratory support in preterm, very low birth weight neonates.<sup>15,16,17</sup>

Hence; under the light of above-mentioned data, the present study was undertaken for assessing the outcome of preterm Infants with Respiratory Distress on CPAP.

### **Gestational age**

In the present study, mean gestational age was found to be 32.13 weeks. Our results were in concordance with the results obtained by previous studies. In a study conducted by Bhatti A et al, the mean gestation age of the preterm infants was 29.6 weeks. In another study conducted by Koti J et al, the mean age of preterm infants with respiratory distress was 30.98 weeks. Similar results were obtained in the study conducted by Moya FR et al, who reported that mean age of the preterm neonates was 31.6 weeks.<sup>18-20</sup>

### **Gender**

In the present study, 57 percent of the neonates were males while 43 were females. Similar results were reported in the past literature by Bhatti et al and Koti J et al who reported that 71 percent and 55.4 percent of the patients in their respective studies were males.<sup>18,19</sup>

### **Delivery**

In the present study, in 68 percent of the patients, cesarean section was performed. In previous studies conducted by Bhatti et al and Koti J et al, Cesarean sections were performed in 53 percent and 80 percent of the cases.<sup>18,19</sup>

### **CPAP outcome**

In the present study, CPAP success occurred in 76 percent of the patients. CPAP failure occurred in 24 percent of the patients. These 24 patients were shifted to mechanical ventilator, after

which, recovery occurred in 11 patients, while mortality occurred in 13 patients. Our results were in concordance with the results obtained by previous authors who have also reported similar results in their respective studies.

In the study conducted by Bhatti et al, authors reported that ventilation was required in 12 percent of the patients while mortality in 18 percent of the patients. In another study conducted by Dargaville PA et al, authors reported that CPAP success occurred in 75 percent of the patients. Koti J et al, in their study, reported the success rate of CPAP to be 75 percent.

In other uncontrolled studies and in the studies comparing INSURE with ventilation, CPAP failure rate ranged from 14% to 40%.<sup>18,19</sup>

In another study conducted by Mazela J et al, authors reported that CPAP failure occurred in 22 percent of the infants.<sup>21</sup>

In a previous study conducted by Myhre J1 et al, authors reported on the introduction of bubble CPAP (BCPAP), a low-cost method of delivering CPAP appropriate to our setting, by comparing survival-to-discharge before and after the technology were introduced. The inpatient hospital records of all preterm infants (<37 weeks) diagnosed with RDS in the AIC Kijabe Hospital Nursery during two 18-month periods before and after the introduction of BCPAP (46 infants enrolled from 1 November 2007 to 30 April 2009 vs. 72

infants enrolled from 1 November 2009 to 30 April 2011) were reviewed. Differences in survival-to-discharge rates between the two time periods were analyzed. The survival-to-discharge rate was higher in Period 2 (after the introduction of BCPAP) than in Period 1 (pre-BCPAP). Similarly, there were lower referral rates of preterm infants with RDS in Period 2 than Period 1. BCPAP had contributed significantly to favorable outcomes for preterm infants with Respiratory distress.<sup>22</sup>

In another study conducted by Hameed NH et al, authors reported that CPAP outcome was successful in 47.1 percent of the preterm neonates.<sup>23</sup>

### **CPAP outcome and gestational age**

In the present study, while correlating the outcome of CPAP with gestational age, significant results were obtained. Our results were in concordance with the results obtained by Dargaville PA et al who also reported similar findings. In their study, CPAP success among neonates with

25 to 28 weeks of gestation was 57 percent, whereas CPAP success among neonates with 29 to 32 weeks of gestation was 79 percent.<sup>13</sup>

In another retrospective study conducted by Ammari, *et al.* none of the babies with gestation >30 weeks failed CPAP.<sup>10</sup>

However; in a study conducted by Koti J et al, contrasting results have been obtained. The authors reported mean gestational age of 30.9 weeks among patients with CPAP success while mean gestational age of 31.1 weeks among patients with CPAP failure. They reported non-significant correlation of CPAP outcome with gestational age.<sup>18</sup>

In another study conducted by Raschetti R et al, authors reported that gestational age of preterm infants with CPAP success was 32.9 weeks and was significantly higher in comparison to the preterm infants with CPAP failure in which gestational age was found to be 29.3 weeks.<sup>24</sup>

**Similar results were reported in the study conducted by Hameed NN et al**, where authors reported that mean gestational age of the pre-term neonates in which CPAP was successful was 34 weeks, and was significantly higher in comparison to the pre-term neonates in whom CPAP was successful and was found to be 31.7 weeks.<sup>23</sup>

### **CPAP outcome and birth weight**

In the present study, mean birth weight of pre-term neonates with CPAP success was found to be significantly higher in comparison to the mean birth weight of the preterm neonates with CPAP failure. Our results were in concordance with the results obtained by Hameed NN et al, who also reported similar findings in their study. They reported that mean birth weight among preterm neonates with CPAP success was 2083 grams and was significantly higher than preterm neonates with CPAP failure where it was found to be 1660 gram.<sup>23</sup>

In a retrospective study by Ammari, *et al.*, the failure rate of Bubble CPAP was 24% in babies'  $\leq 1250\text{g}$  and 50% in babies  $\leq 750\text{g}$ .<sup>10</sup>

Raschetti R et al who reported that mean birth weight of the preterm infants with CPAP success was 1807 gm and was significantly higher than that of infants with CPAP failure in which mean birth weight was found to be 1327 gm.<sup>24</sup>

However; contrasting results were reported in the study conducted by Koti J et al where authors have reported non-significant difference while comparing the mean birth weight among preterm neonates with CPAP success and CPAP failure.<sup>18</sup>

## CPAP OUTCOME AND MODE OF DELIVERY

While correlating the CPAP outcome with mode of delivery, non-significant results were obtained. Our results were in concordance with the results obtained by Koti J et al and Raschetti R who also reported similar findings in their respective studies.<sup>18,24</sup>

In the study conducted by Koti J et al, authors reported that among preterm infants with CPAP success and CPAP failure, mode of delivery in 81 percent and 79 percent of the preterm infants was caesarean section (p-value > 0.05).<sup>18</sup>

In another study conducted by Raschetti R et al, mode of delivery was Caesarean section in 79 percent and 82 percent of the preterm infants with CPAP success and CPAP failure respectively.<sup>24</sup>

Similar results were obtained in the study conducted by Hameed et al where authors non-significant correlation between the CPAP outcome and mode of delivery.<sup>23</sup>

### CPAP and cause of RD

In our study, babies born with RDS and congenital pneumonia showed better CPAP outcome, 81% and 84% respectively, as compared to babies with sepsis (76.2%), MAS (72%) and pulmonary haemorrhage (40%). Higher mortality rate also shown in babies with sepsis (14.3%), MAS (16%) and pulmonary haemorrhage (40%). However, on correlating statistically, the results were found to be non-significant.

In a case-control study by Boo, *et al.*, of the 97 preterm babies (gestation <37 weeks) with RDS on ventilator CPAP or Bubble CPAP, 38% failed CPAP and required ventilator support. Babies were given ventilator support for hypoxia (SpO<sub>2</sub> <90%) on FiO<sub>2</sub> ≥90%. Severe RDS on the chest X-ray was an important predictor of CPAP failure. Pneumothorax and septicemia was higher in the CPAP failures. Although septicaemia predicted CPAP failure in our study too, pneumothorax was seen in 2 babies in the success group.<sup>25</sup>

Similar results were obtained in the study conducted by Koti J et al where authors reported that sepsis was found to be present in 36 percent of the preterm neonates with CPAP failure, while it was found to be present in 4.8 percent of the preterm neonates with CPAP success. Their results also showed that sepsis was a strong risk factor for CPPA failure.<sup>18</sup>

Sepsis or serious infection within the first four weeks of life kills greater than 1 million newborns globally every year. Maternal factors contributing to the risk of neonatal sepsis include prematurity, low birth weight, rectovaginal colonization with group B streptococcus (GBS), prolonged rupture of membranes, maternal intrapartum fever, and Chorioamnionitis. Factors in the postnatal period associated with an increased risk of sepsis or septic shock include male gender, birth weight <1000 grams, hypogammaglobulinemia, intravenous alimentation, central venous catheters, use of steroids or drugs that decrease gastric acid acidity, and prolonged duration of mechanical ventilation.<sup>26</sup>

However; Pillai MS reported contrasting findings in their study. They reported that sepsis did not turn out to be a significant factor in the multivariate analysis. They explained it by stating that the small number of infants with sepsis could have resulted in such contradictory results.<sup>27</sup>

#### **CPAP outcome and weight for gestational age**

Among patients of the SGA group, CPAP success occurred in 55.2 percent of the patients while CPAP failure occurred in 44.8 percent of the patients. While correlating the CPAP outcome among patients divided on the basis of weight for gestational age, it was observed that patients of the SGA group were associated with significantly higher incidence of CPAP failure. Our results were in concordance with the results obtained by Gortner L et al, who also reported similar findings in their respective study. They reported that mortality was significantly higher in SGA-infants in comparison to AGA infants on CPAP. In their study, 4 out of 6 SGA infants with reported mortality, the cause of death was found to be respiratory failure.<sup>28</sup>

In preterm SGA-infants, increased incidence of early neonatal complications e. g. rate and severity of respiratory distress syndrome, cerebral lesions, e. g. intraventricular hemorrhage and periventricular leucomalacia have been described in the past literature.

#### **CPAP outcome and APGAR score**

In the present study, we observed that significantly higher proportion of CPAP failure was seen among neonates with APGAR score of less than 6 at 1 minute. However; at 5 minutes, no significant correlation was observed while correlating the CPAP outcome with APGAR score. Our results were in concordance with the results obtained Mazela J who also reported similar findings in their respective studies. They reported significantly higher mortality among neonates with APGAR score of less than 7.<sup>21</sup>

Similar results were obtained in the study conducted by Raschetti R et al, who also reported non-significant correlation between CPAP outcome and APGAR score at 5 minutes.<sup>24</sup>

A systematic review from the Cochrane collaboration on the effect of continuous distending pressure (which includes CPAP and continuous negative pressure, a technique which is no longer used in newborns) compared to oxygen has shown that CPAP in preterm infants with respiratory distress significantly reduces treatment failure. In addition, there was a reduction in the need for additional mechanical ventilation. With regards to reduction in mortality, the review included two unpowered trials (199 patients in total) from the US to demonstrate the superiority of CPAP. Even though the review showed that continuous distending pressure (CPAP and/or continuous negative pressure) reduces mortality in preterms with respiratory distress, the six trials included in this analysis were all conducted in high-income countries.

Another recent review which examined the effect of CPAP in LMICs identified only one high quality randomised controlled trial (RCT) comparing CPAP to oxygen. The study was a multi-centre trial conducted in 12 South American centres. The study showed that the CPAP group required lower rates of additional mechanical ventilation compared to the group receiving oxygen only.<sup>29,30</sup>

Dargaville PA et al explored the outcomes of CPAP failure in Australian and New Zealand Neonatal Network data from 2007 to 2013. Data from inborn preterm infants managed on CPAP from the outset were analyzed in 2 gestational age ranges (25-28 and 29-32 completed weeks). Outcomes after CPAP failure (need for intubation <72 hours) were compared with those succeeding on CPAP using adjusted odds ratios (AORs). Within the cohort of 19 103 infants, 11 684 were initially managed on CPAP. Failure of CPAP occurred in 863 (43%) of 1989 infants commencing on CPAP at 25-28 weeks' gestation and 2061 (21%) of 9695 at 29-32 weeks. CPAP failure was associated with a substantially higher rate of pneumothorax, and a heightened risk of death, bronchopulmonary dysplasia (BPD) and other morbidities compared with those managed successfully on CPAP. The incidence of death or BPD was also increased. The CPAP failure group had longer durations of respiratory support and hospitalization. CPAP failure in preterm infants is associated with increased risk of mortality and major morbidities, including BPD. Strategies to promote successful CPAP application should be pursued vigorously.<sup>13</sup>

Despite advances in neonatal intensive care, respiratory distress syndrome remains the single, most important cause of mortality among preterm neonates. More than 50% of neonates born before 31 weeks of gestation develop respiratory distress syndrome, which is due to deficiency



of pulmonary surfactant production. Despite the advent of effective prevention and management strategies such as antenatal steroids, exogenous surfactant therapy and newer ventilatory techniques, nearly 40% very-preterm neonates either die or develop bronchopulmonary dysplasia by 36 weeks postconceptional age.

CPAP increases the functional residual capacity of the lung resulting in better gas exchange. CPAP has been shown to reduce the risk of mortality by 48%<sup>6</sup> and the need for surfactant and mechanical ventilation by about 50%. In addition, the use of CPAP has been found to decrease hospital stay and need for referrals and up-transfers to tertiary units. Altogether, these benefits have made CPAP the standard of care in managing sick preterm neonates with respiratory distress in high-income countries.<sup>31</sup>

In another study conducted by Sunil B et al, authors assessed whether the introduction of continuous positive airway pressure (CPAP) results in improved respiratory outcomes in preterm neonates  $\leq 36$  weeks of gestation in KIMS hospital. All babies born  $\leq 36$  weeks of gestational age with respiratory distress were included in this study. Seventy-seven premature newborn babies with  $\leq 36$  weeks of gestation were included in the study and were put on nasal CPAP. The incidence of CPAP failure was 22.1% (95% CI 14.27- 32.54%). The proportion of neonates who required surfactant was 16.9% (10.14-26.77%) and the proportion of children who met with mortality was 6.5% (10.14-26.77%) in this study. Early institution of CPAP in the management of RDS in premature neonates can significantly reduce the need for mechanical ventilation (MV) and surfactant therapy.<sup>32</sup>

## Conclusion

CPAP is an effective way of improving oxygenation of preterm LBW babies with respiratory distress due to various causes. CPAP use can reduce hospital stay and the need for mechanical ventilation.

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