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# Role and Success Rates of Continuous Positive Airway Pressure in Treatment of Respiratory Distress Syndrome in Preterm Babies

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**ABSTRACT** 

The incidence of Respiratory Distress Syndrome (RDS) had a wide geographical variation worldwide. The management of RDS involves a variety of measures that should be initiated promptly upon birth aiming to minimizing the severity and averting any worsening and its related complications. Mechanical ventilation and early or prophylactic use of surfactants have been the standard of management of neonates with respiratory distress syndrome. Since 1980s, observational studies showed that in many centers, the continuous positive airway pressure (CPAP) considered as the primary method of ventilatory assistance had a lower rate of bronchopulmonary dysplasia and provided less ventilation assistance to the neonates. The lack of more solid evidence is one of the reasons why this mode of care has remained restricted to a few perinatal centers. However, in our country few studies assessed the role of CPAP and its success rates in treatment of RDS. Therefore, we conducted this study aiming to shed light on the role of CPAP as a primary treatment for RDS in premature babies. We concluded that CPAP was good success rate. Nonetheless, some factors contributed to failure of CPAP including extreme low birth weight, lower gestational age, severe RDS and longer duration of CPAP treatment. Sepsis and apnea are the main complications of RDS patients on CPAP which may significantly affect the CPAP treatment outcome.

Keywords: continuous positive airway pressure, respiratory distress syndrome, surfactant

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## 1. INTRODUCTION

The incidence of RDS had a wide geographical variation worldwide. The outcome is contingent upon the gestational age of the infant and whether the mother underwent prenatal glucocorticoid therapy. The overall incidence of RDS in premature infants born prior to 30 weeks of gestation is roughly 60%. In premature infants who born after 34 weeks of gestational, the incidence rate is roughly 5%, while respiratory distress syndrome (RDS) is uncommon in full-term infants (1-3). Pathophysiological aspect of RDS based primarily on the surfactant deficit, which involves decreased production and secretion. Elevated surface tension and pulmonary surfactant deficiency cause lungs to collapse and fail to reach functional residual capacity. As gestation advances, type II alveolar cells synthesize and store more phospholipids. Surfactants are released into the alveoli to reduce surface tension and prevent microscopic air spaces from collapsing during end expiration. Immaturity may lead to insufficient production of surfactant that will not meet the postnatal demands. Surfactant is abundant in fetal lung homogenates by the 20th week of gestation, although it is not readily available on the lung surface until later. It is found in amniotic fluid between 28 and 32 weeks. After 35 weeks, pulmonary surfactant reaches mature levels. Rare genetic illnesses may cause respiratory discomfort. A severe and often fatal hereditary respiratory disorder is connected to mutations in surfactant protein B and C genes and ABCA3 (4). There are different risk factors can contribute to RDS such as prematurity, male sex infant, family susceptibility, cesarean sections, birth asphyxia, race (Caucasian), infants born for mothers with diabetes and chorioamnionitis. Some other factors may have associated with lower risk (5). Clinically, the primary symptoms are poor lung function and low oxygen in blood. Symptoms of RDS typically appear shortly after birth, usually within the first few minutes or hours. If not addressed, respiratory distress syndrome (RDS) deteriorates gradually within the initial 48 hours after birth. Expiratory grunting occurs. During inspiration, the rib cage, which is highly flexible, is pulled inward due to the high pressure within the chest. This causes retractions in the intercostal, subxiphoid, and subcostal areas. The purpose of this is to expand the lungs, which are not very flexible. Cyanosis caused by the presence of right-to-left shunting of blood in both the intra- and extra-pulmonary regions. During a physical examination, breath sounds are reduced, and newborns may appear pale with weakened peripheral pulses. During the initial 24 to 48 hours, there is frequently a decrease in urine production and the occurrence of swelling in the extremities, (6,7). Diagnosis mainly based on history, clinical examination, chest X-ray, in which 4 grades can be identified grade I- IV and laboratory investigations; blood gases, hyponatremia, and blood culture (8-12). Before the use of surfactant, uncomplicated RDS would usually proceeded for a duration of 48 to 72 hours. Subsequently, there was an enhancement in respiratory function due to an augmented production of naturally occurring surfactant, leading to the remission. A noticeable increase in urine production usually occurred before the improvement in lung function. There are many complications may arise due to RDS itself or as a result of treatment; acute such as alveolar rupture, pneumothorax, penumopericardium, pneumomediastinum, intestinal or cutaneous, emphysema and air embolism. Chronic complications include bronchopulmonary dysplasia, retinopathy of prematurity and some other complications. Treatment with exogenous surfactant significantly alters the natural progression of RDS, resulting in a remarkable improvement in lung function, remission of symptoms, and a shorter clinical course (13). The management of RDS involves a variety of measures that should be initiated promptly upon birth aiming to minimizing the severity and averting any worsening and its related complications. Treatment of RDS involves delivery room management, surfactant treatment, ventilator support and general supportive care as the major components of treatment (14). Ventilator support specifically CPAP and positive pressure ventilation, is highly successful in reducing mortality rates in infants with RDS. The extensive utilization of prenatal corticosteroids and prophylactic surfactant has rendered these treatments potentially unnecessary (15). CPAP maintains positive pressure during both inhalation and expiration, which leads to a rise in functional residual capacity (FRC) and improves the ability of the lungs to expand and contract. It also reduces airway resistance in infants with unstable lung mechanics. This results in an increased volume change for each unit of pressure change, leading to a larger tidal volume for a given pressure change. As a result, the effort required for breathing is reduced and minute ventilation is stabilized. CPAP elevates the average pressure in the airway, which in turn enhances the connection between ventilation and perfusion, and may potentially decrease the amount of oxygen needed. CPAP is also recommended as an early intervention, along with surfactant administration, for very low birth weight infants who are at risk of developing RDS (15,16). Following the administration of surfactant, it is typically possible to decrease the ventilator settings. In order to mitigate the chances of developing chronic lung disease, it is advisable to utilize the most minimal ventilator settings feasible. Proper humidification of the inspired gases is crucial for newborns who are undergoing mechanical ventilation (15,17). The utilization of continuous positive airway pressure (CPAP) has demonstrated to enhance clinical outcomes in the management of RDS, even in infants who do not undergo surfactant therapy (18). However, some contraindications are found that prohibit the use of CPAP these are upper airway anomalies, severe cardiovascular instability and imminent cardiac arrest, unstable respiratory drive with frequent episodes of apnea leading to desaturation and/or bradycardia, ventilatory failure, untreated congenital diaphragmatic hernia (19,20). The objective of this study is to assess the role of CPAP in management of RDS in preterm Iraqi babies.

#### 2. METHODOLOGY

This prospective study was carried out on premature neonates who admitted to the nursery care unit (NCU) in AL-Imamein kadhimein medical city, Baghdad, Iraq, from first of January 2013 to first of November 2013.

The total number of neonates who received CPAP in NCU during the period of study was 121 neonates .

We enrolled 68 neonates in this study who diagnosed as RDS according to the fallowing inclusion criteria:

- 1) Premature neonate (GA 28 36 week)
- 2) Sign of respiratory distress (grunting , subcostal & intercostal recessions , respiratory rate > 60 cycle per minute , cyanosis ).
- 3) Transcutaneous PO2 < 85% on room air
- 4) Radiological finding RDS include mild, moderate, sever RDS.

## **Exclusion criteria:**

We exclude the neonate patient with one or more of the following:

- 1) Transient tachypnea of newborn
- 2) Birth asphyxia
- 3) Congenital heart disease
- 4) Congenital pneumonia ( which clinically suspect on the presence of maternal leaking liquor > 18 hour ,maternal fever , maternal leukocytosis , gastric fluid aspiration , ear swap , complete blood picture , c-reactive protein and positive blood culture )
- 5) Those with major congenital anomalies.

## **Study protocol and Procedure**

The application of CPAP in our N.I.C.U. was according to the American Association for Respiratory care clinical practice guidelines.

Eligible babies were started on bubble CPAP with bi-nasal prongs, PEEP was started at 5 cm of H2O and adjusted to minimize chest retraction. FiO2 was adjusted to maintain SPO2 between 85% and 95%. The preterm babies with RDS and CPAP therapy were divided into two groups, those with successful CPAP therapy ( CPAP success ) & those with failed CPAP therapy ( CPAP failure). Achieving success with CPAP is determined by the improvement of respiratory distress and the effective weaning of the baby from CPAP within a one-week timeframe. The weaning criteria were the absence of respiratory distress, shown by minimum or no retraction and a respiratory rate between 30 and 60 per minute. Additionally, the patient's SPO2 needed to be above 90%, the FiO2 below 30%, and the PEEP below 5 cm H2O (21). When the CPAP failed, the mechanical ventilator was started (21) when the infant:

- 1. Continued to have hypoxia and SpO2 below 85%, while receiving a high fraction of inspired oxygen (FiO2) above 70% and positive end-expiratory pressure (PEEP) more than 7 cm H2O.
- 2. Experienced significant inward retraction on positive end-expiratory pressure (PEEP) above 7cm H2O.

- 3. Experienced extended apneas lasting more than 20 seconds or repeated apneas (more than two episodes/ 24 hours) with bradycardia, necessitating the use of bag and mask ventilation.
- 4. Death occurring during the course of CPAP treatment.

The studied Neonates' variables include sex, mode of delivery, gestational age at labor (determined using the mother's last menstrual period, early pregnancy ultrasound scan, or New Ballard score), birth weight, chest X-ray findings, and age of starting CPAP, duration of CPAP and PEEP at 20 minute of CPAP.

Other data recorded during management of RDS with CPAP are pneumothorax, sepsis (by blood culture), apnea and mortality.

The severity of RDS was classified based on radiological findings in three grades (62);

- 1. Mild (slight lung granularity)
- 2. Moderate: when the lung showed generalized granularity with air bronchogram and an intact cardiac border.
- 3. Severe: white out lung and obliteration of cardiac borders.

Chest x-ray was taken to all neonates on CPAP to follow up any radiological change & respiratory complications (e.g pneumothorax).

## Statistical analysis:

Data were collected using a pre-constructed data collection sheet to gather relevant information. The collected data were processed using the statistical package for social sciences (SPSS) program version 21, Microsoft Excel program version 2019. Scale variables were denoted by their mean value and standard deviation (SD), whereas nominal variables were expressed as frequencies and percentages. Infant who had successful CPAP were compared to those with failed CPAP regarding their clinical data. Students' t test used to compare means according to CPAP success \ failure for scale variables while Chi-square test used to compare categorical variables between both groups (Success and failure). In all statistical procedures, analysis and tests, level of significance (P. value) of less than or equal 0.05 was considered to be significant difference or correlation.

## 3. RESULTS

A total number of 68 neonates who received CPAP in NCU during the study period and met the inclusion criteria were enrolled in the study. The baseline characteristics of neonates are shown in (Table 1). The median age of starting CPAP was 5 (range: 1-11) hours of life. The CPAP treatment lasted for a median duration of 38 hours, with a range of 8 to 130 hours. Out of the 68 neonate who received CPAP, 37(54%) had success and 31 (46%) had failed. As shown in (Figure 1). We assess the relationship between CPAP success and failure from one side against the characteristics of the neonates from the other side; results of these assessment are demonstrated in (Table 2) where the success rate was significantly associated with gestational age where it increases with the increase in gestational age; the success rate was 32% in neonates with gestational age of 28 – 30 weeks, 60.9% in those with gestational age of > 30 - 33 weeks and the highest rate (75%) in those with gestational of > 33 – 36 weeks, (P. value = 0.011, significant). Similarly, a direct positive association was found between success of CPAP and larger birth weight (BW), neonates with larger BW had the higher success rates; in those with BW of ≤ 1000 (ELBW) gram the success rate was only 16.7% compared to 57.7% in those with BW of 1001 – 1500 gram (VLBW) and the highest success rate of 79.1% was reported in neonates whose BW was 1501 – 2500 gram (LBW), (P. value <0.001, high significant). In male CPAP success was 23(54.8%) and it was not significantly different than that in females which was 14(53.8%), (P. value >0.05, not significant). Regarding mode of delivery CPAP success was 20(48.8%) in neonates delivered by cesarean section (C/S) while in NVD CPAP success was 17 (63%), however, the difference was statistically insignificant (P. value > 0.05, not significant). The success of CPAP according to the chest X-ray findings; mild, moderate and severe were 20(74.1%), 15(60%), 2(12.5%), respectively, with highly significant association reflecting the higher success rate in mild cases, (P. value <0.001, highly significant) (Table 3). The duration of CPAP (mean ±SD) was 34.7±14.34 hours in successful group and 78.1±33.6 hour in failure group, (P. value < 0.001, highly significant). Neither age of starting CPAP nor the PEEP showed significant difference and association with the success/failure of CPAP, in both comparisons, P. value >0.05, not significant, (Table 4).

As complications that occur during treatment of RDS with CPAP, pneumothorax developed in 6 babies, 4 (66.7%) of them from CPAP success group while 2(33.3%) of them from CPAP failure group and this statistically not significant (P. value >0.05, not significant). Also apnea (<20 seconds and <2 episodes within 24 hours) develop in 17 baby, 2(11.8%) of them from CPAP success group while 15(88.2%) of them from CPAP failure group and this statistically was significant the (P. value <0.001, highly significant). Sepsis developed in 16 baby, 4(25%) of them from CPAP success group while 12(75%) of them from CPAP failure group (P. value =0.006, significant). The mortality was significantly lower in CPAP success group compared to failure group, 10.3% vs. 89.7%, respectively, (P. value <0.001, highly significant). All findings regarding complications are shown I (**Table 5**).

Table 1. Baseline neonate's characteristics of the studied group (N=68)

Variable		NO.	%	
Gestational age(week)	28-30	25	36.8	
	>30- 33	23	33.8	
	>33-36	20	29.4	
Birth weight (grams)	≤1000	18	26.5	
	1001- 1500	26	38.2	
	1501-2500	24	35.3	
Mode of delivery	NVD	27	39.7	
	C/S	41	60.3	
Gender	Male	26	38.2	
	Female	42	61.8	
CXR finding	Mild	27	39.7	
	Moderate	25	36.8	
	Severe (white out lung)	16	23.5	
Total		67	100.0	

Birth weight (BW) extreme low BW ≤1000 g, Very low BW 1001- 1500g, Low BW 1501-2500g NVD: normal vaginal delivery, C/S: cesarean section. CXR: chest x-ray

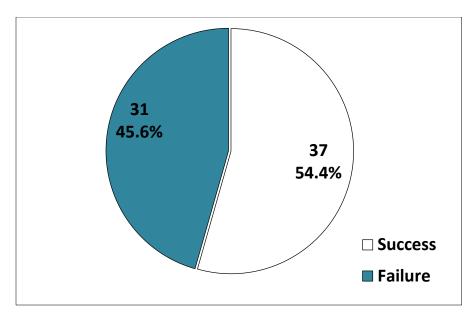


Figure 1. Success and failure rate of Response to CPAP

Table 2. Relationship between CPAP success/Failure and Neonate's characteristics

Variable		CPAP success (n=37)		CPAP failure (n=31)		Divolve
		No.	%	No.	%	P. value
Gestational age (week)	28- 30	8	32.0	17	68.0	0.011
	>30- 33	14	60.9	9	39.1	
	>33- 36	15	75.0	5	25.0	
Birth weight (g)	≤1000	3	16.7	15	83.3	<0.001
	1001- 1500	15	57.7	11	42.3	
	1501-2500	19	79.1	5	20.9	
Gender	Male	23	54.8	19	45.2	0.954
	Female	14	53.8	12	46.2	
Mode of delivery	C/S	20	48.8	21	51.2	0.251
	NVD	17	63.0	10	37.0	

Table 3. Relationship of CPAP success and Failure with chest x-ray findings

Variable	CPAP succ	ess (n=37)	CPAP failure (n=31)		
CXR finding	No.	%	No.	%	
Sever (white out lung)	2	12.5	14	87.5	
Moderate	15	60	10	40	
Mild	20	74.1	7	25.9	

P. value < 0.001

Table 4. Relationship of CPAP success and Failure with CPAP duration, age of starting CPAP and PEEP

Variable	CPAP success (n=37)		CPAP failure (n=31)		P. value
	Mean	SD	Mean	SD	
CPAP duration (hour)	34.7	14.3	78.1	33.6	<0.001
Age of starting CPAP (hour)	6.07	1.6	6.8	1.3	0.834
PEEP (cm H2O)	4.8	0.7	5.1	0.4	0.377

Table 5. Distribution of immediate complications that occur during the course of RDS management with CPAP and their influence on CPAP outcome

Complication	CPAP success		CPAP failure		Total	P.
	No.	%	No.	%	TOLAI	value
Pneumothorax	4	66.7	2	33.3	6	0.528
Apnea	2	11.8	15	88.2	17	<0.001
Sepsis	4	25.0	12	75	16	0.006
Mortality	3	10.3	26	89.7	29	<0.001

## 4. DISCUSSION

This study conducted to evaluate the effectiveness of CPAP therapy in the treatment of RDS in premature neonate and the association between the success of CPAP with the characteristics variables of the neonates. Hence we included 68 neonates who had RDS, admitted to NICU and treated with CPAP. In our study, CPAP was successful in 37 RDS neonates, giving a rate of 54.4%, this rate was lower than that reported by Koti et al. (21) who found a success rate of 75% among neonates treated with CPAP, this difference between our study an Koti et als' study could be attributed to some factors like the studied population, medical facilities, where in our study ELBW were 27% and in Koti, et al. ELBW were 17.9%. Also in our study the mean duration of CPAP treatment was 38 hours and in Koti, et al. was 23.5 hour which can explain the longer duration of CPAP may lead to increase complications of CPAP. Also in Koti, et al. (21) the INSURE (intubate, surfactant, extubate) approach was done in 55.4% of the neonates while it was not perfumed in our study which is not done. Also in URS, et al. (22) the CPAP successful in 80% and CPAP failure in 20% this may be explained by in our study ELBW were 27% and in URS, et al. study was 8% and also in our study gestational age 28-30 week were 37% and in URS, et al. were 18%. In our study we found that the gestational age have a significant effect on CPAP, and CPAP failure was observed in lower gestational age and this agree with Ammari ,et al.(23) and with URS ,et al .(22) but different from Koti, et al .(21), which show that the gestational age not effect on CPAP this may be due to different in the gestational age of neonate in our study (28 -36 week ) and in Koti, et al. (28 – 34 week ). In this study we found that the body weight have a significant effect on CPAP and CPAP failure was observed in (ELBW) and this agree with Ammari, et al.(23) and URS, et al.(22) but different from Koti, et al.(21) such different may be due to in Koti, et al . 55.3% of the neonate were VLBW, 17.9% were ELBW and in our study 38% were VLBW, 27% were ELBW. In our study the sex was not important factor in failure of CPAP and this agree with Koti, et al. (21), Ammari, et al. (23) and URS, et al. (22). In a study conducted by Sandri, et al. (24) it had been demonstrated that respiratory support was more needed in male babies with respiratory distress syndrome. The variation in the findings among studies may be due to total number of neonates in our study were 68, while in Sandri, et al. was 230 so this different in number may affect the results.

We found that the mode of delivery was not significant in CPAP failure and this agreed with Koti, et al. and we may need more neonates to evaluated this factor. According to the chest x ray findings, Koti, et al. (21), Ammari et al. 64), Schimd R, et al.(25) and URS, et al.(22) showed bubble CPAP was effective in treating mild to moderated RDS. From other point of view, the presence of severe RDS on a chest X-ray, was found to be a significant predictor of CPAP failure, however, this contradicts the findings of Boo, et al. (26) study which show CPAP effectiveness in mild RDS while in moderate and severe RDS CPAP was ineffective. In our study CPAP duration in treatment of RDS was significant factor for CPAP failure and this different from Koti, et al. (21) may be due to the main CPAP duration were 38 hours in our center and in Koti, et al the main CPAP duration were 23.5 hour and long duration of CPAP may lead to increase complications of CPAP. In the present study, the CPAP success or failure was not significantly associated with the neonate's age at which the CPAP was initiated and this finding was consistent with that documented by Koti, et al. (21), this may be due to the mean age of start CPAP was high (5 hours), this longer time may be related to the limited number of CPAP machine just three in NICU and there was some delay of application of CPAP because of this limitation. In our study we found that the PEEP is not significant factor for CPAP failure and this agree with Koti, et al. (21). this may be due to the major complications of high PEEP was pneumothorax and in our study the pneumothorax was not have a significant value. Apnea was significant factor for CPAP failure and this different from Koti, et al. (21), this may be due to limited resource to identify the cause of apnea in our center. In Koti, et al. (21) and our study the pneumothorax were not significant factor for CPAP failure may be due to close monitoring of neonates and daily CXR so early diagnosis and management, also availability of cardiothoracic team in our center. while Boo, et.al.(26) study show that the pneumothorax was important factor for CPAP failure. We found that occurrence of septicemia when treating RDS was significantly contributed to the failure of CPAP treatment and this agreed with Koti, et al. and Boo, et.al. because one of the most important complication of CPAP was infection, also some part of CPAP was disposable like nasal prong just use for one patient but in our center we wash this part and reuse in another

patient that well lead to greater risk of infection. In our study the clinical outcome for infants who succeed CPAP are excellent with low mortality and this agree with Koti, et al. (21).

## 5. CONCLUSIONS

The risks of CPAP failure in preterm neonate with RDS is higher in those with: extreme low birth weight, lower gestational age (28-30 week GA), severe RDS (whiteout) on the chest X-ray, and longer duration of CPAP treatment. Sepsis and apnea are the main complications of RDS patients on CPAP which may significantly affect the CPAP failure. The mortality was lower in CPAP successful group. Gender, mode of delivery, age at which CPAP applied, PEEP of CPAP and pneumothorax as a complication that occur during course of treatment had no effect on CPAP outcome. We recommend using CPAP a primary care for treatment of neonates with RDS to decrease mortality and all effort should be paid to avoid sepsis and to determine the cause of apnea to improve CPAP outcome. Mechanical ventilation should be available in NICU beside CPAP because failure of CPAP in treatment of RDS may need mechanical ventilation specially in neonate with extreme low birth weight, lower gestational age (28-30 week GA), whiteout lung on X-ray. Further studies are highly suggested for further more precise assessment particularly larger sample size and multiple center studies.

### **Ethical Approval:**

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association, 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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