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ORIGINAL ARTICLE

Continuous positive airway pressure failure in the management of neonatal respiratory distress in a resource-limited setting: a prospective observational study

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ABSTRACT

Aim To determine the frequency of, and identify predictors for, continuous positive airway pressure (CPAP) failure in neonates of varying gestational ages in a resource-limited setting, where CPAP is often used beyond the preterm population.

Methods A prospective observational study included 119 neonates initiated on CPAP within 24 hours of birth for respiratory distress. We collected demographic, clinical, and perinatal data. CPAP failure was defined by persistent hypoxia or severe respiratory distress despite maximal settings, necessitating mechanical ventilation. Univariate and multivariable binary logistic regression analyses identify predictors of CPAP failure.

Results The CPAP failure rate was 33.6%. Univariate analysis identified lower gestational age (≤ 30 weeks), lower birth weight (≤1200 g), female sex, vaginal delivery, and a 5-minute Apgar score < 7 as significant predictors. However, in the multivariable model, only a 5-minute Apgar score **< 7** remained an independent predictor (Adjusted Odds Ratio AOR 5.315; p=0.006). Antenatal corticosteroid, age at CPAP initiation, and initial fraction of inspired oxygen $(FiO)_2$ were not significant.

Neonates with birth weight <1200g had shorter duration of successful CPAP use as revealed by Kaplan-Meier survival analysis (p<0.001)

Conclusion This study confirms that CPAP failure is a frequent and serious problem in our resource-limited NICU. A low 5-minute Apgar score is a significant predictor of failure. To save more newborns, we must focus on improving neonatal resuscitation and establish clear guidelines for respiratory care in our specific context.

Keywords: Apgar score, continuous positive airway pressure, developing countries, respiratory distress syndrome, newborn.

INTRODUCTION

Continuous positive airway pressure (CPAP) is the main non-invasive respiratory support for neonates with respiratory distress (1). Its primary mechanism is to maintain functional residual capacity by keeping alveoli open and reducing the work of breathing, which will improve oxygenation (2). CPAP effectively supports neonates across a range of respiratory conditions, including transient tachypnoea of the newborn (TTN), respiratory distress syndrome (RDS), congenital pneumonia, meconium aspiration, and apnoea of prematurity (3). TTN typically presents with tachypnoea and signs of respiratory distress within the first two hours of life in term and late-preterm neonates (4). It results from the delayed clearance of foetal lung fluid, leading to increased work of breathing. CPAP is often useful in these cases by providing respiratory support (5). Prematurity-related complications are considered a major factor in global under-5-year mortality. A significant number of these preterm births occurs in low- and middle-income countries (LMICs), where limited healthcare resources often lead to higher risks and poor outcomes (6).

In preterm neonates, RDS presents one of the most immediate and serious challenges caused by insufficient surfactant (7), which leads to the formation of hyaline membranes in the lungs and impairs gas exchange. During the first few days of life, the condition intensifies respiratory effort, leads to hypoxia, respiratory failure, and even death if not managed properly (8). The management strategy for RDS includes early CPAP use, surfactant replacement, and mechanical ventilation if needed (9). However, access to these therapies remains limited

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in many LMICs. The 2022 European Consensus Guidelines on managing respiratory distress syndrome advocate for starting CPAP as early as possible to improve outcomes in all neonates at risk of RDS (10), as it can reduce the need for surfactant replacement and mechanical ventilation (11). Even though implementing CPAP therapy in LMICs is feasible, a concerning 20–40% of neonates fail to respond to CPAP therapy (12). It is noted that CPAP failure has been associated with an increased risk of death and morbidities such as pneumothorax and bronchopulmonary dysplasia (13). Known predictors of CPAP therapy failure include lower gestational age, severe respiratory distress syndrome, high fraction of inspired oxygen (FiO_2), and delay in initiation of CPAP therapy (14).

Given the region's constrained resources, equipment, and healthcare infrastructure, this study aimed to assess the frequency of CPAP failure in neonates with respiratory distress, identify associated risk factors, and improve neonatal care in similar healthcare settings.

PATIENTS AND METHODS

Patients and study design

This prospective observational cohort study was done at Al-Batool Teaching Hospital (ATH), Mosul, Iraq, to assess CPAP failure rates and associated risk factors in neonates with respiratory distress admitted to the Neonatal Intensive Care Unit (NICU). Every year, about 1,500 neonates are admitted to the ATH neonatal unit. Care was provided by a consultant paediatrician and a general paediatrics resident, supported by a nurse-to-patient ratio of 1:5 to 40 neonates simultaneously.

The NICU is equipped to deliver nasal CPAP to up to 14 neonates concurrently, using SLE1000 devices with nasal prongs. Mechanical ventilation is limited to three neonates, and surfactant therapy was not administered due to limited availability.

Eligible newborns included those who received CPAP support in the first 24 hours of life due to clinical signs of respiratory distress, as one or more of the following: tachypnoea (>60 breaths/min), grunting, subcostal or intercostal retractions, central cyanosis, or apnoea.

A total of 119 neonates meeting the inclusion criteria were enrolled in this study from May to December 2024.

Enrolled neonates received routine care, including monitoring of oxygen saturation, heart rate, random blood sugar, and temperature, with respiratory distress assessment.

Every patient received empirical intravenous antibiotics and fluid therapy upon admission. Caffeine citrate was given for apnoea of prematurity.

Exclusion criteria were neonates with multiple congenital anomalies, sepsis, or those with CPAP discontinued for two hours or more. The study was approved by the Ethics Committee of the College of Medicine, University of Mosul.

Methods

Paediatric residents collected data using the New Ballard Score for gestational age (15), the Silverman Andersen Score (SAS) for respiratory distress assessment (16), and completed standardized forms. The measured parameters were gestational age, birth weight, sex, mode of delivery, use of antenatal steroids, 5-minute Apgar score, time of CPAP initiation, initial fraction of inspired oxygen (FiO_2), and type of respiratory distress. CPAP success or failure was the primary outcome.

Chest x-rays were done if symptoms persisted more than six hours, or earlier if pneumothorax or congenital anomalies were suspected. The CPAP began with a Peak End Expiratory Pressure (PEEP) of 5 cmH_2O, with an increase of 1 cmH_2O every 2-4 hours to a maximum limit of 8 cmH_2O. The initial FiO_2 was obtained from the digital oxygen blender integrated into the SLE1000 device (SLE Ltd., United Kingdom). Fraction of inspired oxygen (FiO_2) was then titrated in 5% increments every 30 minutes, up to 60%, and guided by continuous pulse oximetry to maintain Peripheral Oxygen Saturation (SpO_2) ≥ 90%.

The CPAP failure was defined by persistent hypoxia (SpO_2 <90%) despite maximal oxygen on CPAP, or ongoing severe respiratory distress (Silverman Anderson Score; SAS>6), or recurrent prolonged apnoeic episodes despite maximal PEEP. These neonates were put on mechanical ventilation, according to ventilator availability and clinical assessment. The CPAP was weaned when neonates were stable for 12-24 hours on current PEEP, showing no or mild respiratory distress (SAS <3), FiO_2 <27%, and SpO_2 consistently >95%. Nasal oxygen at 0.5 –2 L/min is then used to maintain adequate oxygenation after successful weaning from CPAP.

Statistical analysis

The Shapiro-Wilk test was used to assess the distribution of the continuous variable. The study population's features were described by median and interquartile range (IQR) for continuous variables, frequencies and percentages for categorical variables, presented in a table. The $\chi 2$ test and Fisher's exact test were used to evaluate associations between categorical variables, while the Mann-Whitney U test was used to assess associations for continuous variables.

Univariate binary logistic regression identified factors associated with CPAP failure, and then multivariable logistic regression was done to identify independent predictors of CPAP failure. Kaplan-Meier survival analysis was finally used to compare survival time to CPAP failure. P-value <0.05 is considered statistically significant.

RESULTS

This prospective observational study included 119 neonates. Shapiro-Wilk tests confirmed non-normal distribution for gestational age, birth weight, and CPAP duration ($p<0.05$).

Baseline characteristics stratified by CPAP success and failure reveal that male infants comprised 77 (64.7%) of the cohort. The median gestational age was 33 weeks, with 31 (26.1%) babies ≤30 weeks. Median birth weight was 1800g, and 25 (21%) were <1200g. Seventy (58.8%) neonates were delivered by Cesarean Section (CS) and 49 (41.2%) by normal vaginal delivery (NVD). Respiratory distress etiologies included 85 (71.4%) with RDS and 28 (23.5%) with TTN. Thirty-one (26.1%) neonates had an Apgar score <7. The median CPAP duration was three days. Ninety-six (80.7%) mothers had not received antenatal steroids. Maternal comorbidities included 10 with premature rupture of membranes, seven with hypertension, and two with diabetes. The prevalence of CPAP failure was 33.6% (Table 1).

Factors associated with CPAP failure demonstrate no statistically significant association between sex and CPAP outcome ($p=0.067$). However, a significant association was found with the mode of delivery ($p=0.003$): among CPAP failures, 60% were by NVD and 40% by CS, whereas in the no-failure group,

Table 1. Baseline statistics for the study population

Characteristic	Total 119 (100%)	CPAP success (N=79)	CPAP failure (N=40)	p
Sex (No; %)				
Male	77 (64.7)	56 (70.9)	21 (52.5%)	0.067
Female	42 (35.3)	23 (29.1)	19 (47.5%)	
Median gestational age (IQR)	33 (30-36)	34 (32-36)	29 (27-32)	< 0.001m*
Gestational age group (No; %)				
≤ 30 weeks	31 (26.1)	5 (6.3)	26 (65)	< 0.001*
> 30 weeks	88 (73.9)	74 (93.7)	14 (35)	
Median birth weight (IQR)	1800 (1250-2500)	2300 (1700-2600)	1100 (907.5-1475)	< 0.001m*
		No (%) of patients		
Birth weight group				
< 1200	25 (21)	3 (3.8)	22 (55)	<0.001*
≥ 1200	94 (79)	76 (96.2)	18 (45)	
Mode of delivery				
NVD	49 (41.2)	25 (31.6)	24 (60)	0.003*
CS	70 (58.8)	54 (68.4)	16 (40)	
APGAR score at 5 minutes				
<7	31 (26.1)	12 (15.2)	19 (47.5)	<0.001*
≥7	88 (73.9)	67 (84.8)	21 (52.5)	
Type of respiratory distress				
RDS	85 (71.4)	47 (59.5)	38 (95)	<0.001*
TTN	28 (23.5)	28 (35.4)	0	
MAS	5 (4.2)	4 (5.1)	1 (2.5)	
Pneumonia	1 (0.8)	0	1 (2.5)	
Maternal use of antenatal steroids				
Receive	23 (19.3)	18 (22.8)	5 (12.5)	0.180
Not receive	96 (80.7)	61 (77.2)	35 (87.5)	
PROM				
YES	10 (8.4)	8 (10.1)	2 (5)	0.341
NO	109 (91.6)	71 (89.9)	38 (95)	
Age at initiation of CPAP				
≤ 6 h	104 (87.4)	69 (87.3)	35 (87.5)	0.614
> 6 h	15 (12.6)	10 (12.7)	5 (12.5)	
Initial FiO_2				
≤35%	40 (33.6)	31 (39.2)	9 (22.5)	0.051
>35%	79 (66.4)	48 (60.8)	31 (77.5)	
Median duration of CPAP (IQR)	3 (2-4)	3 (2-4)	3 (2-4.75)	0.337[m]

* statistically significant; m Mann Whitney test

CS, Cesarean Section; FiO2, Fraction of Inspired Oxygen; IQR, Interquartile Range; MAS, Meconium Aspiration Syndrome; NVD, Normal Vaginal Delivery; PROM, Premature Rupture of Membrane; RDS, Respiratory Distress Syndrome; TTN, Transient Tachypnoea of Newborn;

31.6% were NVD and 68.4% CS. The type of respiratory distress was also significantly associated with CPAP outcome (p<0.001); RDS was common in both groups, but constituted 95% of the failure group (Table 2).

Mann-Whitney U tests revealed significant differences in both gestational age and birth weight between the CPAP failure and success groups (both p<0.001). Failure group neonates had a median gestational age of 29 weeks versus 34 weeks for the success group. Also, median birth weight in the failure group was 1100 grams compared to 2300 grams in the success group. CPAP duration showed no significant difference between the two groups (p =0.337).

Initial univariate analysis identified several factors significantly associated with CPAP failure. These included female sex (OR=2.203; p=0.049), gestational age of ≤30 weeks (OR=27.486; p<0.001), birth weight ≤1200 grams (OR=30.663; p<0.001), NVD (OR=3.240, p=0.004), and 5-minute Apgar score <7 (OR=5.052; p<0.001) (Table 2).

Following multivariate adjustment, only the 5-minute Apgar score remained an independent predictor of CPAP failure; neonates with a score <7 had significantly increased odds (adjusted odds ratio AOR=5.315, p=0.006).

There is an adequate model fit (p=0.892) in the Hosmer-Lemeshow test. Nagelkerke's R-squared was 0.599, with a significant overall association (p<0.001) with 84.9% classification accuracy.

Kaplan-Meier survival analysis demonstrated a statistically significant difference in successful CPAP support duration between neonates with birth weights <1200g and those ≥ 1200g (p<0.001). The survival curves showed a significantly higher CPAP failure rate in lower birth weight neonates, indicating a poorer prognosis for sustained non-invasive respiratory support in this vulnerable subgroup (Figure 1).

The forest plot based on multivariate analysis showed that a 5-minute Apgar score below 7 was the only factor independently linked to CPAP failure, as its confidence interval (CI) remained entirely to the right of the line of no effect, while the CI for other risk factors (lower gestational age, lower birth weight, female sex, and mode of delivery) crossed the line of no effect (AOR=1). This indicates that in our final adjusted model, their association with CPAP failure was not statistically significant (Figure 2).

Table 2. Factors associated with Continuous Positive Airway Pressure (CPAP) failure

Baseline characteristic	CPAP failure	CPAP no failure	Univariate regression		Multivariate regression	
			OR (95%CI)	p	AOR (95%CI)	p
	No (%) of patients					
Sex						
Male	21 (27.3)	56 (72.7)	2.203 (1.002-4.843)	0.049*	1.685 (0.521-5.447)	0.383
Female	19 (45.2)	23 (54.8)				
Gestational age						
≤30 weeks	26 (83.9)	5 (16.1)	27.486 (9.17-83.786)	<0.001*	8.340 (0.968-71.822)	0.054
> 0 weeks	14 (15.9)	74 (84.1)				
Birth weight						
≤ 1200 g	22 (88.0)	3 (12.0)	30.663 (8.345-114.884)	<0.001*	7.451 (0.645-86.091)	0.108
> 1200 g	18 (19.1)	76 (80.9)				
Mode of delivery						
NVD	24 (49.0)	25 (51.0)	3.240 (1.469-7.144)	0.004*	3.141 (0.993-9.933)	0.051
CS	16 (22.9)	54 (77.1)				
5-minute APGAR score						
<7	19 (61.3)	12 (38.7)	5.052 (2.110-12.97)	<0.001*	5.315 (1.606-17.594)	0.006*
≥7	21 (23.9)	67 (76.1)				
Antenatal corticosteroids						
receive	5 (21.7)	18 (78.3)	2.066 (0.705-6.049)	0.186	4.223 (0.760-23.458)	0.100
not receive	35 (41.0)	61 (59.0)				
Age at initiation of CPAP						
≤6 h	35 (33.7)	69 (66.3)	1.014 (0.322-3.198)	0.980		
>6 h	5 (33.3)	10 (66.7)				
Initial FiO_2						
≤35%	9 (22.5)	31 (77.5)	0.450 (0.189-1.072)	0.710		
>35%	31 (39.2)	48 (60.8)				

*statistically significant;
AOR, Adjusted Odds Ratio; CI, Confidence Interval; CS, Cesarean Section; FiO2, Fraction of inspired oxygen; NVD, Normal Vaginal Delivery; OR, Odds Ratio;
For statistical purposes, all values presented in the table are calculated and compared against the 'Second Row' (The Reference Category).

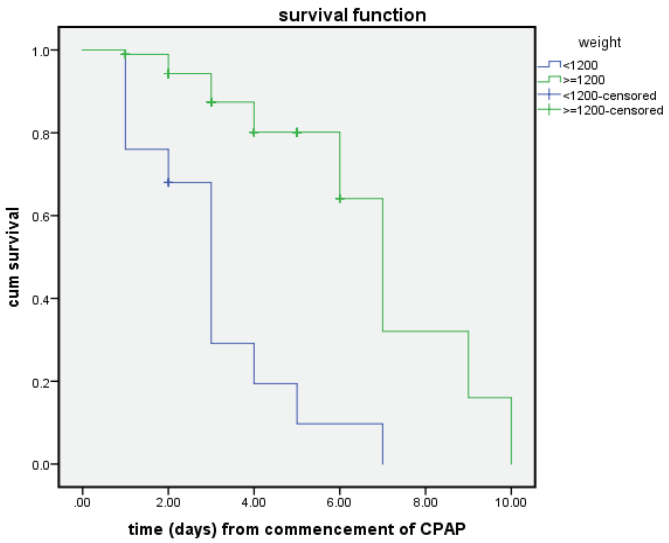

Figure 1. Kaplan-Meier survival curve of Continuous Positive Airway Pressure (CPAP) success in neonates with respiratory distress stratified by birth weight

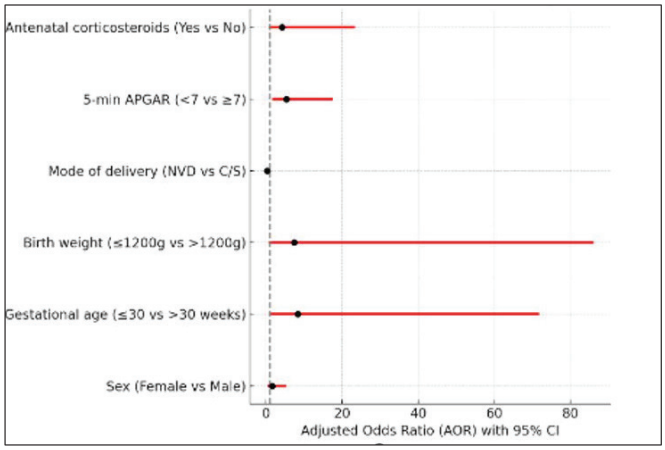

Figure 2. Forest plot of Adjusted Odds Ratio (AORs) for Continuous Positive Airway Pressure (CPAP) failure based on the multivariate analysis
The vertical dashed line at AOR = 1 indicates no effect; points to the right of the line suggest increased odds of CPAP failure; points to the left suggest protective factors (lower odds); only a 5-min APGAR score <7 showed a statistically significant association (CI does not cross 1)

DISCUSSION

This prospective observational study conducted in Mosul, Iraq, revealed a 33.6% CPAP failure rate, aligning with reports from other LMICs like Indonesia and Iran (17,18). The failure rate in our study is more than that in high-income countries, such as 21% in Australia and New Zealand (19), and 28% in Poland (20), due to available resources, including antenatal steroids, prophylactic CPAP use, and surfactant therapy which highlights a big gap in low-resource settings and the urgent need for improving the neonatal care.

In the univariate model, there is a higher risk of CPAP failure with lower gestational age (≤30 weeks), which agrees with studies that identified gestational age (≤30 weeks) as a significant early predictor of CPAP failure in neonates with respiratory distress (8,18). This finding highlights the susceptibility of premature lungs and the challenges in providing adequate respiratory support with CPAP alone.

Another strong predictor of CPAP failure was a very low birth weight of ≤1200 g. This is consistent with some other studies (8,17,20). Our Kaplan-Meier analysis provided further evidence for this, showing significantly shorter successful CPAP support duration in neonates <1200g. This reinforces the clinical reality that infants with very low birth weight often need more aggressive respiratory support and face a higher CPAP failure risk.

Our univariate analysis also indicated that female sex was associated with a higher incidence of CPAP failure. In contrast, some authors did not find sex as a significant risk factor (8,13). The reason for this discrepancy in our population is unclear, and future studies are needed to explore whether specific biological or physiological mechanisms might explain this association.

NVD was a significant risk factor for CPAP failure in univariate analysis, consistent with the higher observed failure prevalence in this group. However, this association lost statistical significance in the multivariate model. This suggests that the increased risk associated with NVD was not independent, but was largely explained by its correlation with other, more strong predictors of CPAP failure. This borderline result needs further investigation in larger, multicentre studies to clarify the independent role of delivery mode.

The lack of a significant association between antenatal corticosteroid administration on CPAP failure is concerning, given the well-established role of steroids in reducing the severity of RDS. However, the low antenatal steroid use rate in our cohort (19.3%) and Abdallah et al.'s cohort (25.5%) (8), likely limited the power to detect a significant effect and probably contributed to the higher overall CPAP failure rate and poorer outcomes.

In the multivariate model, only a 5-minute Apgar score <7 remained an independent predictor of CPAP failure. This suggests that the immediate postnatal condition, reflected by the Apgar score, is a critical determinant of CPAP success in our resource-limited context, potentially mediating prematurity and low birth weight effects. Gulczyńska et al. (20) also identified a low 5-minute Apgar score as a risk factor for CPAP failure. However, Abdallah et al. (8) found no such link, possibly due to differences in neonatal resuscitation practices or the availability of early respiratory supportive care. This finding underscores the importance of early resuscitation and stabilization to increase the likelihood of successful non-invasive ventilation.

On the other hand, the age at CPAP initiation and the initial FiO_2 were not significant predictors of failure, consistent with some other studies (8). This finding is in contrast with reports, which found initial FiO_2 as a significant CPAP failure risk factor (14,21). This discrepancy may be due to differences in CPAP protocols, the timing of the 'initial' FiO_2 assessment, and the resource availability, which could influence the thresholds for defining CPAP failure and escalating care between our resource-limited setting and those of the compared studies.

Limitations of this study include a single-centre study, which limits its generalizability to other settings; the relatively small sample size may have been underpowered to detect weaker independent associations for other significant factors, in addition to a lack of surfactant and limited access to mechanical ventilation, which affect the observed CPAP failure rate and the factors associated with it.

In conclusion, CPAP failure in LMICs is still a serious problem, with a low 5-minute Apgar score as a significant independent predictor, highlighting the importance of immediate postnatal stabilization and care. Further effort is needed to improve delivery room management and provide healthcare equipment to enhance neonatal outcomes.

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TRANSPARENCY DECLARATION

Conflicts of interest: None to declare.

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