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Use of Lung Ultrasound and Thoracic Fluid Content for Prediction of non-Invasive Ventilation Failure in Neonates

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ABSTRACT

Purpose: Non-invasive ventilation (NIV) is commonly employed as the primary respiratory support modality in neonates with respiratory distress due to its lower risk of complications compared to invasive mechanical ventilation. This research aimed to compared between lung ultrasound and thoracic fluid content (TFC) as early predictive tools for identifying NIV failure in premature neonates.

Methods: This prospective cohort observational research involved 60 preterm neonates aged from 28 to 35 weeks old, both sexes, suffered from respiratory distress syndrome which were candidate to NIV. Patients were categorized into two equal groups: Group I: Nasal CPAP (continuous positive airway pressure) and gestational age (GA) 28-35 W and group II: nasal intermittent mandatory ventilation and GA 28-35 W.

Results: Lung ultrasound score (LUS) strongly associated with TFC in the case of NIV failure. The LUS score demonstrated a marked increase in the group that experienced failure opposed to the group that succeeded. Additionally, TFC measured via EC in NIPPV was significantly elevated in the failure group opposed to the success group.

Conclusions: LUS score correlates well with TFC, in the case of NIV failure and it may serve as a valuable tool for tracking changes in lung aeration during the early application of NIV in premature infants.

Keywords: *Lung Ultrasound, Thoracic Fluid Content, Non-Invasive Ventilation Failure, Neonates*

1. INTRODUCTION

Non-invasive ventilation (NIV) is widely used as the primary respiratory support strategy in neonates with respiratory distress due to its lower risk of complications compared to invasive mechanical ventilation [1]. However, considerable number of neonates fail NIV and need escalation to intubation and mechanical support. Early prediction of NIV failure is crucial to prevent delayed intubation, reduce morbidity, and improve clinical outcomes [2].

NIV failure refers to the inability of non-invasive support to maintain adequate gas exchange or relieve respiratory distress, ultimately necessitating escalation to invasive mechanical ventilation [3]. Failure may result from factors such as severe lung disease, inadequate respiratory drive, airway obstruction, or delayed intervention. Timely recognition of high-risk neonates of NIV failure is essential to avoid complications related to delayed intubation, such as hypoxia, acidosis, or increased morbidity and mortality [4].

Currently, there is a pressing need for reliable predictors of non-invasive ventilation (NIV) failure to prevent infants from experiencing respiratory fatigue due to ineffective breathing efforts. Given the frequent discrepancy between clinical assessment and chest radiograph findings in evaluating the severity of neonatal respiratory distress syndrome (RDS), conventional radiology often provides limited diagnostic value. In contrast, the persistence of a 'white lung' pattern on lung ultrasound has been shown to correlate strongly with clinical signs of respiratory distress in preterm neonates [5].

Thoracic Fluid Content (TFC), a non-invasive parameter measured by electrical cardiometry, reflects the amount of fluid in the thoracic cavity, including pulmonary congestion. Elevated TFC levels may indicate excessive lung water, impaired fluid clearance, or evolving pulmonary pathology—all of which are potential contributors to respiratory compromise. Increased TFC may serve as an early predictor of NIV failure in neonates by identifying those with worsening lung fluid status before overt clinical deterioration occurs.

The lung ultrasound score (LUS) has garnered recognition for its utility in diagnostics, with investigations showcasing its reliability in detecting neonatal RDS and various other pulmonary conditions in newborns. [6]

This research aimed to compared between lung ultrasound and TFC as early predictive tools for identifying NIV failure in premature neonates.

2. METHODS

This observational prospectively designed cohort investigation was conducted on 60 preterm neonates, aged 28 to 35 weeks, of both sexes, Identified as having respiratory distress syndrome (RDS) and selected for NIV. The research took place between March 2021 and June 2023, Ethical approval was obtained from the Ethical Committee of Tanta University Hospitals, Tanta, Egypt (approval code: 34645/4/21), and the study adhered to the Declaration of Helsinki guidelines. Informed written consent was obtained from the neonates' relatives before participation.

The study excluded neonates who were intubated for resuscitation and across over among different NIV strategies, neonates with major congenital anomalies, neonates with complex congenital heart disease, congenital anomalies in the lungs or airways and other causes of respiratory distress.

Randomization:

Simple randomization was executed using a computer-generated random number table, with allocations securely enclosed in sealed envelopes. Patients were divided into two equal groups 30 participiants in each group: Nasal CPAP group (group I) and NIMV group (group II) with GA 28-35 W. All newborns were moved to the NICU within 1 hour of delivery. For those placed in the CPAP group, treatment began at a pressure of 6 cmH_2O, with PEEP increased in 1 cmH_2O increments to a maximum of 8 cmH_2O over 2 hours. If SpO_2 levels (90–95%) could not be sustained, FiO_2 was adjusted up to 0.4. Neonates allocated to the NIPPV group, using the NEUMOVENT GRAPHNET TS device (TECME S.A. Company, Atlanta, USA), started with a PEEP of 6 cmH_2O, a PIP of 15 cmH_2O, a maximum FiO_2 of 0.60, and SpO_2 targets set at 90–95%. The duration of inspiration spanned from 0.4 to 0.45 seconds, with an initial rate of 25 breaths per minute.

In all cases Surfactant (Curosurf; 200 mg/kg) was dispensed in the event of elevated. FiO2 greater than 0.40 to a target SpO2 of 90–94%, by the INSURE (intubation, surfactant, extubation) technique. [7] Caffeine citrate was given to infants experiencing apnea, Participants received an initial loading dose of 20 mg/kg, with subsequent maintenance dosing at 5–10 mg/kg daily. Endotracheal intubation and surfactant administration were initiated as indicators of NIV failure, without attempting alternative non-invasive ventilation methods. This intervention was warranted when the Downes score persistently remained at 7 or above. [8]

Laboratory evaluations included a complete blood count (CBC), C-reactive protein (CRP) levels, liver and kidney function tests (LFTs), random blood glucose (RBS), arterial blood gas (ABG) analysis, and serum electrolyte measurement. Additionally, imaging studies such as chest X-rays, echocardiography, and transcranial ultrasound were conducted to support clinical diagnosis and management.

Lung ultrasound:

LUS was conducted within the first three hours of life and repeated either following NIV failure in the failed group or after 24 hours in the successful group. A single neonatologist performed the scans using a Siemens Acuson X300 ultrasound system (Siemens Health Care GmbH, Erlangen, Germany) equipped with a 13-5 MHz transducer. The procedure adhered to standardized vertical planes over the anterior and lateral surfaces of the thorax for both lungs, with the infant positioned supine and calm. LUS scoring involved dividing each lung into three zones (upper anterior, lower anterior, and lateral) and assigning a score of 0 to 3 per zone, resulting in a total score range of 0 to 18.

The ultrasound transducer was aligned perpendicularly toward the ribs and continuing laterally away from the midline for lung assessment. Lung aeration was graded based on distinct imaging patterns. A score of 0 (A-pattern) corresponded to normal lung sliding with visible horizontal A-lines or fewer than three vertical B-lines. A score of 1 (B-pattern) indicated the presence of three or more well-defined, spaced B-lines. A score of 2 (severe B-pattern) was assigned when numerous coalescent B-lines appeared densely packed, often accompanied by subpleural consolidations. A score of 3 signified extensive lung consolidation, displaying a tissue-like echogenic pattern accompanied by static or dynamic air bronchogram.

Electrical Cardiometry:

TFC was measured in all two groups (60 neonates) diagnosed with respiratory distress syndrome (RDS) within the first three hours of life, and these measurements were repeated after either NIV failure in failed group or after 24 hours in successful

group by one experienced neonatologist using EC, ICON (Osypka Medical GmbH, Berlin, Germany).

After cleaning the neonate's skin with alcohol, four electrocardiographic electrodes were applied to the forehead, left cervical region, left mid-axillary line at the xiphoid level, and left thigh to establish connection with the ICON device [9] Continuous monitoring was performed for 30 seconds, during which the infant was quiet and supine; the mean of the maximum and minimum values was subsequently recorded.

Sample Size Calculation:

Using G*Power software version 3.1.9.2 (Universität Kiel, Germany), the sample size was calculated based on data obtained from a pilot study comprising 5 neonates per group. The results showed a mean TFC of 32.9 ± 7.2 in Group I and 27.2 ± 7.7 in Group II during the first 24 hours of life. Sample size estimation was performed using an effect size of 0.764, a 95% confidence interval, 80% statistical power, and an equal group allocation ratio (1:1). To compensate for possible attrition, two extra participants were included in each group, resulting in a final sample of 30 neonates per group.

Statistical analysis

Data analysis was conducted using SPSS software version 27 (IBM©, Chicago, IL, USA), employing a rigorous statistical approach. The normality of data distribution was evaluated through the Shapiro-Wilks test and visualized via histograms. Parametric continuous variables were expressed as mean ± standard deviation (SD) and subjected to ANOVA, supplemented by Tukey's post hoc analysis for multiple comparisons. Non-parametric continuous data were represented as medians with interquartile ranges (IQR) and evaluated using the Kruskal-Walli's test, followed by pairwise comparisons with the Mann-Whitney U test. Categorical data were summarized in frequencies and percentages and analyzed using the Chi-square test. Pearson's correlation coefficient was used to examine relationships between variables. Sensitivity, specificity, PPV, and NPV were computed to evaluate diagnostic performance. Statistical significance was defined as a two-sided p-value < 0.05.

3. RESULTS

An aggregate of 71 subjects was assessed for eligibility, with 11 disqualified from inclusion. The remaining 60 entrants were equitably apportioned into two cohorts, each comprising 30 individuals. All enrolled participants were meticulously observed and integrated into the statistical examination

Patients' characteristics, risk factors, APGAR score at 1st and 5th minutes, vital signs, grading of RDS by X ray, and Downes' no meaningful difference in scores was observed between the two groups. Mode of delivery was significantly different between the two studied groups. Table 1

Table (1): Patients characteristics, risk factors, APGAR score at 1st and 5th minutes, vital signs, grading of RDS by X ray, and Downes' score in all the studied groups

		Group I (n = 30)	Group II (n = 30)	P
Gestational age (weeks)		29.9 ± 2.31	31.27 ± 3.34	0.070
Sex	**Male**	17 (56.67%)	16 (53.33%)	0.795
	Female	13 (43.33%)	14 (46.67%)	
Delivery mode	**Vaginal delivery**	5 (16.67%)	13 (43.33%)	**0.024***
	C-section	25 (83.33%)	17 (56.67%)	
Weight (kg)		1.9 ± 0.23	1.79 ± 0.3	0.107
Recumbenant length(cm)		43.17 ± 2.61	42.87 ± 3.04	0.683
Antenatal steroids		27 (90%)	24 (80%)	0.278
DM		4 (13.33%)	3 (10%)	0.688
HTN		5 (16.67%)	4 (13.33%)	0.718
PROM		5 (16.67%)	4 (13.33%)	0.718
APGAR	**1st**	4.0 (4.0 – 5.0)	4.0 (3.0 – 4.0)	0.086
	5th	9(8 - 9)	8.5(8 - 9)	0.667

Downes score	5.5 (5 - 6)	5 (5 - 6)	0.246
X ray RDS grades	3 (2 - 3)	3 (2 - 3)	0.160

Data are represented using mean ± SD or frequency (%) or median (IQR). * Significant p value <0.05, CS: cesarean section, DM: diabetes mellitus, HTN: hypertension, PROM: Premature rupture of membrane.

FIO2 required, rate and time of failure of failed cases and time of NIV in succeeded cases were insignificantly different among group I and group II. Table 2

Table (2): Fraction of inspired O2 and mean airway pressure in (all groups), success and failure cases as regard time of failure and NIV duration among the groups under investigation

		Group I (n = 30)	Group II (n = 30)	P
FIO_2%		39.93 ± 16.85	36.27 ± 12.81	0.347
FIO_2%	**Succeeded**	39.93 ± 16.85	36.27 ± 12.81	0.347
	Failed	42.67 ± 17.65	35.17 ± 11.4	0.055
NIV	**Success**	16 (53.33%)	20 (66.67%)	0.378
	Failed	14 (46.67%)	10 (33.33%)	
Time of failure (hrs.)		9.79 ± 5.71	11.1 ± 5.02	0.566
Duration of NIV (days)		6.79 ± 3.19	8.3 ± 3.74	0.298

Data are represented as mean ± SD or frequency (%), NIV: Non-invasive ventilation. * Significant p value <0.05.

As regards ultrasound findings; consolidative patterns featuring air bronchograms, along with pleural line irregularities and absence of spared areas were present in all patients 60 (100 %), while absent A lines (white out lungs) were found in 25 (83.33%) cases of group I and 24 (80%) cases of group II. Pleural effusion was observed in 7 (23.33%) cases of group I and 5 (16.67%) cases of group II. Interstitial syndrome was observed in 6 (20%) and 5 (16.67%) cases of group I and group II respectively, Notably, the double lung point sign was not observed in any of the patients as all patients were RDS cases. LUS (1st and 2nd), were insignificantly variant between Group I and Group IITable 3

Table (3): Lung US findings and LUS scores in all investigated groups

		Group I (n = 30)	Group II (n = 30)	p
Consolidation with air bronchogram		30 (100.0%)	30 (100.0%)	--
White out lungs		25 (83.33%)	24 (80%)	0.739
Absence of spared areas		30(100.0%)	30(100.0%)	--
Pleural line abnormalities		30(100.0%)	30(100.0%)	--
Pleural effusion		7 (23.33%)	5 (16.67%)	0.519
Double lungs point sign		0(0.0%)	0(0.0%)	--
Interstitial syndrome		6 (20%)	5 (16.67%)	0.739
LUS score	**1st**	9.3 ± 1.99	10.13 ± 2.97	0.206
	2nd	10.67 ± 4.03	10.7 ± 3.25	0.972

Data are represented using mean ± SD or frequency (%). * Significant p value <0.05.

In group I, LUS (2nd) a meaningful difference existed between the two investegated groups which was significantly elevated in failed group versus succeeded group. In group II, LUS (1st, 2nd), was a significant difference between the two investigated groups which was significantly elevated in failed group versus to succeeded group. Table 4

Table (4): Comparison between succeeded and failed cases of NIV in group I and group II as regard LUS score.

		Succeeded	Failed	P
Group I				
LUS score	**1st**	8.75 ± 1.48	9.93 ± 2.34	0.106
	2nd	7.81 ± 1.33	13.93 ± 3.56	**<0.001***
Group II				
LUS score	**1st**	8.7 ± 1.59	13 ± 3.06	<0.001*
	2nd	9 ± 1.49	14.1 ± 3.18	**<0.001***

Data are represented as mean ± SD. * Significant p value <0.05.

TFC (1st) was insignificant Variation between the groups and TFC (2nd) was a significant higher in group I than group II. Table 5

Table (5): Thoracic fluid content in all studied groups

TFC (1 KOhm^{-1})	**Group I(n = 30)**	**Group II (n = 30)**	**P**
1st (within 3 hours)	30.4 ± 7	30.83 ± 6.99	0.811
2nd (within 24 hours)	33.2 ± 7.38	28.43 ± 7.96	**0.019***

Data are represented as mean ± SD. * Significant p value <0.05

As regard group II, (1st initially and 2nd prior to failure in failed group and after 24 hours in succeeded group), there was a meaningful positive association between LUS and TFC. Table 6

Table (6): Correlation between LUS and Diverse metrics in all groups

	LUS							
	Group I				**Group II**			
	1st		**2nd**		**1st**		**2nd**	
	r	**P**	**r**	**P**	**r**	**P**	**r**	**P**
TFC	0.301	0.10	0.197	0.296	0.387	**0.03***	0.482	**0.007***

r: Pearson coefficient, * Statistically significant at p ≤ 0.05.

4. DISCUSSION

NIV is commonly utilized for treating moderate neonatal respiratory disease, aiming to stabilize spontaneous respiration and reduce complications linked to invasive mechanical ventilation [10].

In this study, the rate of NIV failure and subsequent intubation within the first 72 hours no statistically meaningful difference was found between the two groups. LUS score was unsignificant between 2 studied groups either initially or on the 2nd readings (prior to failure in failed group or after 24 hours in succeeded group). While LUS score was significantly elevated in failed cases versus succeeded cases in 3 studied groups.

LUS is increasingly recognized as a valuable diagnostic tool, with evidence supporting its effectiveness in identifying neonatal RDS and various pulmonary diseases [6]. It also provides reliable prediction of NIV failure and is superior to chest radiography in this context [8].

In concordance with this study Perri et al. [11] who studied LUS score as predictive for CPAP and surfactant need and cut off value for cases who require surfactant was 9 with accuracy 0.86.

Electrical cardiometry (EC) is recognized as a reliable and non-invasive technique for measuring hemodynamic parameters in pediatric populations, including neonates. [12].

In our present study: By comparison between 2 NIV groups, as regard all studied groups there was statistically significant elevation in TFC 2 in CPAP group versus to NIPPV group. Which also significantly increased in failed cases compared to the one succeeded.

The superiority of NIPPV over CPAP can be attributed to its multifaceted benefits, including enhanced pharyngeal dilation, significant reduction in upper airway resistance, and stimulation of spontaneous inspiratory effort via Head's paradoxical

reflex. It also improves lung compliance, reopens partially collapsed airways, and increases functional residual capacity (FRC), tidal volume (Vt), and minute volume. Furthermore, NIPPV facilitates superior alveolar recruitment through elevated MAP, minimizes chest wall distortion, and substantially reduces the work of breathing, resulting in a marked improvement in respiratory function. [13]

In our study, A meaningful direct correlation was observed between the LUS score and TFC in the NIPPV group. However, no such correlation was found in the CPAP group. This agreed with Michard et al.[14] and Hammad et al. [15] who delineated that both LUS and TFC possess exceptional diagnostic acuity for identifying pulmonary edema. Furthermore, TFC demonstrated a robust concordance with lung ultrasound in quantifying extravascular lung water.

This study has several limitations, such as small number of cases, single operator, any neonatologist require proper training for interpretation and scoring of ultrasound findings and sensitivity of LUS and TFC.

5. CONCLUSIONS

LUS score correlates well with TFC, in the case of NIV failure and It may serve as a valuable tool for tracking changes in lung aeration during the early application of NIV in premature infants.

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Conflict of Interest: Nil

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