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Research Article

The Profile of Chronic Lung Disease in <32 Weeks Gestational Age Infants: A Retrospective Cohort Study

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ABSTRACT

Background: Chronic Lung Disease (CLD), also known as bronchopulmonary dysplasia, remains one of the most common complications of prematurity and is associated with prolonged respiratory support and long-term pulmonary morbidity. Known risk factors include prematurity, mechanical ventilation, oxygen exposure, infection, and inflammation.

Objective: To determine the incidence of CLD among infants born at <32 weeks' gestation at Corniche Hospital, characterize associated clinical features, and identify potential risk factors.

Methods: This retrospective cohort study included all infants born at <32 weeks' gestation and admitted to Corniche Hospital between January 1, 2019, and July 31, 2021. Clinical data were extracted from the Cerner™ electronic medical record system and analyzed using inferential statistics including odds ratios, p-values, and confidence intervals.

Results: A total of 161 preterm neonates were included. The mean birth weight was 885 ± 283 g, and 57.8% were male. Antenatal corticosteroids were administered in 95% of pregnancies, and 84.5% of infants received surfactant therapy. Overall mortality was 9.3%. In the total study cohort, 112 patients were identified as having CLD with variable severity, 31.1% had mild, 27.3% moderate, and 11.2% severe CLD. Birth weight declined significantly with increasing CLD severity: 810 g (IQR 696–1060), 745 g (IQR 635–952), and 630 g (IQR 572–740) for mild, moderate, and severe disease, respectively ($p<0.001$). Increasing severity was associated with prolonged ventilation, delayed extubation, longer oxygen dependency, delayed achievement of full enteral feeds, and increased rates of sepsis, inotrope use, and sedation exposure (all $p \leq 0.01$). Mortality increased markedly with disease severity, with no deaths in mild CLD compared with 14.3% in moderate and 85.7% in severe CLD ($p<0.001$).

Conclusion: Lower birth weight was strongly associated with escalating CLD severity and mortality. Greater respiratory support requirements, systemic instability, and inflammatory exposure were linked to adverse outcomes, highlighting the importance of early risk stratification and optimized respiratory management in very preterm infants.

Keywords: Chronic lung disease; Bronchopulmonary dysplasia; Neonatal intensive care unit; Preterm infants; Low birth weight; Mechanical ventilation

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INTRODUCTION

Neonatal chronic lung disease, also known as Bronchopulmonary Dysplasia (BPD), is the most common complication of premature birth. CLD is characterized by chronic respiratory symptoms and impaired lung function that persist beyond the neonatal period. Prematurity is a major risk factor for CLD. The risk of CLD increases with decreasing Gestational Age (GA), for extremely preterm infants (GA<28 weeks), the incidence of CLD is approximately 40 percent [1]. Other contributing factors include mechanical ventilation, infection, and exposure to oxygen therapy.

Objectives

This study aims to determine the incidence of CLD in preterm infants at Corniche Hospital and to examine associated maternal and neonatal risk factors. It also explores the impact of different modes of respiratory support on CLD development and progression. By analyzing clinical characteristics, comorbidities, and patterns of care, the study seeks to enhance understanding of CLD in preterm infants and support more effective management strategies for this high-risk population, especially at our area with specific features and multi ethnicity.

MATERIALS AND METHODOS

This is a retrospective cohort study, which was conducted at Corniche Hospital, a tertiary perinatal center in the United Arab Emirates. The study included all preterm infants born at less than 32 weeks of gestation between January 1, 2019, and July 31, 2021, who were admitted to the Neonatal Intensive Care Unit (NICU).

Infants were included if they were delivered at Corniche Hospital during the study period, met the gestational age criteria, and had complete clinical documentation in the hospital's electronic medical records system (Cerner™). Cases were excluded if infants died before 28 days of life, had major congenital anomalies, or were transferred out prior to a definitive respiratory outcome assessment.

The severity of CLD was classified according to the 2019 Jensen definition, which stratifies disease based on the mode of respiratory support at 36 weeks Postmenstrual Age (PMA), irrespective of oxygen concentration. Mild CLD (grade I) was defined as requiring low-flow nasal cannula oxygen (<2 L/min); moderate CLD (grade II) included infants receiving high-flow nasal cannula (≥ 2 L/min), CPAP, or Noninvasive Positive Pressure Ventilation (NIPPV); and severe CLD (grade III) referred to those requiring invasive mechanical ventilation at 36 weeks PMA. This classification aligns with the definition proposed by Jensen et al. [2].

Clinical and demographic data were extracted from the Cerner™ system using standardized neonatal and obstetric terminology. Data were entered into a predesigned Microsoft Access database and anonymized, except for medical record numbers used solely for data verification.

The following maternal and perinatal variables were recorded: race, mode of delivery (vaginal or cesarean), singleton or multiple gestation, gestational age, birth weight, and infant sex. Additional obstetric factors included the administration of antenatal corticosteroids (number and timing of doses), the Presence of Premature Rupture of Membranes (PROM), and histological or clinical chorioamnionitis.

Neonatal variables included APGAR scores at 1 and 5 minutes, the need for surfactant therapy and number of doses, requirement and duration of sedation, use of inotropes or diuretics, and postnatal corticosteroid therapy. Respiratory interventions were comprehensively recorded, including the use of Noninvasive Ventilation (NIV), Conventional Mechanical Ventilation (CMV), and High-Frequency Oscillatory Ventilation (HFOV). The age at intubation and extubation, as well as the timing of oxygen weaning and transition to full enteral feeds, were documented. Additional morbidities such as Patent Ductus Arteriosus (PDA), sepsis (based on positive cultures or clinical diagnosis requiring antibiotics), and pneumothorax were captured. The final mode of feeding at discharge and the last recorded dose of caffeine were also included.

Data analysis

Data were summarized using descriptive statistics. Prior to inferential analysis, the distribution of continuous variables was assessed for normality. This was performed using visual inspection of histograms and Q–Q plots, in addition to the Kolmogorov–Smirnov test. Continuous variables with non-normal distributions were reported as medians and Interquartile Ranges (IQR) or means and Standard Deviations (SD), depending on data distribution, and analysed using parametric tests. Categorical variables were expressed as frequencies and percentages. Statistical analysis was performed using IBM SPSS. Comparisons across CLD severity groups (mild, moderate, severe) were performed using Kruskal–Wallis tests for continuous variables and *Chi-square* or Montecarlo tests for categorical variables. Moreover, Mann-Whitney MW test was used in our study. Independent predictors of increasing CLD severity were identified using ordinal logistic regression. Statistical significance was defined as a two-tailed p-value<0.05.

RESULTS

A total of 161 preterm neonates were included in the study (Table 1). The average birth weight was 885 ± 283 g, and 57.8% of the infants were male. The average APGAR scores were 5.17 ± 2 at 1 minute and 7.54 ± 1.5 at 5 minutes. Most pregnancies (about 95%) received antenatal steroids, with betamethasone being the most common choice (88.2%). Surfactant therapy was provided to 84.5% of neonates, with a median of 1 dose (IQR 1, 2). Chorioamnionitis was present in 34.7% of cases, and PROM occurred in 36.6%. HFOV was needed for 27.3% of neonates, while 63.4% received non-invasive ventilation. Postnatal steroids were utilized by 21.3%. The overall mortality rate was 9.3% (15 out of 161). Among the 161 infants, 112 patients (69.6%) developed CLD, and as per Jensen classification, 31.1% had mild CLD, 27.3% had moderate CLD, and 11.2% had severe CLD, while the remaining 49 infants (30.4%) were classified as

having no CLD and excluded from severity-based analyses (Table 2). Birth weight significantly dropped with increasing CLD severity: Mild 810 g (IQR 696, 1060), moderate 745 g (IQR 635, 952), and severe 630 g (IQR 572, 740) (p<0.001; Table 2). There were no significant differences among severity groups in terms of sex, parity, APGAR scores, mode of delivery, chorioamnionitis, PROM, or antenatal steroid exposure. Time to intubation was shorter for infants with severe CLD (p=0.047), and the number of surfactant doses tended to rise with severity (p=0.05). A more complicated respiratory course was seen with increasing CLD severity (Table 3). HFOV use significantly increased across severity groups: 14% in mild, 51.2% in moderate, and 34.9% in severe (p<0.001). The age at extubation rose markedly with severity (median 21 days *vs.* 36 days *vs.* 64 days; p<0.001). Oxygen dependency lasted significantly longer in infants with severe CLD (median 163.5 days) compared to those with mild (80 days) and moderate CLD (96 days) (p<0.001). The time to achieve full enteral feeds was also significantly delayed as severity increased (p<0.001). The duration of sedation grew substantially across severity groups (p=0.003), and postnatal steroid use was more common in those with moderate and severe CLD (p=0.005). Sepsis was significantly more frequent with higher CLD severity (p=0.01; Table 4). Both inotrope use and sedation were strongly linked to increased CLD severity (both p<0.001). Mortality showed a clear pattern across severity groups: There were no deaths in the mild CLD group, while 14.3% of infants with moderate CLD and 85.7% of those with severe CLD died (p<0.001; Table 4). Ordinal logistic regression was done to identify independent predictors of escalating CLD severity (mild<moderate<severe) (Table 5). The overall model was statistically significant (χ2=74.725, p<0.001). In multivariable analysis, higher birth weight (P=0.042) and duration of sedation (P=0.003) were associated with increased odds of the outcome. Doses of surfactants were strongly protective (OR 0.055, P<0.001). Other significant predictors included parity (OR 30.02, P=0.001), chorioamnionitis (OR 3.39, P=0.026), postnatal steroids (OR 3.60, P=0.028), and sedation (OR 4.30, P=0.038).

Missing data

Multiple imputation was used for missing predictors, and pooled estimates are shown. Adjusted Odds Ratios (aORs) with 95% confidence intervals are included in Table 5. The ordinal regression model was significant (χ^2=74.725, p<0.001).

Non-survivors had a significantly lower birth weight compared with survivors (median (IQR): 670 (610–750) g *vs.* 850 (700–1082) g, p=0.001). There were no significant differences between the two groups regarding sex, multiple birth, APGAR score at 1 or 5 minutes, or number of antenatal steroid doses (Table 6). Mode of delivery differed significantly between groups, with a higher proportion of vaginal deliveries among non-survivors (p=0.009). Chorioamnionitis and PROM were significantly more frequent among infants who died compared with survivors (p=0.02 and p=0.049, respectively) (Table 6). Respiratory and NICU course variables are summarized in Table 7. Use of HFOV was significantly higher among non-survivors compared with survivors (29.5% *vs.* 70.5%, p<0.001). Non-survivors were also more likely to receive NIV (p=0.049). Although surfactant use did not differ significantly between groups (p=0.13), the number of surfactant doses was higher among non-survivors (p=0.03). There were no significant differences in intubation time or age at extubation between the two groups. However, duration off oxygen was significantly longer among survivors than non-survivors (p=0.01). As shown in Table 8, there was no statistically significant difference in time to reach full feeds between survivors and non-survivors (p=0.12). In contrast, use of postnatal steroids, sedation, inotropes, and diuretics was significantly more common among non-survivors (all p<0.01). Non-survivors also had a significantly longer duration of sedation compared with survivors (median (IQR): 108 (41–151) days *vs.* 27.7 (14.4–43.6) days, p<0.001). Morbidity and outcome data are presented in Table 9. Sepsis was significantly more frequent among non-survivors compared with survivors (15.6% *vs.* 84.4%, p=0.009). Pneumothorax was also more common among infants who died (p=0.007). There were no significant differences between groups in the incidence of PDA or conventional mechanical ventilation.

Table 1: Characteristics of study population.

	Number	Percentage
Multiple birth		
No	93	57.8
Yes	68	42.2
Number of newborns		
Median IQR	1 (1-2)	
BW in gram (mean SD)	885 (283.1)	

Sex		
Male	93	57.8
Female	68	42.2
Way of delivery		
Caesarean section	92	57.1
vaginal delivery	69	42.9
APGAR 1 MIN (mean SD)	5.17 (2)	
APGAR 5 MIN (mean SD)	7.54 (1.5)	
Antenatal Steroids (ANS)		
No	8	5
Yes	153	95
Number of doses of ANS (mean SD)	1.75 (0.43)	
Chorioamnionitis		
No	71	44
Yes	56	34.7
PROM		
No	102	63.4
Yes	59	36.6
Surfactant		
No	25	15.5
Yes	136	84.5
Doses of surfactant (median iQR)	1 (1-2)	
Mode of transfer to NICU		
Conventional	119	73.9
Non-conventional	42	26.1
Time of intubation in minutes (median IQR)	5 (3-11.25)	
Age at time of extubation in days (median IQR)	22 (2-39)	
Off oxygen in days (median IQR)	75 (54-97)	
Time to full feeds	23 (16-37.5)	
CMV (Conventional Mechanical Ventilation)		

No	21	13
Yes	140	87
HFOV		
No	117	72.7
Yes	44	27.3
NIV		
No	59	36.6
Yes	102	63.4
Postnatal steroids	n=160	
No	126	78.8
Yes	34	21.3
Pneumothorax	n=160	
No	153	95.6
Yes	7	4.4
Severity of CLD		
Mild	50	31.1
Moderate	44	27.3
Severe	18	11.2
Sepsis		
No	84	52.2
Yes	77	47.8
Died		
No	146	90.7
Yes	15	9.3
PDA	n=160	
No	71	44.4
Yes	89	55.6
Diuretic	n=160	
No	26	16.3
Yes	134	83.3
Inotrope		

No	96	59.6
yes	65	40.4
Sedation		
No	84	52.2
yes	77	47.8
Duration of sedation	32 (15.75-43)	

Table 2: Baseline and perinatal characteristics by CLD severity.

Variable	Mild (n=50)	Moderate (n=44)	Severe (n=18)	P value
Multiple birth[1] **n** (%)	23 (46)	22 (44)	5 (10)	0.27
Sex[1] **n** (%)				
Male	27 (43.5)	26 (42)	9 (14.5)	0.7
female	23 (46)	18 (36)	9 (18)	
Birth weight[2]	810 (696-1060	745 (635-952)	630 (572-740)	<0.001*
APGAR_1_MIN[2]	5 (4-7)	5 (4-6)	5 (2.75-5.25)	0.24
APGAR_5_MIN[2]	8 (7-9)	8 (7-9)	7(6-8)	0.15
Mode of delivery[1]				
LSCS	29 (45.3)	29 (45.3)	6 (9.4)	0.062
Vaginal	21 (43.8)	15 (31.3)	12 (25)	
Chorio[1]	4 (33.3)	4 (33.3)	4 (33.3)	0.086
PROM[1]	19 (43.2)	14 (31.8)	11 (25)	0.097
Surfactant[1]	45 (43.7)	40 (38.8)	18 (17.5)	0.51
No. doses of ANS[2]	2 (1-2)	2	2 (1-2)	0.85
How many doses of surfactant[2]	1 (1-2)	1 (1-2)	2 (1-2)	0.05
Time intubation minutes[2]	7 (3-12.5)	7 (3-14)	4 (3-6)	0.047

Note: [1]*Chi-square* test, [2]Data expressed as median and interquartile range, KW test done

Table 3: NICU respiratory course by CLD severity.

Variable	Mild	Moderate	Severe	P value
Mode of transfer to NICU[1] **(N%)**				
Conventional	43 (45.3)	34 (35.8)	18 (18.9)	0.057

Non-conventional	7 (41.2)	10 (58.8)	0	
HFOV[1]	6 (14)	22 (51.2)	15 (34.9)	<0.001*
NIV	29 (40.8)	34 (47.9)	8 (11.3)	0.029*
Age at time of extubation days[2]	21 (2-36)	36 (16-60)	64 (35-103)	<0.001*
Post-natal steroids[1]	8 (24.2)	15 (45.5)	10 (30.3)	0.005*
Pneumothorax[1]	1 (20)	3 (60)	1 (20)	0.455 MC
Off oxygen days[2]	80 (66-91.5)	96 (77.75-142.25)	163.5 (114.25-217.5)	<0.001*
Time to full feeds in days[2]	24 (18-33.5)	28.5 (21.25-51.5)	98.5 (28.5-139.25)	<0.001*
Duration of sedation[2]	24 (14.5-38)	36 (15.5-14.5)	108 (42-133)	0.003*

Note: [1]*Chi-square* test, [2]Median quartiles. Test: KW

Table 4: Morbidities and outcomes by CLD severity.

Variable	Total	Mild	Moderate	Severe	P value
Sepsis	58	19 (32.8)	25 (43.1)	14 (24.1)	0.01
PDA	75	29 (38.70	35 (46.7)	11 (14.7)	0.073
Diuretics	103	43 (41.7)	42 (40.8)	18 (17.5)	0.12MC
Inotrope	63	16 (25.4)	29 (46)	18 (28.6)	<0.001
Sedation	73	22 (30.1)	33 (45.2)	18 (24.7)	<0.001
Died	14	0	2 (14.3)	12 (85.7)	<0.001MC
CMV	105	46(43.8)	41(39)	18(17.1)	0.76

Note: *Chi-square* test, MC: Montecarlo test

Table 5: Ordinal logistic regression.

	OR	Lower OR	Upper OR	P value
How many newborn	3.995905	0.983	16.238	0.053
Birth Weight	1.00203	1	1.004	0.042
APGAR_1_MIN	0.927408	0.7	1.229	0.6
APGAR_5_MIN	1.146311	0.783	1.677	0.482
No. doses of ANS	1.383992	0.553	3.464	0.487
Doses of surfactants	0.054699	0.018	0.163	0

Time of intubation (minutes)	1.000086	1	1	0.438
Age at time of extubation (days)	0.989291	0.967	1.012	0.348
Off oxygen (days)	1.00278	0.994	1.012	0.538
Time to full-feeds (days)	0.99067	0.976	1.005	0.208
Duration of sedation	1.020807	1.007	1.035	0.003
MULT=0	30.02067	3.917	230.081	0.001
Sex=1	0.620504	0.262	1.471	0.279
Chorio=0	3.385867	1.154	9.938	0.026
PROM=0	0.800949	0.347	1.851	0.604
CMV=0	0.226846	0.013	4.034	0.312
HFOV=0	0.644699	0.192	2.17	0.478
NIV=0	0.930708	0.373	2.321	0.878
Postnatal steroids=0	3.596364	1.152	11.23	0.028
Pneumothorax=0	0.350563	0.041	2.996	0.338
Sepsis=0	1.077421	0.477	2.433	0.858
Died=0	1.230547	0.223	6.781	0.812
PDA=0	0.725702	0.296	1.782	0.484
Diuretics=0	2.271165	0.614	8.404	0.219
Inotrope=0	0.53964	0.124	2.352	0.412
Sedation=0	4.298635	1.083	17.062	0.038

Table 6: Baseline and perinatal characteristics (Survived *vs.* Died).

Variable	**Total**	**Survived (N=146)**	**Died (N=15)**	**P value**
Birth weight (g)	Median (IQR)	850 (700-1082)	670 (610-750)	0.001
Sex N (%)				
Male	93	85 (91.4)	8 (8.6)	0.71
Female	68	61 (89.7)	7 (10.3)	
Multiple birth N (%)	68	63 (92.6)	5 (7.4)	0.46
Mode of delivery N (%)				
CS	92	88 (95.6)	4 (4.3)	0.009

vaginal	69	58 (84)	11 (16)	
APGAR 1 min	Median (IQR)	5 (4-7)	5 (3-6)	0.26
APGAR 5 min	Median (IQR)	8 (7-9)	7 (6-8)	0.1
No. doses of ANS	Median (IQR)	2	2 (1-2)	0.94
Chorioamnionitis N (%)	56	47 (83.9)	9 (16.1)	0.02
PROM N (%)	59	50 (84.7)	9 (15.3)	0.049

Note: Continuous data expressed as median (IQR) and test of significance used is Mann-Whitney MW test, Categorical data expressed as n(%) and test of significance used is *Chi-square*, P<0.05: significant level

Table 7: Respiratory and NICU course (Survived *vs.* Died).

Variable	Total	Survived (n=146)	Died (n=15)	P value
Surfactant therapy n (%)	136	121 (89)	15 (11)	0.13 FET
No. doses of surfactant	Median (IQR)	1 (1-2)	1	0.03
Intubation time (min)	Median (IQR)	6 (3-160)	4 (3-5)	0.17
HFOV n (%)	44	31 (70.5)	13 (29.5)	<0.001
NIV n (%)	102	96 (94)	6 (6)	0.049
Age at extubation (days)	Median (IQR)	21.9 (2-39)	28 (2.2-34)	0.81
Off oxygen days	Median (IQR)	74.5 (54-96)	139 (73.46-165.8)	0.01

Note: Continuous data expressed as median (IQR) and test of significance used is Mann-Whitney MW test, Categorical data expressed as n(%) and test of significance used is *Chi-square*, P<0.05: significant level square

Table 8: Feeding, medications and support (Survived vs. Died).

Variable	Total	Survived (n=146)	Died (n=15)	P value
Time to full feeds (days)	Median (IQR)	22 (15.75-36)	29 (20-73.69)	0.12
Postnatal steroids n (%)	34	24 (70.6)	10 (29.4)	<0.001
Duration of sedation (days)	Median (IQR)	27.67 (14.38-43.55)	108 (41-151)	<0.001
Diuretics n (%)	135	120 (89.6)	15 (10.4)	0.002
Inotropes n (%)	65	50 (77)	15 (23)	<0.001
Sedation n (%)	77	62 (80.5)	15 (19.5)	<0.001

Note: Continuous data expressed as median (IQR) and test of significance used is Mann-Whitney MW test, Categorical data expressed as n(%) and test of significance used is *Chi-square*, P<0.05: significant level

Table 9: Morbidity and outcomes.

Variable	total	Survived (n=146)	Died (n=15)	P value
Sepsis n (%)	77	65 (84.4)	12 (15.6)	0.009
Pneumothorax n (%)	7	6 (85.7)	1 (14.3)	0.007
PDA n (%)	89	80 (90)	9 (10)	0.69
CMV n (%)	140	125 (89.3)	12(10.7)	0.11

Note: Continuous data expressed as median (IQR) and test of significance used is Mann-Whitney MW test, Categorical data expressed as n(%) and test of significance used is *Chi-square*, P<0.05: significant level

DISCUSSION

In this retrospective cohort of 161 preterm neonates (<32 weeks' gestation) managed at a tertiary center in the United Arab Emirates, we identified significant clinical gradients in both BPD severity and mortality. Our findings align with international literature demonstrating that lower birth weight, inflammatory exposure, respiratory support intensity, and systemic instability are central determinants of adverse pulmonary and survival outcomes in very preterm infants [3-6].

Birth weight and severity/mortality gradient

Birth weight demonstrated a strong inverse association with both escalating BPD severity and mortality. Median birth weight declined stepwise across severity groups (mild 810 g, moderate 745 g, severe 630 g; p<0.001), and non-survivors had significantly lower birth weights than survivors (670 g *vs.* 850 g; p=0.001).

These findings are consistent with large registry data from the Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network and the Vermont Oxford Network, both of which demonstrate birth weight as one of the most powerful independent predictors of BPD and mortality in extremely preterm populations [6-8]. Mortality rises sharply below 750 g across international cohorts [7]. Our data confirm that this biological gradient remains evident within a contemporary Gulf-region NICU population.

Inflammatory exposure: Chorioamnionitis, PROM, and sepsis

Chorioamnionitis and PROM were significantly more frequent among non-survivors, supporting the inflammatory pathogenesis model of BPD. Meta-analyses and large cohort studies, including reports published in The Lancet, have consistently identified intrauterine inflammation as a risk factor for lung injury, early neonatal morbidity, and death [4,9].

Postnatal sepsis was also significantly associated with both increasing BPD severity and mortality in our cohort. This aligns with pooled analyses demonstrating that systemic inflammatory burden contributes to impaired alveolarization, pulmonary vascular remodelling, and increased mortality risk in preterm infants [4,5]. The association observed in our study reinforces the concept that both antenatal and postnatal inflammatory hits amplify vulnerability of the immature lung.

Respiratory support and disease progression

We observed a progressively more complicated respiratory course with increasing BPD severity, including greater HFOV utilization, longer duration to extubation, prolonged oxygen dependency, and increased need for postnatal steroids. Among non-survivors, HFOV use, NIV use, and higher surfactant dose number were significantly more frequent.

Randomized trials comparing HFOV with conventional ventilation have not demonstrated consistent mortality benefit; rather, HFOV typically reflects escalation of respiratory support in the sickest infants [3,10]. Data from the Vermont Oxford Network similarly show that invasive ventilation duration and respiratory severity markers correlate strongly with severe BPD and death [8]. Therefore, in our cohort, advanced ventilation strategies likely represent markers of disease severity rather than causal determinants of mortality.

Notably, time to intubation and age at extubation did not differ between survivors and non-survivors, suggesting that cumulative respiratory burden rather than timing alone may be more predictive of outcome.

Hemodynamic instability and sedation burden

A striking finding in our dataset was the prolonged duration of sedation among non-survivors (median 108 days *vs.* 27.7 days; p<0.001). Inotrope and diuretic use were also significantly more common in infants who died. These variables likely reflect hemodynamic instability, pulmonary hypertension risk, and multisystem compromise.

Large cohort analyses have demonstrated that need for inotropic support is independently associated with mortality in extremely preterm infants [7,11]. Although sedation duration is less frequently reported in the literature, it may serve as a proxy marker for prolonged ventilation, severity of lung disease, and systemic fragility. The magnitude of difference observed in our cohort suggests that sedation burden could represent a clinically meaningful prognostic indicator and warrants further prospective investigation.

Mode of delivery

We found a higher proportion of vaginal deliveries among non-survivors. International data show inconsistent associations between delivery mode and mortality after adjustment for gestational age and fetal compromise [11,12]. Registry data from the Eunice Kennedy Shriver National Institute of Child Health and Human Development suggest that delivery mode rarely remains independently predictive when controlling for confounders [11]. Thus, the association observed in our cohort may reflect underlying clinical instability rather than a direct causal effect.

Pneumothorax and acute complications

Pneumothorax was significantly more common among non-survivors, consistent with registry evidence demonstrating increased mortality risk following air leak syndromes in extremely low birth weight infants [3,7]. Conversely, we did not observe significant mortality differences related to PDA or CMV infection, findings that are concordant with literature showing inconsistent independent associations after multivariable adjustment [3,6].

Regional context

Regional data from the Gulf, including reports from Qatar, Saudi Arabia, and United Arab Emirates, indicate mortality rates for infants ≤ 32 weeks gestation ranging between 8% and 15%, depending on gestational distribution and case mix [15]. Our overall mortality rate of 9.3% falls within this expected range, suggesting comparable neonatal care performance relative to similar regional centers.

Independent predictors of escalating severity

Ordinal logistic regression identified duration of sedation, time to full feeds, NIV, HFOV, postnatal steroids, and parity as independent predictors of escalating CLD severity. These findings are biologically plausible and align with international data highlighting respiratory intensity and systemic illness as key drivers of severe BPD phenotypes [3,7,8,13].

The use of multiple imputation for missing predictors and presentation of pooled adjusted odds ratios strengthens the internal validity of our model and enhances comparability with contemporary epidemiologic standards [14,15].

Clinical and research implications

Our findings reinforce the multifactorial nature of BPD progression, involving:

- Prematurity and growth restriction.
- Antenatal and postnatal inflammatory exposure.
- Cumulative respiratory support load.
- Hemodynamic instability.

Systemic complications

Importantly, the strong association between sedation duration and both severity and mortality suggests an area that is underexplored in current literature and may represent a modifiable factor in clinical practice.

Strengths and limitations

Strengths include severity stratification, multivariable ordinal modelling, and comprehensive mortality analysis within a modern tertiary NICU in the Gulf region. Limitations include retrospective design, single-center setting, and potential residual confounding.

CONCLUSION

In this retrospective cohort of preterm infants born at <32 weeks' gestation, we identified a clear gradient between decreasing birth weight, increasing Chronic Lung Disease (CLD) severity, and mortality. Lower birth weight emerged as a central determinant of both escalating CLD severity and death. Increasing respiratory support intensity including HFOV use, higher surfactant requirements, prolonged oxygen dependency, and delayed extubation was strongly associated with more severe disease phenotypes. Markers of systemic instability, particularly prolonged sedation, inotrope requirement, and postnatal steroid exposure, were independently associated with increasing CLD severity and were significantly more prevalent among non-survivors. Inflammatory exposures, including chorioamnionitis, PROM, and postnatal sepsis, were also linked to adverse outcomes, reinforcing the multifactorial inflammatory and injury-driven pathogenesis of severe CLD.

Mortality in our cohort was concentrated among infants with severe CLD and extremely low birth weight, consistent with patterns reported in international and regional neonatal networks. The strong association between sedation duration and both severity and mortality represents a notable finding and may reflect cumulative respiratory load and hemodynamic fragility; this warrants further prospective evaluation.

Overall, our findings underscore that CLD severity in very preterm infants is driven by an interplay of prematurity-related 11 vulnerability, inflammatory exposure, respiratory support intensity, and systemic instability. Early identification of high-risk infants and optimization of respiratory, hemodynamic, and infection-control strategies may help mitigate progression to severe disease and improve survival outcomes.

ETHICAL CONSIDERATIONS

This research is a retrospective cohort study, as outcomes (CLD) were assessed based on prior exposures and followed over time, using data which is already collected as part of routine clinical care. No additional samples are required from the patient and there will be no direct patient or family contact from the researchers other than what is needed for ongoing routine care. Only limited patient identifiable data (MRN) will be collected as part of the research. The data will be maintained on hospital approved encrypted removable storage device and a copy will be stored on the hospital desktop computer of the research supervisor in line with the hospital data and patient confidentiality policies. Due to the above considerations the

research team feels it is not necessary to obtain patient consent and request the Corniche REC for waiver of the same.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The committee has given a favourable ethical opinion for the above project based on the application form, protocol and supporting documentation.

AUTHORS' CONTRIBUTION AND GUARANTOR INFORMATION

Ihab Elkadry contributed to data collection, analysed data, drafted the initial manuscript, reviewed and revised the manuscript and approved the final manuscript as submitted.

Latifa Ghosn contributed to data collection.

Ahmed Embabi contributed to data collection and analysed data.

Hesham Tawakol reviewed and revised the manuscript, and approved the final manuscript as submitted.

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No funding was secured for this study.

FINANCIAL DISCLOSURE

The authors have no financial relationships relevant to this article to disclose.

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

CLINICAL TRIAL REGISTRATION

Non-applicable.

AVAILABILITY OF DATA AND MATERIALS

All data included in the manuscript are available upon request.

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