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ORIGINAL ARTICLE

Epidemiology of neonatal pneumothorax developed spontaneously and during respiratory supports in neonatal intensive care units

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Abstract

Background: Information on incidence and risk factors associated with different types of neonatal pneumothorax were lacking globally. Objectives: To determine incidences of pneumothorax developed spontaneously and during different modes of respiratory support, and risk factors associated with each type of pneumothorax. Study Design: Retrospective observational study of neonates in the Malaysian National Neonatal Registry. Setting: 44 Malaysian neonatal intensive care units (NICUs). Participants: All neonates born in 2015-2020 and admitted to NICUs. Results: Pneumothorax developed in 3265 neonates: 37.5% occurred spontaneously, 62.5% during respiratory support. The incidence of all types of pneumothorax was 1.75 per 1000 livebirths, and of spontaneous pneumothorax was 0.58 per 1000 livebirths. Pneumothorax developed in 0.6% (450/70512) of neonates during continuous positive air way pressure therapy (nCPAPt), 1.8% (990/54994) of neonates during conventional mechanical ventilation (CMV), and 7.0% (599/8557) of neonates during high frequency ventilation (HFV). Term neonates had significantly higher pneumothorax rate than preterms ($p<0.001$). Multiple logistic regression analyses show that exposure to intermittent positive pressure ventilation and chest compression at birth were significant independent factors associated with increased risk of spontaneous pneumothorax and CMV, and persistent pulmonary hypertension was associated with increased risk of spontaneous pneumothorax and pneumothorax during CMV and HFV. Conclusions: The most common type of pneumothorax was spontaneous in-onset. Neonates on HFV had the highest and those on nCPAPt the lowest rate of pneumothorax. Improving training of resuscitation techniques at birth and strategies of use of invasive modes of respiratory support may reduce incidences of all types of pneumothorax.

Keywords: neonates, spontaneous-onset pneumothorax, pneumothorax during respiratory support, risk factors, Malaysian NICUs.

INTRODUCTION

Globally, neonatal pneumothorax is a common problem in neonatal intensive care units (NICUs) and an important cause of morbidity and mortality. The reported incidence of pneumothorax varied from 0.13% to 8.6%[1-7], with higher incidence in extremely low birthweight (ELBW, <1000g) neonates.[7] In Malaysian NICUs, pneumothorax continues to be a significant independent factor associated with increased risk of mortality in both preterm[8] and term neonates.[9]

Population studies from different countries reported several factors associated with pneumothorax. These include prolonged rupture of amniotic membrane[3,5], chorioamnionitis[5], higher birthweight[5], male[5], outborns[5], surfactant administration[3,5], respiratory distress syndrome (RDS)[5], and meconium aspiration syndrome (MAS).[5,8] In Malaysia, a study conducted ten years ago reported sepsis[7], conventional mechanical ventilation (CMV)[7] and high frequency ventilation (HFV)[7] as significant risk factors associated with pneumothorax. However, in that study[7], it was unclear whether the association of CMV or HFV with pneumothorax was due to their being used as a rescue treatment for pneumothorax or as a causal factor of pneumothorax. Given that such

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information is crucial for strategising effective preventive measures against development of pneumothorax, the MNNR has since requested participating NICUs to submit information on whether pneumothorax occurred spontaneously or during a specific mode of respiratory support. The present study aimed to a) determine the incidences of pneumothorax developed spontaneously and during different modes of respiratory support in Malaysian NICUs, and b) the risk factors associated with each of these types of pneumothorax.

MATERIALS AND METHODS

This was a retrospective observational study of all neonates born during a six-year period (1 January 2015 and 31 December 2020) and admitted to 44 NICUs participating in the MNNR. The inclusion criteria were all neonates with any of the following characteristics: gestational age<32 weeks, birthweight of 500-1500g, requiring respiratory support (nasal continuous positive airway pressure therapy (nCPAPt), conventional mechanical ventilation CMV), or high frequency ventilation (HFV)), gestation ≥35-week with hypoxic ischaemic encephalopathy (HIE), sepsis, or congenital heart disease. The exclusion criteria were all inborns who died in delivery rooms (DR), outborns who died before arrival in the participating hospitals, gestation <22 weeks or >44 weeks, or birthweight <500g.

Data of the following variables of all eligible neonates were retrieved from the MNNR database: birthweight, gestation, intrauterine growth status, gender, ethnic group, inborn/outborn, mode of delivery, chorioamnionitis, antenatal steroids, types of resuscitation received in DR, surfactant therapy, pneumothorax (yes, no), pneumothorax developed during respiratory support (no, yes), types of respiratory support when pneumothorax developed, respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), persistent pulmonary hypertension of neonates (PPHN), culture positive early-onset sepsis (EOS), HIE, outcome (alive, dead), and duration of hospital stay. Cases were all eligible neonates who developed pneumothorax, and controls were those who did not have pneumothorax.

Definitions

Pneumothorax was diagnosed by chest radiograph or needle aspiration. Gestation was reported in completed weeks based on antenatal ultrasound findings or maternal last menstrual period or the New Ballard scores[10] in those unsure of dates. Antenatal steroids (ANS) were any steroids given before birth. Outborns were neonates transferred-in to a participating centre. Early nasal continuous positive airway pressure therapy (enCPAPt) was defined as receiving nCPAPt shortly after birth in DR. Sepsis was diagnosed in symptomatic neonates with a positive blood culture. EOS was sepsis developed at age ≤72 hours. Bronchopulmonary dysplasia (BPD) was diagnosed in neonates on continuous oxygen therapy during first 28 days of life and still oxygen- or ventilator-dependent at 36 weeks' gestation.[11] HIE was diagnosed clinically based on Sarnat's criteria.[12]

Ethics approval

Parental consent was not obtained for this study as the database was anonymised. Ethical clearance for the study was granted by the Malaysian Ministry of Health and registered under the National Medical Research Registry (NMRR-05-04-168).

Statistical analysis

The IBM SPSS software (version 29.0) was used for statistical analysis. Data were summarised as number and percentage for categorical variables, and as mean±SD for continuous variables with normal distribution and as median and interquartile range (IQR) for those with skewed distribution. For between group comparison, the Chi Square test (or Fisher's Exact test for expected number of <5) was used for univariate analysis of categorical variables; Student t test for continuous variables with normal distribution and Mann-Whitney U test for skewed distribution. Potential risk factors (demographic characteristics, resuscitation procedures in DR, and clinical problems detected shortly after birth (RDS, MAS, HIE, EOS, PPHN, pneumonia, congenital malformations)) were compared between those developing pneumothorax during each mode of respiratory support and those without pneumothorax. Outcome of neonates with and without pneumothorax were also compared. Multiple logistic regression analysis was used to identify significant independent factors associated with pneumothorax developed during each mode of respiratory support (dependent variables), after controlling for various potential confounders (independent variables). P values of <0.05 was considered statistically significant.

RESULTS

During this six-year period, there were 98355 neonates from 45 centres in the MNNR database. We present here the data of 97340 neonates, after excluding 887 who died in DR and 128 neonates from a centre with irregular data submission. Table 1 shows the demographic characteristics of the 97340 neonates from the remaining 44 centres.

Pneumothorax developed in 3.4% (3265/97340) of neonates: 37.5% (n=1226) occurred spontaneously, 13.8% (n=450) during nCPAPt, 30.3% (n=990) during CMV, and 18.3% (n=599) during HFV. Pneumothorax was significantly more common in term neonates (4.9%, n=2148/43988) than preterm neonates (2.1%, n=1117/53352, p<0.001).

Incidences of pneumothorax

Majority (86.2%) of the neonates with pneumothorax were inborn (spontaneous-onset n=1043, during nCPAPt n=406, CMV n=849, and HFV n=516). Out of 1,792,002 livebirths born in the participating hospitals during these six years, the incidence of all types of pneumothorax was 1.75 per 1000 livebirths, and of spontaneous pneumothorax was 0.58 per 1000 livebirths.

The most common modes of respiratory support used by all neonates (inborn and outborns) was nCPAPt (n=70512); next were CMV (n=54994) and HFV (n=8557).

Spontaneous-onset pneumothorax

Spontaneous-onset pneumothorax was significantly more common in term neonates than the preterm (2.0% or 899/43988 versus 0.6% or 327/53352; p<0.001). Table 2 compares the potential risk factors between neonates with spontaneous-onset pneumothorax and those without pneumothorax in preterm (<37 weeks) and term neonates, respectively.

Pneumothorax during nCPAPt

Of the 70512 neonates who received nCPAPt in NICUs, 68612 (97.3%) did not have pneumothorax; 450 (0.6%) developed pneumothorax during nCPAPt, and 2.1% developed pneumothorax during CMV (n=499), HFOV (n=271) or spontaneously (n=680). Majority of the neonates on nCPAPt (59.8% or n=42201) were preterm (<37 weeks) and 40.2% (n=28311) were term gestation.

TABLE 1: Demographic characteristics of all neonates admitted to 44 Neonatal Intensive Care Units in Malaysian Neonatal Registry in 2015-2020

Characteristics	Neonates n=97340
Birthweight, g	
Median (range)	2350 (500-6000)
Gestation, weeks (range)	
Median (range)	36 (22-44)
Males, n (%)	57145 (58.7)
Ethnic groups, n (%)	N=97311
Malay Malaysian	65894 (67.7)
Chinese Malaysian	7196 (7.4)
Indian Malaysian	5912 (6.1)
Malaysian of other ethnic groups	11283 (11.6)
Foreigners	7026 (7.2)
Missing data	29 (0.03)
Outborn, n (%)	9968 (10.2)
Modes of delivery, n (%)	N=97301
Lower segment Caesarean section	50469 (51.8)
Spontaneous vertex delivery	39077 (40.1)
Vacuum extraction	5826 (6.0)
Breech extraction	1248 (1.3)
Forceps delivery	681 (0.7)
Missing data	39 (0.04)

TABLE 2: Comparison of potential risk factors associated with development of spontaneous pneumothorax in preterm (<37 weeks) and term neonates, respectively, in the Malaysian National Neonatal Registry, 2015-2020

Gestation groups	Preterm Gestation <37 weeks N=52562			Term Gestation ≥37 weeks N= 42739		
Potential risk factors	Developed spontaneous pneumothorax. N= 327 (%)	No pneumothorax during NICU stay. n= 52235 (%)	P values	Developed spontaneous pneumothorax. n= 899 (%)	No pneumothorax during NICU stay. n= 41840 (%)	P values
Birthweight groups						
<1000 g	44 (13.5)	5774 (11.1)	<0.001	0	10 (0)	0.378
1000-1499 g	66 (20.2)	14108 (27.0)		0	126 (0.3)	
1500-2499 g	162 (49.5)	26509 (50.7)		115 (12.8)	5152 (12.3)	
≥2500 g	55 (16.8)	5844 (11.2)		784 (87.2)	36552 (87.4)	
Gestation				-	-	
<28 weeks	39 (11.9)	4592 (8.8)	0.031	-	-	
28-31 weeks	73 (22.3)	14347 (27.5)		-	-	
32-36 weeks	215 (65.7)	33296 (63.7)				
Intrauterine growth						
AGA	245 (74.9)	38442 (73.6)	0.479	545 (60.6)	27485 (65.7)	<0.001
SGA	63 (19.3)	11256 (21.5)		332 (36.9)	12107 (28.9)	
LGA	19 (5.8)	2537 (4.9)		22 (2.4)	2248 (5.4)	
Males	212 (64.8)	29418/52223 (56.3)	0.002	605 (67.3)	25666/41830 (61.4)	<0.001
Ethnic groups		N=52218			N=41829	
Chinese Malaysian	21 (6.4)	4423 (8.5)	0.338	57 (6.3)	2571 (6.1)	0.012
Malay Malaysian	218 (66.7)	34454 (66.0)		596 (66.3)	29212 (69.8)	
Indian Malaysian	18 (5.5)	3203 (6.1)		45 (5.0)	2545 (6.1)	
Malaysians of other ethnic groups	41 (12.5)	6718 (12.9)		113 (12.6)	4170 (10.0)	
Foreigners	29 (8.9)	3420 (6.5)		88 (9.8)	3331 (8.0)	

Outborn	43 (13.1)	4500 (8.6)	0.004	140 (15.6)	5017/41837 (12.0)	0.001
Chorioamnionitis	10/315 (3.2)	1814/51292 (3.5)	0.878	7/878 (0.8)	615/41163 (1.5)	0.117
Antenatal steroids	181/318 (56.9)	34288/51379 (66.7)	<0.001	-	-	-
Resuscitation at birth						
Oxygen therapy	246/319 (77.1)	38870/51382 (75.6)	0.543	671/878 (76.4)	28992/40859 (71.0)	<0.001
eCPAPt	151/319 (47.3)	29381/51380 (57.2)	<0.001	374/878 (42.6)	17995/40851 (44.1)	0.391
B & M IPPV	183/319 (57.4)	21990/51360 (42.8)	<0.001	436/875 (49.8)	15348/40821 (37.6)	<0.001
IPPV via ETT	179/319 (56.1)	20422/51361 (39.8)	<0.001	444/878 (50.6)	14003/40848 (34.3)	<0.001
Chest compression	18/319 (5.6)	1081/51346 (2.1)	<0.001	34/879 (3.9)	756/40842 (1.9)	
Surfactant therapy	162 (49.5)	20523 (39.3)	<0.001	-	-	-
EOS	4 (1.2)	547/52232 (1.0)	0.590	6 (0.7)	404/41838 (1.0)	0.487
MAS	-	-	-	300 (33.4)	7738 (18.5)	<0.001
RDS	191 (58.4)	32730 (62.7)	0.113	-	-	-
Pneumonia	108 (33.0)	13430/52180 (25.7)	0.003	332 (36.9)	16466/41703 (39.5)	0.121
HIE	-	-	-	84 (9.3)	3833/41832 (9.2)	0.852
PPHN	42 (12.8)	1151/52207 (2.2)	<0.001	165 (18.4)	2905/41828 (6.9)	<0.001
Major congenital malformations	57 (17.4)	4731 (9.1)	<0.001	72 (8.0)	5657 (13.5)	<0.001

Note: NICU, neonatal intensive care unit; AGA, appropriate-for-gestational age; SGA, small-for-gestational age; LGA, large-for-gestational age; eCPAPt, early continuous positive pressure therapy; B&M IPPV, intermittent positive pressure ventilation via bag-and-mask; IPPV via ETT, intermittent positive pressure ventilation via endotracheal tube; EOS, early-onset sepsis; MAS, meconium aspiration syndrome; RDS, respiratory distress syndrome; HIE, hypoxic-ischemic encephalopathy; PPHN, pulmonary hypertension of newborn.

Compared with preterm neonates, significantly more term neonates developed pneumothorax during nCPAPt than preterm neonates (1.0% or 283/28311 versus 0.4% or 167/42201, p<0.001). Table 3 compares the potential risk factors between neonates who developed pneumothorax during nCPAPt and those without pneumothorax, in preterm and term neonates respectively.

Pneumothorax during mechanical ventilation

Of the 54994 neonates who received CMV in NICUs, 1.8% (n=990) developed pneumothorax during CMV; 3.1% were put on CMV due to pneumothorax developed spontaneously (n=954), or during nCPAPt (n=294), or HFV (n=479). Majority (55.0% or n=30225) of neonates receiving CMV were preterm and 45.5% (n=24769) were term gestation. A significantly higher proportion of term neonates developed pneumothorax during CMV than preterm neonates (2.6% or n=639 versus 1.2% or n=351; p<0.001). Table 4 compares the potential risk factors between neonates who developed pneumothorax during MCV and those without pneumothorax in preterm and term neonates, respectively.

Pneumothorax during HFV

Of the 8557 neonates who received HFV, 7.0% (n=599) developed pneumothorax during HFV; 7.5% were on HFV because they developed pneumothorax spontaneously (n=274), or during nCPAPt (n=69), or CMV (n=300). Majority of neonates on HFV were preterm (57.9% or n=4953) and 42.1% (n=3604) were term. However, term neonates had a significantly higher rate of developing pneumothorax during HFV (10.1% or n=327) than preterm neonates (5.8% or n=272; p<0.001). Table 5 compares the potential risk factors between neonates who developed pneumothorax during HFV and those without pneumothorax in preterm and term neonates, respectively.

Multiple logistic regression analysis

Table 6 shows the results of multiple logistic regression analysis of significant independent factors associated with various types of pneumothorax, after controlling for various potential confounders listed in Tables 2-5 in preterm and term neonates, respectively.

In preterm neonates with spontaneous-onset pneumothorax, the significant independent factors associated with increased risk of pneumothorax were males, Malaysian Malays, non-Malaysians, intermittent positive pressure ventilation (IPPV) via bag-and-mask in DR, chest compression in DR, surfactant therapy, PPHN and major congenital malformations. In term neonates, the significant independent factors associated with increased risk of spontaneous-onset pneumothorax were small-for-gestational age (SGA), males, outborns, IPPV via endotracheal ventilation (ETT) in DR, chest compression in DR, MAS, and PPHN. The significant factors associated with decreased risk in term neonates were LGA and major malformations.

In preterm neonates with pneumothorax developed during nCPAPt, the significant independent factors associated with increased risk of pneumothorax were RDS and PPHN. In term neonates, the significant independent factors associated with increased risk of pneumothorax during nCPAPt were SGA and eCPAPt in DR. Large-for gestational age, HIE or major congenital malformations were significant independent factors associated with lower risk.

In preterm neonates with pneumothorax developed during CMV, extremely preterm gestation <28 weeks, pneumonia, and PPHN were significant independent factors associated with increased risk; IPPV via ETT in DR was associated with significantly lower risk of developing pneumothorax during CMV. In term neonates with pneumothorax developed during CMV, the significant independent factors associated with increased risk of pneumothorax were SGA, IPPV via ETT in DR, chest compression in DR, MAS, pneumonia, and PPHN.

In preterm neonates with pneumothorax developed during HFV, the only significant independent factor associated with increased risk was PPHN. In term neonates, the significant independent factors associated with increased risk were MAS and PPHN.

Outcome

In both term and preterm neonates, mortality was significantly higher in neonates with pneumothorax than those without pneumothorax (term neonates: 19.2% versus 6.5%, p<0.001; preterm neonates: 35.5% versus 10.0%; p<0.001), respectively. The duration of hospitalisation of term-gestation survivors with pneumothorax (median duration: 8 days, IQR: 6, 15) were significantly longer than those without pneumothorax (median duration: 6 days, IQR: 4,11; p<0.001). The duration of hospitalisation

TABLE 3: Comparison of potential risk factors associated with development of pneumothorax during CPAP therapy in preterm neonates (<37 weeks) and term neonates, respectively, in the Malaysian National Neonatal Registry, 2015-2020

Gestation groups	Preterm Gestation <37 weeks N=41636			Term Gestation ≥37 weeks N=27426		
Potential risk factors	**Developed pneumothorax during CPAP N=167 (%)**	**No pneumothorax during NICU stay n=41469 (%)**	**P values**	**Developed pneumothorax during CPAP n=283 (%)**	**No pneumothorax during NICU stay n=27143 (%)**	**P values**
Birthweight groups						
<1000 g	11 (6.6)	3675 (8.9)	<0.001	0	7 (0)	0.774
1000-1499 g	28 (16.8)	11719 (28.3)		0	63 (0.2)	
1500-2499 g	98 (58.7)	21853 (52.7)		37 (13.1)	3217 (11.9)	
≥2500 g	30 (18.0)	4222 (10.2)		246 (86.9)	23856 (87.9)	
Gestation						
<28 weeks	6 (3.6)	2721 (6.6)	0.004	-	-	
28-31 weeks	34 (20.4)	12321 (29.7)		-	-	
32-36 weeks	127 (76.0)	26427 (63.7)		-	-	
Intrauterine growth						
AGA	125 (74.9)	31088(75.0)	0.855	179 (63.3)	18029 (66.4)	<0.001
SGA	33 (19.8)	8501 (20.5)		100 (35.3)	7496 (27.6)	
LGA	9 (5.4)	1880 (4.5)		4 (1.4)	1618 (6.0)	
Males	97 (58.1)	23429/41464 (56.5)	0.681	184 (65.0)	16861/27136 (62.1)	0.320
Ethnic groups		N=41456			N=27140	
Chinese Malaysian	16 (9.6)	3557 (8.6)	0.261	19 (6.7)	1640 (6.0)	0.319
Malay Malaysian	120 (71.9)	27361 (66.0)		211 (74.6)	19027 (70.1)	
Indian Malaysian	10 (6.0)	2506 (6.0)		12 (4.2)	1819 (6.7)	
Malaysians of other ethnic groups	13 (7.8)	5458 (13.2)		24 (8.5)	2749 (10.1)	
Foreigners	8 (4.8)	2574 (6.2)		17 (6.0)	1905 (7.0)	

Outborn	17 (10.2)	3115 (7.5)	0.192	27 (9.5)	2647/27140 (9.8)	0.905
Chorioamnionitis	5 /163 (3.1)	1439/40841 (3.5)	1.000	2/277 (0.7)	403/26789 (1.5)	0.450
Antenatal steroids	102 (61.1)	28538/40863 (69.8)	0.014	-	-	-
Resuscitation at birth				N=280		
Oxygen therapy	123/163 (75.5)	31784/40901 (77.7)	0.491	205 (73.2)	19298/26649 (72.4)	0.766
Early CPAP therapy	104/163 (63.8)	26086/40899 (63.8)	0.995	194 (69.3)	13836/26644 (51.9)	<0.001
B&M IPPV	63/163 (38.7)	16885/40882 (41.3)	0.493	80 (28.6)	7730/26630 (29.0)	0.867
IPPV via ETT	50/164 (30.5)	14961/40880 (36.6)	0.105	64 (22.9)	5653/26642 (21.2)	0.505
Chest compression	2/164 (1.20)	540/40868 (1.3)	1.000	3 (1.1)	215/26640 (0.8)	0.497
Surfactant therapy	63 (37.7)	16901 (40.8)	0.426	-	-	-
EOS	1/167 (0.6)	368/41466 (0.9)	1.000	2 (0.7)	229/27142 (0.8)	1.000
MAS	2 (1.2)	345 (0.8)	0.406	62 (21.9)	5052 (18.6)	0.157
RDS	115 (68.9)	27625 (66.0)	0.539	-	-	-
Pneumonia	57/167 (34.1)	11162/41423 (26.9)	0.037	126 (44.5)	11693/27048 (43.2)	0.662
HIE	-	-	-	3 (1.1)	1314 (4.8)	0.001
PPHN	10/167 (6.0)	673/41453 (1.6)	<0.001	22 (7.8)	1620/27139 (6.0)	0.203
Major congenital malformations	10 (6.0)	2749 (6.6)	0.740	14 (4.9)1314	2671 (9.8)	0.006

Note: CPAP, continuous positive pressure; NICU, neonatal intensive care unit; AGA, appropriate-for-gestational age; SGA, small-for-gestational age; LGA, large-for-gestational age; B&M IPPV, positive pressure ventilation via bag and mask; IPPV via ETT, intermittent positive pressure ventilation via endotracheal tube; EOS, early-onset sepsis; MAS, meconium aspiration syndrome; RDS, respiratory distress syndrome; HIE, hypoxic-ischaemic encephalopathy; PPHN, pulmonary hypertension of newborn.

TABLE 4: Comparison of potential risk factors associated with pneumothorax developed during conventional mechanical ventilation in preterm (<37 weeks) and term neonates, respectively, in the Malaysian National Neonatal Registry, 2015-2020

	Preterm Gestation<37 weeks N=29608			**Term Gestation ≥37 weeks N=23659**		
Potential risk factors	**Pneumothorax occurred during CMV. N= 351 (%)**	**No pneumothorax N= 29257 (%)**	**P values**	**Pneumothorax occurred during CMV. N= 639**	**No pneumothorax N= 23020**	**P values**
Birthweight, g Median (IQR)						
<1000	75 (21.4)	4364 (14.9)	0.003	1 (0.2)	6 (0,0)	0.135
1000-1499	91 (25.9)	8618 (29.5)		2 (0.3)	42 (0.2)	
1500-2499	140 (39.9)	13109 (44.8)		90 (14.1)	2886 (12.5)	
≥2500	45 (12.8)	3166 (10.8)		546 (85.4)	20086 (87.3)	
Gestation, weeks						
<28	75 (21.4)	3521 (12.0)	<0.001	-	-	-
28-31	96 (27.4)	9940 (34.0)		-	-	-
32-36	180 (51.3)	15796 (54.0)		-	-	-
Intrauterine growth, n (%)						
AGA	272 (77.5)	22593 (77.2)	0.403	365 (57.1)	15023 (65.3)	<0.001
SGA	56 (16.0)	5151 (17.6)		262 (41.0)	6945 (30.2)	
LGA	23 (6.6)	1513 (5.2)		12 (1.9)	1052 (4.6)	
Males	216 (61.5)	16873/29251 (57.7)	0.146	394/638 (61.8)	14289/23013 (62.1)	0.896
Ethnic groups		N=29245		N=638	N=23013	
Chinese Malaysian	27 (7.7)	2507 (8.6)	0.898	21 (3.3)	1453 (6.3)	0.007
Malay Malaysian	234 (66.7)	19654 (67.2)		481 (75.4)	16051 (69.7)	
Indian Malaysian	20 (5.7)	1696 (5.8)		32 (5.0)	1169 (5.1)	
Malaysians of other ethnic groups	42 (12.0)	3400 (11.6)		52 (8.2)	2251 (9.8)	
Foreigners	28 (8.0)	1988 (6.8)		52 (8.2)	2089 (9.1)	

Outborns	40 (11.4)	3005 (10.3)	0.490	101 (15.8)	3504/23017 (15.2)	0.686
Chorioamnionitis	22/344 (6.4)	1168/28643 (4.1)	0.031	16/630 (2.5)	350/22581 (1.5)	0.049
Antenatal steroids	228/347 (65.7)	19382/28766 (67.4)	0.509	-	-	
Resuscitation at birth:						
Oxygen therapy	272/345 (78.8)	22447/28615 (78.4)	0.859	448/601 (74.5)	16071/22290 (72.1)	0.187
Early CPAP therapy	164/344 (47.7)	14575/28613 (50.9)	0.229	239/601 (39.8)	7885/22283 (35.4)	0.027
B&M IPPV	212/345 (61.4)	17592/28600 (61.5)	0.981	360//600 (60.0)	11962/22258 (53.7)	0.002
IPPV via ETT	213/344 (61.9)	18817/28606 (65.8)	0.134	397/601 (66.1)	12960/22282 (58.2)	<0.001
Chest compression	17/344 (4.9)	918/28595 (3.2)	0.071	30/601 (5.0)	685/22277 (3.1)	0.008
Surfactant therapy	241 (68.7)	18130 (62.0)	0.010	-	-	-
EOS	4 (1.2)	416/29256 (1.4)	1.000	3 (0.5)	278/23018 (1.2)	0.095
MAS	-	-	-	289 (45.2)	5135 (22.3)	<0.001
RDS	267 (76.1)	21710 (74.2)	0.427	-	-	-
Pneumonia	143/350 (40.9)	8301/29213 (28.4)	<0.001	247/637 (38.8)	9068/22939 (39.5)	0.700
PPHN	50 (14.2)	962/29247 (3.3)	<0.001	207 (32.4)	2445/23015 (10.6)	<0.001
HIE	-	-	-	95 (14.9)	3359/23015	0.848
Major congenital malformations	52 (14.8)	3264 (11.2)	0.031	96 (15.0)	3547 (15.4)	0.790

Note: CMV, conventional mechanical ventilation; CPAP, early continuous positive pressure; B&M IPPV, intermittent positive airway pressure ventilation via bag and mask; IPPV via ETT, intermittent positive pressure ventilation via endotracheal tube; EOS, early onset sepsis; MAS, meconium aspiration syndrome; RDS, respiratory distress syndrome; HIE, hypoxic-ischaemic encephalopathy; PPHN, pulmonary hypertension of newborn.

TABLE 5: Comparison of potential risk factors associated with pneumothorax developed during high frequency ventilation in preterm (<37 weeks) and term neonates, respectively, in the Malaysian National Neonatal Registry, 2015-2020

	Preterm Gestation <37 weeks N=4664			**Term Gestation ≥37 weeks N=3250**		
Potential risk factors	**Developed Pneumothorax During HFV N= 272 (%)**	**No pneumothorax N= 4392 (%)**	**P values**	**Developed Pneumothorax During HFV N= 327 (%)**	**No pneumothorax N= 2923 (%)**	**P values**
Birthweight, g Median (IQR)						
<1000	82 (30.1)	1504 (34.2)	0.046	0	1 (0.0)	0.141
1000-1499	78 (28.7)	1356 (30.9)		3 (0.9)	7 (0.2)	
1500-2499	77 (28.3)	1165 (26.5)		48 (14.7)	376 (12.9)	
≥2500	35 (12.9)	367 (8.4)		276 (84.4)	2539 (86.9)	
Gestation, weeks						
<28	80 (29.4)	1333 (30.4)	0.164	-	-	
28-31	87 (32.0)	1598 (36.4)		-	-	
32-36	105 (38.6)	1461 (33.3)		-	-	
Intrauterine growth, n (%)						
AGA	216 (79.4)	3414 (77.7)	0.245	191 (58.4)	1882 (64.4)	0.014
SGA	35 (12.9)	708 (16.1)		125 (38.2)	897 (30.7)	
LGA	21 (7.7)	270 (6.1)		11 (3.4)	144 (4.9)	
Males	166 (61.0)	2639/4390 (60.1)	0.765	187 (57.2)	1786 (61.1)	0.167
Ethnic groups		N=4391				
Chinese Malaysian	27 (9.9)	492 (11.2)	0.942	14 (4.3)	193 (6.6)	0.014
Malay Malaysian	166 (61.0)	2607 (59.4)		202 (61.8)	1920 (65.7)	
Indian Malaysian	16 (5.9)	254 (5.8)		11 (3.4)	137 (4.7)	
Malaysians of other ethnic groups	45 (16.5)	710 (16.2)		65 (19.9)	403 (13.8)	
Foreigners	18 (6.6)	328 (7.5)		35 (10.7)	270 (9.2)	

Outborn	23 (8.5)	536 (12.2)	0.065	60 (18.3)	592/2922 (20.3)	0.413
Chorioamnionitis	16/265 (6.0)	233/4257 (5.5)	0.696	6/315 (1.9)	42/2847 (1.5)	0.472
Antenatal steroids	172/268 (64.2)	2940/4325 (68.0)	0.197	-	-	
Resuscitation at birth:						
Oxygen therapy	202/264 (76.5)	3312/4267 (77.6)	0.677	239/316 (75.6)	1983/2785 (71.2)	0.098
Early CPAP therapy	108/264 (40.9)	1860/4265 (43.6)	0.390	110/316 (34.8)	838/2784 (30.1)	0.085
B&M via IPPV	191/264 (72.3)	2866/4262 (67.2)	0.086	184/314 (58.6)	1304 /2777 (47.0)	<0.001
IPPV via ETT	197/264 (74.6)	3023/4265 (70.9)	0.193	183/316 (57.9)	1308/2783 (47.0)	<0.001
Chest compression	20/264 (7.6)	242/4259 (5.7)	0.201	11/316 (3.5)	91/2781 (3.3)	0.844
Surfactant therapy	217 (79.8)	3454 (78.6)	0.657	-	-	-
EOS	10 (3.7)	149 (3.4)	0.802	4/327 (1.2)	82/2922 (2.8)	0.091
MAS	-	-	-	165 (50.5)	1124 (38.5)	<0.001
RDS	212 (77.9)	3586 (81.6)	0.127	-	-	-
Pneumonia	82 (30.1)	1350/4383 (30.8)	0.821	110 (33.6)	1126/2907 (38.7)	0.082
PPHN	79 (29.0)	636/4387 (14.5)	<0.001	240 (73.4)	1644/2919 (56.3)	<0.001
HIE	-	-	-	39 (11.9)	248 (8.5)	0.037
Major congenital malformations	60 (22.1)	706 (16.1)	0.010	70 (21.4)	692 (23.7)	0.359

Note: HFV, high frequency ventilation; AGA, appropriate-for-gestational age; SGA, small-for-gestational age; LGA, large-for-gestational age; CPAP, continuous positive pressure; B&M IPPV, intermittent positive pressure ventilation via bag and mask; IPPV via ETT, intermittent positive pressure ventilation via endotracheal tube; EOS, early-onset sepsis; MAS, meconium aspiration syndrome; RDS, respiratory distress syndrome; HIE, hypoxic-ischaemic-encephalopathy; PPHN, pulmonary hypertension of newborn.

TABLE 6: Significant independent factors associated with pneumothorax developed during different modes of respiratory support identified by multiple logistic regression analysis

Modes of respiratory support when pneumothorax developed	Gestation group	Risk factors	Adjusted Odds Ratio (95% CI)	P values
Spontaneous breathing	Preterm	Males	1.39 (1.09, 1.77)	0.007
		Malays	1.68 (1.01, 2.80)	0.046
		Foreigners	1.98 (1.04, 3.76)	0.038
		IPPV via face mask in DR	1.37 (1.00, 1.87)	0.049
		Received chest compression in DR	1.72 (1.03,2.87)	0.040
		Surfactant therapy	1.58 (1.15, 2.18)	0.005
		PPHN	4.45 (3.11, 6.37)	<0.001
		Congenital malformations	1.67 (1.22, 2.27)	0.001
	Term	SGA	1.51 (1.28, 1.78)	<0.001
		Males	1.28 (1.11, 1.49)	<0.001
		Outborn	1.41 (1.14, 1.74)	0.002
		IPPV via ETT in DR	1.65 (1.37, 1.99)	<0.001
		Received chest compression in DR	1.92 (1.31, 2.81)	<0.001
		MAS	1.67 (1.41, 1.96)	<0.001
		PPHN	2.51 (2.07, 3.03)	<0.001
		LGA	0.57 (0.37, 0.87)	0.010
		Major malformations	0.52 (0.40, 0.68)	<0.001
CPAPt in NICU	Preterm	RDS	1.80 (1.20, 2.70)	0.005
		PPHN	3.75 (1.92, 7.30)	<0.001
	Term	SGA	1.48 (1.10, 1.98)	0.009
		eCPAPt in DR	2.20 (1.68, 2.90)	<0.001
		LGA	0.20 (0.06, 0.61)	0.005
		HIE	0.20 (0.06, 0.64)	0.007
		Major malformation	0.52 (0.30, 0.91)	0.022
Mechanical ventilation in NICU	Preterm	Gestation <28 weeks	1.83 (1.07, 3.13)	0.029
		Pneumonia	1.73 (1.38, 2.17)	<0.001
		PPHN	4.52 (3.26, 6.25)	<0.001
		IPPV via ETT in DR	0.66 (0.50, 0.88)	0.005
	Term	SGA	1.66 (1.36, 2.01)	<0.001
		IPPV via ETT in DR	1.37 (1.09, 1.72)	0.007
		Chest compression in DR	1.62 (1.06, 2.48)	0.026
		MAS	2.51 (2.07, 3.04)	<0.001
		Pneumonia	1.32 (1.10, 1.59)	0.003
		PPHN	3.81 (2.65, 3.88)	<0.001
High frequency ventilation in NICU	Preterm	PPHN	2.21 (1.63, 3.01)	<0.001
	Term	MAS	1.38 (1.04, 1.84)	0.027
		PPHN	2.17 (1.64, 2.88)	<0.001

Note: CI, confidence intervals; CPAPt, continuous positive airway pressure therapy; DR, delivery room; eCPAPt, early continuous positive airway pressure therapy; ETT, endotracheal tube; HIE, hypoxic-ischaemic encephalopathy; IPPV, intermittent positive pressure ventilation; LGA, large-for-gestational age; MAS, meconium aspiration syndrome; PPHN, persistent pulmonary hypertension of newborns; RDS, respiratory distress syndrome; SGA, small-for-gestational age.

of preterm-gestation survivors were also significantly longer in those with pneumothorax (median duration: 25 days, IQR: 13, 56) than those without pneumothorax (median duration: 23 days, IQR: 11, 42; p<0.001).

DISCUSSION

In this large multicentre population study of neonates admitted to 44 Malaysian NICUs, the incidence of all types of pneumothorax was higher than those reported in high-income countries where the incidences ranged from 0.34-1.4 per 1000 livebirths.[1,13,14] One-third of the pneumothorax in the Malaysian NICUs were spontaneous onset, and two-third developed during respiratory support. Term neonates had higher rates of all types of pneumothorax than preterm, as reported by others.[5] However, mortality was higher in preterm neonates with pneumothorax. Although nCPAPt was the most used mode of respiratory support and HFV the least used, neonates on nCPAPt had the lowest rate of pneumothorax, and HFV the highest rate. These confirm that nCPAPt is a much safer mode of respiratory support than both CMV and HFV as reported elsewhere.[15] Many neonates in the present study who developed spontaneous-onset pneumothorax had either underlying lung conditions at birth and/or exposure to resuscitative procedures in DR with possibility of sustaining some degree of lung trauma as reported by other investigators.[4]

Our study was the first to investigate the risk factors associated with spontaneous-onset pneumothorax and pneumothorax developed during the three common modes of respiratory supports in both term and preterm neonates. Given that most pneumothorax occurred during the first 48 hours of life[1,4,16,17], we evaluated demographic characteristics, DR resuscitative procedures and neonatal conditions present during the first 48 hours of life as potential risk factors associated with development of pneumothorax. In preterm neonates, we found male gender, ethnicity, major congenital malformations, and surfactant therapy were significant independent factors associated with increased risk only in spontaneous-onset pneumothorax unlike studies reported elsewhere.[3,5] RDS was only significantly associated with increased risk of pneumothorax developed during nCPAPt. Pneumonia was only significantly associated with increased risk of pneumothorax developed during CMV. PPHN was a significant factor associated with increased risk in all types of pneumothorax. In term neonates, male gender and outborn were significant independent factors associated with increased risk of spontaneous-onset pneumothorax. SGA was significantly associated with increased risk of spontaneous-onset pneumothorax and pneumothorax developed during nCPAPt and CMV. Pneumonia was significantly associated with increased risk of developing pneumothorax only during CMV. MAS was significantly associated with increased risk of spontaneous-onset pneumothorax and pneumothorax developed during CMV and HFV. PPHN was a significant independent factor associated with increased risk in all types of pneumothorax.

We have also identified four resuscitative procedures in DR as significant independent factors associated with increased risk of pneumothorax. IPPV via face mask was associated with increased risk of spontaneous-onset pneumothorax only in preterm neonates. Chest compression was associated with increased risk of spontaneous-onset pneumothorax of both term and preterm neonates, and of pneumothorax during CMV in term neonates as reported by others.[17,18] According to the Malaysian national guidelines[19], eCPAP in DR was recommended only for preterm neonates. In this study a high proportion of term neonates were given eCPAPt (Table 3) which was a significant independent factor associated with increased risk of pneumothorax developed during nCPAPt. Although nCPAPt was a safer mode of respiratory support than CMV and HFV, our findings suggest that its use on term neonates in DR should be applied with caution.

Our study confirms that many neonates who developed spontaneous-onset pneumothorax often had underlying lung conditions or exposure to more aggressive types of resuscitative procedures in DR than those without pneumothorax. Our findings suggest that following exposure to these procedures, these neonates should be monitored closely for the development of pneumothorax.

Systematic training of all perinatal health care providers on neonatal resuscitation was implemented in Malaysia since 1996.[20,21] However, there is no similar national training program on use of nCPAPt, CMV and HFV for neonatal healthcare providers in Malaysian hospitals. Most young doctors learned on the job. Given the findings in the present study, to reduce the incidence of neonatal pneumothorax and its associated morbidities and mortalities, there is a need to fine-tune the training of the techniques of applying IPPV (via face mask and ETT) and chest compression during resuscitation, and monitor the competency levels of trained healthcare providers in neonatal resuscitation, review and improve our ventilatory strategies, and introduce a systematic training program for all neonatal doctors on the use of nCPAPt, CMV and HFV, particularly in neonates with PPHN and pneumonia.

The strengths of the present study include its large sample size, it being a national multicentre population study, and its prospectively collected data using a standardised format. There were several limitations in this study. Information on the age of onset of pneumothorax, BPD and LOS were not included in the MNNR database. Without this information, the temporal relationship of onset of BPD and LOS with the development of pneumothorax was unclear. For this reason, these variables were not evaluated as potential risk factors associated with the development of pneumothorax in multiple regression analyses.

In conclusion, the most common type of pneumothorax was spontaneous in-onset. During respiratory support, HFV had the highest and nCPAPt the lowest rate of pneumothorax. Improving training and strategies on use of all modes of respiratory support and resuscitation techniques in delivery rooms may reduce incidences of all types of pneumothorax.

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REFERENCES

1. Joshi A, Kumar M, Rebekah G, Santhanam S. Etiology, clinical profile & outcome of neonatal pneumothorax in tertiary care centre in South Indian: 13-year experience. J Matern Fetal Neonatal Med 2022;35(3):520-4.
2. Shen A, Yang J, Chapman G, Pam S. Can neonatal pneumothorax be successfully managed in regional Australia? Rural and Remote Health 2020;20:5615.
3. Garcia-Munoz Rodrigo F, Urquia Marti L, Galan Henriquez G, Rivero Rodriquez S, Tejera Carreno P, Molo Amoros S. Perinatal risk factors for

pneumothorax, morbidity and mortality in very low birth weight infants. J Matern Fetal Neonatal Med 2017;30(22):2679-85.
4. Vibede L, Vibede E, Bendtsen M, Pedersen L, Ebbesen F. Neonatal pneumothorax: a descriptive regional Danish study. Neonatology 2017;111:303-8.
5. Duong HH, Mirea L, Shah PS, Yang J, Lee SK, Sankaran K. Pneumothorax in neonates: trends, predictors, and outcomes. J Neonat-Perinat Med. 2014;7:29-38.
6. Al Matary AR, Munshi HH, Abozaid S, Qaraqei M, Wani TA, Abdu-Shaheen AK. Characteristics of neonatal pneumothorax in Saudi Arabia: three years' experience. Oman Med J. 2017;2:135-9.
7. Boo NY, Cheah IGS. Risk factors associated with pneumothorax in the Malaysian neonatal intensive care units. J Paedr Child Health 2011;47:183-90.
8. Boo NY, Chee SC, Neoh SH, *et al*. Ten-year trend of care practices, morbidities, and survival of very preterm neonates in the Malaysian National Neonatal Registry: a retrospective cohort study. BMJ Paediatr Open 2021;5:e001149.
9. Boo NY, Neoh SH, Chee SC. An observational study of therapeutic hypothermia and factors associated with mortality in late-preterm and term neonates with hypoxic-ischaemic encephalopathy in a middle-income country. Front Pediatr. 2022;10:894735.
10. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard score, expanded to include extremely premature infants. J Pediatr 1991;119:417-23.
11. Jobe A, Bancalari E. NICHD/NHLBI/ORD Workshop Summary: bronchopulmonary dysplasia. Am J Respir Crit Care Med. 2001;163:1723–29.
12. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. Arch Neurol 1976;33:696-705.
13. Acun C, Nusairat L, Kadri A, *et al*. Pneumothorax prevalence and mortality per gestational age in newborn. Pediatr Pulmono 2021;56:2583-8.
14. Zanardo V, Padovani E, Pittini C, Doglioni N, Ferrante A, Trevisanuto D. The influence of timing of elective Caesarean section on risk of neonatal pneumothorax. J Pediatr 2007;150:252-5.
15. Thome UH, Carlo WA, Pohlandt F. Ventilation strategies and outcome in randomised trials of high frequency ventilation. Arch Dis Child Fetal Neonatal Ed 2005;90(6):F466–73.
16. Kim EA, Jung JH, Lee SY, Park SH, Kim JS. Neonatal pneumothorax in late preterm and full-term newborns with respiratory distress: a single-center experience. Neonatal Med 2022;29:18-27.
17. Ngerncham S, Kttiratsatcha P, Pacharn P. Risk factors of pneumothorax during the first 24 hours of life. J Med Assoc Thai 2005;88:S135-41.
18. Watkinson M, Tiron I. Events before the diagnosis of a pneumothorax in ventilated neonates. Arch Dis Child Fetal Neonatal Ed 2001;85: F201–3.
19. The premature infants. In: Paediatric Protocols for Malaysian Hospitals, 3rd Ed. Editors: Ismail MHI, Ng HP, Thomas T, Kuala Lumpur: Ministry of Health Malaysia, 2012; pp. 63-64.
20. Boo NY, Pong KM. Neonatal resuscitation training program in Malaysia: results of the first 2 years. J Paediatr Child Health 2001; 37: 118-124.
21. Boo NY. Neonatal resuscitation programme in Malaysia: an eight-year experience. Singapore Med J 2009; 50: 152-159.

- What is already known?
  - Mortality rates of neonatal pneumothorax are high.
  - Mechanical ventilation is associated with increased risk of neonatal pneumothorax.
  - Early continuous positive airway pressure is associated with low incidence.
- What this study adds?
  - Spontaneous pneumothorax accounts for one-third of the neonatal pneumothorax.
  - Chest compression is a significant risk factors associated with spontaneous-onset pneumothorax in both term and preterm neonates.
  - Neonates on high frequency ventilation have the highest rate of developing pneumothorax than other modes of respiratory support.
  - Preterm neonates with pneumothorax have higher mortality than term neonates.