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Original article

Pneumothorax in neonates: a level III Neonatal Intensive Care Unit experience

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Abstract

Introduction: Pneumothorax occurs more frequently in the neonatal period than in any other period of life and is associated with increased mortality and morbidity. Several risk factors for pneumothorax, including respiratory pathology, invasive and non-invasive respiratory support, and predictors of mortality have been described.

Objective: To evaluate the prevalence of pneumothorax, to assess risk factors and to describe the clinical characteristics, management and outcome of newborn infants with pneumothorax, as well as to identify predictors of mortality in these newborns.

Methods: This retrospective case-control study included all newborns hospitalized in the Neonatal Intensive Care Unit (NICU) of "Centro Hospitalar São João", Porto, Portugal, between 2003 and 2014, with the diagnosis of pneumothorax. A control group was selected among the newborns without pneumothoraces, admitted to the same NICU during the same period. The collected data included: demographics and perinatal data, pneumothorax characteristics, classification, treatment and clinical outcomes.

Results: Our study included 240 neonates (80 with pneumothoraces and 160 controls), of whom 145 were male (60.4%). Median gestational age was 37 (24-40) weeks and median birthweight 2,613 (360-4,324) grams. The prevalence in our NICU was 1.5%. Pneumothorax was significantly associated with respiratory distress syndrome (RDS) ($p = 0.010$) and transient tachypnea of the newborn (TTN) ($p < 0.001$). Invasive mechanical ventilation (MV) ($p = 0.016$) and $FiO_2 \geq 0.4$ ($p = 0.003$), were independent risk factors for the development of pneumothoraces. The mortality rate was 13.8%. Hypotension, MV and thoracentesis followed by a chest tube insertion were found to be predictors of mortality in newborns with pneumothoraces, but pneumothorax *per se* was not a predictor of mortality.

Conclusion: Pneumothorax is relatively frequent in the NICU. Its risk factors and predictors of mortality should be known in order to prevent and treat

this critical situation. Pneumothorax itself was not a predictor of mortality, probably due to the adequate and prompt management used in the NICU.

Keywords

Pneumothorax, newborn, risk factors, mechanical ventilation, neonatal intensive care, mortality.

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Introduction

Pneumothorax occurs more frequently in the neonatal period than in any other period of life and is associated with increased mortality and morbidity. It begins with the rupture of an over-distended alveoli. The air escapes along the perivascular connective tissue sheath into the pleural space, causing pneumothorax and less commonly pneumomediastinum, pneumopericardium, subcutaneous emphysema, and pneumoperitoneum, altogether known as air leak syndromes [1, 2].

Pneumothorax is a relatively frequent critical situation in the Neonatal Intensive Care Unit (NICU). Symptomatic pneumothorax occurs in about 0.05% to 0.1% of all live births, and in very low birthweight infants this rate can achieve 3.8% to 9% [3, 4].

Several risk factors for pneumothorax have been described and include among others immaturity, respiratory distress syndrome (RDS), invasive and non-invasive respiratory support, chorioamnionitis. For moderate-late preterm infants, risk factors also include high birth weight, male gender, and rupture of membranes longer than 24 hours [5].

Common clinical manifestations of pneumothorax are RDS signs. Hypoxemia and hypercapnia are usually observed in arterial blood gases. In some cases, there is a mediastinal shift that compromises the cardiovascular system and carries a significant risk of an impaired outcome and death. Tension pneumothorax causes a rise in intrapleural pressure and subsequent lung collapse, as well as impaired venous return, systemic hypotension and cardiac arrest. It is, therefore, essential to recognize these risk infants in order to prevent and treat properly this critical situation [1, 4].

The diagnosis of pneumothorax relies on clinical judgment, transillumination and chest radiogram [6].

The treatment of neonatal pneumothorax is not fully defined. Three approaches are the common practice in NICUs. The expectant approach for small and asymptomatic pneumothorax, and active intervention to a significant one, such as needle (14–16 G) aspiration and thoracic drainage [7, 8]. Needle aspiration is an option in cases of mild to moderate pneumothorax when the infant is hemodynamically stable. In hypertensive pneumothoraces the common therapeutic approach is chest tube placement [1].

The aim of this study was to evaluate the prevalence, to identify risk factors and to describe the clinical characteristics, management and outcome of newborn infants with pneumothorax as well as to identify the predictor factors of mortality in these newborns.

Material and methods

This retrospective case control study included all newborns hospitalized in the NICU (a level III unit with 17 beds and 450 admissions per year) of "Centro Hospitalar São João", Porto, between 1st January 2003 and 31st December 2014, with the diagnosis of pneumothorax.

All data were collected from the hospital electronic clinical database and medical records of the patients. A control group was selected among newborns without pneumothoraces admitted to the NICU in the same years (more or less 1 year), gender, gestational age (more or less 2 weeks) and birthweight (more or less 500 g). These data includes: information regarding pregnancy and delivery (gestational age, multiple births, type of delivery), gender, birth weight, Apgar score at 1 and 5 minutes, the need of resuscitation, antenatal corticosteroid therapy, need for surfactant, oxygen therapy, nasal continuous positive airway pressure (nCPAP), conventional mechanical ventilation (MV) and high frequency oscillation ventilation (HFOV) use.

Pneumothorax characteristics were also obtained (day of life and the duration of the pneumothorax) and classified as spontaneous (primary or secondary), iatrogenic (positive airway pressure or

surgery), hypertensive (or tension) and persistent pneumothorax. We defined pneumothorax as primary spontaneous if it occurred without obvious cause, as secondary spontaneous if there was an underlying disease and as iatrogenic if it was caused by a medical (MV) or surgical procedure. Hypertensive or tension pneumothorax was considered whenever a mediastinum shift was observed; persistent pneumothorax if it persisted more than 7 days. Data about treatment, neonatal morbidity and mortality were also collected. Pneumothoraces were diagnosed by chest radiography and the type of pneumothorax was assessed according to clinical setting and medical history [1].

Gestational age was assessed by post-menstrual age, ultrasound examination or the New Ballard Score (in the absence of obstetrical indexes) [9, 10]. Small for gestational age was defined as a birth weight below the 3rd centile of Fenton's growth charts [11]. Our NICU has a protocol for positive pressure ventilation that includes different ventilatory strategies according to different lung diseases and favors the use of permissive hypercapnia. For the very low birth weight infants nCPAP just after birth is the preferable mode of ventilation [12]. nCPAP is performed using Infant Flow (Pulmocor, USA), for invasive MV we use Babylog® (Dräger, Germany). HFOV is performed as rescue ventilation (Sensor Medics®, USA).

Sepsis was considered in the presence of a positive blood culture, combined with clinical and laboratory parameters [13]. Intraventricular hemorrhage (IVH) was defined according to Papile [14] and Volpe [15] (before and after 2010, respectively), intraventricular bleeding with ventricular dilatation is classified as IVH 3 and with parenchymal involvement as IVH 4. Retinopathy of prematurity (ROP) was diagnosed and classified according to the International Classification of Retinopathy of Prematurity revised [16]. Patent ductus arteriosus (PDA) was diagnosed according to SIBEN consensus [17]. Necrotizing enterocolitis (NEC) was defined by clinical findings and radiological features, according to the modified Bell criteria [18]. Cystic periventricular leukomalacia (PVL) was diagnosed by ultrasound [19].

RDS was defined based on the European guidelines [20] and bronchopulmonary dysplasia (BPD) according to the NIH Consensus definition [21]. Transient tachypnea of the newborn (TTN) was diagnosed according to the criteria of Machado and Fiori [22]. Pneumonia was diagnosed based on combination of clinical, radiological and laboratory parameters [23]. Meconium aspiration syndrome (MAS) was characterized based on El Shahed's criteria [24]. Pulmonary hypoplasia (PH) was defined according to clinical, radiologic, and pathologic criteria [25].

Hypotension was defined according to Cayabyab et al. [26].

All statistical analyses were performed using SPSS® for Windows®, version 23. Categorical variables were evaluated by absolute and relative frequencies and continuous variables were reported as median (minimum-maximum). All variables were compared between neonates with (cases) or without (controls) pneumothorax. Chi-Squared or Fisher's exact test were used to compare categorical variables and Mann-Whitney U test (non-parametric test) to compare continuous variables. Risk factors for pneumothorax were evaluated by a multivariate analysis by logistic regression. Statistically significance was considered for a p-value less than 0.05.

Results

Our study included 240 neonates (80 with pneumothoraces and 160 controls), of whom 145 were males (60.4%). Their median gestational age was 37 (24-40) weeks and the median birthweight was 2,613 (360-4,324) grams. The prevalence of pneumothorax in our NICU was 1.5%, varying from 11 (2.4%) cases in 2003 to 4 (0.9%) cases in 2014. The analysis of demographic and perinatal data of both groups showed statistically significant differences in Apgar score at 5th minute ($p = 0.002$) and in resuscitation at birth ($p < 0.001$), as shown in **Tab. 1**.

Tab. 2 shows the characterization and treatment of pneumothoraces. They were spontaneous (primary or secondary to lung disease) in 46 (57.5%) neonates and iatrogenic in 34 (42.5%) neonates. Fifty-seven (71.3%) were hypertensive and 2 (2.5%) persistent. We observed 37 (46.3%) pneumothoraces in the right lung, 35 (43.8%) in the left lung. Eight (10%) cases were bilateral. Oxygen therapy was delivered in 68 (85%) neonates, nCPAP in 15 (18.8%) and MV in 60 (75%) newborns. All patients treated with MV also received oxygen therapy. Eight newborns received nCPAP and oxygen therapy and 7 of them only were treated with nCPAP. Five newborns with pneumothorax recovered without any respiratory treatment. To treat the pneumothoraces, 57 (71.3%) neonates needed drains and 3 (3.8%) thoracentesis

Table 1. Demographic and perinatal data.

	Total (n = 240)	Cases (n = 80)	Controls (n = 160)	p-value
Gender, n (%)				
Male	145 (60.4)	50 (62.5)	95 (59.4)	0.641[a]
Female	95 (39.6)	30 (37.5)	65 (40.6)	
Gestational age (weeks), median (min-max)	37 (24-40)	37 (24-40)	37 (24-40)	0.948[b]
Gestational age (weeks), n (%)				
< 37	117 (48.8)	39 (48.8)	78 (48.8)	0.999[a]
< 28	29 (12.1)	9 (11.3)	20 (12.5)	0.779[a]
Birth weight (g), median (min-max)	2,613 (360-4,324)	2,588 (360-4,260)	2,643 (450-4,324)	0.836[b]
Parity, n (%)				
Single	208 (86.7)	65 (81.3)	143 (89.4)	0.081[a]
Multiple	32 (13.3)	15 (18.8)	17 (10.6)	
Antenatal steroids, n (%)	72 (30)	24 (30)	48 (30)	0.976[a]
Full cycle	53 (22.1)	18 (22.5)	35 (21.9)	0.912[a]
Type of delivery, n (%)				
Vaginal	129 (53.8)	36 (45)	93 (58.1)	0.055[a]
C-section	111 (46.3)	44 (55)	67 (41.9)	
Apgar Score, n (%)				
1st min < 7	76 (31.7)	32 (40)	44 (27.5)	0.050[a]
5th min < 7	27 (11.3)	16 (20)	11 (6.9)	**0.002**[a]
Resuscitation at birth, n (%)	64 (26.7)	37 (46.3)	27 (16.9)	**< 0.001**[a]
Endotracheal Intubation	31 (48.4)	22 (59.5)	9 (33.3)	**0.039**[a]

$p < 0.05$, statistical significance.
[a]Chi-square test; [b]Mann-Whitney U test.

Table 2. Characterization and treatment of cases (n = 80).

Characterization of pneumothoraces	
Spontaneous, n (%)	46 (57.5)
Primary	6 (13)
Secondary to lung disease	40 (87)
Iatrogenic, n (%)	34 (42.5)
Positive pressure ventilation	32 (94.1)
During surgery	2 (5.9)
Laterality, n (%)	
Right	37 (46.3)
Left	35 (43.8)
Bilateral	8 (10)
Treatment of pneumothoraces	
Oxygen therapy, n (%)	68 (85)
FiO_2 after pneumothorax, median (min-max)	0.4 (0.21-1)
Days, median (min-max)	4 (1-83)
nCPAP, n (%)	15 (18.8)
Days, median (min-max)	9 (1-32)
MV, n (%)	60 (75)
Days, median (min-max)	4 (1-48)
Thoracentesis with needle aspiration, n (%)	3 (3.8)
Drain, n (%)	57 (71.3)
Days, median (min-max)	3 (1-21)

nCPAP: nasal continuous positive airway pressure; MV: mechanical ventilation

with needle aspiration. Actually, thoracentesis with needle aspiration was performed in 10 (12.5%) pneumothoraces, but 7 of them also had to be drained.

In **Tab. 3** we present the clinical and management data in cases and controls. There were statistically significant differences between both groups concerning respiratory pathology (pneumonia, MAS, RDS, PH, TTN). IVH ≥ 3 grade, PDA, cystic PVL and hypotension were also more frequent in newborns having pneumothorax. Use of oxygen therapy ($p < 0.001$), nCPAP ($p < 0.001$) and MV ($p < 0.001$) also showed a significant increase in pneumothorax cases. Statistical significance between the two groups was also found for $FiO_2 \geq 0.4$ ($p < 0.001$). An association of pneumothorax was observed with two major congenital malformations: congenital cardiopathy (CHD) and diaphragmatic hernia. The median days of hospitalization was 9.5 in pneumothorax group and 4 in controls ($p < 0.001$). The prevalence of death was 24 (30%) in cases and 9 (5.6%) in controls ($p < 0.001$).

The two respiratory pathologies, RDS (OR 3.512, 95% CI 1.353-9.118, p = 0.010) and TTN (OR 8.677, 95% CI 2.752-27.354, p < 0.001) were significantly associated with pneumothorax. MV was also significantly associated with pneumothorax (OR 3.824, 95% CI 1.285-11.376, p = 0.016), as was $FiO_2 \geq 0.4$ (OR 5.614, 95%CI 1.828-17.238, p = 0.003), **Tab. 4**. Pneumothorax was not identified as a predictor of death (OR 1.284, 95% CI 0.409-4.032, p =

Table 3. Clinical and management data.

	Total (n = 240)	Cases (n = 80)	Controls (n = 160)	p-value
Pneumonia, n (%)	6 (2.5)	6 (7.5)	0	**0.001**[b]
MAS, n (%)	3 (1.3)	3 (3.8)	0	**0.036**[b]
RDS, n (%)	35 (14.6)	24 (30)	11 (6.9)	**< 0.001**[a]
Severe PH, n (%)	7 (2.9)	7 (8.8)	0	**< 0.001**[a]
TTN, n (%)	16 (6.7)	10 (12.5)	6 (3.8)	**0.010**[a]
Sepsis, n (%)	48 (20)	16 (20)	32 (20)	0.999[a]
BPD, n (%)	9 (3.8)	5 (6.3)	4 (2.5)	0.999[b]
IVH ≥ 3, n (%)	10 (4.2)	8 (10)	2 (1.3)	**0.003**[b]
ROP ≥ 2, n (%)	6 (2.5)	2 (2.5)	4 (2.5)	0.999[b]
NEC ≥ 2, n (%)	10 (4.2)	3 (3.8)	7 (4.8)	0.999[b]
PDA, n (%)	16 (6.7)	9 (11.3)	7 (4.4)	**0.044**[a]
Cystic PVL, n (%)	6 (2.5)	6 (7.5)	0	**0.001**[b]
Hypotension, n (%)	18 (7.5)	12 (15)	6 (3.8)	**0.002**[a]
Vasopressors, n (%)	16 (6.7)	11 (13.8)	5 (3.1)	**0.002**[a]
Surfactant, n (%)	41 (17.1)	30 (37.5)	11 (6.9)	**< 0.001**[a]
Doses, median (min-max)	1 (1-4)	1 (1-3)	2 (1-4)	**< 0.001**[c]
Oxygen therapy, n (%)	85 (35.4)	59 (73.8)	26 (16.3)	**< 0.001**[a]
Days of oxygen, median (min-max)	2 (1-75)	2 (1-25)	5 (1-75)	**< 0.05**[c]
FiO_2, median (min-max)	0.21 (0.21-1)	0.4 (0.21-1)	0.21 (0.21-1)	**< 0.001**[c]
FiO_2 ≥ 0.4, n (%)	54 (22.5)	43 (53.8)	11 (6.9)	**< 0.001**[a]
nCPAP, n (%)	51 (21.3)	28 (35)	23 (14.4)	**< 0.001**[a]
Days, median (min-max)	2 (1-35)	1 (1-15)	3 (1-35)	**0.006** [c]
MV, n (%)	64 (26.7)	47 (58.8)	15 (9.4)	**< 0.001**[a]
Days, median (min-max)	1.5 (1-25)	2 (1-25)	1 (1-24)	0.141[c]
PIP max, median (min-max)	24.5 (0-40)	25 (16-40)	22 (0-35)	0.161[c]
PEEP max, median (min-max)	4 (0-7)	4 (2-6)	4 (0-7)	0.582[c]
Thoracic congenital malformation, n (%)	25 (10.4)	23 (28.8)	2 (1.3)	**< 0.001**[b]
CHD	11 (4.6)	11 (13.8)	0	**< 0.001**[b]
Diaphragmatic hernia	9 (3.8)	9 (11.3)	0	**< 0.001**[b]
Esophageal atresia	5 (2.1)	3 (3.8)	2 (1.3)	0.337[b]
Days of hospitalization, median (min-max)	5 (1-167)	9.5 (1-167)	4 (1-149)	**< 0.001**[c]
Death, n (%) (3)	33 (13.8)	24 (30)	9 (5.6)	**< 0.001**[a]

$p < 0.05$, statistical significance.
[a]Chi-square test; [b]Fisher's exact test; [c]Mann-Whitney U test.
MAS: meconium aspiration syndrome; RDS: respiratory distress syndrome; PH: pulmonary hypoplasia; TTN: transient tachypnea of the newborn; BPD: bronchopulmonary dysplasia; IVH: intraventricular hemorrhage; ROP: retinopathy of prematurity; NEC: necrotizing enterocolitis; PDA: patent ductus arteriosus; PVL: periventricular leukomalacia; nCPAP: nasal continuous positive airway pressure; MV: mechanical ventilation; PIP: positive inspiratory pressure; PEEP: positive end expiratory pressure; CHD: congenital cardiopathy.

0.669). Hypotension, thoracentesis and MV were found to be predictors of death in newborns with pneumothoraces, as shown in **Tab. 5**.

Discussion

This study aimed to compare clinical characteristics between neonates with and without pneumothoraces and to identify risk factors of pneumothoraces and predictors of death in these patients.

As expected, there were no significant differences between cases and controls in terms of gender, gestational age and birth weight. Statistically significant differences in Apgar score at 5th minute occurred due to the need of resuscitation at birth, which was found to be a risk factor ($p < 0.001$). According to clinical practice, the use of

Table 4. Risk factors of pneumothorax.

	OR[a]	95% CI	p-value
RDS	3.512	1.353-9.118	**0.010**
TTN	8.677	2.752-27.354	**< 0.001**
$FiO_2 \geq 0.4$	5.614	1.828-17.238	**0.003**
MV	3.824	1.285-11.376	**0.016**

$p < 0.05$, statistical significance (multivariate analysis).
[a]Logistic regression.
OR: odds ratio; CI: confidence interval; RDS: respiratory distress syndrome; TTN: transient tachypnea of the newborn; MV: mechanical ventilation.

Table 5. Predictors of mortality in newborns with pneumothorax.

	OR[a]	95% CI	p-value
Pneumothorax	1.284	0.409-4.032	0.669
Hypotension	6.165	1.702-22.327	**0.006**
Thoracentesis and chest tube insertion	8.195	1.280-52.478	**0.026**
MV	29.551	8.257-105.765	**< 0.001**

$p < 0.05$, statistical significance (multivariate analysis).
[a]Logistic regression
OR: odds ratio; CI: confidence interval; MV: mechanical ventilation.

invasive ventilation with endotracheal intubation in neonatal resuscitation is less and less used and increasingly replaced by noninvasive ventilation with the minimum effective pressure [12]. Indeed we observed in our NICU that the prevalence of pneumothoraces decreased from 11 (2.4%) cases in 2003 to 4 (0.9%) cases in 2014, probably due to adoption of less invasive procedures. The type of delivery had no influence in pneumothorax occurrence. These, results that are consistent with previous studies [2, 27]. Antenatal steroids use wasn't associated with pneumothorax ($p = 0.976$), which is in agreement with other studies [28].

The treatment of pneumothorax is not fully defined. In this study we described 80 pneumothoraces, spontaneous in 46 (57.5%) neonates and iatrogenic in 34 (42.5%). However, only 68 (85%) received oxygen therapy, because pneumothoraces with very small size in chest X-ray solved spontaneously. As described in literature, another option for treatment is the expectant management for non-hypertensive pneumothoraces in patients who are ventilated [3], and this approach was used in 15 (18.8%) neonates with nCPAP and in 60 (75%) with CMV. The use of needle aspiration and chest tube are common options of treatment. Thoracentesis was performed in 10 (12.5%) pneumothoraces, however this treatment wasn't effective in 7 of them. Hence, thoracentesis only treated 3 (3.8%) non-hypertensive pneumothoraces. It is known that, frequently, neonates treated with needle aspiration can require subsequent chest-tube insertion [29]. In our study, 57 (71.3%) neonates needed drains to be effectively treated.

As described in **Tab. 3**, there was a statistically significant difference between cases and controls in respiratory pathology. When adjusted by multivariate analyses, RDS showed an OR = 3.512 and TTN was OR = 8.677, which means that they were positively related with pneumothorax. This is consistent with other studies [2, 28]. BPD was not statistically different between the two groups, as observed in other studies [28, 30]. This finding can be due to the few BPD cases in each group. The risk of developing pneumothorax was also increased in newborns with other pathologies (IVH ≥ 3 grade, PDA, cystic PVL and hypotension), showing that pneumothoraces can occur in patients with more severe diseases. Concerning IVH and PVL, the vascular cerebral effects of intrathoracic hemodynamic changes justified the significant differences observed between cases and controls. As we expected, the administration of surfactant was more frequent in patients with pneumothoraces, probably due to the lung pathology associated with cases. In the present study, oxygen therapy, nCPAP and CMV were related with the development of pneumothorax. Linear regression analyses indicate

that neonates who received MV were 3.8 times more likely to develop pneumothorax, and those who received oxygen therapy with a $FiO_2 \geq 0.4$ had an 5.6 times higher risk of pneumothorax. Terzic et al. showed that infants who needed higher FiO_2 were more likely to develop pneumothorax [28]. These results suggest that high pressures in nCPAP and CMV and a high FiO_2 should be avoided. Congenital heart disease and diaphragmatic hernia were also statistically significant risk factors for pneumothorax, probably because of the pathophysiological disturbances of these pathologies, or their surgical repair. Congenital diaphragmatic hernia is a risk factor for PH once it occupies space, prevents lung expansion and causes changes in the thoracic cavity [31]. Neonates with pneumothorax had a prolonged stay in NICU (average of 9.5 days). Possibly they were more likely to have associated pathology and need of treatment.

We found that 30% of cases died, compared to 5.6% of controls ($p < 0.001$). Hypotension, MV and thoracentesis associated with chest tube insertion were found to be predictors of mortality in newborns with pneumothoraces. These neonates had a bad prognosis since the beginning. However, in our study, pneumothorax was not identified as a predictor of mortality as it has been shown by others [2, 6]. The appropriate management used in the NICU was probably the explanation for this result.

The limitations of this study are the retrospective and single-centre design, the small sample size.

Conclusion

Pneumothorax is relatively frequent in the NICU. Its risk factors (RDS, TTN, invasive MV and a $FiO_2 \geq 0.4$) and predictors of mortality (hypotension, MV and thoracentesis followed by a chest tube insertion) should be well known, in order to prevent and treat this critical situation.

Pneumothorax itself was not a predictor of mortality, probably due to the adequate and prompt management used in the NICU.

Declaration of interest

The Authors declare that there is no conflict of interest. Funding: none.

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