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ORIGINAL ARTICLE

# Neonatal pneumothorax: symptoms, signs and timing of onset in the post-surfactant era

J. Andersson[a]  (iD), A. Magnuson[b] and A. Ohlin[c]

[a]Karlskoga Hospital, Örebro, Sweden; [b]Clinical Epidemiology and Biostatistics Department, School of Medical Sciences, Örebro University, Örebro, Sweden; [c]Department of Pediatrics, Örebro University Hospital, Faculty of Medicine and Health, Örebro University, Örebro, Sweden

**ABSTRACT**

**Aim:** The primary objective was to describe the incidence, symptoms, clinical signs, and time of onset of neonatal pneumothorax in Örebro County during 2011–2017. Secondary objectives were to describe risk factors, diagnostic procedures, treatments, and mortality and to compare preterm with term/post-term neonates.

**Materials and methods:** This retrospective population-based descriptive study included all neonates born in Örebro County during 2011–2017 and admitted to the neonatal intensive care unit at Örebro University Hospital at age <28 days with an x-ray verified diagnosis of "Pneumothorax originating in the perinatal period" in their medical record.

**Results:** Seventy-five neonates matched the inclusion criteria. The incidence of neonatal pneumothorax in Örebro County during the study period was 3.1 (95% CI: 2.5–3.8) per 1000 live births. All neonates were <48 h at debut of respiratory symptoms and the most common symptom was tachypnea. Twelve (16%) received invasive treatment. The mortality rate was 2 (3%), none due to pneumothorax.

**Conclusion:** The incidence of 3.1 per 1000 live births was relatively high, but the frequency of invasive treatment and mortality was low, indicating a high proportion of mild pneumothoraces. The lack of patients aged >48 h indicates that most neonatal pneumothoraces now occur very early in life.

## Introduction

Pneumothorax (PT) is more common in neonates than in any other age group [1]. Previous reports have shown the regional incidence of symptomatic neonatal PT to be 0.8–1.9 per 1000 live births [2–5].

Risk factors for neonatal PT include respiratory distress syndrome, meconium aspiration syndrome, congenital malformations, infections, transient tachypnea of the newborn, immaturity [6], and specific respiratory procedures such as mechanical ventilation, intubation, endotracheal suctioning [6], and fraction of inspired oxygen ≥0.4 [7]. Delivery by cesarean section [8,9] and the mode of anesthesia during cesarean section [10] are other predisposing factors. PT is known to be most common immediately after birth, when higher distending pressures may be needed to ventilate the neonate, and in the resolution period of respiratory distress syndrome, when pulmonary compliance may rise quickly [1].

The symptoms and clinical signs of PT have been known for a long time, and are well described in the literature. Symptoms include tachypnea, grunting, flaring, retractions, cyanosis, apnea, and bradycardia, while clinical signs comprise chest asymmetry, shift of cardiac impulse, and decreased breath sounds [1]. However, respiratory care for newborns has developed tremendously during recent years, and interventions such as CPAP, prenatal steroids, and surfactant treatment have had a substantial impact on how patients are treated today. Against this background, it is surprising that only two relevant studies have been published in the post-surfactant era: one small study on the symptoms of PT [11] and one on time of symptom onset [12]. It therefore seems warranted to examine whether symptoms, clinical signs and time of onset remain the same as when the disease was described in the dawn of neonatology.

CONTACT J. Andersson ✉ jnswnstn@gmail.com 💬 Intern Physician, Karlskoga Hospital, S-691 44 Karlskoga, Örebro, Sweden

The gold standard for confirming a PT diagnosis is a chest x-ray, unless the clinical condition requires emergency drainage [13]. Depending on the severity of a symptomatic PT, choice of treatment varies from expectant management to invasive treatment with either thoracentesis and/or thoracostomy [13]. The mortality rate in neonatal PT with study populations similar to the population in the present study varies from 6.6% to 13.6% [2–5].

## Methods

This was a retrospective population-based descriptive study including all neonates born in Örebro County during 2011–2017 and admitted to the neonatal intensive care unit at Örebro University Hospital at age <28 days with an X-ray verified PT diagnosis. Information on the number of births was provided by Statistics Sweden [14]. Patients whose medical record had the diagnosis "Pneumothorax originating in the perinatal period" (ICD-10 code 25.1) were included. This study was performed in two stages; first, all patients from 2011 to 2015 were analyzed in a quality improvement project which sparked the idea of the present study, and the cohort was then expanded to include all patients from 2011 to 2017. The study was approved by the ethical review board in Uppsala (2019-02595)

All data were registered in the spreadsheet software Excel (version 15 for Mac). The 95% confidence interval of the incidence was determined by calculating the Wilson score interval using the Epitools epidemiological calculator [15]. Due to a small sample size, continuous variables were summarized with median and interquartile range (IQR). Differences between preterm and term/post term infants were tested with the Mann–Whitney $U$-test for continuous variables and Fisher's exact test for categorical variables. $p$-values of <.05 were assumed to indicate statistical significance. Version 23 of SPSS for Mac was used for the statistical analysis.

## Results

A total of 24411 live births and 75 cases of neonatal PT were registered in Örebro County between 2011 and 2017, giving a mean incidence for PT of 3.1 (95% CI: 2.5–3.8) per 1000 live births per year. The yearly incidence varied from 1.8 per 1000 live births in 2012 to 4.5 per 1000 live births in 2016.

Background characteristics of the 75 patients in the study cohort are presented in Table 1. 10 (13%) were preterm. None of the patients were more than 48 h of age at the onset of symptoms. 39 (53%) had low APGAR scores (<7) after one minute, and 19 (25%) had low scores after 10 min. 57 (76%) patients were resuscitated and 68 (91%) received ventilatory support.

The most common symptom or clinical sign manifested was tachypnea with 58 (77%) cases, followed by 42 (56%) with cyanosis, 35 (47%) with grunting and retractions, 30 (40%) with bradycardia, 16 (21%) with decreased breath sounds, 14 (19%) with nasal flaring and five (7%) with apnea.

Half (51%) of the patients were x-rayed once, 33 (44%) were X-rayed between two and five times, and four (5%) were X-rayed between five and nine times.

**Table 1.** Background characteristics of 75 neonates evaluated for pneumothorax.

| | |
|---|---|
| Hospital of birth[a] | |
|   Karlskoga Hospital | 10 (13) |
|   Örebro University Hospital | 65 (87) |
| Mode of delivery[a] | |
|   Emergency Cesarean section | 22 (29) |
|   Elective Cesarean section | 5 (7) |
|   Vaginal delivery | 28 (37) |
|   Instrumental delivery | 20 (27) |
| Transported to another hospital[a] | 3 (4) |
| Singleton or twin at birth | |
|   Singleton | 72 (96) |
|   Twin | 3 (4) |
| Sex[a] | |
|   Female | 23 (31) |
|   Male | 52 (69) |
| Birth weight, g[b] | 3394 (3015–3770) |
| Low birth weight[a] | 7 (9) |
| Weight for gestational age[a] | |
|   Small for gestational age | 5 (7) |
|   Appropriate for gestational age | 70 (93) |
|   Large for gestational age | 0 |
| Birth length, cm*[b] | 51 (49–53) |
| Head circumference, cm*[b] | 35 (34–36) |
| Preterm, term, or post-term[a] | |
|   Preterm | |
|   - Moderate to late preterm | 9 (12) |
|   - Very preterm | 1 (1) |
|   - Extremely preterm | 0 (0) |
|   Term | 56 (75) |
|   Post-term | 9 (12) |
| Gestational age, days[b] | 283 (272–290) |
| APGAR score[a] | |
|   APGAR1* | 39 (53) |
|   ≥7 | 35 (47) |
|   APGAR5 | 30 (40) |
|   ≥7 | 45 (60) |
|   APGAR10 | 19 (25) |
|   ≥7 | 56 (75) |
| Age at symptom debut[a] | |
|   ≤24 h | 71 (95) |
| | 4 (5) |
| | 0 |
| Resuscitation[a] | 57 (76) |
| Ventilatory support[a] | 68 (91) |

[a]n (%).
[b]Median (interquartile range).
*1 patient.

**Table 2.** Subgroup analysis comparing preterm and term/post-term neonates with pneumothorax.

| | Preterm (n = 10) | Term/post-term (n = 65) | p-value |
|---|---|---|---|
| Mode of delivery[a] | | | .099 |
| Cesarean section | 5 (50) | 22 (34) | |
| Vaginal delivery | 5 (50) | 23 (35) | |
| Instrumental delivery | – | 20 (31) | |
| Hospital of birth[a] | | | >.999 |
| Karlskoga Hospital | 1 (10) | 9 (14) | |
| Örebro University Hospital | 9 (90) | 56 (86) | |
| Sex[a] | | | >.999 |
| Female | 3 (30) | 20 (31) | |
| Male | 7 (70) | 45 (69) | |
| APGAR score[a] | | | |
| APGAR1* | | | .040 |
| | 2 (20) | 37 (58) | |
| ≥7 | 8 (80) | 27 (42) | |
| APGAR5 | | | .044 |
| | 1 (10) | 29 (45) | |
| ≥7 | 9 (90) | 36 (55) | |
| APGAR10 | | | .057 |
| | – | 19 (29) | |
| ≥7 | 10 (100) | 46 (71) | |
| Weight for gestational age[a] | | | .521 |
| Small for gestational age | 1 (10) | 4 (6) | |
| Appropriate for gestational age | 9 (90) | 61 (94) | |
| Large for gestational age | – | – | |
| Transported to another hospital[a] | 1 (10) | 2 (3) | .353 |
| Age at symptom debut[a] | | | .007 |
| ≤24 h | 7 (70) | 64 (98) | |
| | 3 (30) | 1 (2) | |
| Resuscitation[a] | | | .104 |
| Intubated | – | 9 (14) | |
| Ventilated | 5 (50) | 43 (66) | |
| No resuscitation | 5 (50) | 13 (20) | |
| Respiratory support[a] | | | .845 |
| Invasive | 1 (10) | 9 (14) | |
| Non-invasive | 9 (90) | 45 (69) | |
| Oxygen | – | 4 (6) | |
| No ventilatory support | – | 7 (11) | |
| Number of X-rays performed[b] | 3 (1–4.25) | 3 (1–1.25) | .080 |
| Invasive PT treatment[a] | 4 (40) | 8 (12) | .048 |
| Comorbidities | | | |
| Asphyxia | 2 (20) | 26 (40) | .304 |
| Respiratory distress syndrome | 6 (60) | 14 (22) | .019 |
| Meconium aspiration syndrome | – | 14 (22) | .192 |
| Congenital malformations | – | 3 (5) | >.999 |
| Pneumonia | – | 1 (2) | >.999 |
| Sepsis | – | 1 (2) | >.999 |
| Transient tachypnea of the newborn | 2 (20) | 16 (25) | >.999 |
| None | 3 (30) | 14 (22) | .686 |
| Other thoracic air leak | – | 11 (17) | .341 |
| Mortality[a] | – | 2 (3) | >.999 |
| Number of days in hospital[b] | 18.5 (8.25–34.00) | 4 (3–8.5) | <.001 |

[a]n (%) and Fisher's exact test.
[b]median (interquartile range) and the Mann–Whitney U-test.
*1 patient.

Thirty-seven (49%) patients had a right-sided PT, 19 (25%) had a left-sided PT, 16 (21%) had a bilateral PT, and in three cases (4%) the location of the PT was not determined. Other than pneumomediastinum and subcutaneous emphysema, no other thoracic air leaks were identified in any of the patients. Twelve patients received invasive treatment: nine (12%) received drainage, two (3%) received needle aspiration, and one (1%) received both treatments.

Two patients (3%) died, but neither due to PT. One died due to severe asphyxia at birth, where an X-ray revealed a small PT that was not considered clinically significant, and the death of the other was primarily due to a genetically verified alveolar capillary dysplasia rather than to PT. The median number of days of hospital treatment was 5.00 (IQR: 3.00–11.00), and 23 patients (31%) were followed up at the hospital's neonatal clinic.

A subgroup analysis comparing preterm with term/post-term infants showed significant differences in APGAR score after 1 and 5 min, age at symptom debut, percentage of infants receiving invasive PT treatment, and median number of days spent in hospital (Table 2).

## Discussion

This was a retrospective population-based study including more than 24,000 live births with a focus on epidemiology, symptoms, clinical signs, and age of onset. One interesting finding was that a large majority of the cases were ≤24 h of age at debut of respiratory symptoms, and none were >48 h of age. It has been well known since long before the introduction of surfactant therapy that neonatal PT presents later in preterm neonates than in term neonates. For example, one study from 1959 reported that neonatal PT had an average symptom onset of 24 days in neonates weighing <1500 g while term neonates debuted early after birth [16]. Although the care of preterm infants have improved tremendously in the decades since, the timing of onset has only been described once in the post-surfactant era, in a relatively small study from Turkey which showed that 20% of neonates developed pneumothorax after 48 h [12]. However, it should be noted that the Turkish study seemed to have a very different comorbidity profile from the present material, with a mortality rate of 33% (10 of 30). We therefore felt that it would be of interest to present our population-based material from a country with very frequent use of prenatal corticosteroids, surfactant, and nasal CPAP.

The finding that all cases were aged <48 h at symptom onset could be of value to everyday clinical practice, as clinicians may find it worthwhile to consider diagnoses other than PT when a neonate has a debut of respiratory symptoms at >48 h of age. If our finding concerning time of onset of symptoms could be repeated in other studies, this might lead to a decreased need for chest X-rays prescribed to exclude PT after 48 h of life. However, it should be noted that a recent study proposed lung ultrasound as more than an equivalent to X-ray in detecting neonatal PT, offering a way to eliminate the adverse effect of radiation [17].

Another crucial issue in any diagnostic procedure is detailed knowledge about the presenting symptoms. Since PT is a reasonably common complication, the most common clinical signs are well known to all experienced neonatologists. Still, scientific data on which symptoms and clinical signs are most common have only previously been presented in one small study comprising just 10 neonates [11]. The data on symptoms and clinical signs that have been presented should therefore be of both clinical and scientific interest. Most of the reported symptoms were very unspecific, but it is worth pointing out that decreased breath sounds, which according to previous

knowledge has a strong association with PT, were only noted in 16 (21%) of the patients.

The incidence in this study was higher than in previous regional-based studies from the post-surfactant era [2–5]. However, in comparison to those studies, the present study also showed lower rates of invasive treatment (16% [12 of 75] vs. 41%–95%) and mortality (3% [2 of 75] vs. 6.6%–13.6%), suggesting that our study included a large proportion of cases with less severe PT.

A variation in incidence could depend on different comorbidity profiles and routines for x-ray performance, delivery mode, and ventilatory support [5]. The grade of hypoxemia around birth, resuscitation technique, and the quality and interpretation of the X-ray images could also affect the incidence [18]. In one previous study, premature infants born before week 32 more often had PT compared to preterms born at ≥32 weeks [19], and the majority of premature infants (90%) in the present study were born at or after week 32. We do not know the reason for the low proportion of early preterm infants in our study, but one could speculate that factors such as prenatal steroids, surfactant use, and ventilator strategies might have an impact. We cannot exclude the possibility that some cases were missed due to the attending physician making an incorrect diagnosis.

The rate of mortality varies between studies. However, information on whether PT was the cause of death has only been presented in one other study, which also found no cases of death caused by PT [5]. This could indicate that the risk of dying as a direct result of neonatal PT might be lower than the current understanding.

Our finding of significant differences in APGAR scores between preterm and term/post-term patients suggests that preterm infants develop PT as a complication of premature birth while term/post-term infants develop PT as a complication of asphyxia. Unsurprisingly, preterm subjects had a later onset of symptoms and a higher incidence of respiratory distress syndrome. Preterm patients more often received invasive treatment, as has been previously reported [5]; the reason for this is perhaps that preterm infants becoming ill with a PT is often more critical, and expectant management is too much of a risk.

## Study limitations

This study was a retrospective single-center study with a small study population. The true incidence of PT is not presented here, since asymptomatic cases were

not included and premature infants born before 25 weeks of gestation were referred to another hospital. Only patients with a correct diagnosis were included, and there is a risk that some are missing because of an incorrect diagnosis. Another limitation is the fact that this was a retrospective study based on chart reviews.

## Conclusion

In this population-based regional study we found a relatively high incidence of PT but a low frequency of invasive treatment and mortality, suggesting that a high proportion of cases with mild PT were included. All subjects were <48 h of age at debut of respiratory symptoms, suggesting that PT occurring after 48 h is fairly rare. Most patients showed unspecific symptoms, and the presence of decreased breath sounds was recorded in only 16 (21%) of cases.

## ORCID

J. Andersson  http://orcid.org/0000-0003-1461-2262

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