Pneumothorax Prevalence and Mortality per Gestational Age in the Newborn

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Abstract

Objectives: Pneumothorax (PTX) in newborns is a life-threatening condition associated with high morbidity and mortality especially in premature infants. The frequency of PTX in neonates at different gestational ages (GA) and its impact on neonatal mortality have not been quantified. We aimed to determine: 1) the prevalence of PTX in neonates at different GA from ≤24 weeks to ≥37 weeks, 2) the impact of PTX on mortality per GA, and 3) the impact of PTX on the length of stay (LOS) per GA.

Methods: The national Kids' Inpatient Database (KID) for the years of 2006 to 2012 were used. We included all infants admitted to the hospital with a documented GA and ICD9 code of pneumothorax. Bivariate and multivariate analyses were conducted and odds ratios (OR) were calculated.

Results: A total of 10 625 036 infants were included; of them 3665 infants (0.034 %) had a diagnosis of PTX, with highest prevalence at ≤24 weeks GA (0.67%), and lowest at term (0.02%). The overall mortality rate of patients with PTX was 8.8%, and greater in preterm (16.3%) vs. term infants (2.7%). The association of mortality with PTX was greatest at GA of 29−32 weeks (OR = 8.55 (95% CI: 6.56−11.13). Infants who survived until discharge had a median of 2–12 days longer length of stay depending on GA category.

Conclusions: The prevalence of PTX peaks in infants <24 weeks, however its impact on mortality is greatest at 29-32 weeks. PTX is associated with longer length of stay in survivors.

Introduction

Pneumothorax (PTX) in newborns is a life−threatening condition associated with high morbidity especially in premature infants, like intra-ventricular hemorrhage (IVH) and chronic lung diseases.[1,2] It is also associated with high mortality.[3,4] In all live births, the incidence of spontaneous symptomatic PTX was reported to be between 0.05−1%.[5-7] However, in infants admitted to neonatal intensive care unit (NICU), reported PTX rates were 2.8−9%.[8-10] The incidence of PTX varied widely depending on the underlying lung disease, birth weight, resuscitation techniques, and methods of administering assisted ventilation.[11,12] The prevalence and mortality rates associated with PTX at different gestational ages (GA) have not been well described. Moreover, studies that examined the outcomes of PTX are mostly small sampled. Utilizing a United States national dataset, we aimed to determine the prevalence of PTX at different GA, as well as the association of PTX with mortality and length of stay (LOS) in each GA group.

Materials and methods

Database:

We used the de−identified Kids' Inpatients Database (KID) for the years of 2006 to 2012. The KID is a part of the Healthcare Cost and Utilization Project, which is sponsored by the Agency for Healthcare Research and Quality. This is an all−payer database that contains information from millions of inpatient discharges from approximately 1000 hospitals across the United States. Hospitals were sampled to represent a 20% stratified sample of all community hospitals, and national U.S. estimates were produced by using sampling weights provided by the KID.[13] Data represents about 37 states across the nation. During the specified study time, data was coded using the International Classification of Disease 9 (ICD−9) for different clinical variables. The database includes more than 100 data elements for each patient for every hospital stay, such as patients' demographics, primary and secondary diagnoses, source of admission, discharge status, expected payment source, and total charges. As these data are de–identified and publicly available, the need for informed consent and institutional review board approval was waived.

Patient selection and identification:

We included hospital discharge records of infants who have an ICD−9 diagnostic codes referring to the newborn period. Using ICD−9 diagnostic and procedural codes, we identified GA, PTX, birth asphyxia, chorioamnionitis, necrotizing enterocolitis (NEC), sepsis, persistent pulmonary hypertension (PPHN), IVH, and the use of invasive and noninvasive mechanical ventilation. We excluded newborns with: (a) congenital lung anomalies (b) diaphragmatic hernia and/or (c) abdominal wall defect.

Data management and analysis:

We classified newborns according to their GA into 5 groups: ≤24 weeks, 25−28 weeks, 29−32 weeks, 33−36 weeks and ≥37 weeks. We calculated the prevalence of PTX in the overall sample and then in each GA group. Categorical variables (prevalence and mortality of PTX) were expressed as percentages, and compared using Chi−square and Fisher's Exact tests whenever appropriate. Continuous variables with

abnormal distribution were expressed as median and interquartile range (interquartile range [IQR]) and compared using Mann−Whitney test. We used bi-variable and multivariable logistic regression analyses to evaluate the association between infant characteristics and mortality. Variables with $p<0.2$ in bivariable analyses were considered eligible to enter the multivariable model. Associations were expressed as odds ratio (OR) with 95% confidence intervals (CIs). A $p<0.05$ was considered statistically significant. Statistical analyses were performed with SPSS version 25.0 (IBM, New York, NY U.S.A).

Results

Data for 21 604 237 hospitalizations for the years 2006−2012 was obtained. We excluded infants >1-month-old (n = 10 955 736), infants with anomalies of diaphragm (n = 4437), infants with congenital lung anomalies (n = 9260), and infants with congenital anomalies of abdominal wall (n = 10 998). A total of 10 625 036 infants met the inclusion criteria (Figure 1). The majority of infants with PTX (62.2%) were males, white (60.5%) and received mechanical ventilation (64.7%). Associated clinical diagnoses included: respiratory distress syndrome (RDS) (34%), sepsis (28.3%), PPHN (9.7%), IVH (8.3%), meconium aspiration (4.5%), necrotizing enterocolitis (2.4%), birth asphyxia (1%) and chorioamnionitis (0.6%) (Table 1).

The overall prevalence of PTX in neonates (GA from ≤24 weeks to ≥37 weeks) was 0.034%. There was an inverse relationship between the frequency of PTX and GA group; with highest incidence at ≤24 weeks GA (0.67%), and lowest at term (0.02%). The overall mortality rate was significantly greater in infants with PTX (8.8%) vs. infants without (0.4%), $p < 0.001$ (Table 2). Furthermore, the mortality rate associated with PTX was greater in preterm (16.3%) vs. term infants (2.7%), $p < 0.001$. The mortality rate in infants with PTX decreased with increasing GA group. However, when compared to the mortality rate in infants without PTX, the contribution of PTX to mortality rate at different GA groups was complex. Overall across all age groups, PTX was associated with greater risk of mortality (OR = 2.33; 95% CI: 2.02−2.67, p< 0.001). However, while in infants ≤24 week GA group, the presence of PTX was associate with less mortality (OR=0.64; 95% CI= 0.45−0.93, $p = 0.018$), in all other age groups the presence of PTX increased the odds of mortality to varying degrees with greatest impact at GA group of 29−32 weeks (OR = 8.55; 95% CI: 6.56−11.13, p< 0.001) (Table 2).

In infants diagnosed with PTX, other factors associated with increased mortality included; Black race (OR = 1.88; 95% CI: 1.28−2.76), birth asphyxia (OR = 3.98; 95% CI: 1.47−10.76), sepsis (OR = 1.69; 95% CI: 1.28−2.23), PPHN (OR= 2.8; 95% CI: 1.99−3.94) and invasive mechanical ventilation (OR = 2.65;

95% CI = 1.82−3.87); whereas male sex (OR = 0.52; 95% CI = 0.4−0.68) and meconium aspiration (OR = 0.32; 95% CI = 0.14−0.74) were associated with lower risk of mortality (Table 3).

In infants who survived until hospital discharge, PTX increased the median length of stay (LOS) from 2 (IQR 2−3) to 12 (IQR 4−36) days, ($p < 0.001$) according to GA groups; the highest median LOS in PTX infants was at ≤24 weeks GA group (106 days, IQR 39−136) (Table 4). This increase in LOS was also associated with higher overall cost. The median cost of admission in infants with PTX who survived until hospital discharge was significantly increased in all GA groups (Figure 2). The median cost of admission in infants with PTX was $82,579 (IQR $20,778−$295,727) that is significantly greater than in those without PTX ($2,680, IQR $1,746−$4,749), $p < 0.001$.

Discussion

This study highlights the prevalence rate of PTX in neonates, and the association of PTX with mortality, and LOS according to GA, in a large nationally representative sample. The overall prevalence of PTX in neonates was 0.034%. It decreased with advancing gestational age with the greatest frequency at ≤24 weeks, while the odds of mortality associated with PTX was greatest at 29−32 weeks of GA. Furthermore, PTX was associated with increased LOS and, accordingly increased the cost of hospitalization.

A wide range of PTX rates have been reported in the literature, as the studies vary according to population and methodology. Chernick et al.[6] reported symptomatic spontaneous pneumothorax incidence rate of 0.05%. In term infants, Katar et al.[7] and Al Tawil et al.[14] reported symptomatic spontaneous pneumothorax rates of 0.6% and 0.17% respectively. While in preterm infants, Bhatia et al.[4] reported PTX rate of 9.2%, and the rate was even higher (20%) in ventilated extremely low birth−weight infants[2]. Furthermore, in infants diagnosed with hyaline membrane disease, Mandasky et al.[3] reported an incidence of air leak of 27%, while in infants admitted to NICU, Cizmeci et al.[15] reported PTX incidence of 2.8%. The overall incidence in this study was lower than what was previously published, this could be attributed to the large sample size of this study and should be reflective of the true national rate independent of the health facility. The low incidence could also reflect improved neonatal care as the data is much more recent than previous reports.

In infants diagnosed with PTX, the overall mortality rate was 8.8%. As expected, our results showed that the mortality rate was higher in preterm babies, and it was the highest at 29–32 weeks. Bhatia et al.[4] reported a mortality rate of 43% “very preterm” infants with PTX vs 13% in control group. Moreover, Apiliogullari et al.[16] reported mortality rate of 32% in term infants compared to 40% in preterm infants. In the pre–surfactant era, Mandasky et al.[3] reported a mortality rate of 68% in infants with alveolar rupture and birth weight less than 1.5 kg. The differences between our results and previously reported mortality rates could, again, be attributed to the large population sample and better ventilation approach. Our sample

showed that infants with PTX had lower mortality rate than infants without PTX at age of ≤ 24 weeks (OR=0.64; 95% CI= 0.45−0.93), (p = 0.018). This could possibly be explained by the temporal relationship of PTX and mortality; immature infants who dies in the delivery room or early in life did not have the time to develop PTX.

The association of mortality with PTX has been sporadically reported. There is not consistent data to describe such relationship to provide a reference guide or national benchmark. Yu et al.[2] reported that only 36% of infants who have PTX and ventilated had survived. This study was performed in the pre-surfactant era that did not reflect the current practice. The current study showed that birth asphyxia, sepsis, PPHN and invasive mechanical ventilation were significantly associated with higher rates of mortality, while male sex and meconium aspiration were associated with lower rates of mortality.

There is also limited data on the relationship between PTX, LOS and hospital cost. Katar et al.[7] reported an average increased length of stay in infants diagnosed with PTX of 7.7 days. The current study reports increased median LOS by 2 to 12 days in infants with PTX. The current study does not explore the temporal relationship between PTX and increased LOS. However, investigators may speculate that infants diagnosed with PTX have increased need for mechanical ventilation that might pose increased respiratory and non-respiratory complications. These complications would also have an associated increase in the LOS and cost of hospitalization. Of note, previous studies showed less impact on the need for mechanical ventilation when PTX occurred in premature infants with BW >2500g.[17]

This study has several limitations. KID database by its nature is an administrative billing database. There is a possibility of under coding the diagnosis of PTX. This could be attributed to the fact that many PTX cases are asymptomatic, and only symptomatic cases would be coded. Furthermore, the current study design did not allow for determination of the time when PTX occurred and whether mechanical ventilation preceeded PTX or followed it. However, this data set is considered the most comprehensive national

database available, and therefore it represents the national values rather than being center–specific as published in other reports.

In conclusion, this study highlights the prevalence of PTX in neonates, and the association of PTX with mortality, cost and LOS according to GA, in a large nationally−representative sample. PTX decreased with advancing gestational age with the highest rate at ≤24 weeks, while the association of PTX with mortality was the greatest at 29−32 weeks of GA. Furthermore, the presence of PTX was associated with a prolonged LOS and increased cost of hospitalization. This data could be of a great value when consulting with families of infants with PTX.

Disclosure: The authors declare no conflict of interest.

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