Risk Factors of Pneumothorax during the First 24 Hours of Life

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Background: *Pneumothorax is one of the air leak syndrome and is more common in the newborn period than in any other childhood periods. It can be divided into spontaneous pneumothorax and secondary pneumothorax from underlying lung pathology or assisted ventilation. Pneumothorax results in longer hospital stays and even deaths in some cases. To date, there are few studies that focus on identifying risk factors of pneumothorax. We conducted this study to ascertain risk factors for pneumothorax, in order to create a guideline to prevent this condition.*

Material and Method: *This is a retrospective case-control study. Cases were infants with the diagnosis of pneumothorax (P25.1 Pneumothorax originating in the perinatal period) between January 2001 and December 2004. Controls were those whose birth times followed in the immediate chronology to the cases. Case:control ratio was 1:2. Univariate analysis was used to compare the two groups. Odds ratio and 95% confidence interval were used to identify possible risk factors. Statistical significance was considered as $p < 0.05$.*

Results: *There are 44 cases and 88 controls. Risk factors are shown as Odds ratio and 95% confidence interval. Infant factors associated with higher risk of pneumothorax are male (2.6; 1.2, 5.6), low birth weight (19.3; 2.3, 160.2), vacuum extraction (20.9; 1.1, 403.4), meconium-stained amniotic fluid (4.5; 1.8, 11.0), low 1-minute Apgar score (78.3; 4.5, 1357.8), and the administration of bag and mask positive-pressure ventilation (29.0; 3.6, 233.5). Maternal factor associated with higher risk of pneumothorax is poor antenatal care (3.5; 1.04, 11.9).*

Conclusion: *All pregnant women should be encouraged to have good antenatal care. Mother who has complication(s) during pregnancy and delivery should receive special care to prevent perinatal depression. For mothers with meconium-stained amniotic fluid, close fetal monitoring and tracheal suction for meconium after delivery should be appropriately considered to prevent meconium aspiration. Finally, neonatal resuscitation, when needed, should be done very carefully by following the American Heart Association and the American Academy of Pediatrics guidelines, especially for bag and mask positive-pressure ventilation.*

Keywords: *Pneumothorax, Newborn, Risk factors*

J Med Assoc Thai 2005; 88(Suppl 8): S135-41
Full text. e-Journal: *http://www.medassocthai.org/journal*

Pneumothorax is the most common air leak syndrome found in newborn infants. An important etiology is alveolar over-inflation then rupture of air into the intrapleural space. Pneumothorax can be divided into two groups, spontaneous or idiopathic and secondary. Spontaneous pneumothorax can be found in the same family. Secondary pneumothorax can occur secondary to congenital lung cyst, pulmonary hypoplasia, hyaline membrane disease, or meconium aspiration syndrome. It occurs more commonly in males than females and in infants who are term or post-term more commonly than in those that are preterm. The incidence increases in infants who need positive-pressure ventilation or mechanical ventilation. Pneumothorax is also

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reported to be associated with urinary tract anomalies, for example, multicystic dysplastic kidney and horseshoe kidney[1].

Infants with pneumothorax can appear asymptomatic. Such infants are found in 1%-2% of all newborn infants and the pneumothorax usually is unilateral[2]. Occasionally, the patient can be symptomatic, with respiratory distress, irritability, and apnea. Onset of symptoms can be sudden or gradual. Once occur, infants often suffer a wide range of complications, including ARDS and sepsis. We conduct this study in order to ascertain the possible risk factors for the occurrence of pneumothorax in our newborn population. We hope that the results obtained from this study will help guide us towards effective and timely preventive measures for this disease.

Material and Method

This was a retrospective case-control study. All newborn infants diagnosed with pneumothorax between January 1, 2001 and December 31, 2004 were cited by using ICD-10 code of "P25.1 Pneumothorax originating in the perinatal period". All the charts were reviewed by the investigators. Pneumothorax cases with onset within the first 24 hours of life and before the institution of mechanical ventilation were included in our study group. Infants in the control group were those whose birth times followed in the immediate chronology to the cases with no matching.

The infant data included sex, birthweight, gestational age, mode of delivery, characteristic of amniotic fluid, Apgar scores, and resuscitation needed. Clinical course, treatment and outcome of all cases were also recorded. Maternal data include age, gravida, antenatal care, and any complications during pregnancy and delivery.

Sample size calculation

Sample size was calculated by PS: power and sample size calculation program, (Vanderbilt University, Nashville, Tennessee). Estimated numbers of meconium-stained amniotic fluid as a risk factor of pneumothorax were 30% and 10% in case and control groups, respectively. Power is 80%. Significance level is at $p < 0.05$. Case:control ratio is 1:2. Number of case is 44 and control is 88.

Statistical analysis

Statistical analysis was performed using SPSS" 10.0, (Chicago, Illinois). When appropriate, a variety of methods were used to compare the two groups, including Pearson's chi-square, Fisher's exact test, independent t-test and Mann-Whitney's test. Odds ratio and 95% confidence interval were used to identify possible risk factors. Statistical significance was considered as $p < 0.05$.

Results

Demographic data and delivery characteristics of all infants are shown in Table 1. Most pneumothorax cases were male. Birthweight and Apgar scores at 1 and 5 minute were significantly lower in the cases than in the controls. Gestational age and the number of cases with prolonged rupture of membranes were not significantly different. Most of the infants in both groups were born by normal labor and none in control group was born by vacuum extraction. The number of infants with a history of meconium-stained amniotic fluid (MSAF) with and without the administration of bag and mask positive-pressure ventilation (BM-PPV) was significantly higher in the study group. There were more infants in the study group who needed neonatal resuscitation other than BM-PPV. However, no infants in either group needed chest compressions. There was no difference in the number of infants who received Narcan between the two groups.

Mean maternal age in both groups was not different. The number of mothers who received good antenatal care (≥ 4 visits) is higher in the control group. The prevalence of complications during pregnancy and delivery in the two groups were not different except for oligohydramnios (Table 2).

Infants' factors which were univariately associated with greater risk of pneumothorax included male, low birthweight, vacuum extraction (compared to normal labor), MSAF, Apgar score at 1 minute lower than 7, tracheal suction for meconium, and neonatal resuscitation including oxygen tubing and BM-PPV (Table 3). MSAF together with BM-PPV was associated with greater risk than MSAF alone (Table 3).

The only maternal factor associated with a greater risk of pneumothorax is poor antenatal care (Table 4). Oligohydramnios had a trend of greater risk but did not reach statistical significance.

Two subgroup analyses were done. The first subgroup was selected by excluding infants with the history of MSAF plus having received BM-PPV. There were 39 and 78 infants in study and control groups, respectively. Male, low birth-weight, MSAF, Apgar score at 1 minute less than 7, tracheal suction for meconium and BM-PPV were associated with a greater risk

Table 1. Demographic data and delivery characteristics

	Case (n=44)	Control (n=88)	p-value
Sex			
- Male	31 (70.5%)	42 (47.7%)	0.01*
Gestational age (week)	39.0 (2.1)	38.5 (1.4)	0.11
Birthweight (gram)	2,884.3 (473.7)	3,080.0 (382.3)	0.01*
Apgar score at 1 min (n=131)	8 (6, 9)	9 (9, 10)	< 0.001*
Apgar score at 5 min (n=131)	10 (8, 10)	10 (10, 10)	< 0.001*
Mode of delivery			
- Normal labor	23 (52.3%)	54 (61.4%)	
- Cesarean section	17 (38.6%)	34 (38.6%)	
- Vacuum extraction	4 (9.1%)	0	0.02*
Rupture of membranes > 18 hour	2 (4.5%)	0	0.11
MSAF	16 (36.4%)	10 (11.4%)	0.001*
Neonatal resuscitation needed			
- Tracheal suction for meconium	9 (20.5%)	0	< 0.001*
- Oxygen tubing			
- Bag-mask positive pressure	36 (81.8%)	29 (33.0%)	< 0.001*
ventilation (BM-PPV)	11 (25%)	1 (1.1%)	< 0.001*
- Narcan administration			
	8 (18.2%)	11 (12.5%)	0.38
MSAF and PPV	5 (11.4%)	1 (1.1%)	0.02*

Data is shown as number of cases (%), mean (standard deviation) or median (percentiles 25, 75).
* Significant level, $p < 0.05$

Table 2. Maternal data

	Case (n=44)	Control (n=88)	p-value
Age (year)	27.7 (6.5)	26.5 (6.0)	0.31
Antenatal care ≥ 4 visits (n=128)	33 (82.5%)	83 (94.3%)	0.048*
Complications during pregnancy and delivery			
- Twin pregnancy	1 (2.3%)	0	0.33
- Oligohydramnios	3 (6.8%)	0	0.04*
- Breech presentation	3 (6.8%)	4 (4.5%)	0.79
- Pethidine administration	9 (20.5%)	13 (14.8%)	0.41
- Fetal distress	3 (6.8%)	1 (1.1%)	0.11
- Cephalopelvic disproportion	5 (11.4%)	9 (10.2%)	1.0
- Birth before admission	1 (2.3%)	1 (1.1%)	1.0

Data is shown as mean (standard deviation) or number of cases (%). * Significant level, $p < 0.05$

Table 3. Odds ratio of infant factors

Factors	Odds Ratio	95% CI
Male	2.6	1.2, 5.6*
Prematurity	1	0.2, 4.2
Low birthweight (< 2,500 g)	19.3	2.3, 160.2*
Cesarean section	1.2	0.5, 2.5
Vacuum extraction	20.9	1.1, 403.4*
Rupture of membranes > 18 hr.	10.4	0.5, 221.7
MSAF	4.5	1.8, 11.0*
Apgar score at 1 min d< 7	78.3	4.5, 1357.8*
Apgar score at 5 min d< 7	6.2	0.2, 156.6
Tracheal suction for meconium	47.4	2.7, 835.7*
Oxygen tubing	9.2	3.8, 22.2*
BM-PPV	29.0	3.6, 233.5*
Narcan administration	1.6	0.6, 4.2
MSAF and BM-PPV	11.2	1.3, 98.6*

* Significant level, $p < 0.05$

Table 4. Odds ratio of maternal factors

Factors	Odds Ratio	95% CI
Teenage mother (<18 yr)	0.7	0.1, 3.5
Advanced maternal age (> 35 yr)	1.3	0.4, 5.0
Poor antenatal care (< 4 times)	3.5	1.04, 11.9*
Fetal distress	6.4	0.6, 63.1
Twin pregnancy	6.1	0.2, 152.9
Oligohydramnios	14.9	0.8, 295.7
Breech presentation	1.5	0.3, 7.2
Pethidine administration	1.5	0.6, 3.8
Cephalopelvic disproportion	1.1	0.4, 3.6
Birth before admission	2.0	0.1, 33.1

* Significant level, $p < 0.05$

Table 5. Odds ratio of infant and maternal factors (subgroup analysis)

Factors	Odds ratio (95% C.I.)	
	Subgroup 1	Subgroup 2
Infant factors		
Male	3.0 (1.3, 6.8*)	2.4 (1.01, 5.9*)
Low birthweight	16.8 (2.0, 142.5*)	14.4 (1.7, 125.8*)
MSAF	3.4 (1.3, 9.4*)	5.0 (1.7, 15.1*)
Apgar score at 1 min d< 7	43.8 (2.4, 781.5*)	NS
Tracheal suction	25.0 (1.3, 465.3*)	25.7 (1.4, 479.8*)
Oxygen tubing	8.2 (3.3, 20.4*)	7.2 (2.8, 18.7*)
BM-PPV	30.5 (1.7, 556.3*)	NA
Maternal factor		
Poor antenatal care	3.8 (1.01, 14.6*)	5.5 (1.3, 23.7*)

* Significant level, $p < 0.05$

of pneumothorax (Table 5). Maternal poor antenatal care was associated with greater risk of pneumothorax.

The second subgroup was selected by excluding infants who received BM-PPV during neonatal resuscitation since the procedure, in itself, is a possible predisposing factor of pneumothorax. There were 33 and 66 infants in case and control groups, respectively. Table 5 showed only the statistically significant data. Male, low birthweight, MSAF, and neonatal resuscitation including oxygen tubing and tracheal suction of meconium, were associated with greater risk of pneumothorax (Table 5). Maternal poor antenatal care was also associated with greater risk of pneumothorax (Table 5).

In all the cases, the diagnosis of pneumothorax was made by attending neonatologist using chest radiographs since clinical findings were not specific and mostly subtle. These chest radiographs were reviewed by a radiologist in 42 cases (95%). Of the 44 cases of pneumothorax, 27 (61.4%) were on the right side, 11 (25%) were on the left side and 6 (13.6%) had bilateral involvement. Pneumomediastinum was found in 3 cases together with pneumothorax.

In almost all cases (95.5%), the pneumothorax was manifested with tachypnea. Only two cases were manifested with sudden onset of cyanosis. Fourteen cases (32.6%) had onset at birth, 38 cases (88.4%) within the first 6 hours of life and 41 cases (95.3%) within 12 hours. Oxygen saturations on room air were between 74-98%. Treatment was mainly supportive and symptomatic in most cases. Oxygen therapy to keep oxygen saturation between 95% and 98% was given via oxygen hood or incubator in 43 cases (97.7%). Mean duration of oxygen therapy was 3.6 ± 2.1 days (range 1-11 days). Pleural tapping was done in 6 cases; one was on NCPAP for 4 days, four were on oxygen via oxygen hood for 2-11 days and one patient expired. All cases were initially kept NPO and were put on intravenous fluid. Mean NPO days was 2.1 ($\pm$ 2.5). Empirical antibiotics were started in 13 cases (29.5%), with the mean duration of 6.5±3.9 days (range 3-14 days). Mean length of hospital stay in the study group was significantly higher than in control group (9.2 ± 4.8 vs. 3.2 ± 1.1, $p < 0.001$). Two patients expired, giving the mortality rate of 4.5%. Both patients expired within 48 hours of life and cause of death was most likely persistent pulmonary hypertension of the newborn.

Discussion

In our study, as in earlier reports[1, 3], there is an increased prevalence in male (71%). Mean gestational age of study group is 39 weeks which is not different from control group. However, in our study, the mean birthweight is significantly lower in cases than that in controls. This phenomenon is in contrast to those previously reported in the literature[1], but could be easily explained since previously published study included only term newborn infant. Pneumothorax cases had lower Apgar scores at 1 and 5 minutes and more were born by vacuum extraction. These may explain the higher need of neonatal resuscitation in study group.

Pneumothorax can be a complication of vigorous neonatal resuscitation. It should be considered in infant who does not respond to BM-PPV, chest compressions and epinephrine or who is improving during the initial resuscitation and then suddenly get worse[4, 5]. None of our 132 cases received chest compressions. Twenty five percent of cases and 1% of controls received BM-PPV which, by some standard, may be considered as vigorous resuscitation. However, it could imply that the good Apgar scores in our study mean that BM-PPV was administered only once or twice (30 seconds each). BM-PPV, in this study, was demonstrated to increase risk of pneumothorax by 29 fold (Table 5). MSAF increased the risk of pneumothorax by 5 times while MSAF plus BM-PPV increased it by 11 fold. Aspiration of meconium can cause partial obstruction in small airways (a ball-valve obstruction) which relates to the development of pneumothorax[6]. In order to decrease this bias, we excluded all infants with history of MSAF together with BM-PPV in subgroup 1. BM-PPV, without MSAF, was still shown to increase the risk of pneumothorax by 31 fold (Table 5). However, in the literature, only 5% of the infants with MSAF developed meconium aspiration syndrome[7]. BM-PPV should be cautiously performed with optimal positive pressure especially in infants with MSAF. Use of pressure manometer and observation of chest movements during BM-PPV has been recommended to determine optimal pressure[4]. Tracheal suction for meconium and oxygen tubing are not causes of pneumothorax but they are confounders because more infants in the study group needed neonatal resuscitation.

Spontaneous pneumothorax occurs in infants without underlying lung disease and without vigorous resuscitation. Subgroup 2 was selected by excluding all infants who received BM-PPV. Male, low birthweight and a history of MSAF are associated with a greater risk of spontaneous pneumothorax by 2, 14, and 5 fold, respectively (Table 5). These factors are robust risks of pneumothorax.

Poor antenatal care (< 4 visits) is the only maternal factor which is associated with greater risk of pneumothorax by 3.5 fold (Table 4). Pregnant women should be encouraged to start their antenatal care as early as possible. Oligohydramnios had a trend to increase risk but did not reach statistical significance. The possibility is reaffirmed in the literature where the relationship between KUB anomaly and spontaneous pneumothorax was also reported[1,8]. We had four infants with oligohydramnios but only one of them had ultrasound done and the result was normal. In all subgroup analysis, poor antenatal care is the only maternal factor which associates with a greater risk of pneumothorax.

The propensity for pneumothorax occuring on the right side may be due to the unequal distribution of air during the first few breaths. Oxygen was given in all cases in order to increase adsorption of free air in the pleural cavity. However, high oxygen concentration can cause complications such as, tracheitis, damaged airway epithelium, atelectasis, and impaired mucociliary

clearance. In preterm infants, oxygen increases the risk of retinopathy of prematurity and bronchopulmonary dysplasia. Mortality rate was 4.5% and survivors had a longer length of hospital stay.

Conclusions

To prevent pneumothorax in the first 24 hours of life, we propose that all pregnant women should be encouraged to have good antenatal care, in order to decrease the prevalence of preterm delivery and low birthweight infants. Mother who has complication during pregnancy and delivery should receive special care to prevent perinatal depression so less neonatal resuscitation will be needed. For mothers with MSAF, close fetal monitoring should be done. When the infant is born, tracheal suction for meconium, when indicated, should be performed to prevent meconium aspiration. Finally if neonatal resuscitation is inevitable, it should be done very carefully following the American Heart Association and the American Academy of Pediatrics guidelines[4], especially for BM-PPV.

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ปัจจัยเสี่ยงของภาวะโพรงเยื่อหุ้มปอดมีอากาศที่เกิดภายในอายุ 24 ชั่วโมง

โสภาพรรณ เงินฉ่ำ, พรพัฒน์ กิตติรัตน์สัจจา, ปรียชาต์ ปาจารย์.

ความเป็นมา: *ภาวะโพรงเยื่อหุ้มปอดมีอากาศ (pneumothorax) เป็นภาวะหนึ่งในกลุ่ม air leak syndrome ที่พบในวัยทารกแรกเกิดได้บ่อยกว่าวัยอื่น ๆ อาจแบ่งออกเป็นสองกลุ่มคือ กลุ่มที่เกิดเอง (spontaneous pneumothorax) กับกลุ่มที่เกิดเนื่องจากมีพยาธิสภาพที่ปอดหรือได้รับการช่วยหายใจด้วยแรงดันบวก ทารกที่มีภาวะโพรงเยื่อ หุ้มปอดมีอากาศจะต้องอยู่ในโรงพยาบาลนานขึ้นและอาจมีบางรายที่เสียชีวิต การศึกษาเกี่ยวกับปัจจัยเสี่ยงของภาวะโพรงเยื่อหุ้มปอดมีอากาศมีอยู่ไม่มากนัก การศึกษานี้จึงมีวัตถุประสงค์เพื่อหาปัจจัยเสี่ยงของการเกิดภาวะโพรงเยื่อหุ้มปอดมีอากาศภายใน 24 ชั่วโมงแรกหลังเกิด เพื่อนำไปสู่แนวทางการป้องกันการเกิดภาวะดังกล่าว*

วัสดุและวิธีการ: *การศึกษานี้เป็นการศึกษาย้อนหลังแบบ case-control (retrospective case-control study) กลุ่มศึกษาคือทารกที่ได้รับการวินิจฉัยภาวะโพรงเยื่อหุ้มปอดมีอากาศตาม ICD-10 (P25.1 Pneumothorax origi- nating in the perinatal period) ที่เกิดระหว่างเดือนมกราคม 2544 ถึงเดือนธันวาคม 2547 กลุ่มควบคุมคือทารก ที่เกิดถัดจากทารกในกลุ่มศึกษาโดยใช้อัตราส่วน 1:2 การวิเคราะห์ข้อมูลใช้ univariate analysis ในการเปรียบเทียบ และใช้อัตราส่วนเสี่ยง (Odds ratio, 95% confidence interval) ในการบอกขนาดและทิศทางของความ สัมพันธ์ของปัจจัยต่าง ๆ ระหว่างสองกลุ่ม กำหนดระดับนัยสำคัญทางสถิติที่ $p < 0.05$*

ผลการศึกษา: *จำนวนทารกในกลุ่มศึกษาและกลุ่มควบคุมคือ 44 และ 88 ราย ตามลำดับ ปัจจัยเสี่ยงแสดงด้วยอัตราส่วนเสี่ยงดังนี้ ปัจจัยทางทารกที่เป็นปัจจัยเสี่ยงได้แก่ เพศชาย (2.6; 1.2, 5.6) น้ำหนักแรกเกิดน้อยกว่า 2,500 กรัม (19.3; 2.3, 160.2) การคลอดด้วยการดึงออกด้วยสูญญากาศ (20.9; 1.1, 403.4) น้ำคร่ำมีขี้เทาปน (4.5; 1.8, 11.0) คะแนน Apgar ที่ 1 นาที น้อยกว่า 7 (78.3; 4.5, 1357.8) และการช่วยหายใจด้วย bag and mask positive-pressure ventilation (29.0; 3.6, 233.5). ปัจจัยทางมารดาที่เป็นปัจจัยเสี่ยงได้แก่ การฝากครรภ์น้อยกว่า 4 ครั้ง (3.5; 1.04, 11.9)*

สรุป: *หญิงตั้งครรภ์ทุกรายควรได้รับการส่งเสริมให้มาฝากครรภ์อย่างถูกต้อง เพื่อลดอัตราทารกเกิดก่อนกำหนด และทารกน้ำหนักตัวน้อย มารดารายใดที่มีภาวะแทรกซ้อนระหว่างการตั้งครรภ์หรือการคลอด ควรได้รับการดูแลอย่างใกล้ชิดเพื่อป้องกันทารกขาดอากาศระหว่างการคลอด ซึ่งจะส่งผลให้มีทารกที่ต้องการการกู้ชีพหลังเกิดน้อยลง มารดาที่พบว่าน้ำคร่ำมีขี้เทาปน ทารกในครรภ์ควรได้รับการเฝ้าติดตามอย่างใกล้ชิด และหลังคลอดควรพิจารณา ทำการดูดขี้เทาออกจากหลอดลมคอตามข้อบ่งชี้อย่างถูกต้องเพื่อป้องกันภาวะสูดสำลักขี้เทา หากไม่สามารถหลีกเลี่ยงการทำการกู้ชีพได้ ต้องทำอย่างระมัดระวังที่สุด โดยเฉพาะในการทำ bag and mask positive-pressure ventilation โดยปฏิบัติตามคำแนะนำของ American Heart Association ร่วมกับ American Academy of Pediatrics อย่างเคร่งครัด*