# Nosocomial Pneumonia in a Newborn Intensive Care Unit

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**Abstract**

Nosocomial pneumonia is a major cause of morbidity and mortality in hospitalized patients. The risk is especially high in the neonatal intensive care unit (NICU) particularly in infants with mechanically assisted ventilation. During the 5-year period of the study, 160 infants with problems including prematurity (60.6%), respiratory distress (55.6%) and birth asphyxia (45.0%) were admitted to the NICU. One hundred and thirty-three infants (83.1%) received mechanical ventilation. Nosocomial pneumonia was found in 65 infants (40.6%) or 88.3 cases per 1,000 ventilator-days. Low birth weight, prematurity, respiratory distress and hyperbilirubinemia were found more significantly in the pneumonia group. They underwent more manipulations such as the placement of an umbilical catheter and orogastric tube. Infants with pneumonia received mechanical ventilation at a higher percentage and for a longer period than those without pneumonia (96.9% *vs* 73.7%, odds ratio=11.2, p=0.000) with a mean duration of 11.7 and 3.5 days respectively (p=0.000). The etiologic organisms recovered from hemoculture were *Acinetobacter calcoaceticus* var. *anitratus* 44.0 per cent, *Enterobacter* spp. 16.0 per cent, *Klebsiella pneumoniae* 16.0 per cent, coagulase-negative staphylococci 12.0 per cent. There was no concordance of the bacteriologic results in endotracheal aspirate culture and hemoculture in each infant. Leukocytosis and granulocytosis as well as blood gas values could not differentiate the presence of pneumonia. The mean hospital stay for the infants with pneumonia was longer (23.0 days *vs* 6.4 days, p=0.000). Nosocomial pneumonia did not only prolong hospital stay but also contributed to mortality. Twenty-seven (41.5%) of the infants with pneumonia died, compared with 46 (48.4%) of the other group without pneumonia (p=0.422). The risk of nosocomial pneumonia can be reduced by using infection control measures, including meticulous hand washing and gloving during respiratory manipulation, heat-treated water supply in a nebulizing unit of the ventilator and proper care of umbilical catheterization.

**Key word :** Nosocomial, Pneumonia, Newborn, Intensive Care Unit, NICU

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Pneumonia is the second most common nosocomial infection, trailing only urinary tract infection, and is usually fatal[1]. In addition, nosocomial pneumonia causes considerable morbidity, prolonged hospital stay, and adds million of baht to the health care costs. Danchaivijitr et al[2] carried out a national prevalence study on nosocomial infection in 1988 and estimated that it was the main health problem affecting more than 200,000 patients annually in Thailand, 14.6 per cent of which were nosocomial pneumonia, a number that was likely to increase given the ability of medicine to keep severely ill patients alive. The study was repeated in 1992 to evaluate the efficacy of the control program. Lower respiratory tract infections were the commonest infection in this study[3]. Sophisticated and complex techniques in the NICU allow many infants to survive their initial injury only to die later of nosocomial pneumonia. The risk factors for nosocomial pneumonia in newborn intensive care are fairly clear; infants in this unit have a higher incidence of nosocomial pneumonia than other pediatric hospital patients[4,5].

The purpose of this study is to examine nosocomial pneumonia in the NICU, its incidence, clinical characteristics and outcome so that measures regarding prevention and control of nosocomial pneumonia can be instituted.

## METHOD

### Patient Population

The study population consisted of 160 sick newborn and premature infants, 54 females and 106 males, admitted to the NICU at Prachomklao Hospital, Phetchaburi Province, Thailand, between October 1993 and April 1998 with problems including prematurity (60.6%), respiratory distress (55.6%) and birth asphyxia (45.0%). The infants were born at 35.0 ± 4.9 (22 to 42) weeks gestational age, as determined by obstetrical dates and confirmed by the Dubowitz examination. The mode of delivery was mostly normal labor (51.4%) and caesarean section (37.0%). Their body weights were 2,199± 873 g, with a range of 700 to 5,200 g. (Table 1) More than 90 per cent of them were admitted within the first 3 days of life.

The infants who were at risk for respiratory failure were given supplemental oxygen, which was administered with hoods. Those with severe symptoms were intubated and supported by mechanical ventilation with conventional time-cycled, pressure-limited infant ventilators (BearCub Infant Ventilator, Bear Medical Systems, Riverside, CA, or Sechrist Infant Ventilator, Sechrist Industries, Inc, Anaheim, CA). Arterial capillary blood gas analysis and pulse oximetry were monitored. Tracheal aspirates were collected in specimen traps during endotracheal tube suctioning. The suction catheter was introduced through the endotracheal tube and advanced as far as possible to aspirate lower respiratory secretions. The aspirate sample was immediately transported to the laboratory for culture. Collection of endotracheal aspirates and hemocultures were initiated at the suspicion of pneumonia before specific antibiotics were administered.

The chest radiographs of each infant were evaluated for the presence of pneumonia.

Infants were diagnosed as having nosocomial pneumonia if they satisfied the CDC's definition[6]. (Patients less than 12 months of age with two of the following:

Apnea, bradycardia, cough, tachypnea, wheezing or rhonchi

OR

Chest radiologic examination that shows new or progressive infiltrate, cavitation, consolidation, or pleural effusion

AND

Any of the following:

1. Increased production of respiratory secretions.
2. New onset of purulent sputum or change in character of sputum.
3. Organism isolated from blood culture.
4. Isolation of pathogen from specimen obtained by transtracheal aspiration, bronchial brushing, or biopsy.)

### Statistical Analysis

The statistical analyses were carried out by using the SPSS statistical program (SPSS for Windows ver 7.5.1, SPSS Inc., Chicago, IL). Values are

**Table 1. Birth weight of the infants.**

| Birth weight (g) | Per cent | Cumulative |
|---|---|---|
| <1,000 | 4.0 | 4.0 |
| 1,000-1,499 | 20.5 | 24.5 |
| 1,500-1,999 | 17.9 | 42.4 |
| 2,000-2,500 | 21.2 | 63.6 |
| >2,500 | 36.4 | 100 |

presented as group means ± 1 SD. Differences in clinical parameters between the two groups were determined by the Student *t* test, chi-square analysis, or by the Fisher Exact Test. Values were considered to differ significantly when the p value was < 0.05.

## RESULTS

One hundred and thirty-three of the 160 infants (83.1%) received mechanically assisted ventilation, 63 of them had pneumonia as well as another 2 infants from the other group of 27 infants who did not receive it. The rate of nosocomial pneumonia was 40.6 per cent or 88.3 cases per 1,000 ventilator-days.

Table 2 shows the characteristics of the infants in the 2 groups. There were no differences in sex distribution, gestational age, and incidence of birth asphyxia and hypoglycemia. On the other hand, low birth weight, prematurity, respiratory distress, and hyperbilirubinemia were found more significantly in the pneumonia group. Infants with pneumonia underwent more manipulations other than endotracheal intubation, such as the placement of umbilical catheter and orogastric tube.

For laboratory investigation, leukocytosis and granulocytosis were not different in the 2 groups of infants, as well as the blood gas values, i.e. pH, $pO_2$, $pCO_2$, $pO_2/FiO_2$ and hematocrit, although $HCO_3$ was higher in the pneumonia group.

Sixty-three (96.9%) of 65 infants with pneumonia and 70 (73.7%) of 95 infants without pneumonia were mechanically ventilated (odds ratio, OR=11.3, 95% Confidential Interval, 95%CI =2.6-49.4, p=0.000) with a mean duration of 11.7 and 3.5 days respectively (p=0.000).

The frequency of organisms recovered from hemoculture and endotracheal aspiration is shown in Table 3. In 25 specimens of hemoculture, the organisms recovered were *Acinetobacter calcoaceticus* var. *anitratus* 44.0 per cent, *Enterobacter* spp. 16.0 per cent, *Klebsiella pneumoniae* 16.0 per cent, coagulase-negative staphylococci 12.0 per cent. In 33 specimens of endotracheal aspirate, the most commonly isolated agents were *Pseudomonas aeruginosa* 33.3 per cent, *Klebsiella pneumoniae* 21.2 per cent, and *Acinetobacter calcoaceticus* var. *anitratus* 18.2 per cent. Polymicrobial cultures were found in 21.2 per cent. There was no concordance of the bacteriologic results in endotracheal aspirate culture and hemoculture in each infant.

The mean hospital stay in the NICU for the infants with pneumonia was 23.0 days (range, 6 to 74 days) while the mean for the group without was 6.4 days (range, 1 to 24 days) (p=0.000). In infants with pneumonia due to *Pseudomonas aeruginosa*, the mean length of stay in the NICU was 35.5 days (range, 23 to 48 days), all were fatal, while that of cases due to other organisms was 16.3 days (range, 1 to 40 days).

**Table 2. Characteristics of infants with and without pneumonia.**

| Categories | With pneumonia (65) | Without pneumonia (95) | OR(95%CI) | p |
|---|---|---|---|---|
| Male:Female | 47:18 | 59:36 | 1.6(0.8-3.2) | 0.233 |
| Gestational age (wk) | 34.2±4.3 | 35.8±5.2 | | 0.054 |
| Birth weight (g) | 1,887.0±692.4 | 2,452.9±914.9 | | 0.000 |
| Low birth weight | 78.5%(51) | 47.4%(45) | 4.0(2.0-8.3) | 0.000 |
| Prematurity | 78.5%(51) | 48.4%(46) | 3.9(1.9-7.9) | 0.000 |
| Respiratory distress | 78.5%(51) | 40.0%(38) | 5.5(2.7-11.2) | 0.000 |
| Hyperbilirubinemia | 69.2%(45) | 32.6%(31) | 4.6(2.4-9.2) | 0.000 |
| Birth asphyxia | 44.6%(29) | 45.3%(43) | 1.0(0.5-1.8) | 1.000 |
| Hypoglycemia | 20.0%(13) | 10.5%(10) | 2.1(0.9-5.2) | 0.111 |
| Umbilical catheter | 78.5%(51) | 42.1%(40) | 5.0(2.4-10.3) | 0.000 |
| Orogastric tube | 30.8%(20) | 9.5%(9) | 4.2(1.8-10.1) | 0.001 |
| Mechanical ventilation | 96.9%(63) | 73.7%(70) | 11.2(2.6-49.4) | 0.000 |
| Duration of ventilation (days) | 11.7±7.8 | 3.5±2.7 | | 0.000 |
| Leukocytes (cells/$mm^3$) | 13,365.6±9,237.9 | 10,560.3±8,876.5 | | 0.178 |
| Granulocytes | 56.0±19.9% | 47.2±26.4% | | 0.093 |
| Hospital stay (days) | 23.0±13.6 | 6.4±5.3 | | 0.000 |
| Deaths | 41.5%(27) | 48.4%(46) | 0.8(0.4-1.4) | 0.422 |
| Days before death | 18.5±11.0 | 2.5±1.7 | | 0.000 |

**Table 3. Organisms recovered from infants with pneumonia.**

| Bacteria | Hemoculture(25) | Endotracheal aspirate(33) |
|---|---|---|
| *Acinetobacter calcoaceticus* var. *anitratus* | 44.0%(11) | 18.2%(6) |
| *Enterobacter* spp. | 16.0%(4) | 3.0%(1) |
| *Klebsiella pneumoniae* | 16.0%(4) | 21.2%(7) |
| *Pseudomonas aeruginosa* | 8.0%(2) | 33.3%(11) |
| Coagulase-negative staphylococci | 12.0%(3) | 3.0%(1) |
| Group D streptococci | 4.0%(1) | - |
| Polymicrobials | - | 21.2%(7) |

Seventy-three (45.6%) of the 160 infants admitted to the NICU died. Twenty-seven (41.5%) of the infants with pneumonia died at an average age of 18.5 days, 59.3 per cent of them were less than 1,500 g in birth weight. In the non-pneumonia group, 46 (48.4%) infants died, most of them had severe birth asphyxia and were mechanically ventilated at an average duration of 2.5 days before death.

## DISCUSSION

Infants receiving continuous, mechanically assisted ventilation had a higher risk (47.4%) of developing nosocomial pneumonia compared with infants not receiving ventilatory support (7.4%). Prematurity (78.5%) and respiratory distress syndrome (78.5%) made the infants dependent on mechanical ventilatory support. In the pneumonia group, 96.9 per cent of them were mechanically ventilated, a number that was significantly different from the group without pneumonia (73.7%).

The incidence of nosocomial pneumonia was 40.6 per cent or 88.3 cases per 1,000 ventilator-days. The rate varies with the diagnostic criteria of nosocomial pneumonia and patient groups. The National Nosocomial Infection Surveillance (NNIS) [7] stratified the incidence density of nosocomial pneumonia from 1986 to 1990, and revealed a median rate of 4.7 cases per 1,000 ventilator-days in pediatric ICUs. Hemming et al[8] diagnosed nosocomial pneumonia at a rate of 29.3 per cent in 222 infections in NICU, while Horpaopan et al[9] studied 89 neonates with a body weight less than 2,000 g who required mechanical ventilation with pneumonia complicated in 70 per cent.

The risk of pneumonia was also increased with the number of days the infants were receiving mechanical support. In the pneumonia group, it was 11.7 days compared with that of the non-pneumonia group, 3.5 days.

Placement of an enteral tube may increase nasopharyngeal colonization, cause reflux of gastric contents, or allow bacterial migration *via* the tube from the stomach to the upper airway[10]. In infants with pneumonia, orogastric tube placement (30.8%) significantly exceeded the other group (9.5%).

In infants with pneumonia, 33 (50.7%) of endotracheal aspirates were positive. *Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Acinetobacter* comprised 72.7 per cent of the isolates from endotracheal aspirates with 21.2 per cent being polymicrobial. Microorganisms cultured from tracheal aspirate were not found in lung tissue obtained by open lung biopsy in 56 per cent of 48 patients in a study published by Hill et al[11]. With their low specificity, the significance of endotracheal aspirates remained the least reliable specimen[12].

Because the infants had been treated with antibiotics, hemocultures were positive in only 25 (38.5%) of infants with pneumonia, all were in pure culture. Although a culture of blood has very low sensitivity but greater specificity, short of tissue obtained by the above methods, the only reliable bacterial cultures were those obtained from blood, the organisms isolated were considered etiological for pneumonia if evidence of a nonpulmonary infection was lacking[12]. *Acinetobacter calcoaceticus* var. *anitratus*, *Enterobacter* spp., *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* comprised 84 per cent of the isolates from neonates for whom nosocomial pneumonia was diagnosed. Coagulase-negative staphylococci and group D streptococci accounted for the remainder.

Results of cultures of endotracheal aspirates and hemocultures obtained simultaneously all showed substantial differences in this study.

Another major change is the increasing importance of coagulase-negative staphylococcus and the growing appreciation of this organism as a pathogen[13,14], since it reflects possible catheter-associated infection especially umbilical catheterization. Avila-Fugueroa et al reported that mechanical ventilation was also a risk factor for coagulase-negative staphylococci in very low birth weight newborns in the NICU[15].

Other tests of potential value in the evaluation of neonates with possible nosocomial pneumonia include complete blood count (CBC) and the differential count of white blood cells. With bacterial infection, the white blood cell count tends to be elevated and the granulocytes tend to be shifted toward more immature forms. However, the mean value of blood leukocytes and percentage of granulocytes were not different in neonates who had pneumonia and those who did not.

The length of stay in the NICU was significantly different in the 2 groups of infants. Infants with nosocomial pneumonia were hospitalized for an average of 3.5 times that of noninfected infants. A correlation has been reported between nosocomial pneumonia and prolonged hospitalization[16].

It was not clearly determined in our patients whether the occurrence of nosocomial pneumonia itself contributed to a longer period of hospitalization, or whether the lower birth weight, sicker infants, many of whom were exposed to varieties of manipulations and devices, required a more prolonged hospitalization.

Patients with nosocomial pneumonia had mortality rates of 55 per cent to 70 per cent[16,17]. In the present study, the mortality rate was 41.5 per cent, low and very low birth weight infants were particularly at higher risk, most (59.3%) of the 27 infants who died of pneumonia were less than 1,500 g in birth weight. The presence of high-risk antibiotic-resistant pathogens, *Pseudomonas aeruginosa, Acinetobacter* and *Enterobacter* spp., was the most important predictor of hospital mortality.

Infants who have severe underlying disease and who are receiving intensive care have a greater risk of nosocomial pneumonia. Provided that the major group of etiologic bacteria in our hospital setting were gram-negative enteric bacteria and coagulase-negative staphylococci, potential useful infection control measures might include meticulous hand washing and gloving during respiratory manipulation, heat-treated water supply in a nebulizing unit of the ventilator and proper care of umbilical catheterization.

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# โรคปอดบวมที่เกิดในโรงพยาบาลในหน่วยผู้ป่วยหนักเด็กแรกเกิด

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โรคปอดบวมที่เกิดในโรงพยาบาลเป็นสาเหตุสำคัญของการเจ็บป่วยและเสียชีวิตในหน่วยผู้ป่วยหนักเด็กแรกเกิดที่ได้รับเครื่องช่วยหายใจ ในระยะเวลา 5 ปีของการศึกษาโรคนี้มีทารกแรกเกิดจำนวน 160 คนที่มีปัญหาคลอดก่อนกำหนด (60.6%) หายใจลำบาก (55.6%) และขาดออกซิเจนขณะคลอด (45.0%) ทารก 133 คน (83.1%) ได้รับการรักษาด้วยเครื่องช่วยหายใจ พบปอดบวมที่เกิดจากการติดเชื้อในโรงพยาบาล 65 คน (40.6%) หรือ 88.3 รายต่อ 1,000 วันของการใช้เครื่องช่วยหายใจ ในกลุ่มที่มีปอดบวมพบทารกน้ำหนักน้อย คลอดก่อนกำหนด หายใจลำบาก และตัวเหลืองมากกว่าทารกในกลุ่มนี้ได้รับหัตถการมากกว่าเช่นการใส่สายสวนเข้าหลอดเลือดสะดือ การใส่สายเข้ากระเพาะอาหาร ทารกในกลุ่มที่มีปอดบวมได้รับเครื่องช่วยหายใจมากกว่า (96.9% *vs* 73.7%, odds ratio=11.2, p=0.000) เป็นเวลา 11.7 วัน ส่วนอีกกลุ่มหนึ่งเพียง 3.5 วัน (p=0.000) เชื้อที่แยกได้จากเลือดคือ *Acinetobacter calcoaceticus* var. *anitratus* 44.0%, *Enterobacter* spp. 16.0%, *Klebsiella pneumoniae* 16.0%, coagulase-negative staphylococci 12.0% ไม่มีความเกี่ยวข้องกันระหว่างเชื้อที่เพาะได้จากเสมหะที่ดูดจากหลอดลมและจากเลือด จำนวนเม็ดเลือดขาว ร้อยละของ granulocytes และค่าของก๊าซในเลือด ไม่สามารถบ่งบอกว่ามีการติดเชื้อปอดบวมหรือไม่ ระยะเวลาในการพักรักษาตัวของทารกที่มีปอดบวมนานกว่า คือ 23.0 วันเมื่อเทียบกับ 6.4 วัน ในกลุ่มไม่มีปอดบวม (p=0.000) ทารกที่มีปอดบวมเสียชีวิต 27 คน (41.5%) และที่ไม่มีปอดบวมเสียชีวิต 46 คน (48.4%) จะเห็นได้ว่าโรคปอดบวมที่เกิดในโรงพยาบาลนอกจากจะเป็นสาเหตุที่ทำให้สูญเสียทรัพยากรเป็นจำนวนมากในการรักษาแล้วยังทำให้มีการเสียชีวิตอีกมากด้วย ปัจจัยเสี่ยงที่จะเกิดโรคปอดบวมที่เกิดในโรงพยาบาลจะลดลงได้โดยมีมาตรการควบคุมการติดเชื้อที่เหมาะสมได้แก่ การล้างมืออย่างพิถีพิถันและการใส่ถุงมือในหัตถการที่เกี่ยวกับระบบหายใจ การเพิ่มอุณหภูมิของน้ำในเครื่องทำฝอยละอองของเครื่องช่วยหายใจ และการดูแลสายสวนเข้าหลอดเลือดสะดือ

**คำสำคัญ** : ปอดบวม, เกิดในโรงพยาบาล, หน่วยผู้ป่วยหนัก, เด็กแรกเกิด

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