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Neonatal morbidity and mortality of very low birth weight infants at King Chulalongkorn Memorial Hospital

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- Background** : *The number of very low birth weight (VLBW) infants in tertiary care hospitals in Thailand is rising continuously. Nevertheless, available data about their morbidity and mortality have not yet been established.*
- Objective** : *To determine the neonatal morbidity and mortality of VLBW infants admitted at a tertiary care hospital in Bangkok.*
- Methods** : *Medical records of all newborns with birth weight of <1500 grams (VLBW) at King Chulalongkorn Memorial Hospital during 2003 - 2005 were analyzed. Care provided to the infants was based on the same practical guideline. Early nasal continuous positive airway pressure (CPAP) was the common practice and exogenous surfactant was only used as a rescue therapy for Idiopathic Respiratory Distress Syndrome (IRDS). Five items of morbidity, i.e., bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), osteopenia and intra-ventricular hemorrhage (IVH) were included. All deaths occurred during hospitalization were included irrespective of postnatal age.*

- Result** : There were 284 VLBW infants including 15 out - borns. The ratio of infants with birth weight ≤ 1000 grams to 1001-1499 grams was 97:187. Their gestational age ranged between 22 - 41 weeks. The total incidence of BPD, ROP, NEC, osteopenia, IVH and death were 39 (13.7%), 27 (9.5%), 50 (17.6%), 14 (4.9%), 32 (11.3%) and 35 (12.3%) respectively. In comparison with the group of larger infants, infants with birth weight ≤ 1000 grams had higher incidence of BPD (21.6% vs 9.6%), (OR 2.59; 95%CI, 1.31 - 5.15), ROP (16.5% vs 5.9%), (OR 3.16; 95%CI, 1.40 - 7.11) and IVH (26.8% vs 3.2%), (OR 11.05; 95%CI, 4.36 - 27.97), p-value < 0.005 for all. The incidence of NEC and osteopenia were not statistical different. Their mortality rate was also higher (28.9% vs. 3.7%), (OR 10.43; 95%CI, 4.36 - 24.99), p-value < 0.005 . Major causes of death were extreme immaturity, severe birth asphyxia, severe IRDS and nosocomial infection. Among the survival infants, none of them had blindness, hydrocephalus, bone deformity or requires oxygen supplement.
- Conclusion** : This study demonstrates a satisfactory outcome of the VLBW infants at a tertiary care hospital. Survival rate is 87.7%. Their survival with relatively mild degree of morbidity is encouraging.
- Keywords** : Very low birth weight infant, Neonatal mortality, Neonatal morbidity.

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พิมลรัตน์ ไทยธรรมยานนท์, สันติ ปุณณะหิตานนท์. ภาวะแทรกซ้อนและการเสียชีวิต
ของทารกแรกเกิดน้ำหนักน้อยมากในโรงพยาบาลจุฬาลงกรณ์. จุฬาลงกรณ์เวชสาร 2551
ก.ค. - ส.ค; 52(4): 255 - 64

หลักการและเหตุผล : จำนวนทารกแรกเกิดน้ำหนักน้อยมากในโรงพยาบาลระดับตติยภูมิใน
ประเทศไทยเพิ่มขึ้นอย่างต่อเนื่อง แต่ข้อมูลที่เกี่ยวข้องกับภาวะแทรกซ้อน
และการเสียชีวิตยังไม่ชัดเจน

วัตถุประสงค์ : แสดงข้อมูลเหล่านี้ในโรงพยาบาลจุฬาลงกรณ์ ซึ่งเป็นโรงพยาบาลระดับ
ตติยภูมิแห่งหนึ่งในกรุงเทพฯ เพื่อเป็นข้อมูลให้บุคลากรทางการแพทย์ที่
เกี่ยวข้องนำไปปรับใช้

วิธีทำการศึกษา : ทำการวิเคราะห์เวชระเบียนของทารกแรกเกิดน้ำหนักน้อยมากทุกคน
(น้ำหนักแรกเกิดต่ำกว่า 1500 กรัม) ที่ได้รับการรักษาในระหว่าง ปี พ.ศ.2546
ถึง 2548 ในโรงพยาบาลจุฬาลงกรณ์ แนวทางการรักษาทารกทุกคนเป็น
แบบอย่างเดียวกัน ทารกป่วยด้วยภาวะ Idiopathic Respiratory Distress
Syndrome (RDS) จะได้รับการรักษาด้วย Early nasal continuous positive
airway pressure และได้รับการพ่นสารลดแรงตึงผิว (Exogenous surfactant)
ถ้ามีอาการภาวะนี้รุนแรง ภาวะแทรกซ้อนที่นำมาวิเคราะห์มี 5 ชนิดคือ
Bronchopulmonary dysplasia (BPD), Retinopathy of prematurity (ROP),
Necrotizing enterocolitis (NEC), Osteopenia และ Intraventricular
hemorrhage (IVH) อัตราเสียชีวิตนับจาก ทารกทุกรายที่ตายไม่ว่าจะมีอายุ
เท่าใดขณะอยู่โรงพยาบาล

ผลการศึกษา : พบว่ามีทารกทั้งหมด 284 ราย รวมถึงทารกที่รับย้ายมาจากโรงพยาบาลอื่น
15 ราย อายุครรภ์อยู่ระหว่าง 22 ถึง 41 สัปดาห์ สัดส่วนทารกน้ำหนัก
 ≤ 1000 กรัม ต่อทารกน้ำหนัก 1001-1499 กรัมเท่ากับ 97 ต่อ 187 อัตราการ
เกิด BPD, ROP, NEC, osteopenia (rickets), IVH และอัตราการเสียชีวิต
เท่ากับ 39 (13.7%), 27 (9.5%), 50 (17.6%), 14 (4.9%), 32(11.3%)
และ 35 (12.3%) ตามลำดับ เมื่อเปรียบเทียบอัตราเหล่านี้ระหว่างทารก
น้ำหนัก ≤ 1000 กรัมกับทารกน้ำหนัก 1001-1499 กรัม ปรากฏว่ากลุ่มทารก
น้ำหนักน้อยกว่าเกิด BPD (21.6% vs 9.6%), (OR 2.59; 95%CI, 1.31 -
5.15), ROP (16.5% vs 5.9%), (OR 3.16; 95%CI,1.40 - 7.11), IVH
(26.8% vs 3.2%), (OR 11.05; 95%CI, 4.36 - 27.97), และเสียชีวิต

(28.9% vs 3.7%), (OR 10.43; 95%CI, 4.36 - 24.99). มากกว่ากลุ่มที่มี น้ำหนักมากกว่าอย่างมีนัยสำคัญทางสถิติ (ทั้งหมด $p < 0.005$) แต่อัตราเกิด NEC และ osteopenia ไม่แตกต่างกัน สาเหตุตายที่สำคัญได้แก่ อายุครรภ์ น้อยมาก ขาดออกซิเจนเมื่อแรกเกิดอย่างรุนแรง IRDS ชนิดรุนแรง และการติดเชื้อในโรงพยาบาล ทารกรอดชีวิตทุกรายไม่มีอาการตาบอด หัวบาตร กระดูกผิดปกติหรือต้องการออกซิเจนเสริม

สรุป : การศึกษานี้แสดงให้เห็นว่าผลการรักษาทารกน้ำหนักน้อยมากใน โรงพยาบาลระดับตติยภูมิเป็นที่น่าพอใจ เกิดภาวะแทรกซ้อนไม่รุนแรง และมีอัตราการรอดชีวิตสูงถึงร้อยละ 87.7

คำสำคัญ : ทารกน้ำหนักแรกเกิดน้อยมาก, อัตราการเกิดภาวะแทรกซ้อน, อัตราการ เสียชีวิต

Very low birth weight (VLBW) infants have a large impact on both neonatal mortality and morbidity. Care for these infants is very special. They demand high technology and consume a great amount of resource. Reports from both developed and developing countries have shown that the improved survival rate of VLBW infants — particularly of the extremely low birth weight infants — is likely associated with modern perinatal technology and care. And the improvement of survival rate is not associated with an increase in major morbidities.⁽¹⁻³⁾ Thailand is a developing country where regionalized system of perinatal-neonatal healthcare and neonatal intensive care network have not been established. With the new health reform system, delivery rate in the tertiary care hospital in Thailand has been decreasing. But the proportion of high-risk infants especially the very low birth weight (VLBW) infants in these hospitals continue to rise. It is due to increased transferring of high-risk mothers and infants from most general hospitals to the tertiary care centers. Some sick neonates are still transferred by unskilled personnel with inadequate facilities. Data concerning the neonatal outcome of VLBW is still unavailable as nationwide databases or reports. Our hospital, King Chulalongkorn Memorial Hospital — a Red Cross Hospital — is also operated by the Faculty of Medicine, Chulalongkorn University, is one of the major tertiary care center in Thailand. A large number of high-risk pregnant women including sick newborn infants are referred to our institute from most of hospitals in Bangkok and all over the country. The purpose of this study is to demonstrate the neonatal death rate and some important selected short-term morbidity of VLBW infants admitted to a tertiary care center in Bangkok.

We expect the result can be used as relevant information for the obstetricians, pediatricians and their patients. It should help them on decision making concerning their healthcare and management plan for these high-risk infants.

Material and Method

Medical records of all newborn infants with birth weight of less than 1500 grams (VLBW) admitted to either the neonatal intensive care unit (NICU) or a special care unit for low birth weight infants between January 1, 2003 and December 31, 2005 were analyzed. All infants with detectable heart rate were resuscitated and admitted to the neonatal intensive care unit. Infants with a major malformation were not excluded. Care provided to the infants was based on the same guideline. Early nasal continuous positive airway pressure (CPAP) was the common practice and exogenous surfactant was used as a rescue therapy for severe Idiopathic Respiratory Distress Syndrome (IRDS) only. Gestational age in completed weeks was determined by obstetric measures (e.g., last menstrual period, ultrasonography) or by clinical assessment using Ballard score system.⁽⁴⁾ Five items of morbidity were selected, i.e., bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), necrotizing enterocolitis (NEC), osteopenia (rickets) and intra-ventricular hemorrhage (IVH). BPD was defined as receiving supplement oxygen at 36 week post-conceptual age with characteristic chest radiograph abnormalities.⁽⁵⁾ ROP was defined according to International Classification of Retinopathy of prematurity,⁽⁶⁾ all stages were included. All stages of NEC defined according to the criteria of Bell *et al.*⁽⁷⁾, and all stages of IVH defined according to the criteria

of Papile *et al.*⁽⁸⁾ were also included. Cranial sonograms were performed on every infant admitted to NICU during the first week of life or when IVH was suspected. Osteopenia was defined as a condition of de-mineralized bone accompanied with abnormal blood chemistry.⁽⁹⁾ Morbidity in both demised and survived infants were reported. The incidence of each item was calculated from the number of event. Death occurred during hospitalization regardless of their postnatal age was counted for mortality rate.

Statistical analyses were performed using Chi-square test. Odd ratio and 95% Confidence Interval were calculated. P-value <0.05 was considered statistical significant.

Result

There are 284 VLBW infants, 269 inborns and 15 out-borns are included. The ratio of infants with birth weight ≤ 1000 grams to 1001-1499 grams is 97:187. Their gestational age ranged between 22 - 41 weeks. The smallest infants weighed 390 grams. Number distribution of all VLBW infants by gestational age and by birth weight is shown in table 1 and table 2. IRDS is diagnosed in 81/97 (83.5%) infants and 94/187 (50.3%) infants of those with birth weight ≤ 1000 grams and 1001-1499 grams, respectively. The total incidence of BPD, ROP, NEC, osteopenia, IVH, and death are 39 (13.7%), 27 (9.5%), 50 (17.6%), 14

(4.9%), 32 (11.3%) and 35 (12.3 %) respectively, (Figure 1). In comparison with the group of larger infants, infants with birth weight ≤ 1000 grams have significantly higher incidence of BPD (21.6% vs. 9.6%), (OR2.59; 95%CI, 1.31, 5.15), ROP (16.5% vs. 5.9%), (OR3.16; 95%CI, 1.40, 7.11) and IVH (26.8% vs. 3.2%), (OR11.05; 95%CI, 4.36, 27.97). The incidence of NEC and osteopenia are not statistical different. Their mortality rate is also higher (28.9% vs. 3.7%), (OR10.43; 95%CI, 4.36, 24.99) (Table 3). The birth weight-specific mortality for all infants in 250-gram birth weight intervals is shown in figure 2. Mortality rate decreased as birth weight increased. The gestational age-specific mortality for all infants is shown in figure 3. Percentage of death among infant gestational age ≥ 35 weeks is unusually high. They were severe intrauterine growth retarded infants with multiple congenital anomalies, one of them also had trisomy 18 chromosome. Most of the non-survival infants weighed under 750 grams (14 out of 26 infants) or had gestational age less than 26 weeks (16 out of 30 infants). Overall survival rate was 87.7%. The major causes of death were extreme immaturity, severe birth asphyxia, severe IRDS, congenital anomalies and nosocomial infection. Among the survival infants, none of them had blindness, hydrocephalus, bone deformity or oxygen dependency at the time of discharge.

Table 1. Number distribution of all VLBW infants by birth weight (BW) and survival rate.

BW (grams)	No. of infants	Survival rate, n (%)
≤ 500	3	0
501-750	23	12 (52.2)
751-1000	71	57 (80.3)
1001-1250	92	88 (95.6)
1251-1499	95	92 (96.8)
Total	284	249 (87.7)

Table 2. Number distribution of all VLBW infants by gestational age (GA) and survival rate.

GA (weeks)	No. of infants	Survival rate, n (%)
≤25	30	14 (46.7)
26-28	91	79 (86.8)
29-31	98	96 (97.9)
32-34	51	49 (96.1)
≥35	14	11 (78.6)
Total	284	249 (87.7)

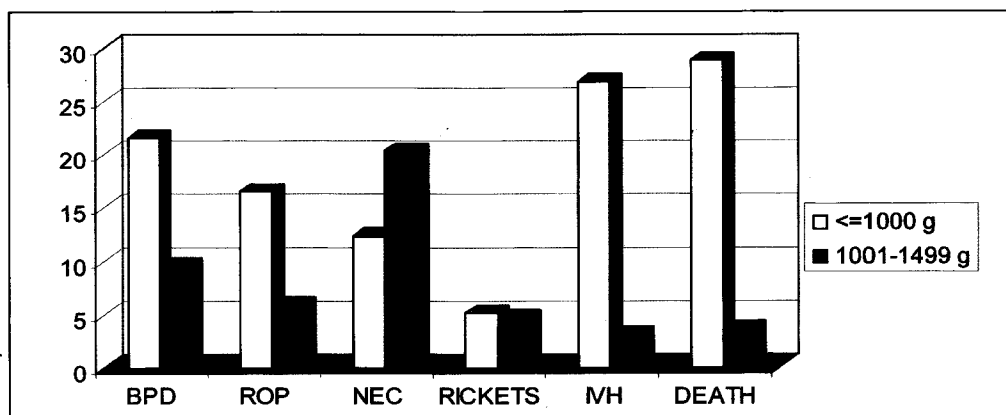


Figure 1. Morbidity and mortality rate (%) of VLBW infants

Table 3. Comparison of the morbidity and mortality rates between infants ≤ 1000 grams and 1001-1499 grams.

Morbidity & Mortality	Birth weight		OR (95% CI) * p-value <0.005
	≤1000, (n=97) (%)	1001-1499, (n=187) (%)	
BPD	21 (21.6)	18 (9.6)	2.59 (1.31,5.15)*
ROP	16 (16.5)	11 (5.9)	3.16 (1.40,7.11)*
NEC	12 (12.4)	38 (20.3)	0.55 (0.27,1.12)
Osteopenia	5 (5.2)	9 (4.8)	1.07 (0.35,3.30)
IVH total	26 (26.8)	6 (3.2)	11.05 (4.36,27.97)*
Grade I	6 (6.2)	2 (1.1)	
Grade II	8 (8.2)	3 (1.6)	
Grade III	10 (10.3)	1 (0.5)	
Grade IV	2 (2.1)	0	
Deaths	28 (28.9)	7 (3.7)	10.43 (4.36,24.99)*

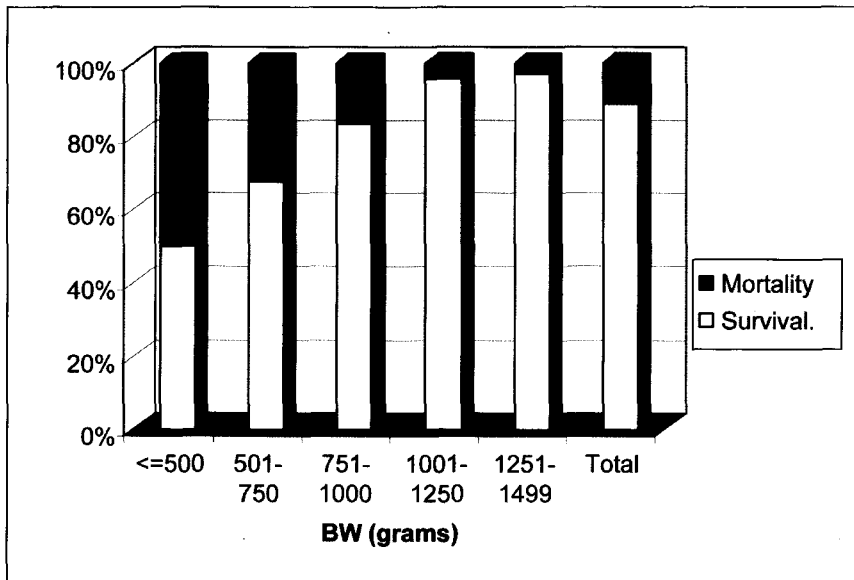


Figure 2. Mortality by birth weight

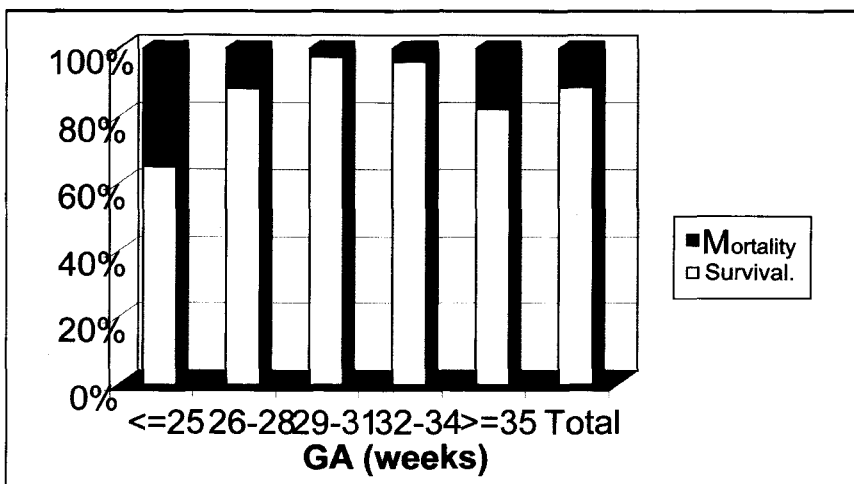


Figure 3. Mortality by gestational age

Discussion

We report the mortality and morbidity among VLBW infants born at a tertiary care hospital in Bangkok where its resource is very limited. However, it shows an encouraging outcome. The overall survival rate is favorably comparable with reported cases from both developing and developed countries.^(1-3, 10) It has been suggested that there are many factors that improve pulmonary outcome and decrease IVH which are also associated with improving ROP outcome in

VLBW infants. These factors include the use of prenatal steroid, surfactant and continuous pulse oximetry, and providing adequate nutritional support.^(1,13,14) We agree and we are assured that better obstetric care and the recent advances in neonatology influenced this outcome. Prenatal steroid has been used more often in our institute during this study period. But the detailed information cannot be reported because of the data is highly fragmented. Although, we used exogenous surfactant for infants with severe RDS only

the proportion of survivor VLBW infants and the morbidity rate is comparable with other reports in the medical literatures.^(1-3, 10) However, the incidence of BPD (13.7%) and its severity in our infants seem to be less than those reported from North America or Taiwan.^(1, 10) Their incidences were 23% and 16.5%, respectively. We believe it could be due to the difference in genetic factor or the method of assisted ventilation. We speculate that the common use of early nasal CPAP in our center was contributed to this favorable outcome. It has been demonstrated that early use of nasal CPAP in extremely low birth weight infants is associated with reduction in BPD rate.^(11, 12) The incidence of NEC and IVH in this report are higher than those of other studies.^(1, 2) Because we include all stage of NEC and IVH. For example, if we had excluded IVH stage I and II, the incidence would be similar to the outcomes of other reports. Our incidence of IVH stage III and IV is only 4.5%. The overall incidence of NEC is 17.6% which is much higher than those reported from NICHD and Neonatal Research Network. Their incidence of proven NEC (Bell's stage: \geq II) was 7% and inversely related to birth weight which was different from our result. The incidence of NEC among larger infants in our study is higher than those infants \leq 1000 grams. This is probable due to the high early death rate of smaller infants. They could develop NEC if they had survived longer. Common nosocomial infection and relatively small number of breast feeding in our infants could be also other risk factors of NEC. We realized that there was some limitation of our data since it came from only a single tertiary care center in Bangkok. National data are required and the long-term outcomes of these survival infants still need to be emphasized.

Conclusion

This study demonstrates a satisfactory outcome of VLBW infants in a tertiary care hospital. The overall survival rate is 87.7% and morbidity among the survivors is relatively minimal.

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