Survival and Outcome of Very Low Birth Weight Infants Born in a University Hospital with Level II NICU

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Objectives: *Determine the survivals, neonatal outcomes to hospital discharge, and perinatal risks of death among VLBW infants born in the Thammasat University Hospital.*
Material and Method: *This was a retrospective longitudinal study. Data were colleted from medical charts of all neonates with a gestational age of more than 25 weeks and birth weight of less than 1500 grams, who were born in Thammasat University Hospital for a 3-year period between July 1st, 2003 and June 30th, 2006. Antenatal history, perinatal data, and neonatal outcome until hospital discharge were extracted and analyzed.*
Results: *Seventy-eight neonates with a birth weight between 600-1,485 grams were analyzed. Survival rate of very-low-birth-weight (VLBW) infants and extremely-low-birth-weight (ELBW) infants were 81% and 52% respectively. Respiratory distress syndrome (RDS) was the major cause of death. Major morbidity was found in 35% of survived infants to hospital discharge. Unfavorable outcome was documented in infants with a birth weight < 750 grams. Perinatal risks of mortality among VLBW infants included no use of antenatal steroids ($p = 0.015$), gestational age of < 28 weeks ($p = 0.012$), ELBW ($p < 0.001$), congenital abnormalities ($p = 0.002$), Apgar score at 5 minute ≤ 5 ($p = 0.019$), needed endotracheal intubation in the delivery room ($p < 0.001$), and first temperature at NICU $\leq 35.0^{o}C$ ($p = 0.023$).*
Conclusion: *Overall survival and outcome among very-low-birth-weight infants born in Thammasat University Hospital is acceptable. The mortality and morbidity in extremely-low-birth-weight infants remained high. A continuing audit of these measures should be encouraged.*

Keywords: *Survival, Outcome, Very low birth weight infants, Mortality, Morbidity, Intensive neonatal care*

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Very-low-birth-weight (VLBW) infants (birth weight < 1,500 grams) are at high risk of mortality and morbidity because of problems associated with prematurity and treatment complications[1,2]. Implementation of neonatal intensive care in neonatal intensive care unit (NICU), use of mechanical ventilation and exogenous surfactant has been reported to improve the outcome especially for extremely low birth weight (ELBW) infants (birth weight < 1,000 grams[2,3]). The survival to hospital discharge of VLBW infants has been well documented in developed countries with an increasing survival trend, especially in ELBW infants[1-6]. The survival and outcomes of VLBW varied from hospital to hospital or from country to country regarding the quality of antenatal, intrapartum, and neonatal care[7]. In Thailand, survival data of VLBW infants have been reported with lower survival, especially in ELBW infants[8-11]. Thammasat University Hospital provided maternal and neonatal services for the population of Patumthanee Province and surrounding areas. All live-born VLBW infants were admitted to the NICU (level 2 by AAP classification) for intensive care with availability of mechanical ventilation. Exogenous surfactant was provided only for affordable patients when indication has been met as in developing countries.

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The objectives of the present study were to determine the survivals, neonatal outcomes to hospital discharge and perinatal risks of death among VLBW infants born in Thammasat University Hospital.

Material and Method

This was a retrospective longitudinal study. All live-born premature infants who had a birth weight < 1,500 grams were identified by reviewing the delivery room registry of Thammasat University Hospital between July 1st, 2003 and June 30th, 2006. Outborn VLBW infants were excluded. The present study was approved by the Faculty of Medicine Thammasat University Human Ethics Committee.

The medical records were reviewed and extracted retrospectively for antenatal and perinatal characteristics, neonatal mortality, and morbidity. The gestational ages were determined by obstetric assessment or modified Ballard score[12]. A birth weight less than the 10th percentile for gestational age was classified as small for gestational age (SGA). Diagnosis of respiratory distress syndrome (RDS) was based on clinical and radiological evidence. Infants who received supplemental oxygen at 36 weeks' postmenstrual age as determined by the gestational age at birth were diagnosed as chronic lung disease (CLD). Necrotizing entercolitis (NEC) was diagnosed by Bell's classification[13]. Intraventricular hemorrhage (IVH) was graded according to Papile's classification[14]. The stage of retinopathy of prematurity (ROP) was classified according to the International of Retinopathy of Prematurity[15]. Major morbidity in the present study was defined as infants who had one of these following conditions: CLD, severe IVH (grade $\geq$ 3), NEC grade $\geq$ 2 and severe ROP (grade $\geq$ 3).

All data were analyzed using the STATA version 9.0 statistical package. Overall survival rate and stratified survival rates by gestational age and birth weight were calculated. Kaplan Meier survival curves were presented and a log-rank test was used to compare the survival curves between birth weight groups. Perinatal risks of mortality were explored and presented with odds ratios and 95% confidence interval (95% CI). Chi-square test and Fisher's exact tests were used to test an association between risk factors and the survival outcome at statistical significant level of 0.05.

Results

There were 16,114 live births in the hospital over a 3-year period with the incidence rate of live-born VLBW infants of 4.9 cases per 1,000 live births. Of all 78 VLBW infants, 47% were boys and 53% were girls. The median birth weight and gestational age were 1,200 grams (range 600-1485 grams) and 30 weeks (range 25-37 weeks) respectively. The birth weight distribution included 6% who weighed between 600 and 749 grams, 20% who weighed between 750 and 999 grams, 31% who weighed between 1,000 and 1,249 grams, and 42% who weighed between 1,250 and 1,499 grams. By gestational age estimated, 32% of the VLBW infants was < 28 weeks, 49% was 28 to 32 weeks, and 19% was > 32 weeks. The mean maternal age in the present study was 27.5 years (SD 10.3 years). Fifteen percent had no antenatal care and 18% had severe preeclampsia. Among VLBW infants, 27% were ELBW, 24% were SGA, 56% were born by cesarean section, and 27% required resuscitation in the delivery room at birth. Antenatal use of full course steroids was 33%.

There were 15 deaths and 63 survivals to discharge home. The overall survival of VLBW infants was 81%. The survival rate of VLBW infants improved with increasing birth weight ($p < 0.001$). Survivals to hospital discharge stratified by birth weight are presented in Table 1. Survivability correlated significantly

Table 1. Survivals and outcomes among 78 VLBW infants according to birth weight

	< 750 g (n = 5)	750-999 g (n = 16)	1,000-1,249 g (n = 24)	1,250-1,499 g (n = 33)	Total (n = 78)
Deaths	4 (80%)	6 (38%)	3 (13%)	2 (6%)	15 (19%)
Survivals	1 (20%)	10 (62%)	21 (87%)	31 (94%)	63 (81%)
Survivals without morbidity	0	3 (30%)	15 (71%)	23 (74%)	41 (65%)
Survivals with morbidity	1	7 (70%)	6 (29%)	8 (26%)	22 (35%)
CLD	0	6	6	4	16
Severe IVH (grade $\geq$ 3)	1	0	0	0	1
NEC (stage $\geq$ 2)	0	1	0	4	5
Severe ROP (grade $\geq$ 3)	0	0	0	0	0

with gestational age (p = 0.031). Sixty-four percent of infants born at a gestational age of less than 28 weeks survived, 87% of those born between 28 to 32 weeks, and 93% of those born between 32 to 37 weeks. Survival curves stratified by birth weight are shown in Fig. 1. The survival curves were significantly better according to increasing birth weight ($p < 0.001$ by log-rank test). All fatal VLBW infants died within 48 days and 80% died within the first 5 days. The major cause of death among the VLBW infants was RDS and followed by congenital abnormalities as summarized in Table 2.

The median duration of hospital stay of all VLBW was 31.5 days (inter-quartile range: 15-46 days).

Table 2. Causes of death among VLBW infants

Causes of death, n=15	Frequency (%)
RDS	7 (47%)
Severe sepsis	3 (20%)
Culture proven	1
Congenital abnormalities	5 (33%)
Suspected Edward syndrome	1
Hypoplastic left heart syndrome	1
Hydranencephaly	1
Congenital cytomegalovirus infection	1
Congenital rubella infection	1

Overall neonatal outcome to hospital discharge improved when birth weight increased as presented in Fig. 2. Major morbidity was noted in 35% of VLBW infants who survived to hospital discharge. Percent survival with and without neonatal morbidity according to birth weight is shown in Table 1. There were three survived infants having ROP grade 1-2 assessed at hospital discharge.

Antenatal and perinatal factors associated with mortality are presented in Table 3. By univariate analysis, the significant perinatal risks of mortality included no use of antenatal steroids ($p = 0.015$), gestational age of < 28 weeks ($p = 0.0123$), ELBW ($p < 0.001$), congenital abnormalities ($p = 0.002$), Apgar score at 5 minute ≤ 5 ($p = 0.019$), needed endotracheal intubation in the delivery room ($p < 0.001$) and first temperature at NICU $\leq 35.0^{o}C$ ($p = 0.023$).

Discussion

The overall survival of VLBW infants in the present study was 81%, which is comparable to the survival of 72%-90% from other countries[2-6,13,14]. The relatively low survivals of 63% -76% were reported from other hospitals in Thailand[8-11]. The favorable survival can be explained by improvement of neonatal care including increasing use of continuous positive airway pressure (CPAP) as a form of ventilation in practice, willingness, and ability of the care team in the NICU[18].

Table 3. Antenatal and perinatal risks of mortality

Characteristics	Survivors n = 63	Deaths n = 15	Odds ratio (95% CI)
Antenatal factors			
Maternal age $\leq$ 20 years	15 (24%)	5 (33%)	1.6 (0.5-5.4)
Primigravida	32 (51%)	9 (60%)	1.5 (0.5-4.6)
No antenatal attendance	14 (22%)	2 (13%)	0.5 (0.1-2.7)
Severe pre-eclampsia	13 (21%)	1 (7%)	0.3 (0-2.2)
Antenatal steroids	25 (40%)	1 (7%)	0.1 (0-0.9)*
Perinatal factors			
Caesarean-section	28 (44%)	6 (40%)	0.8 (0.3-2.6)
Male gender	29 (46%)	8 (53%)	0.7 (0.2-2.3)
GA $\leq$ 28 weeks	16 (25%)	9 (60%)	4.4 (1.4-14.3)*
ELBW	11 (18%)	10 (67%)	9.5 (2.7-33.2)*
SGA	16 (25%)	3 (20%)	0.7 (0.2-2.9)
Congenital anomaly	1 (2%)	4 (27%)	22.2 (2.3-221)*
Apgar score at 1 minute $\leq$ 5	25 (40%)	8 (53%)	1.7 (0.5-5.3)
Apgar score at 5 minute $\leq$ 5	3 (5%)	4 (27%)	7.2 (1.4-36.5)*
Endotracheal intubation in delivery room	13 (21%)	10 (67%)	7.5 (2.2-25.9)*
First temperature at NICU $\leq 35.0^{o}C$	11 (18%)	7 (47%)	4.1 (1.2-13.8)*

* Significant level at $p < 0.05$

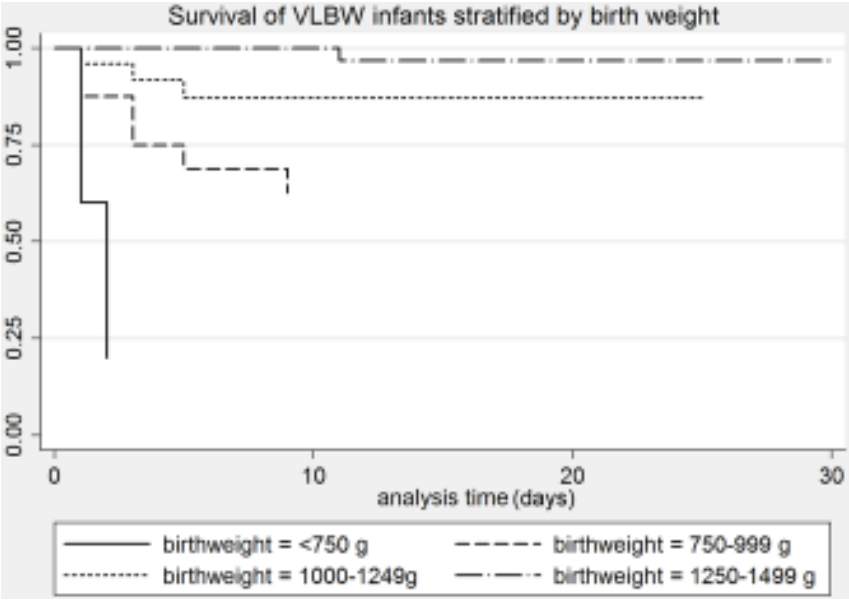

Fig. 1 Survival curves of VLBW infants according to birth weight

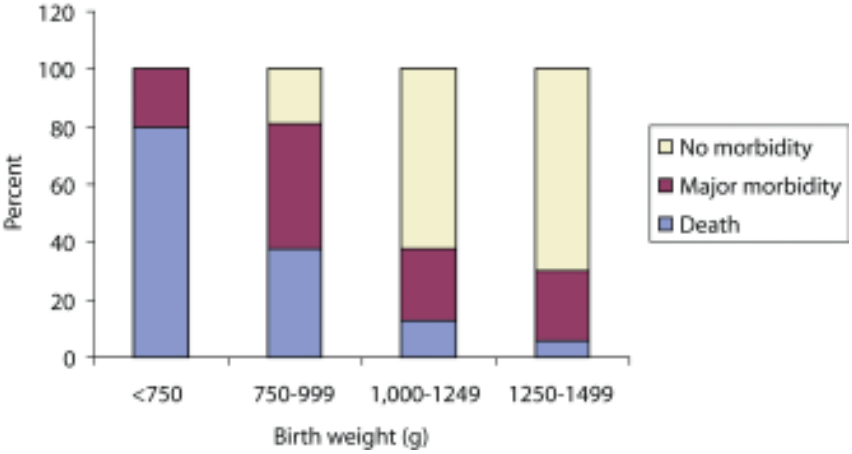

Fig. 2 Outcomes of VLBW infants to hospital discharge

Since 2002, all VLBW infants born in Thammasat University Hospital have been admitted to the NICU with a neonatologist and a well-trained intensive care nurses team. Reports of the survivals of VLBW infants and ELBW infants are summarized and compared in Table 4. The mortality and morbidity of VLBW varied from hospital to hospital and country to country reflecting the quality of antenatal, intrapartum and neonatal care[7]. In developing countries and areas where the availability of exogenous surfactant, NICU beds, mechanical ventilation, and equipment are limited, the survivals of especially ELBW tend to be low[6,10-12]. The survival of ELBW infants to hospital discharge of 23%-63% in Thailand is relatively low compared to the survival of 60%-70% in developed countries[2,4,5].

A continuing audit of survival and outcome stratified by birth weight or gestational age among VLBW infants should be encouraged in every hospital to reflect the quality of care. However, the authors preferred to use birth weight rather than gestational age because discrepancy between antenatal and postnatal

Table 4. Reports of survivals among VLBW and ELBW infants

References	Cohort year	Number of infants	Overall survival of VLBW infants	Survival of ELBW infants
Panadda Labcharoenwongs	2001	29	76%	63%
Kitichai Uruwankul	2000-2	54	63%	23%
Rossukon Charearnsutsiri	2000-3	202	63%	25%
Somchai Laouthaiwathana	2004-6	111	70%	36%
Present study	2003-6	78	81%	52%
Maureen Hack, USA	1989-90	1,804	78%	60%
Lemons JA, USA	1995-6	4,438	84%	71%
Svenningsen NW, Sweden*	1986-94	325	-	70%
Darlow BA, New Zealand	1998-9	1,084	90%	-
Tsou KI, Taiwan	1996	613	76%	49%
Atasay B, Turkey	1997-2000	133	84%	-
Velaphi SC, South Africa	2000-2	2,164	72%	32%

* Only ELBW infants were studied

assessment of gestational age existed[19]. Gestational age assessment needs to have early antenatal care and routinely antenatal ultrasound, which is not the case in the present setting. The marked difference in survival and outcome of VLBW babies according to birth weight is clearly seen in Fig. 1-2. These measures have an important role to decide a cutoff birth weight below which it may be inadvisable to offer the intensive care since birth when resources, facilities, and budgets are limited[6]. In the present setting, the authors suggest using a birth weight cut off point of 750 grams when deciding whether to get access or receive the limited facilities in the NICU. This issue should be discussed locally to further implement in the unit. Providing facilities, which are limited for all infants, may compromise the care and therefore the outcome not only for the ELBW infants but also for all ill neonates who shared the resources.

Mortality and major morbidity (CLD, severe IVH, severe ROP, and NEC) was high among ELBW infants. The rate of CLD of 25% among survived VLBW infants is rather high compared to the reports of 8-23% from developed countries but is comparable to the report in Thailand by Labcharoenwongs et al[2-4,8]. However, no severe ROP has been documented in the present study. Screening program for ROP with indirect ophthalmoscopy at bedside has been available since 2003 by a pediatric ophthalmologist. However, reliability of these morbidity figures is limited because of the small sample size of the present study. The incidence of severe IVH of 2% among survived VLBW infants in the present study might be under-diagnosed. Routine screening of IVH among ELBW infants by cranial ultrasonography was not available. Only clinically suspected IVH cases had cranial ultrasonography.

No use of antenatal steroids, gestational age of < 28 weeks, ELBW, congenital abnormalities, Apgar score at 5 minute ≤ 5, needed endotracheal intubation in the delivery room and the first temperature at NICU $\leq 35.0^{o}$C were associated with lower survival. These findings are consistent with the study of Laouthaiwathana. Doye et al who reported the substantially higher survival and better prognosis of VLBW infants who had antenatal steroids[20]. Only 24% of ELBW infants in the present study had a full course of antenatal steroids. Some mothers presented late in labor, resulting in inadequate time for antenatal steroids to be used.

In conclusion, the overall survival and outcome among VLBW infants born in Thammasat University Hospital is acceptable. The mortality and morbidity in ELBW remained high. A continuing audit of these measures should be encouraged and the results should go to all health workers working in obstetrics and neonatology. The information will be helpful to improve the care with limited facilities and resources.

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การรอดชีวิตและผลการรักษาของทารกน้ำหนักน้อยมากที่คลอดในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

สุธิดา ศรีทิพย์สุโข, ทิพย์วภา เสือรอด, ภาสกร ศรีทิพย์สุโข

วัตถุประสงค์: เพื่อศึกษาการรอดชีวิต ผลการรักษาและปัจจัยที่เกี่ยวกับการเสียชีวิตในทารกน้ำหนักน้อยมากที่คลอดและรับการรักษาในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ

วัสดุและวิธีการ: เป็นการศึกษาโดยเก็บข้อมูลย้อนหลังจากแฟ้มทารกแรกเกิดที่มีอายุครรภ์ตั้งแต่ 25 สัปดาห์และมีน้ำหนักน้อยกว่า 1,500 กรัม ที่คลอดมีชีวิตในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติทุกรายเป็นเวลา 3 ปีตั้งแต่ 1 กรกฎาคม พ.ศ. 2546 ถึง 30 มิถุนายน พ.ศ. 2549 โดยเก็บข้อมูลเกี่ยวกับการตั้งครรภ์ การคลอด การรอดชีวิตและผลการรักษาก่อนจำหน่ายออกจากโรงพยาบาล

ผลการศึกษา: ทารกที่มีน้ำหนักแรกเกิดตั้งแต่ 600-1,485 กรัมมีจำนวน 78 ราย อัตราการรอดชีวิตของทารกทั้งหมดและทารกที่มีน้ำหนักน้อยกว่า 1,000 กรัมเป็นร้อยละ 81 และร้อยละ 52 ตามลำดับ สาเหตุการตายที่สำคัญคือภาวะปอดขาดสารลดแรงตึงผิว โดยร้อยละ 35 ของทารกที่รอดชีวิตมีภาวะแทรกซ้อนที่สำคัญก่อนจำหน่ายกลับบ้าน ผลการรักษาในกลุ่มทารกที่มีน้ำหนักแรกเกิดน้อยกว่า 750 กรัมไม่เป็นที่น่าพอใจ ปัจจัยเสี่ยงในช่วงปริกำเนิดที่เกี่ยวกับการเสียชีวิตของทารกน้ำหนักน้อยมากได้แก่ การไม่ได้รับ steroids ก่อนคลอด ($p = 0.015$), อายุครรภ์ < 28 สัปดาห์ ($p = 0.012$), ทารกที่มีน้ำหนักแรกเกิดน้อยกว่า 1,000 กรัม ($p < 0.001$), มีความพิการที่พบแต่กำเนิด ($p = 0.002$), ค่าคะแนน Apgar ที่ 5 นาที ≤ 5 ($p = 0.019$), ต้องใส่ท่อช่วยหายใจเพื่อการกู้ชีพในห้องคลอด ($p < 0.001$), และอุณหภูมิร่างกายแรกรับ $\leq 35.0^{\circ}$ซ ($p = 0.023$)

สรุป: อัตราการรอดชีวิตและผลการรักษาทารกน้ำหนักน้อยมากที่คลอดในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติเป็นที่ยอมรับได้ อัตราการเสียชีวิตและภาวะแทรกซ้อนที่สำคัญยังเป็นปัญหาในกลุ่มทารกที่มีน้ำหนักแรกเกิดน้อยกว่า 1,000 กรัม การติดตามดัชนีชี้วัดเหล่านี้ควรกระทำอย่างต่อเนื่อง