

Outcome of Very Low Birth Weight Infants Over 3 Years Report From an Iranian Center

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Abstract

Objective: Very low birth weight (VLBW) infants are at high risk for morbidity and mortality. This article determines the frequency of disease, rate of survival, complications and risk factors for morbidity and mortality in VLBW neonates admitted to a level III neonatal intensive care unit (NICU) at Mahdiah Hospital in Tehran.

Methods: This cross-sectional retrospective study was performed from April 2007 to March 2010 on all hospitalized VLBW neonates. Relevant pre- and peri-natal data up to the time of discharge from the hospital or death, including complications during the course of hospitalization, were collected from the case notes, documented on a pre-designed questionnaire and analyzed.

Findings: Out of 13197 neonates, 564 (4.3%) were VLBW with 51.4% males. Mean gestational age was 29.6±2.5 weeks; mean birth weight 1179±257 grams. Mean birth weight, gestational age and Apgar scores were significantly higher in babies who survived than in those who died, (1275±189 vs. 944±253 grams; 30.5±2.2 vs. 27.5±2 weeks and 6.9±1.7 vs. 5±2.1 respectively, $P<0.001$ in all instances). Overall survival was 70.9%; in extremely low birth weight (ELBW) newborns this figure was 33.3% rising to 84.1% in infants weighing between 1001-1500 grams. Respiratory failure resulting from RDS in ELBW babies was the major factor leading to death. Need for mechanical ventilation, pulmonary hemorrhage and gastro-intestinal bleeding were also significant predictive factors for mortality.

Conclusion: Birth weight and mechanical ventilation are the major factors predicting VLBW survival.

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Key Words: Neonatal Mortality; Low Birth Weight; Very Low Birth Weight; Infant; Risk Factors; NICU

Introduction

Very low birth weight (VLBW) infants comprise between 4-8% of live-births but about one-third of deaths during the neonatal period occur in this group of newborns^[1,2]. Although, recent advances in medical technology and innovations in the quality of care for premature neonates have resulted in increasing life expectancy for these small infants, especially for babies weighing under 1000 grams at birth (ELBW infants) during the

last two decades, frequency of complications associated with premature birth have remained stationary^[3]. Studies have reported normal outcomes in approximately 73% of these preterm neonates, figures vary widely from country to country with reports of up to 90% survival from developed countries to 40% in the developing world^[4].

Normal outcomes with no or minimal complications in a VLBW infant depend largely on the quality of prenatal and perinatal care. The aim

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of this study is to determine the frequency of disease, rate of survival, complications and risk factors for morbidity and mortality in VLBW neonates admitted to a level III neonatal intensive care unit at Mahdiah Hospital in Tehran.

Subjects and Methods

This cross-sectional retrospective study was performed for duration of 3 years from April 2007 to March 2010 in the NICU of Mahdiah Hospital in Tehran, Iran. This center is teaching hospital of Shahid Beheshti University of Medical Sciences in south Tehran with 40 level III NICU cubs, and more than 95% inborn admissions and about 5000 deliveries per year.

All VLBW neonates hospitalized in the NICU of this hospital were enrolled in the study including those with congenital anomalies. We excluded infants with birth weight less than 500 grams, death within 12 hours of life and multiple congenital anomalies incompatible with life.

All relevant pre- and peri-natal data was collected from the case notes, and together with all information from the time of birth, admission to the NICU, hospital course up to the time of discharge from the hospital or death was documented on a pre-designed questionnaire. In our center CPR team are present in delivery room for all VLBW neonates, CPR is performed in accordance with the NRP algorithm^[12], if developed RDS, NCPAP was applied by Neopuffor, the neonate intubated and transferred to the NICU, no surfactant was administered in delivery room. In NICU spontaneously breathing neonates received NCPAP (PEEP 4-6 cmH₂O, FIO₂<0.4). If failure happened (need for PEEP >6cmH₂O or FIO₂ >0.4, respiratory distress, ABG deterioration and SPO₂ <85%) INSURE was done. Mechanical ventilation was started in those with poor respiratory effort at birth and those with NCPAP and INSURE failure (PEEP >6cmH₂O, FIO₂ >0.6 and PIP >14cmH₂O).

All complications during the course of hospitalization were recorded. Retinopathy of prematurity (ROP) was diagnosed by a single ophthalmologist with indirect ophthalmoscopic examination at bedside according to AAP guide

line (at age 4-6 weeks) and classified according to the international criteria for retinopathy^[5]. Chronic lung disease (CLD) was diagnosed if the infant continued to need oxygen by the 28th postnatal day or at 36 weeks after the mother's last menstrual period^[11]. Necrotizing enterocolitis (NEC) was diagnosed on compatible clinical, laboratory and radiological manifestations according to the modified Bell criteria^[6]. Bed-side intracranial sonography was done through the anterior fontanel by a single radiologist on days 3, 7, 14 and 28 to detect intra-ventricular hemorrhage (IVH), the severity of which was classified in accordance with Papile staging^[7]; if necessary, the sonography was repeated every week till discharge from the hospital. After documentation, data from newborns who survived were compared with those who died.

Categorical data were reported as count and percentage and continuous data as mean±standard deviation (SD). To detect mortality risk factors we performed simple and multiple logistic regressions, and odds ratio (OR) with related 95% confidence interval (95%CI) were reported. *P*-values less than 0.05 considered as statistically significant.

Findings

During a period of 3 years 13197 neonates were delivered in the Mahdiah Hospital; 564 (4.3%) were VLBW and 51.4% males. Mean gestational age was 29.6±2.5 weeks; mean birth weight was 1179±257 grams. Average duration of hospitalization was 29.7±23.6 days (Table 1).

Average birth weight of babies who survived was significantly higher than of those who died, (1275±189 vs. 944±253 grams respectively; *P*<0.001); similar pattern was noticed for gestational age (30.5±2.2 vs. 27.5±2 weeks, respectively; *P*<0.001); and also for the mean Apgar scores, (6.9±1.7 vs. 5±2.1; *P*<0.001). In contrast, need for resuscitation was significantly higher in the latter group, *P*<0.001 (Table 2).

On simple regression analysis, co-morbidities and complications associated with a rise in mortality included respiratory distress syndrome, (RDS), pneumothorax, pulmonary hemorrhage,

Table1: Demographic and perinatal characteristics of study population

Characteristic	No. (%)	
Gender	Female	274 (48.6%)
	Male	290 (51.4%)
Birth weight (mean± SD)	1179.26±258.04	
	<=750	42 (7.4%)
	751-1000	105 (18.6%)
	1001-1250	153 (27.1%)
	1251-1500	264 (46.8%)
Gestational age (Weeks; mean± SD)		29.68±2.58
	≤28	196 (34.8%)
	29-32	301 (53.4%)
	33-36	62 (11%)
	≥ 37	5 (0.9%)
Delivery mode	Cesarean	416 (73.8%)
	Vaginal	148 (26.2%)
Primigravida	No	241 (42.7%)
	Yes	323 (57.3%)
Plurality	Singleton	334 (59.2%)
	Twin	123 (21.8%)
	Triple and more	107 (19.0%)
Place of birth	Inborn	471 (83.5%)
	Outborn	93 (16.5%)
Maternal age (Years; mean± SD)	28.27±6.03	
Antenatal steroid	562 (99.6%)	
Maternal disease	332 (58.9%)	
Preeclampsia	125 (22.2%)	
Premature rupture of membranes	49 (8.7%)	
Prolonged labor	33 (5.9%)	
Infertility	133 (23.6%)	
Chorioamnionitis	11 (2%)	
Abruption placenta	59 (10.5%)	
Apgar score at one minute (mean± SD)	6.36±2.07	
Apgar score at five minute (mean± SD)	7.86±1.7	
Apgar score	≥6	388 (68.8%)
	<6	176 (31.2%)
Resuscitation at birth	246 (43.6%)	
Surfactant therapy	366 (64.9%)	
Mechanical ventilation only	38 (6.7%)	
Duration of mechanical ventilation (mean± SD)	0.56±4.02	
Duration of hospital stay (mean± SD)	29.72±23.60	
Age at time of discharge .median (Min-Max)	32d; (1-185d)	
Age at time of death, median (Min-Max)	4d; (1-75d)	
Outcome	Age of regain birth weight; Median (Min-Max)	15d; (1-84d)
	Survive	400 (70.9%)
	Death	164 (29.1%)

CLD, repeated seizures, IVH, renal failure, gastrointestinal bleeding, anemia, homeostatic imbalance and metabolic abnormalities; while treatment modalities revealed as risk factors associated with increase in mortality were surfactant replacement therapy, nasal continuous positive airway pressure, (NCPAP), INSURE,

(INTubation SURfactant Extubation), and mechanical ventilation (Table3).

On multiple regression analysis, lower birth weight, need for mechanical ventilation, pulmonary hemorrhage and gastro-intestinal bleeding remained as factors significantly associated with the risk of mortality. Other

Table 2: Antenatal and perinatal risk factors (variables) in dead and alive neonates

Parameter	Characteristic	Alive (n=400)	Dead (n=164)	OR	95%CI	P. Value
Gender	Female	201 (73.4%)	73 (26.6%)	1		
	Male	199 (68.6%)	91 (31.4%)	1.26	0.87-1.81	0.2
Birth weight (gm)		1275.53(189.15)	944.45(253.37)	0.54		
	<=750	3 (7.1%)	39 (92.9%)	167.63	0.48-0.6	<0.001
	751-1000	46 (43.8%)	59 (56.2%)	16.54	47.38-593.14	<0.001
	1001-1250	106 (69.3%)	47 (30.7%)	5.72	9.03-30.3	<0.001
	1251-1500	245 (92.8%)	19 (7.2%)	1	3.2-10.21	<0.001
Gestational age (w)		30.55(2.25)	27.56(2.03)	0.49		
	≤28	72 (36.7%)	124 (63.3%)	6.89	0.43-0.56	<0.001
	29-32	264 (87.7%)	37 (12.3%)	0.56	0.76-62.83	0.09
	33-36	60 (96.8%)	2 (3.2%)	0.13	0.06-5.15	0.6
	≥ 37	4 (80%)	1 (20%)	1	0.01-1.8	0.1
Gestational age	<28w	27 (24.5%)	83 (75.5%)	14.16	8.62-23.25	<0.001
	≥28w	373 (82.2%)	81 (17.8%)			
Delivery mode	Cesarean	314 (75.5%)	102 (24.5%)	1	1.49-3.3	<0.001
	Vaginal	86 (58.1%)	62 (41.9%)	2.22		
Primigravida	Yes	230 (71.2%)	93 (28.8%)	0.97	0.67-1.4	0.9
	No	170 (70.5%)	71 (29.5%)			
Plurality	Singleton	233 (69.8%)	101 (30.2%)	1	0.6-1.26	0.5
	Multiple	167 (72.6%)	63 (27.4%)	0.87		
	Maternal age	28.26(5.61)	28.3(6.98)	1	0.97-1.03	0.9
Maternal age	<20yrs	15 (60%)	10 (40%)	1.67	0.73-3.79	0.2
	≥20yrs	385 (71.4%)	154 (28.6%)			
Maternal disease	Yes	242 (72.9%)	90 (27.1%)	0.79	0.55-1.15	0.2
	No	158 (68.1%)	74 (31.9%)			
Preeclampsia	Yes	100 (80%)	25 (20%)	0.54	0.33-0.87	0.01
	No	300 (68.3%)	139 (31.7%)			
PROM	Yes	40 (81.6%)	9 (18.4%)	0.52	0.25-1.1	0.09
	No	360 (69.9%)	155 (30.1%)			
Prolonged labor	Yes	28 (84.8%)	5 (15.2%)	0.42	0.16-1.1	0.08
	No	372 (70.1%)	159 (29.9%)			
Infertility	Yes	92 (69.2%)	41 (30.8%)	1.12	0.73-1.7	0.6
	No	308 (71.5%)	123 (28.5%)			
Chorioamnionitis	Yes	3 (27.3%)	8 (72.7%)	6.79	1.78-25.91	0.005
	No	397 (71.8%)	156 (28.2%)			
Abruption placenta	Yes	37 (62.7%)	22 (37.3%)	1.52	0.87-2.67	0.1
	No	363 (71.9%)	142 (28.1%)			
Meconium stain amniotic fluid	Yes	11 (68.8%)	5 (31.3%)	1.11	0.38-3.25	0.8
	No	389 (71%)	159 (29%)			
Apgar score at five minute		6.91(1.78)	5.02(2.13)	0.53	0.46-0.6	<0.001
Apgar score (5')	≥6	317 (81.7%)	71 (18.3%)	1		
	<6	83 (47.2%)	93 (52.8%)	5	3.38-7.41	<0.001
Resuscitation at birth	Yes	126 (51.2%)	120 (48.8%)	5.93	3.96-8.89	<0.001
	No	274 (86.2%)	44 (13.8%)			
Intubation at delivery room	Yes	18 (26.1%)	51 (73.9%)	9.58	5.38-17.05	<0.001
	No	382 (77.2%)	113 (22.8%)			

CI: Confidence Interval

variables associated with the risk of neonatal death were, maternal pre-eclampsia or hemorrhage, vaginal delivery, Apgar <6 at 5 minutes, need for intubation at birth, NCPAP, surfactant replacement therapy, CLD, intractable seizures and hematological abnormalities, (Table 4).

Overall survival was 70.9%; in ELBW newborns this figure was 33.3% rising to 84.1% in infants weighing between 1001-1500 grams. Respiratory failure resulting from RDS in babies with extremely low birth weight was the major factor leading to death (Tables 5 and 6).

Table 3: Mortality rates according to the disease/treatment characteristics in neonatal period

	Characteristic	Alive (n=400)	Dead (n=164)	OR	95%CI	p-Value
Respiratory distress syndrome	Yes	252 (62.2%)	153 (37.8%)	8.17	4.29-15.56	<0.001
	No	148 (93.1%)	11 (6.9%)			
Surfactant therapy	Yes	229 (62.6%)	137 (37.4%)	3.79	2.4-5.99	<0.001
	No	171 (86.4%)	27 (13.6%)			
Intubation-Surfactant-Extubation	Yes	123 (85.4%)	21 (14.6%)	0.33	0.2-0.55	<0.001
	No	277 (66%)	143 (34%)			
Nasal continuous positive airway pressure	Yes	166 (76.5%)	51 (23.5%)	0.64	0.43-0.94	0.02
	No	234 (67.4%)	113 (32.6%)			
Mechanical ventilation	Yes	19 (50%)	19 (50%)	2.63	1.35-5.1	0.004
	No	381 (72.4%)	145 (27.6%)			
Mechanical Ventilation + Surfactant	Yes	134 (50.2%)	133 (49.8%)	8.52	5.47-13.26	<0.001
	No	266 (89.6%)	31 (10.4%)			
Patent Ductus Arteriosus	Yes	131 (71.6%)	52 (28.4%)	0.95	0.65-1.41	0.81
	No	269 (70.6%)	112 (29.4%)			
Necrotizing enterocolitis ≥ 2	Yes	3 (50%)	3 (50%)	2.47	0.49-12.35	0.27
	No	397 (71.1%)	161 (28.9%)			
Intra-ventricular hemorrhage (All Grade)	Yes	139 (73.5%)	50 (26.5%)	2.78	1.24-6.24	0.01
	No	261 (69.6%)	114 (30.4%)			
Periventricular leukomalacia	Yes	4 (57.1%)	3 (42.9%)	1.84	0.41-8.33	0.43
	No	396 (71.1%)	161 (28.9%)			
Pneumothorax	Yes	20 (35.1%)	37 (64.9%)	5.54	3.1-9.89	<0.001
	No	380 (75%)	127 (25%)			
Pulmonary hemorrhage	Yes	16 (17.4%)	76 (82.6%)	20.73	11.53-37.27	<0.001
	No	384 (81.4%)	88 (18.6%)			
Chronic Lung Disease	Yes	84 (81.6%)	19 (18.4%)	0.49	0.29-0.84	0.01
	No	316 (68.5%)	145 (31.5%)			
Renal failure	Yes	42 (47.7%)	46 (52.3%)	3.32	2.08-5.3	<0.001
	No	358 (75.2%)	118 (24.8%)			
Seizure	Yes	36 (37.9%)	59 (62.1%)	5.68	3.56-9.07	<0.001
	No	364 (77.6%)	105 (22.4%)			
Gastrointestinal bleeding	Yes	11 (29.7%)	26 (70.3%)	6.66	3.21-13.84	<0.001
	No	389 (73.8%)	138 (26.2%)			
Apnea	Yes	155 (73.5%)	56 (26.5%)	0.82	0.56-1.2	0.31
	No	245 (69.4%)	108 (30.6%)			
Infection (Pneumonia +/- Meningitis +/- Sepsis)	Yes	106 (71.1%)	43 (28.9%)	0.99	0.65-1.49	0.95
	No	294 (70.8%)	121 (29.2%)			
Anemia	Yes	211 (82.7%)	44 (17.3%)	0.33	0.22-0.49	<0.001
	No	189 (61.2%)	120 (38.8%)			
Hematologic complication	Yes	232 (75.8%)	74 (24.2%)	0.6	0.41-0.86	0.006
	No	168 (65.1%)	90 (34.9%)			
Metabolic complication	Yes	258 (66.3%)	131 (33.7%)	2.18	1.42-3.37	<0.001
	No	142 (81.1%)	33 (18.9%)			
Surgical operation	Yes	9 (69.2%)	4 (30.8%)	1.09	0.33-3.58	0.89
	No	391 (71%)	160 (29%)			

CI: Confidence Interval

Discussion

Prevalence of VLBW neonates (4.3%) and ELBW infants (1.1%) in our study is comparable to reports from other countries; world-wide prevalence of VLBW babies has been reported between 5-7% and that of ELBW as 1%; however, studies from the United States set the figures at 1.1% and 0.7% respectively^[1,8]. This study was done in a level III NICU in a hospital that is a referral center for high risk pregnancies,

therefore, our figures are not representative of nation-wide prevalence of very low birth weight infants, that is about 0.98% in our country with birth rate of 1.3% and NMR around 17/1000 live births according to UNICEF report at 2009.

Maternal co-morbidities are linked with neonatal morbidity and mortality^[9,10]; in the present study 58.9% of mothers were considered at high risk because of pregnancy-associated complications including pre-eclampsia (22.2%) abruptio placentae (10.5%), infertility (23.6%),

Table 4: Multiple regression analysis with adjusted estimates of odds ratio (95% CI)

Characteristic	OR	95%CI	P. Value	
Birth weight (gm)	<=750	11.09	3.83-32.08	<0.001
	751-1000	63.53	17.07-236.45	<0.001
	1001-1250	11.09	3.83-32.08	<0.001
	1251-1500	1		
Vaginal delivery mode	2.55	1.05-6.18	0.04	
Preeclampsia	0.34	0.12-0.95	0.04	
Maternal Bleeding(placenta abruption)	5.18	1.41-19.07	0.01	
Apgar score <6 in 5 minute	3.51	1.41-8.73	0.007	
Intubation at delivery room	3.52	1.04-11.94	0.04	
nCPAP	0.27	0.11-0.63	0.003	
Mechanical ventilation +Surfactant	47.08	14.35-154.42	<0.001	
Mechanical ventilation only	35.75	6.56-194.77	<0.001	
Pulmonary hemorrhage	45.57	14.38-144.41	<0.001	
Chronic Lung Disease	0.05	0.02-0.16	<0.001	
Gastrointestinal bleeding	11.66	3.03-44.88	<0.001	
Seizure	3.82	1.42-10.24	0.008	
Hematologic complication	0.12	0.05-0.31	<0.001	

CI: Confidence Interval; nCPAP: Nasal continuous positive airway pressure

PROM (8.7%), prolonged labor (5.9%) and chorioamnionitis (2%) (Table1).

Optimal mode of delivery for VLBW neonates is controversial but most authorities regard cesarean section as the method of choice for these infants^[11]; however, 26.2% of our patients had been delivered normally with increased mortality rate (41.9% vs 24.5%) and NVD was an independent risk factor for neonatal mortality (Table 4).

Team of personnel well-trained in recognition of need to resuscitate and prompt appropriate measures to establish adequate respiration is crucial for survival of VLBW infants with minimal long and short term complications. One and five minute Apgar scores are generally used to assess the respiratory status of the newborn and to define the outcome for cardio-pulmonary

resuscitation^[12]. An Apgar score of <6 at 5 minutes, which is a risk factor for neonatal mortality, was observed in approximately one-third (31.2%) of the VLBW infants in our study; in a 10-year research performed in USA by Daksha et al, 46.9% of VLBW newborns had an Apgar score of <6 at 5 minutes^[14]. This difference may be due to lower gestational age and birth weight infants in Daksha study or our successful resuscitation in delivery room.

During the last few years Delivery Room Cardio-Pulmonary Resuscitation, (DR-CPR) has named for advanced resuscitation (intubation, chest compression and adrenaline administration) of VLBW infants. 82.1% of Finer's 27707 newborns in 196 neonatal units needed chest compression and 66.7% adrenaline administration, 63.3% survived^[14]. In our study out of 69 infants that had

Table5: Overall survival and survival with selected complication among VLBW according to birth weight

Characteristic	Birth weight groups				
	501-750	751 -1000	1001 -1250	1251-1500	Total (n=400)
Outcome					
Overall survival	3.42 (7.1%)	46.105 (43.8%)	106.153 (69.3%)	245.264 (92.8%)	400.564 (70.9%)
Survival without complication	2 (66.7%)	21 (45.7%)	71 (67%)	204 (83.3%)	298 (74.5%)
Survival with complication					
CLD	1 (33.3%)	23 (50%)	32 (30.2%)	28 (11.4%)	84 (21.0%)
Intra-ventricular hemorrhage ≥ 3	0 (0%)	2 (4.3%)	4 (3.8%)	6 (2.4%)	12 (3.0%)
NEC ≥ 2	0 (0%)	1 (2.2%)	1 (0.9%)	1 (0.4%)	3 (0.8%)
Sever ROP (treated by laser)	1 (33.3%)	10 (21.7%)	14 (13.2%)	8 (3.3%)	33 (8.3%)

Table 6: Distribution of died babies in relation of birth weight and primary cause of death

Characteristic	Birth weight groups				Total(n=164)
	501-750	751 -1000	1001 -1250	1251-1500	
Cause of death					
Respiratory failure	30 (76.9%)	47 (79.7%)	32 (68.1%)	13 (68.4%)	122 (74.4%)
Sepsis	2 (5.1%)	0 (0%)	1 (2.1%)	1 (5.3%)	4 (2.4%)
Congenital anomalies	0 (0%)	0 (0%)	1 (2.1%)	1 (5.3%)	2 (1.2%)
Others	7 (17.9%)	12 (20.3%)	13 (27.7%)	4 (21.1%)	36 (22.0%)

needed endotracheal intubation 51 (73.9%) died later during hospital course showing that improvement of quality of post-resuscitation care is needed in our NICU.

RDS has been reported to occur in up to 90% of VLBW infants^[15], this was 71.8% in our study which is acceptable due to the higher gestational age of our infants. Optimal management requires teamwork between obstetricians and neonatologists and includes meticulous prenatal care, timely administration of steroids, planned delivery in a center equipped with a level III NICU, presence of trained resuscitation team in the delivery unit, initiation of NCPAP at birth, prompt administration of surfactant (INSURE) and mechanical ventilation if needed^[16]. We followed this recommended guidelines in 405 of our patients who developed RDS, with NCPAP (in 53.6%) and INSURE (in 35.5%); however, we had to start mechanical ventilation in 267 (65.9%) of these newborns. Despite these measures 153 (37.8%) died, this underlines the severity of RDS in our patients, although NCPAP and INSURE failure was compatible with some other studies^[17-20], NCPAP and mechanical ventilation (with or without surfactant) were independent risk factors for neonatal mortality (Table 4).

Short term complications seen in our surviving patients included CLD in 21%, ROP in 8.3%, IVH in 3% and NEC in 0.8%. Prevalence of CLD was comparable to the figures quoted in other studies from the industrialized countries, but the other complications were lower than reported in other studies^[1,3,4,15,21,22], which may be due to more mature neonates in our study and respecting the standard care for prevention of ROP, IVH and NEC.

In multiple regression analysis, pulmonary hemorrhage, gastrointestinal bleeding, seizures, hematologic complications were also independent risk factors for neonatal mortality (Table 4), which are similar in one or more complications compared with other studies, however, In most

studies very low birth weight and need for mechanical ventilation have been quoted as risk factors for mortality^[15,25], the same as in our study.

Rate of overall survival for VLBW newborns has been widely different in studies from different parts of the world; 63% from India ^[23], 35.6% from a study in Iran^[24], 70% and 71% in 2006 and 2003 from South Africa^[25], 74.5% from Turkey ^[26], 81% from Thailand^[21], 87.5 and 85% from the USA^[27,28], 84% from Spain^[29], and 90% from New Zealand and the Netherlands^[30,31]. Survival of ELBW infants in our study was 33.3% while it has been reported as 34.9% from South Africa^[25], 36.6% in an Iranian study^[32], 44% from Italy^[33], and 51.8% from the United States^[28]. These differences mainly related to gestational age, birth weight and associated diseases of the newborns and standard care of NICU in different studies.

Neonates weighing ≤ 750 grams at birth had the highest mortality rate; only 3 out of 42 (7.1%) infants in this group survived; this figure is comparable to studies from other developing countries^[1,2]. due to limited facilities and NICU bed. Similar to other studies^[25,30,34] main cause of mortality in our patients was RDS leading to respiratory failure; sepsis and major congenital anomalies were also common causes of death, which need improving quality of care in our NICU with available facilities.

Limitations of our study were: 1) retrospective study, 2) limited to short term outcome during hospital course, 3) lack of neonatal network in our NICU.

Conclusion

Our findings reveal that birth weight and mechanical ventilation are the 2 major factors responsible for mortality. Although survival of

VLBW infants in our study is comparable to other studies around the world, a decline in the mortality and morbidity of these newborns (especially the ELBW neonates) can only be made possible through optimizing perinatal care including regionalization, CPR at birth, early NCPAP and quality improved collaborative (QIC) in our NICU.

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Conflict of Interest: None

References

1. Fanaroff AA, Stoll BJ, Wright LL, et al. Trend in neonatal morbidity and mortality for very low birth weight infants. *Am J Obstet Gynecol* 2007;196(2): 147-8.
2. United Nations: Reduce Child Mortality. The Millennium. Development Goals Report New York. New York: UN, 2008. Available at: <http://www.un.org/millenniumgoals/2008highlevel/pdf/newsroom/Goal%204%20FINAL.pdf>. Access date: Sep 2008.
3. Eichenwald EC, Stark AR. Management and outcomes of very low Birth weight. *N Engl J Med* 2008;358(16):1700-11
4. Ruegger C, Hegglin M, Adams M, et al. Population based trends in mortality ,morbidity and treatment for very preterm and very low birthweight infants over 12 years. *BMC Pediatr* 2012;12:17.
5. Section on Ophthalmology American Academy of Pediatrics; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus American Academy of Pediatrics, Section on Ophthalmology; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus. Screening examination of premature infants for retinopathy of prematurity. *Pediatrics* 2006;117(2):572-6.
6. Bell MJ, Ternberg JL, Feigin RD, et al. Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging. *Ann Surg* 1978;187(1): 1-7.
7. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weight less than 1,500 gm. *J Pediatr* 1978;92(4):529-34.
8. Behram RE, Stith Butler A. Preterm birth: Causes, consequence, and prevention. Washington, DC: National Academies Press. 2007; Pp:31-52.
9. Liu CM, Jen CP, Dyh C. Maternal complications and perinatal outcomes associated with gestational hypertension and severe preeclampsia in Taiwanese women. *Formosan Medical Association* 2008;107(2):129-38
10. Sheiner E, Shoham-Vardi I, Hadar A, et al. Incidence, obstetric risk factors and pregnancy outcome of preterm placental abruption; a retrospective analysis. *J Matern Fet Neonat Med* 2002;11(1):34-9.
11. Lee HC, Gould JB. Survival advantage associated with cesarean Delivery in very low birth weight Vertex Neonates. *Obstetric Gynecol* 2006;107(1):97-10.
12. American Academy of Pediatrics and American Heart Association. Kattwinkel J (Ed). Textbook of Neonatal Resuscitation, the 2010 American Academy of Pediatrics and American Heart Association Guidelines for Neonatal. 6thed. American Academy of Pediatrics. 2011.
13. Patel D, Piotrowski ZH. Positive Changes among very low birth weight infant apgar score that are associated with the neonatal resuscitation program in Illinois. *J Perinatol* 2002;22(5):386-90.
14. Finer NN, Horbar JD, Carpenter JH. Cardiopulmonary resuscitation in the very low birth weight infant: the Vermont Oxford Network Experience. *Pediatrics* 1999;104(3 Pt 1):428-34.
15. Stool BJ, Hansen NI, Bell EF, et al. Neonatal outcomes of extremely preterm infants from NICHD neonatal research network. *Pediatrics* 2010;126(3): 443-56.
16. Sweet DG, Carnielli V, Greisen G, et al. European consensus guidelines on the management of neonatal respiratory Syndrome in preterm infants. 2010 update. *Neonatology* 2010;97(4):402-17.
17. Morley CI, Davis PG, Doyle LW, et al. Nasal CPAP or intubation at birth for very preterm infants. *N Engl J Med* 2008;358(7):700-8.
18. Kugelman A, Ferferkorn I, Riskin A, et al. Nasal intermittent mandatory ventilation versus nasal continuous positive airway pressure for respiratory distress syndrome: A randomized controlled, prospective study. *J Pediatric* 2007;150(5):521-6.
19. Ramanathan R, Sekar KC, Rasmussen M, et al. Nasal intermittent positive pressure ventilation after surfactant treatment for respiratory distress syndrome in preterm infant <30 weeks' gestation: A randomized, controlled trial. *J Perinatol* 2012;32(5): 336-43.

20. Afjeh SA, Sabzehei MK. The INSURE method in VLBW preterm infant with RDS. *Pejouhandeh* 2010;15(5):199-203. [In Persian]
21. Sritipsukho S, Suarod T, Sritipsukho P. Survival and outcome of very low birth weight infants born in a university hospital with level II NICU. *J Med Assoc Thai* 2007;90(7):1323-9
22. Chedid F, Shanteer S, Haddad H, et al. Short-term outcome of very low birth weight infants in a developing country: comparison with the Vermont Oxford Network. *J Trop Pediatr* 2008;55(1):15-9.
23. Basu S, Rathore P, Bhatia BD. Predictors of mortality in very low birth weight neonates in India. *Singapore Med J* 2008;49(7):556-60.
24. Navaei F, Aliabady B, Moghtaderi J, et al. Early outcome of preterm infants with birth weight of 1500g or less and gestational age of 30 weeks or less in Isfahan city, Iran. *World J Pediatr* 2010; 6(3):228-32.
25. Ballot ED, Chirwa TF, Cooper PA. Determinants of survival in very low birth weight neonates in public sector hospital in Johannesburg. *BMC Pediatr* 2010;10:30.
26. Canbak Y, Silfeler I, Dorum BA, et al. The Ratio of Mortality and Morbidity in very low birth weight infants in a public hospital *Turk Arch Pediatr* 2011;46:137-43.
27. Grupo Collaborative Neocosur. Very low birth weight infant outcome in 11 South American NICUS. *J Perinatol* 2002;22(1):2-7
28. Jeffrey D, Horba MD, Joseph H, et al. Mortality and neonatal morbidity Among infants 501 to 1500 Grams from 2000 to 2009 *Pediatrics* 2012;129(6); 1019-21.
29. Moro M, Figueras-Aloy J, Fernandez C, et al. Mortality for newborns of birth weight less than 1500 g in Spanish neonatal units (2002-2005). *Am J Perinatol* 2007;24(10):593-601
30. Darlow BA, Cut AE, Danoghue DA. Improved outcome for very low birth weight infant: evidence from New Zealand national population based data. *Arch Dis Child Fetal Neonatal Ed* 2003;88(1):23-8.
31. Anthony S, Ouden L, Brand R, et al. Changes in perinatal care and survival in very preterm and extremely preterm infants in The Netherlands between 1983 and 1995. *Eur J Obstet Gynecol Reprod Biol* 2004;112(2):170-7.
32. Nayeri F, Amini E, Shariat M, et al. Life expectancies and outcome in extremely low birth weight neonates. *Tehran Uni Med J* 2008;66(4):288-93. [In Persian]
33. Vonderweid U, Carta A, Chiandotto V, et al. Italian multicenter study on very low birth weight babies. *Ann IST Super Sanita* 1991;27(4):633-50.
34. Battin MR, Knight DB, Kuschel CA, Howie RN. Improvement in mortality of very low birthweight infants and the changing pattern of neonatal mortality: The 50-year experience of one perinatal centre. *J Paediatr Child Health* 2012;48(7):596-9.