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Mortality and Short-Term Outcomes of Very Low Birth Weight Infants at a Tertiary Care Center in Jordan: Comparison with Other Countries

Manar Al-lawama*, Tariq Abdelghani and Eman Badran

Department of Pediatrics, School of Medicine, University of Jordan, Jordan

***Corresponding author:** Manar Al-lawama, Department of Pediatrics, School of Medicine, University of Jordan, Amman, Jordan, Tel: 962799068565; E-mail: manar-76@hotmail.com

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Abstract

Purpose: Very low birth weight infants (VLBWI) are the most fragile group of neonates with high rate of mortality and morbidity. Neonatal mortality rate in Jordan is still high. This is the first study from Jordan that aims to assess VLBWI mortality rate and the factors contributed to it and to report on the short outcomes and morbidities of those newborns in comparison to other countries to identify potential areas of improvement.

Methods: A prospective study of all newborns with birth weight 500-1500 g, admitted to our level three neonatal intensive care unit (NICU) at Jordan university hospital over 14 months period. The results were compared to reports from other countries.

Results: The study included 71 neonates admitted to our neonatal intensive care weighing from 500-1500 g during the study period. Most of them (88.7%) were inborn infants. Gestational ages mean ± SD was 28.6 ± 2.3 week. Birth weights mean ± SD was 1086.7 ± 262 g. Mortality rate was 35.2%. Short outcomes of survivors are for CLD 4.2%, sever ROP 3.8%, proven NEC 2.8%, PVL 1.9% and sever IVH rate was 10.6%.

Conclusions: Mortality rate in our cohort is high. Multiple factors are involved. The care of very low birth infants in Jordan needs a lot of efforts to decrease mortality and improve morbidities. This is a prospective single center study. A multicenter study is needed that involves all health sectors in Jordan.

Keywords: Infant; Very low birth weight; Mortality; Short term outcome; Neonatal mortality

Introduction

Very low birth weight infants (VLBWI) are the most fragile group of neonates, with a high rate of mortality and morbidity. Studies investigating the health outcomes of those neonates from the Arab countries are scarce [1-3], with none being from Jordan. VLBWI represent 1.4% of total live births in Jordan [4]. Despite all of the efforts to improve neonatal care by national and international organizations, the neonatal mortality rate in Jordan is still high (14.8/1000 live births) [4] and 50% of those mortalities are in VLBWI [4].

In this study, we compare our findings to reports from two Arab countries; United Arab Emirates (UAE) [2] and Kingdome of Saudi Arabia (KSA) [3]. And we also compare it to the data published by the national institution of child health and development (NICHD) in the United States [5].

National data on VLBWI are not available. This is the first study from Jordan addressing the care of VLBWI. Our objective is to assess the mortality rate of VLBWI and the factors that contributed to it and to report on the short term outcomes and morbidities of those newborns to identify areas of improvement. This study should be the beginning of the development of a new culture in Jordan in which people believe in the less fortunate newborns and understand the importance of improving their care.

Materials and Methods

We conducted a prospective study of all newborns with a birth weight 500-1500 g, who were admitted to our level-three neonatal intensive care unit (NICU) at Jordan University Hospital over a 14-month period from March 2015 to June 2016. No infants were excluded from the study. We have approximately 6000 deliveries per year. Our hospital has a fetal medicine unit and is a referral center of high-risk pregnancies. Infants were enrolled from birth and followed prospectively until death or discharge home.

Definitions

Gestational age was determined by last menstrual period and antenatal ultrasound and new Ballard scoring [6] was used to confirm gestational age in case no antenatal care was provided.

Prolonged rupture of membranes (PROM) was defined as rupture of membranes more than 18 hours before delivery. Chronic lung disease (CLD) was defined as requirements for supplemental oxygen or dependency on CPAP at 36 weeks post-menstrual age. Intraventricular hemorrhage (IVH) was determined by cranial ultrasound performed on day 7 after birth or whenever the newborn is symptomatic, with grades from 1-4 defined according to Levene's classification [7]. Periventricular leukomalacia (PVL) was defined as acquired periventricular cystic lesions diagnosed by cranial ultrasound done postnatally at 1 month of age or before discharge. Retinopathy of prematurity (ROP) was diagnosed by screening all infants born at 1500

g or below, or those under 32 weeks gestational age. Screening done at 4 weeks of age or at 32 weeks postmenstrual age, whichever is later, was diagnosed by ophthalmologists and reported according to international classification [8]. Necrotizing enterocolitis (NEC) was classified and recorded according to Bell's classification [9], with proven NEC being at least Bell's classification stage 2 with pneumatosis intestinalis.

Small for gestational age (SGA) was defined as birth weight below the tenth percentile. Extra uterine growth restriction (EUGR) was defined as weight less than the tenth percentile at discharge according to INTERGROWTH charts [10].

Feeding protocol

Total parenteral nutrition starts at birth with 10% pediatric amino acid solution, because neonatal solution is unavailable, at a dose of 2.4 g/kg/day, reaching maximum dose of 4.5 g/kg/day. Feeding starts as soon as the newborn is hemodynamically stable. We fortify breast milk once full feeds are reached by premature discharge formula Similac NeoSure 22 kcal/oz. Breast milk fortifiers are not available and premature formulas are not available in Jordan. A premature discharge formula was used as a substitute for breast milk. The feeding increment was 20 cc/kg/day.

Mortality included all deaths that occurred before discharge. Early neonatal mortality is defined as death within the first 7 days of life. Late neonatal mortality is defined as death after day 7 of life and before 28 days of life.

The results of this study were compared to available studies from other Arab countries and with data from NICHD study.

The data in this study is part of the patent ductus arteriosus study data. It was approved and funded by the deanship of scientific research at the University of Jordan and it was approved by the IRB committee at the University of Jordan Hospital.

Statistical analysis

Numerical data were represented by the mean ± standard deviation (SD). Categorical data were represented by their respective rates or proportions. Rates of CLD, PVL and ROP were measured as a proportion of surviving infants at the screening age. The P-value was considered significant at <0.05.

Results

The study included 71 consecutive neonates admitted to our neonatal intensive care weighing between 500 and 1500 g between March 2015 and June 2016, comprising 1.2% of total live births and 6.1% of total admissions. Most of them (88.7%) were inborn infants. The gestational ages mean ± SD was 28.6 ± 2.3 week. The birth weight mean ± SD was 1086.7 ± 262 g. The antenatal steroids rate was 29.6%. Basic characteristics are presented in Table 1. The mortality rate was 35.2%, which is 47% of the overall mortality in the unit. The early neonatal mortality was 17% and the late neonatal mortality was 12.7%. Mean birth weight ± SD were 1195 ± 253 g and 876 ± 265 g for survivors and non survivors respectively, with a P-value <0.0001. Mean gestational age ± SD was 29.7 ± 2.1 week and 26.5 ± 1.9 week for survivors and non-survivors respectively, with a P value <0.0001 (Tables 2 and 3). The short outcomes of survivors for CLD, severe ROP, proven NEC and PVL are 4.2%, 3.8%, 2.8% and 1.9%, respectively. The severe IVH rate was 10.6%. The overall outcome of all VLBWI is shown in Table 4.

Patients characteristics	Jordan (71)	UAE (173)	KSA (468)	NICHD (9575)
Birth weight Mean ± SD g	1086.7 ± 262	1113 ± SD 264	992 ± SD 287	836 ± 241
Gestational age Mean ± SD week	28.6 ± 2.3	29.1 (2.8)	27.5 (NA)	NA
Male gender	56.3	55	NA*	53
Out born	11	NA	NA	NA
Multiple births	31.8	33.9	29.6	25
Antenatal steroids	29.6	85.3	77.5	80
Post-natal steroids	2.8	NA	27.9	10
Prolonged rupture of membranes > 18 hours	8	25.7	3.5**	25**
Cesarean section	71.8	55.5	47.8	59
ELBWI	43.7	36.4	NA	NA
SGA	22.5	NA	12.5	8
Apgar score				
First minute	6	NA	5	NA
Fifth minute	8	NA	7	NA
Post conceptional age at discharge(weeks)	36	NA	NA	NA

Average length of stay of survivors (days)	48	56.1	71	NA
Average length of stay of died(days)	11.6	21.4	NA	NA

Percentages are presented when available, unless otherwise specified.

*NA: Not available/Not applicable.

**Definition is different >24 hours.

ELBWI: Extremely low birth weight infants <1000 g.

SGA: Small for gestational age.

Table 1: Basic patient characteristics with comparison to UAE, KSA and NICHD studies.

Characteristics	**No (%)**
Overall mortality rate	25 (35.2)
Early Mortality	12 (17.0)
Late Mortality	9 (12.7)
Mortality rate by gestational age	
<26	7 (77.8)
26-27	8 (50)
28-29	7 (36.8)
30-31	2 (18.2)
≥ 32	0 (0)
Mortality rate by birth weight	
500-1000	18 (58.1)
1001-1500	7 (17.5)

Table 2: Analysis of mortality among very low birth infants according to birth weight and gestational age.

Characteristics	**Survivors**	**Non-survivors**	**P-value**
Birth weight	1195 ± 253	876 ± 265	<0.0001
Gestational age	29.7 ± 2.1	26.5 ± 1.9	<0.0001
C/S delivery	33	18	0.981
Male gender	23	17	0.144
Multiple births	14	8	0.981

Table 3: Comparison between survivors and non survivors in very low birth weight infants.

Neonatal outcome	**Jordan (N=71)**	**UAE (N=173)**	**KSA (N=468)**	**NICHD (N=9575)**
Mortality	35.2	26.6	11.2	28
Respiratory distress management and complications				
No CPAP*, no ventilator	2.8	19.7	NA**	9
CPAP, no ventilator	31.1	30.1	NA	29
Mechanical Ventilator	66.2	50.2	NA	62

surfactant administration	67.6	41.4	80	76
Pneumothorax	1.4	NA	5	7
Pulmonary Hemorrhage	8.5	NA	NA	7
Chronic lung disease (CLD)				
36 definition	4.2	12.1	27.4	42
CLD or Death	38	26.6	NA	70
Patent ductus arteriosus (PDA)				
Screened for PDA	90.1	NA	NA	NA
Any PDA	43.7	NA	31	46
PDA treated medically	77.4	NA	48.3	71
Surgical PDA	0	NA	12.4	27
Gastroenterology and nutrition				
Proven NEC	2.8	5.8	15.6	11
Average age of Initiation of feeds	3.7 ***	NA	1	NA
Full feeds age	11.6 ***	NA	39.4	NA
Any breast milk before discharge	58.7	NA	NA	NA
Exclusive breast milk on discharge	15.2	NA	NA	NA
EUGR	56.5	NA	NA	79
Intraventricular hemorrhage (IVH)				
Screened with sonogram	93.1	92.5	90	97
IVH any grade	36.4	17.5	13.9	36
Sever grade 3 or 4	10.6	5	7.8	16
IVH grade 1	16.7	8.1	2.7	10
IVH grade 2	9.1	4.4	3.4	6
IVH grade 3	7.6	1.9	4.4	7
IVH grade4	3	3.1	3.4	9
Periventricular leukomalacia (PVL)				
Screened for PVL with sonogram	76	83.3	NA	NA
PVL rate in screened pts	1.9	2.8	1.3	3
Retinopathy of prematurity (ROP)				
Screened for ROP	96.2	71.1	NA	94
ROP any stage	7.8	11.3	34.5	59
Sever ROP §	3.8	1.6	NA	16
Hematological				
Red blood cells transfusion	47.9	NA	NA	NA
Phototherapy for hyperbilirubinemia	62.7	NA	NA	NA

Infectious disease				
Culture proven sepsis	10	NA	48	38 $$
Rates of IVH, PVL and ROP were calculated from survivors to screening age.				
*CPAP: Continuous positive airway pressure.				
** NA: Not available. NEC: Necrotizing enterocolitis.				
***Days				
EUGR: Extra uterine growth restriction.				
§ Our definition of sever ROP is if laser therapy was needed, UAE study defined sever ROP as stage 3, 4 or 5, NICHD stage 3 or 4.				
$$ definition was not provided in the article.				

Table 4: Mortality and short term morbidity rates, comparison of the percentage of outcomes with the reported rates in the UAE, KSA and NICHD studies.

Discussion

Our findings showed higher mortality rate than reports from the UAE, KSA and NICHD (Table 2). Deaths were significantly more in the smaller and less mature infants. The most contributing factor is the low administration rate of antenatal steroids, which is significantly lower in our cohort, 29.6% versus 77.5% , 85.3% and 80% in the KSA, UAE and NICHD reports, respectively (Table 1). Antenatal steroid therapy caused a huge improvement in neonatal mortality and morbidity, yet other factors that were not studied in our paper, such as the admission temperature and high patient-to-nurse ratio, might have a role [11]. The higher rate of early mortality is similar to reports from many developing countries [12].

Although VLBWI comprise only 1.2% of live births and only 6.1% of total NICU admissions, their mortality rate comprise half of the deaths in all neonates. This is a consistent finding in both the national mortality study [4] and our study. Improvement in the care of VLBWI should significantly impact the overall neonatal mortality rate in Jordan.

Regarding other short-term outcomes, except for IVH, our cohort shows much better short-term outcomes than the other reported studies. Although this might be partially explained by our higher early mortality rates of smaller infants who are the highest-risk group for those morbidities, this cannot explain all of the differences. Genetic factors are of major importance when discussing neonatal morbidities [13] and they might explain some of the differences.

The IVH rate is higher than the other Arab countries. The low rate of antenatal steroids, higher rate of mechanical ventilation, absence of delayed cord clamping policy and high patient-to-nurse ratio, all might have contributed to this higher rate. Considering the higher survival rate in NICHD report, the similarities of the reported IVH rate might only be due to survival of more vulnerable VLBWI to screening age.

Our respiratory outcomes are lagging behind those of our neighbors; we have higher rate of mechanical ventilation and surfactant administration. The UAE population is bigger and more mature and they have a higher rate of antenatal steroids. The KSA cohort had a higher rate of antenatal steroids, but they report a higher rate of surfactant administration, which might not reflect current practice, because it used a 9-year period of study. NICHD report similar high rate of mechanical ventilation and surfactant administration although their antenatal steroid rate is high. This might reflect more premature population than ours.

The pneumothorax rate is low, which is most likely due to the gentle ventilation strategies applied in the unit. However, there is a significant number of pulmonary hemorrhages, which might be explained by a high rate of mechanical ventilation and surfactant administration. Pulmonary hemorrhage caused 20% of all mortalities.

The study took place at the same time as a study investigating patent ductus arteriosus, which explains the high rate of screened newborns. During the study period, we had strict criteria for treatment; we applied intravenous fluid and feeding protocols. These factors in addition to early loss of the most premature infants might explain the absence of surgical PDA in our cohort. Enteral feeding was initiated as early as possible and whenever breast milk was available, although we used a slow progression protocol (increments of 20 cc/kg/day); however, we reached full feeds sooner than reports presented. A good percentage of our newborns were fed expressed breast milk, which should have a role in the lower incidence of proven NEC. This important intervention and feeding protocol were not reported in the other studies. Still, our rate of breast milk use is lagging behind other countries [9], which might be explained by the absence of lactation consultants, the high cost of electrical breast pumps and the high patient-to-nurse ratio that leaves no time for family education.

Twenty-two percent of the study population were SGA infants and the EUGR rate was high, which was not reported in the UAE or KSA studies, but its lower than reported rate of EUGR in NICHD data, the lack of breast milk fortifiers, premature infant formula and the absence of neonatal solutions for total parenteral nutrition are all factors for the considerable rate of EUGR in our cohort.

Regarding retinopathy of prematurity, 52 babies survived to the screening age and 50 (96.2%) were screened. The remaining two infants were discharged before the screening age and were screened as outpatients. Our unit oxygen targets ranged from 88-94%, yet we did not have high saturations alarms. Also, due to the high patient-to-nurse ratio, it is most likely that our babies spend most of the time on ranges higher than that. Nevertheless, during the study period, only two of our babies required laser therapy with excellent outcome.

Conclusion

The care of very low birth infants in Jordan requires a lot more effort to decrease mortality and improve morbidities. Continuous assessment of this vulnerable group is needed. This is a prospective single-center

study. A multicenter study is needed that involves all health sectors in Jordan.

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