Risk Factors for Neonatal Mortality Among Very Low Birth Weight Neonates

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Abstract- The objective of this study is to determine risk factors causing increase in very low birth way (VLBW) neonatal mortality. The medical files of all neonates weighing ≤1500 g, born in Vali-e-Asr hospital (2001-2004) were studied. Two groups of neonates (living and dead) were compared up to the time of hospital discharge or death. A total of 317 neonates were enrolled. A meaningful relationship existed between occurrence of death and low gestational age (*P*=0.02), low birth weight, lower than 1000 g (*P*=0.001), Apgar score <6 at 5th minutes (*P*=0.001), resuscitation at birth (*P*=0.001), respiratory distress syndrome (*P*=0.001) need for mechanical ventilation (*P*=0.001), neurological complications (*P*=0.001) and intraventricular hemorrhage (*P*=0.001). Regression analysis indicated that each 250 g weight increase up to 1250 g had protective effect, and reduced mortality rate. The causes of death of those neonates weighting over 1250 g should be sought in factors other than weight. Survival rate was calculated to be 80.4% for neonates weighing more than 1000 g. The most important high risk factors affecting mortality of neonates are: low birth weight, need for resuscitation at birth, need for ventilator use and intraventricular hemorrhage.

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Key words: Neonatal mortality rate (NMR); Risk factor; Very low birth weight (VLBW)

Introduction

Survival rate of very low birth weight (VLBW) neonates has been increasing day to day, during the recent four decades, because of developments in the neonate's medical care. Therefore, the lowest gestational age and birth weight for survival are reported 22-23 weeks and 350 g in developed countries, respectively (1). According to some statistics the rate of low birth weight (LBW) and VLBW for neonates are 6-7% and 1% of all births respectively (2). In spite of that and in spite of all progress made, more than 50% of neonates death are among VLBW neonates (2).

VLBW may be associated with some factors such as maternal anemia, pure prenatal care, socioeconomic factors and obstetric history (3,4). LBW is also associated with disabilities such as cardiovascular diseases and acute renal injury in adulthood, even their mechanism is poorly understood (3,5).

Organ malfunctions, different causes of preterm delivery, and even the type of therapies used for these neonates have had reverse effects upon mortality rate of neonates. Complications among VLBW neonates are reversely related to birth weight and gestational age, so that complications such as respiratory distress syndrome, intraventricular hemorrhage, duration of hospitalization, moderate to severe deficit in academic achievement, attention and behavioral problems and poorer self perceived physical health are increased by reduction of birth weight and gestational age (6-9).

Several factors may reduce mortality rate of VLBW neonates, including the improvement in quantity and quality of prenatal care and maternal nutrition regionalization of neonatal care, antenatal steroid administration, widespread use of surfactant and equipping 3rd level neonatal care centers and

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improvement of neonatal transport system.

In this study we intended to evaluate the situation of VLBW neonates in Vali-e-Asr hospital by investigating mortality rate and complications that VLBW neonates have experienced in the time of hospitalization during a period of 4 years. The result of this study will help us to find out our weak points and evaluate and improve the health care for VLBW neonates.

Material and Methods

The society under the study consisted of all neonates born from 21st march 2001 to 20th March 2004 in Vali-e-Asr hospital, weighing 500 to 1500 g. Tt was a cross sectional, descriptive analytic study. Vali-e-Asr hospital is an academic general hospital part of Imam Khomeini hospital complex with primary, secondary and tertiary neonatal care levels. In this study, neonates were also included who were in the above mentioned range weight and died in delivery room or suffered from congenital anomalies. Several variables were scrutinized through a questioner. Including the followings: weight, gestational age, type of delivery, sex, apgar score <6 at 5th minutes, cardiopulmonary resuscitation (CPR) at birth, need for respirator and assisted ventilation, complications such as respiratory distress syndrome, sepsis, necrotizing enterocolitis, neurological, intraventricular hemorrhage, cardiac, metabolic, hematological, congenital anomalies and the final outcome (discharge or death). Maternal information such as age, prenatal care, antenatal steroid administration, complications related to pregnancy and delivery and underlying chronic diseases noted in the questioner were also examined.

Statistical analysis was carried out using Student's t-test, Fisher's exact test, Chi-square test and logistic regression to the meaningful level of 95%. The study was confirmed to be in accordance with medical ethics measure by the research council of the Reproductive Health Center at Imam Khomeini hospital and then it was approved by research council of the Tehran University of Medical Sciences.

Definitions

Resuscitation at birth was defined as the use of positive pressure ventilation or cardiac massage, in case neonate required any form of ventilators including CPAP (continuous positive airway pressure) or SIMV (synchronized intermittent mandatory ventilation) or assisted ventilation after birth until point of discharge from ward. Sepsis is the term used when neonate, in addition to poor general condition suffered from one of the followings: (a) positive culture of sterile body liquids, (b) leukocyte count with WBC > 28000/mm^3 or < 5000 mm^3 (c) positive CRP or high ESR (d) thrombocytopenia (e) CXR indicating pneumonia.

Necrotizing entrocolitis was diagnosed and classified according to Bell's staging (10).

Intraventricular hemorrhage is applied to the presence of slights amount of blood in ventricles detected by ultrasonography.

Neurologic complications are any of the following: (a) any from of seizure from the time of birth until hospital discharge, accompanied by impaired EEC, (b) Apgar score <6 at the 5th minutes of life accompanied with a seizure on the first on the first day of life, (c) intraventricular hemorrhage.

Metabolic complications in this study consisted of hypoglycemia, hyperglycemia, hypocalcaemia, hypo and hypernatremia, hypo and hyperkalemia and uremia during hospitalization.

Hematological complications consisted of thrombocytopenia, leucopenia, leucopenia <5000/mm^3, neutropenia <1500/mm^3, anemia requiring packed cell infusion.

Jaundice was any case requiring medical intervention (phototherapy or exchange transfusion).

Cardiac complications were considered for neonates with patient ductus arteriosus based on echocardiography findings or heart failure.

Results

A total of 317 VLBW neonates, whose mothers had received prenatal care during pregnancy, were enrolled in the study. Their birth weights ranged from 500 g to 1500 g. The mean weight was 1158±246.4 g. Gestational age was between 22 to 40 weeks. The mean gestational age was 30.2±3.1 weeks (Table 1). Overall alive rate was 67%. This was 80.4% for weights over 1000 g. Alive rates were calculated 62.5% and 71% for boys and girls respectively. Highest mortality rate was observed among neonates of lowest gestational age (68% in neonates ≤26 weeks of gestational age), and lowest birth weight (89.7%) was seen in neonates weighing less than 750 g. Mean gestational age and birth weight were meaningfully lower among those who died than those alive. Mean birth weight was 990 g in those who died against 1236 g in those remained alive (P=0.001); and mean gestational age in the group who died was 28.52 weeks compare to 31 weeks among those alive (P=0.001) (Table 2).

Table 1. Mortality and viability rates based on gestational age and birth weight.

Viability and birth weight (g)	Total	Living newborns N (%)	Dead newborns N (%)
500-750	29 (100)	3 (10.3)	26 (897)
751-1000	97 (100)	30 (47.6)	33 (52.4)
1001-1250	97 (100)	72 (74.2)	25 (25/8)
1251-1500	117 (100)	100 (85.5)	17 (14.5)
Total	306 (100)	205 (67)	101 (33)
Gestational age	Total	Viable N (%)	Dead N (%)
<_26	25 (100)	8 (32)	17 (68)
27-29	116 (100)	60 (51.7)	56 (48.3)
30-32	97 (100)	75 (77.3)	22 (22.7)
33-35	50 (100)	42 (84)	8 (16)
>35	18 (100)	18 (100)	0 (0)
Total	306 (100)	203 (66.3)	103 (33.7)

The logistic regression model for risk estimation of weight in categorical groups showed that alive rate meaningfully increased with each 250 g increase of weight in groups starting from basic group (500-750) to 1250 g of weight by each 250 g of body weight, so that odds ratio would be 0.08 (group 2 as compared to group 1), and 0.233 (group 3 as compared to group 2). This protective effect is lost in neonates weighting over 1250 g and the cause of death should be sought in other factors (Table 3).

Mortality rate is meaningfully higher in cases of RDS (respiratory distress syndrome), neurological complications, intraventricular hemorrhage, need for resuscitation at birth, low Apgar score and need for ventilator (Table 4). Meanwhile no significant relation was observed between mortality rate and icter, hematological, cardiac complications or sepsis (Table 4).

Table 2. Characteristics of newborns under study.

Study grow Characteristics	Total	Living newborns	Dead Newborns	*P*-value
Mean maternal age	27.61 ± 6.14	27.64 ± 6.03	6.29 ± 6.56	0.775
Antenatal steroid use N (%)	55 (17.4)	40 (19.5)	14 (13.5)	0.482
SGA [N (%)]	103 (32.7)	71 (70.3)	30 (29.7)	0.369
Mean gestation al age (weeks)	30.20 ± 3.1	31.03 ± 3.04	28.52 ± 2.53	0.022
Mean birth weight (g)	1158.76 ± 264.44	1236.49 ± 195.46	990.40 ± 285.15	0.001
Cesarean sections N (%)	224 (70.7)	149 (27.7)	71 (68.3)	0.311
Gender				0.133
Girl N (%)	171 (54.1)	120 (58.5)	49 (47.6)	
Boy N (%)	142 (44.9)	85 (41.5)	51 (49.5)	

Table 3. Results of Logistic Regression analysis in different age groups.

Groups (grams)	B	EXP(β)	CI
Group 1 (500-750)	-	-	-
Group2 (751-1000)	-2.524	0.080	0.011-0.589
Group 3 (1001-1250)	-1.502	0.223	0.055-0.901
Group 4 (1251-1500)	0.199	1.221	0.366-4.073

Table 4. Overall Incidence prevalence of complications and risk factors of mortality based on complications among VLBW newborns.

Complication	Overall prevalence N (%)	Mortality rate due to complications to all deaths N (%)	*P*-value	Odds Ratio	Confidence Interval (95%)
Low Apgar score	64 (21.5)	38 (37 3)	0.000	3.882	2.183-6.904
Need for resuscitation at birth	168 (58.1)	83 (84.7)	0.000	6.900	3.714-12.821
Need of respirator use	130 (42.2)	87 (83.7)	0.000	19.161	10.317-35.589
					3.930-14.243
					2.717-7.921
RDS	186 (61)	89 (87.3)	0.000	7.481	3.930-14.243
Neurological complication	84 (27.6)	49 (49)	0.000	4.639	2.717-11/660
IVH	65 (21)	44 (42.3)	0.000	6.425	3.541-11.660
					0.340-0.946
Hematological Complications	215 (70.5)	63 (62.4)	0.033	0.567	0.340-0.946
Septicemia	198 (64)	62 (59.6)	0/375	0.375	-
Metabolic complications	171 (53.9)	48 (46.2)	0/039	0.039	-
Icter	245 (80.3)	57 (56.4)	0/000	0.110	0.058-0.210
Cardiac complications	26 (8.6)	3 (3)	0/016	0.243	0.071-0.831 I
PDA	15 (4.9)	2 (1.9)	0/09	0.288	0.064-1.301
NEC	21 (6.6)	5 (23.8)	0/473	0.473	4.24-12.60
Birth weight< 1000 g	93 (30.06)	59 (58.4)	0/000	7.32	4.24-12.60
Gestational age less than 30 weeks 30 weeks gestation	141 (46.07)	73 (70.9)	0/000	4.83	2.88-0.08

Table 5. Neonatal mortality Rate based on risk factors.

Risk factor	Need for respirator use	RDS	Low Apgar score	Need for resuscitation on at birth	Neurological complications	Birth weight <1000 g
No (%)	87 (67)	89 (48)	38 (60)	83 (50)	49 (58)	59 (58)
β	2.808	0.660	-0.874	1.437	-1.994	-1.502
Exp (β)	16.583	1.934	0.417	4.206	0.136	0.223
P value	0.000	0.238	0.114	0.005	0.035	0.035

Regarding maternal factors, the ages of the mothers were 16 to 46 with an average of 27.61±6.14 years. There were no significant statistical differences between the two groups of dead and alive on average mother's age, type of delivery (vaginal or cesarean/section) and antenatal steroid administration (Table 2).

Moreover, all maternal files under study showed one risk factor during pregnancy or delivery, but the groups did not show a significant difference in this respect. Logistic regression analysis showed that in addition to weight lower than 1000 g, other factors such as the use of ventilator, resuscitation at birth and intraventricular hemorrhage are independently associated with mortality in neonates. However, low Apgar score and respiratory distress syndrome did not independently increase mortality rate (Table 5). According to this analysis, 50% of gestational age more than 26 weeks old and birth weight over 1000 g has the chance of being alive.

Discussion

This study showed that the survival chance is 67% for VLBW neonates in our ward, and it decreases with lower gestational age and especially with lower weight at birth. The chance is lower than 32% for neonates with gestational age ≤26 weeks. It is difficult to compare this result with some other studies performed on neonates hospitalized in NICU wards. This is because death of

live birth in delivery room, death within the first 24 hours of life and death due to congenital anomalies are omitted in those studies, and as a result the VLBW neonate's death rate has been reported low. For instance, survival chances were reported 39% and 41% for neonates hospitalized in NICU wards with gestational ages 26 weeks and lower by Manzar and colleagues (11) from Oman, and Kook and colleagues (12) from England respectively. A similar study carried out in networks of NICU wards in Canada (13) and Latin American (14) have reported survival chance for neonates of 26 weeks gestational ages or less, hospitalized in NICU wards as 63% and 27% (10-5%) respectively. However, another study carried out in 2000 (15) in the United States, showed survival rate of 35% for neonates of 26 weeks gestational age and less including death in delivery room, which is very close to our findings. In general, studies carried out in America (16), Canada (17), New Zealand (18), Turkey (19) have reported the survival chances for VLBW neonates to be between 70%-90% which are higher than our results, but the study carried out in Taiwan (20) indicates results very close to ours.

Another point which makes such comparisons difficult is that VLBW neonates are not a homogenous group. They include neonates weighting less than 1000 g as well as those with intra-uterine growth retardation, which affect death rate. Average weight of neonates inr our study was lower than those of most other studies (17,19,21). This may explain the reason for higher mortality rate in our study. Comparisons of weight groups under study, more or less, indicates that our results are quite similar to those of other studies for weights over 1250 g, while for weights under 1000 g, our results are in agreement with those of Taiwan and Turkey. Among the risk factors of death, the most important factor is low birth weight and low gestational age based on previous studies (14-16,19-23). In our study, low birth weight exhibited more influence in causing death compared to low gestational age. This finding has been reported previously (21). We also found that the use of CPR at birth was another risk factor causing death, this is similar to two other studies (11,20). In one of them the risk of death is stated to be 2.3 times higher in neonates who received resuscitation at birth, which is similar to our results. Ventilator use which increased the death risk of our neonates 20 times has also been pointed out in one study (18). Neurological complications and intraventricular hemorrhage, the mortality risk factors observed in our study, were not reported as death risk factors in other studies. On the hand sepsis (2,20,24), pneumothorax (18,24), respiratory distress syndrome (20,24), multiple gestation (22,23) , delivery type (25) and gender (15,22,23) were not detected as prognostic factors in our study, they were regarded as mortality factors in other studies. In present study, significant reverse relationship between metabolic, cardiac, hematological complications, jaundice and death, means that death of neonate must have been occurred in the first hours or days of birth, before any such complications could have been appeared. Therefore, such complications have occurred more frequently among those remained alive. The effect of disuse of surfactant and steroid, which were reported as death risk factors, could not be measured in our study as their use were limited in both groups of dead and alive. Totally, this study and its comparison with other studies showed that, VLBW neonates are heterogeneous and not a homogeneous group regarding their weight, gestational age and other complications, that it is difficult to compare studies of different parts of the world, but the most determining factors in the outcome of neonates are birth weight, and probably gestational age, and each area should evaluate other death risk factors for these neonates separately and frequently, and improve the outcome according to its condition. Meanwhile, this study showed that our pregnant mothers have received much less antenatal steroid than mothers in other studies, and their use of surfactant have been very limited probably due to high cost and unavailability, and both these two factors have effective role in reducing mortality of VLBW neonates all over the world. In conclusion, in our hospital, neonate's mortality rate, especially for neonate group weighing lower than 1000 g is higher than those reported for developed countries. To some extent it may be attributed to lesser use of antenatal steroid and limited use of surfactant after birth.

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