Causes and Risk Factors Associated to Neonatal Mortality in Neonatal Intensive Care Unit (NICU) in Besat Hospital Hamadan-Iran in 2015 to 2016

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Abstract

Background
Advances in the perinatal and neonatal cares have brought about considerable reductions in the neonatal mortality. The present study aimedto determine the disease patterns, outcomes and factors influencing the neonatal mortality in single neonatal intensive care unit.

Materials and Methods
This descriptive research was retrospective and cross-sectional in type. The study population enrolled all neonates who had been hospitalized in the neonatal intensive care unit (NICU) of the Besat hospital, Hamadan city, Iran, for a period of one year from October 1, 2015 to September 31, 2016 and the mothers and infants information (such as maternal diseases, delivery mode, neonatal age, birth weight, the causes and duration of hospitalization) were extracted from the Medical records and analyzed using SPSS software version 16.0

Results
The study population included 600 infants and 13% (78) of whom were died. The results of the multivariate logistic regression analysis for the risk factors associated to the neonatal deaths indicated that there was a significant relationship between neonatal deaths and the use of mechanical ventilation, gastrointestinal bleeding, birth weight less than 2500 grams, positive urine cultures, need for surgery, administration of dopamine, anticonvulsant drugs, and surfactant (P<0.05).

Conclusion
The present study indicated that sepsis, surfactant administration and ventilator use significantly influence neonatal death; additionally, to underlying diseases, the occurrence of complications and their number increase the probability of neonatal deaths.

Key Words: Iran, Mortality, Neonates, NICU, Risk factor.

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1- INTRODUCTION

Neonatal period, incorporating the first 28 days of the infant's life, is the most important time for the children's survival worldwide and it accounts for nearly 50% of the deaths of the children below five years of age (1). About 3.8 million neonatal deaths are reported around the globe every year some 98% of which occurs in the developing countries. The neonatal mortality rates in developing and developed countries are 28.2 and 3.5 per 1000 live births, respectively (2). The reduction in neonatal mortality over the last two decades is owed to the progresses made in prenatal and perinatal care as well as the enhancement of the quality of services in neonatal intensive care units (3). Worldwide, the main causes of neonatal mortality are prematurity, infection and perinatal asphyxia (4).

Although the recent advances in medical technologies as well as innovations in the quality of premature infants' care have led to an increase in the life expectancy of them, especially for the infants born with weights less than 1,000 gr (Extremely Low Birth Weight infants), the frequency of the complications accompanied by preterm birth is still high (5). Recent studies have shown different rates of mortality in the NICUs (6-9). These differences in the mortality rates are important in that conclusions can be made based thereupon concerning the quality and quantity of care provided. The survey of the medical care methods associated with the mortality rates can provide us with solutions to discover how medical care methods can lead to improved outcomes.

Due to the same reason, the present study aimed to determine the disease patterns and outcomes as well as the factors influencing the mortality rates of the neonates hospitalized in NICU of Besat hospital, Hamadan city, Iran, during a one-year period.

2- MATERIALS AND METHODS

Incorporated all the neonates who had been hospitalized in neonatal intensive care unit of Besat hospital, Hamadan city, Iran, during a one-year period spanning from 1st of October 2015 to 31st of September 2016. The inclusion criteria of the study was being admitted to neonatal intensive care unit during the study period and the infants who were discharged with their parents' personal consent and the infants who had been dispatched for such reasons as their need for more advanced facilities or cardiac surgery were excluded from the study.

The mothers and infants' information, including neonatal age, birth weight, gender, maternal diseases, delivery mode, the causes and duration of hospitalization, complications development during stay, surfactant administration, use of mechanical ventilation, type of treatment and the disease outcomes, was collected through a checklist from their medical records by medical student and analyzed using SPSS software version 16.0, and p-values <0.05 were considered statistically significant. The present study has been approved by the Ethics Committee of Hamadan University of Medical Science, No. P/16/35/9/305.

3-RESULTS

The present study, undertaken based on a census method, a total of 600 infants were investigated as the study population; 13% (78) of the hospitalized infants died and the rest (522) were dismissed. Sepsis, respiratory distress syndrome resulting from prematurity and major congenital anomalies were the most common causes of deaths in our study. The frequency distribution of the admission and death causes are presented in **Table.1** and the frequency distribution of the infants' demographic characteristics are summarized in **Table.2**. The results of the univariate regression analyses of the

factors correlated with the neonatal mortality, given in **Table.3**, indicated that the neonatal death was substantially associated with the age of the first day after birth,weighsless than 2,500 gr, multiple delivery, preterm birth and normal vaginal delivery; moreover, the occurrence of sepsis, seizure, pulmonary hemorrhage, gastrointestinal bleeding, pneumothorax, acute kidney injury, disseminated intravascular coagulation disorder, positive blood and urine cultures, the use of mechanical ventilation, ultrasonography requirement, surgery requirement and administration of dopamine, surfactant and anticonvulsant drugs all of which can bring about an increase in the neonatal death (p<0.05).

The results of multivariate logistic regression analysis regarding the risk factors associated with neonatal mortality, as summarized in **Table.4**, indicated that the neonatal death is increased by 13.94 times with the use of mechanical ventilation [odds ratio (OR):13.94, 95% confidence interval (CI) (3.45-56.21), P=0.001], 11 times with the gastrointestinal bleeding [OR:11.07,95%CI(1.95-62.62), P=0.007], 3.99 times with birth weights less than 2,500 gr [OR:3.99,95%CI(1.32-12.08), P=0.014], 139.57 times with positive urine cultures [OR:139.57,95%CI(29.56-658.89), P=0.001], 0.27 times with the ultrasonography requirement [OR:0.27,95%CI(0.09-0.82), P=0.021], 8.39 times with the need for surgery [OR:8.39,95%CI(2.58-27.26), P=0.001], 15.34 times with administration of dopamine [OR:15.34,95%CI(3.07-76.51), P=0.001], 13.01 times with use of anticonvulsant drugs [OR:13.01,95%CI(3.58-47.28), P=0.001] and 21.63 times with surfactant administration [OR:21.63,95%CI(3.87-120.84), P=0.001].

Table-1: The frequency distribution of the hospitalization and death causes in the neonates admitted to neonatal intensive care unit of Besat Hospital, Hamadan (2015 to 2016)

Causes of admission	Out come		Total Number (%)
	Survive Number (%)	Death Number (%)	
Sepsis and meningitis	84(14)	21(3.5)	105(17.5)
Urinary tract infection	25(4.2)	0(0)	25(4.2)
Pneumonia	24 (4)	0(0)	24 (4)
Respiratory distress syndrome	72(12)	24(4)	96(16)
Transient tachypnea of the newborn	34(5.6)	0(0)	34(5.6)
Congenital heart disease	30(5)	5(0.8)	35(5.8)
Asphyxia	30(5)	6(1)	36(6)
Seizure	50(8.3)	0(0)	50(8.3)
Metabolic disorder	20(3.3)	5(0.8)	25(4.2)
Diaphragmatic hernia	8(1.3)	3(0.5)	11(1.8)
Esophageal atresia	17(2.8)	8(1.3)	25(4.2)
Duodenal atresia	8(1.3)	0(0)	8(1.3)
Midgut volvulus	5(0.8)	0(0)	5(0.8)
Hirschsprung	10(1.7)	0(0)	10(1.7)
Jejunoileal atresia	14(2.3)	0(0)	14(2.3)
Imperforated anus	21(3.5)	2(0.3)	23(3.8)
Hypertrophic pyloric stenosis	10(1.7)	0(0)	10(1.7)
Gastroschisis	5(0.8)	0(0)	5(0.8)
Hydrocephalus	5(0.8)	0(0)	5(0.8)
Myelomeningocele	10(1.7)	0(0)	10(1.7)
Choanal atresia	6(1)	0(0)	6(1)

Cleft palate	5(0.8)	0(0)	5(0.8)
Vesicoureteral reflux	8(1.3)	0(0)	8(1.3)
Renal mass	10(1.7)	0(0)	10(1.7)
Neonatal thrombocytopenia	5(0.8)	0(0)	5(0.8)
Multiple congenital anomalies	6(1)	4(0.7)	10(1.7)
Total	522(87)	78(13)	600(100)

Table-2: The frequency distribution of the infants' demographic characteristics, Besat Hospital, Hamadan (2015 to 2016)

	Out come		Total
Variables	Survive, Number (%)	Death, Number (%)	Number (%)
Gender	304 (87.4)	44 (12.6)	348 (58.0)
	218 (86.5)	34 (13.5)	252 (42.0)
Neonatal age (day)			
1	150 (76.9)	45 (23.1)	195 (32.5)
2-7	191 (93.2)	14 (6.8)	202 (34.2)
> 7	181 (90.5)	19 (9.5)	200 (33.3)
Birth weight (gr)			
≥2,500	389(93.8)	26 (6.2)	415 (69.2)
<2,500	133 (71.9)	52 (28.1)	185 (30.8)
Gestational age			
Term	368(92.9)	28 (7.1)	396 (66.0)
preterm	154 (75.5)	50 (24.5)	204 (34.0)
Multiple birth			
Yes	19 (54.3)	16 (45.7)	35 (5.8)
No	503 (89.0)	62 (11.0)	565(94.2)
Primigravid			
Yes	239 (88.8)	30 (11.2)	269(44.8)
No	283 (85.5)	48 (14.5)	331 (55.2)
Mode of delivery			
NVD	231 (85.6)	39 (14.4)	270 (45.0)
Cesarean section	291 (88.2)	39 (11.8)	330 (55.0)
Seizure			
Yes	106 (88.3)	14(11.7)	120 (20.0)
No	416 (86.7)	64 (13.3)	480 (80.0)
Sepsis			
Yes	202 (79.2)	53 (20.8)	255(42.5)
No	320(92.8)	25 (7.2)	345 (57.5)
Use of mechanical ventilation			
Yes	55 (45.8)	65 (54.2)	120 (20.0)
No	467 (97.3)	13 (2.7)	480 (80.0)
Pulmonary hemorrhage			
Yes	4 (40.0)	6 (60.0)	10 (1.7)
No	518 (87.8)	72 (12.2)	590 (98.3)
Pneumothorax			
Yes	12 (48.0)	13 (52.0)	25 (4.2)
No	510 (88.7)	65 (11.3)	575 (95.8)
Gastrointestinal bleeding			
Yes	9 (45.0)	11 (55.0)	20 (3.3)
No	513 (88.4)	67 (11.6)	580 (96.7)
Acute kidney injury			
Yes	14 (56.0)	11 (44.0)	25 (4.2)
No	508 (88.3)	67 (11.7)	575 (95.8)
Disseminated intravascular coagulation			
Yes			

No	7 (35.0)	13 (65.0)	20 (3.3)
	515 (88.8)	65 (11.2)	580 (96.7)
Positive blood culture			
Yes	51 (70.8)	21 (29.2)	72 (12.0)
No	471 (89.2)	57 (10.8)	528 (88.0)
Positive urine culture			
Yes	31 (41.3)	44 (58.7)	75 (12.5)
No	491 (93.5)	34 (6.5)	525 (87.5)
Positive CSF culture			
Yes	13 (72.2)	5 (27.8)	18 (3.0)
No	509 (87.5)	73 (12.5)	582 (97.0)
Brain CT- scan			
Yes	132 (88.0)	18 (12.0)	150 (25.0)
No	390 (86.7)	60 (13.3)	450 (75.0)
Ultrasonography			
Yes	304 (90.7)	31 (9.3)	335 (55.8)
No	218 (82.3)	47 (17.7)	265 (44.2)
Echocardiography			
Yes	195 (88.6)	25 (11.4)	220 (36.7)
No	327 (86.1)	53 (13.9)	380 (63.3)
Need for Surgery			
Yes	71 (78.0)	20 (22.0)	91 (15.2)
No	451 (88.6)	58 (11.4)	509 (84.8)
Use of dopamine			
Yes	7 (17.9)	32 (82.1)	39 (6.5)
No	515 (91.8)	46(8.2)	561 (93.5)
Use of anticonvulsant			
Yes	84 (80.8)	20 (19.2)	104 (17.3)
No	438 (88.3)	58 (11.7)	469 (82.7)
Surfactant administration			
Yes	5 (15.6)	27 (84.4)	32 (5.3)
No	517 (91.0)	51 (9.0)	568 (94.7)

NVD: Normal Vaginal Delivery.

Table-3: Univariate logistic regression of risk factors for neonate mortality, Besat Hospital, Hamadan (2015 to 2016)

Variables	Crude OR	95% CI	P - value
Gender			
Male	-	-	0.760
Female	1.07	0.66 - 1.74	
Neonatal age (day)			
1	2.85	1.60 – 5.09	0.001
2-7	0.69	0.34 – 1.43	0.328
>7	–	–	–
Birth weight (g)			
≥ 2,500	–	–	–
< 2,500	7.79	4.29 – 14.14	0.001
Gestational age			
Term	–	–	0.001
preterm	4.26	2.59 – 7.03	
Multiple birth			
Yes	6.83	3.34 – 13.97	0.001
No	–	–	

Primigravid			
Yes	–	–	–
No	1.35	0.83 – 2.20	0.226
Mode of delivery			
NVD	4.15	2.23 – 7.72	0.001
Cesarean section	–	–	
Seizure			
Yes	0.85	0.46 – 1.59	0.628
No	–	-	
Sepsis			
Yes	3.35	2.02 -5.57	0.001
No	–	–	
Use of mechanical ventilation			
Yes	42.45	21.99 – 81.95	0.001
No	–		
Pulmonary hemorrhage			
Yes	10.79	2.97 – 39.16	0.001
No	–		
Pneumothorax			
Yes	8.50	3.72 – 19.41	0.001
No	–	–	
Gastrointestinal bleeding			
Yes	9.35	3.74 – 23.41	0.001
No	–		
Acute kidney injury			
Yes	5.95	2.59 – 13.65	0.001
No	–		
Disseminated intravascular coagulation			
Yes			
No	14.71	5.66 – 38.21	0.001
	–		
Positive blood culture			
Yes	3.40	1.90 – 6.06	0.001
No	–		
Positive urine culture			
Yes	20.49	11.52 – 36.47	0.001
No	–		
Positive CSF culture			
Yes	2.68	0.92 – 7 .74	0.068
No	–		
Brain CT scan			
Yes	0.88	0.50 – 1.55	0.674
No	–		
Ultrasonography			
Yes	0.47	0.29 – 0.76	0.003
No	–		
Echocardiography			
Yes	0.79	0.47 – 1.31	0.365
No	–		

Surgery
    Yes
    No
	2.19
	-
		1.24 – 3.86	0.007

Use of dopamine
    Yes
    No
	51.18
	-
		21.40 – 122.36	0.001

Use of anticonvulsant
    Yes
    No
	1.79
	-
		1.02 – 3.14	0.001

Surfactant administration
    Yes
    No
	54.74
	-
		20.20 – 148.30
		-
			0.001

NVD: Normal Vaginal Delivery; 95% CI: 95% confidence interval; OR: Odds ratio.

Table-4: The multivariate logistic regression of risk factors for neonate mortality, Besat Hospital, Hamadan (2015 to 2016)

Variables	Adjusted OR	95%CI	P - value
Birth weight (g) ≥2,500 <2,500	- 3.99	- 1.32-12.08	- 0.014

Use of mechanical ventilation
    Yes
    No
	13.94
	-
		3.45-56.21	0.001

Pulmonary hemorrhage
    Yes
    No
	7.22
	-
		0.97 – 53.84
		-
			0.054

Gastrointestinal bleeding
    Yes
    No
	11.07
	-
		1.95 – 62.62	0.007

Positive urine culture
    Yes
    No
	139.57
	-
		29.56 – 658.89	0.001

Ultrasonography
    Yes
    No
	0.27
	-
		0.09 – 0.82	0.001

Need to Surgery
    Yes
    No
	8.39
	-
		2.58 – 27.26
		-
			0.001

Use of dopamine
    Yes
    No
	15.34
	-
		3.07 – 76.51	0.001

Use of anticonvulsant
    Yes
    No
	13.1
	-
		3.58 – 47.28	0.001

Surfactant administration
    Yes
    No
	21.63
	-
		3.87-120.84	0.001

95% CI: 95% confidence interval; OR: Odds ratio.

4- DISCUSSION

The infants are admitted to neonatal intensive care units for such reasons as prematurity, low birth weights, medical diseases and need for surgery. The present study indicated that the overallmortality rate of the neonates have been 13% that is consistent with the rate, 14.2%, obtained by Ekwochi et al. (10) in Nigeria and lower than the mortality rate, 26%, obtained by Musookoet al. (11) in Uganda as well as mortality rate, 27.2%obtained by Al-Sadi (12) in Iraq and 19.2%, figured out by Babaei et al. (13) in Iran; furthermore, the mortality rate estimated herein was found higher than the mortality rate,8.1%, obtained by Manktelow et al. (14) in England as well as the rate, 9.2%, figured out by Feng et al. (15) in Australia.

Generally, the mortality rates of newborns in neonatal intensive care units differ between 3.1% and 29% in the world (16). The difference seen between the mortality rates estimated by various centers and countries are due to the availability of the equipment and skilled humanresources.

The neonates' deaths reported in our study predominantly occurred during the early days postpartum and the same finding was also observed in the other studies that reported the most frequent deaths on the first day, on the first week and between 1 and 12 days postpartum (8, 16-18); moreover, in a study by Sridhar et al. (8), 42.2% of the neonatal deaths were reported for the first day after birth, and 82.4% of them happened during the first three days postpartum. As for the very immature and preterm infants featuring weights below 1,500 gr, the death age was most often found longer than the term infants in such a way that in a study by Zhou et al. (19), almost 50% of the very preterm infantsdied after the first week (within 7 to 28 days postpartum), and in another study undertaken by Navaei et al. (20), the average death age of the preterm infants with weights below 1,500 gr was 28.9 days and this increase might have been due to the enhancement of care quality (21). Sepsis, respiratory distress syndrome stemming from prematurity and congenital anomalies were the most common causes of deaths in our study. Prematurity and low birth weight were pointed out as the major causes of neonatal death in the study conducted by Navaei et al. (20), as well, and in the study by Battin et al. (22), prematurity and very low birth weights, neonatal sepsis and congenital anomalies constituted the major neonatal death factors which were asphyxia, prenatal and neonatal sepsis as well as infection in the study by Ekwochi et al. (10), and also respiratory distress syndrome, congenital anomalies and sepsis were enumerated amongst the most common causes of neonatal deaths in the study performed by Basiri et al. (23), and as it can be seen the results conform to what was found herein.

In terms of the risk factors and complications, associated with diseases development during hospital stays, that are influential on the neonatal deaths, there was found a significant relationship between neonatal deaths and the respiratory failures requiring mechanical ventilation and respiratory distress syndrome requiring surfactant administration, seizure in need of anticonvulsant drugs, shocks requiring dopamine, infants in need of surgery, infants with deteriorated statuses along with pulmonary and gastrointestinal bleeding and urinary infections. Respiratory distress syndrome, neonatal infections, Necrotizing enterocolitis (NEC), pneumonia and pneumothorax, neonatal seizure, shock and intraventricular hemorrhage were pointed out as the major factors giving rise to neonatal deaths in the study performed by Shrestha et al. (24); also, Tagare et al. (25) in a study recounted pulmonary hemorrhage, respiratory distress syndrome,

intraventricular hemorrhage, neonatal infections, Bronchopulmonary dysplasia and pneumothorax as associated with the neonatal deaths. Nayeri et al. (26) in a study found the need for mechanical ventilation, respiratory distress syndrome and neurological symptoms correlated with neonatal deaths. Afjeh et al. (5) pinpointed the need for mechanical ventilation only and the need for mechanical ventilation plus surfactant administration, pulmonary hemorrhage, gastrointestinal bleeding, seizure and the need for surgery as predictors of neonatal deaths and in another study by Basiri et al. (23), the need for mechanical ventilation, the need for early-birth resuscitation, pneumothorax and weights below 1000 gr as being associated with the neonatal deaths. In another study carried out by Demisse et al. (27), as well, sepsis and respiratory distress syndrome were realized as factors contributing to the neonatal deaths. The results of our study are in compliance with what has been found in the similar studies, so it can be concluded that the occurrence and the multiplicity of the complications in the hospitalized infants causes an increase in their death likelihoods.

5- CONCLUSION

The current research indicated that neonatal infection and respiratory distress syndrome and congenital anomalies are the major causes of the neonatal deaths of the hospitalized infants and the appearance of complications such as respiratory failure, seizures, shock, which is why it is recommended to improve the quality of prenatal care and the quality of the NICU service to decrease the number of neonatal deaths.

6- CONFLICT OF INTEREST: None.

7-ACKNOWLEDGEMENT

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