

Original Paper

Factors Related to Neonatal Mortality at Discharge Among Premature Neonates in a Tertiary Care Hospital in North of Iran





Ali Roshani Tabrizi¹ (10), Seyedeh Hajar Sharami^{2*} (10), Shadi Sabetghadam³ (10), Mandana Mansour Ghanaei⁴ (10), Reza Sharafi⁵ (10), Seyedeh Fatemeh Dalil Heirati⁶ (10), Habib Eslami-Kenarsari⁷ (10)

- 1. Pediatrician, Reproductive Health Research Center, Al-zahra Hospital, Guilan University of Medical Sciences, Rasht, Iran.
- 2. Professor, Reproductive Health Research Center, Department of Obstetrics & Gynecology, Al-zahra Hospital, School of Medicine, Guilan University of Medical Sciences. Rasht. Iran.
- 3. Assistant Professor, School of Nursing and Midwifery, Guilan University of Medical Sciences, Rasht, Iran.
- 4. Professor, Reproductive Health Research Center, Department of Obstetrics & Gynecology, Alzahra Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran.
- 5. Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran.
- 6. Midwifery (MSc), Reproductive Health Research Center, Al-zahra Hospital, Guilan University of Medical Sciences, Rasht, Iran.
- 7. Biostatistics (MSc), Vice-chancellor for Research and Technology, Guilan University of Medical Sciences, Rasht, Iran.



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Running Title Factors Related to Mortality Among Iranian Preterm Neonates

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ABSTRACT

Introduction: The neonatal period is vital for child survival. In Iran, neonatal mortality rate is high in preterm births. Various factors influence the risk of neonatal mortality in preterm births in different populations but these factors are poorly documented.

Objective: This study aimed to determine predictors of neonatal mortality at discharge among preterm neonates admitted to a tertiary care hospital in Rasht, north of Iran.

Materials and Methods: This is a retrospective cross-sectional study. The medical records of 1145 premature neonates admitted to a tertiary care hospital in Rasht from 2017 to 2022 were examined and the data were collected using a checklist. Descriptive statistics, chi-square test, and Fisher's exact test were used to analyze the data. Multiple logistic regression was used to identify the predictors of neonatal mortality at discharge.

Results: Most of the neonates had an age ≥33 weeks (71.9%) with a birth weight above 2500 g (94.1%). In most cases, the preterm birth was spontaneous (74.2%). The neonatal mortality frequency at discharge was 78 per 1000 live births. Respiratory distress syndrome was the most common cause of death in all age groups (61 per 1000 live births). Predictors of neonatal mortality were fetal sex (OR=0.24, 95% CI; 0.08%, 0.69%, P=0.008), gestational age (OR=0.57, 95% CI; 0.47%, 0.71%, P=0.001), mode of delivery (OR=3.50, 95% CI; 1.04%, 11.78%, P=0.042), five-minute Apgar score (OR=0.40, 95% CI; 0.21%, 0.77%, P=0.006), fetal distress (OR=0.18, 95% CI; 0.04%, 0.73%, P=0.016), and neonatal intensive care unit (NICU) admission (OR=0.26, 95% CI; 0.08%, 0.78%, P=0.016).

Conclusion: Neonatal mortality at discharge among premature neonates is high in the study hospital in northern Iran. Improving the quality of services and resource allocation are recommended to increase the survival rate of premature neonates.

Keywords:

Neonatal mortality, Preterm birth, Neonatal intensive care unit (NICU)

* Corresponding Author:

Seyedeh Hajar Sharami, Professor.

Address: Reproductive Health Research Center, Department of Obstetrics & Gynecology, Al-zahra Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran.

Tel: +98 (911) 1500433 E-mail: sharami@gums.ac.ir



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Highlights

- The neonatal mortality at discharge among premature neonates in northern Iran is 5.5%.
- Neonatal mortality at discharge is higher in neonates with iatrogenic preterm birth compared to spontaneous preterm birth
- Fetal sex, gestational age, mode of delivery, five-minute Apgar score, fetal distress and neonatal intensive care unit admission are predictors of neonatal mortality at discharge

Plain Language Summary

This study aimed to investigate the death rate of premature babies in a tertiary care hospital in northern Iran and find the related factors. The medical records of 1145 premature babies admitted to the hospital from 2017 and 2022 were examined. We assessed the death rate before they left the hospital. The most common reason for death was respiratory distress syndrome. We found fetal sex, gestational age, mode of delivery, five-minute Apgar score, fetal distress, and neonatal intensive care unit admission could predict the death rate. Based on the results, there is a high rate of death among newborns at the study hospital. There is a need to improve the quality of services and provide resources to hospitals to increase the chances of survival for premature babies.

Introduction

remature birth is one of the most critical and challenging problems faced by obstetricians and gynecologists. It is associated with the neonatal death and lifelong complications, such as learning disabilities and visual, hearing, and cognitive problems, and is considered as a public health problem [1-4]. Premature birth also affects the economy, health care system, and society [5]. There is a clinical challenge in dealing with premature birth and reducing its complications due to problems in identifying preventable or modifiable factors. The overall prevalence of preterm birth is increasing worldwide, with about 15 million cases reported annually, leading to the deaths of about 1.1 million children [6]. Perinatal deaths account for about 7% of the global burden of disease [7]. It is estimated that globally four million neonatal deaths and stillbirths occur every year. Almost all these deaths occur in developing countries [8, 9] The neonatal death rate in Iran has been declined in past decades, but the decline has been slowed down, recently [10, 11].

Knowing the causes and predisposing factors of neonatal death can help identify, control, or reduce the death rate. Prematurity is a critical predisposing factor for neonatal death, which, despite the vast advances in midwifery science, is still a serious problem and requires extensive planning before birth and during pregnancy. Complications of prematurity, such as infection, respiratory distress syndrome, and intraventricular hemor-

rhage, are important causes of neonatal death [12]. Due to the progress in midwifery and quality of services dedicated to newborns, the survival rate of premature neonates has increased dramatically. Today, more than 95% of premature neonates who born before 28 weeks of pregnancy survive [13].

Many studies in Iran have reported the predictors of neonatal death [14, 15]. To the best of our knowledge, neonatal death rate and its associated factors in the tertiary hospitals are poorly documented, particularly at the institutional level. The ability of a premature neonate to survive is different among countries depending on hospital facilities. Therefore, the health centers that accept the admission of premature neonates should plan according to their conditions and decide whether these neonates survive or not, especially in the settings with limited beds in the neonatal intensive care units (NICUs). This study aims to investigate the factors related to death among premature neonates admitted to a tertiary care hospital in Rasht, north of Iran.

Materials and Methods

This is a retrospective cross-sectional study that was conducted at a tertiary care hospital in Rasht, north of Iran, from April to October 2022. The Pediatrics Department of this hospital has two major wards: Premature neonates unit and NICU. There are 50 beds in the two wards, where the NICU has 10 beds. Premature neonates in good general conditions receive care



beside their mothers. The minimum sample size was determined 1126, by considering the premature birth prevalence of 7.1% According to the results of Rezaeian et al. [16], an error rate of 0.05, a test power of 0.80, and acceptable error rate of 0.015. All medical records of neonates admitted from May 2017 to March 2022 were examined. All neonates reach gestational age of 25-37 weeks whose information was registered by the neonatal registry form from May 2017 to March 2022 in the hospital were included. The newborns older than 28 days, out-of-hospital birth cases, and revisits were excluded.

The data were collected by two trained midwives and one experienced intern who had undergone the necessary training before the study. A data collection form was used to extract the demographic and maternal/fetal and treatment-related factors. The maternal/fetal factors included the mother's age, obstetric history, mode of delivery, cause of preterm birth, pregnancy and childbirth complications, gestational age, birth weight, the admission unit, neonate's sex, congenital malformation, and neonatal complications during hospitalization such as electrolyte disorder, hyperglycemia (blood glucose >200 mg/dL), hypoglycemia (blood glucose <47 mg/dL), sepsis, and abnormal brain ultrasound findings (e.g. germinal matrix hemorrhage, intraventricular hemorrhage, cerebral parenchymal hemorrhage, periventricular leukomalacia, hydrocephalus). The treatment-related factors included respiratory support, breastfeeding, the given treatment, and length of hospitalization.

The collected data entered into SPSS software, version 25 and were expressed as Mean±SD and number (percentage). Chi-square test and Fisher's exact test were used to analyze the relationships between nominal variables. The factors related to fetal death were analyzed using multivariate logistic regression.

Results

There were 1161 premature neonates registered in the NICU and Premature Neonates Unit's database, of whom 16 were excluded (five due to revisit, and 11 due to birth outside the hospital). Finally, the data of 1145 neonates were analyzed. Most of the neonates were 33 weeks and older (71.9%). The birth weight of most of them were above 2500 g (94.1%). In most cases, the preterm births happened spontaneously (74.2%). The mean age of mothers was 30.90±6.24 years. In most cases, the mode of delivery was cesarean section (77%), and in one-third of cases, the cause was repeated cesarean section (Table 1).

There were 63(5.5%) deaths during the study period. Among the deceased neonates, 27.7% died during the first 24 hours and 69.8% died during 48 hours. The youngest survived neonate was a 750-g female with a gestational age of 25 weeks. The mean gestational age of survived and dead neonates was about 34 and 28 weeks, respectively. The average time between birth and admission to the NICU was 23 hours (ranged from 22 min to 90 hours). Among neonates, 676(59%) were hospitalized for more than seven days. Eleven neonates had retinopathy of prematurity that needed treatment, 7 had grade-1 necrotizing enterocolitis (NEC), one had grade-2 NEC, and 73(6.4%) had abnormal brain ultrasound findings. Moreover, 346(30.2%) used mechanical ventilation, and 5.2% did not receive breastfeeding and were discharged with infant formula packs. Of all neonates, 212(18.5%) were admitted to NICU, of whom 19(9%) died (Table 2).

Of neonates who were admitted to the NICU, 83(39%) aged ≤28 weeks, and most of them (63.8%) were primarily admitted to the NICU. Of those who received NICU care, 20.8% died, while 93.3% of neonates who did not receive NICU care died. The most common diagnosis for neonates admitted to the premature neonates unit was icter (73%), while respiratory distress (72.2%) was the most common diagnosis for neonates admitted to NICU. The final diagnosis of 247(21.57%) neonates was respiratory distress (Table 3).

Variables with a P<0.2 in the univariate analysis were included in the logistic regression model. The results of analysis (Table 4) showed the significant association of fetal sex (OR=0.24, 95% CI; 0.08%, 0.69%, P=0.008), gestational age (OR=0.57, 95% CI; 0.47%, 0.71%, P=0.001), mode of delivery (OR= 3.50, 95% CI; 1.04%, 11.78%, P=0.042), five-minute Apgar score (OR= 0.40, 95% CI; 0.21%, 0.77%, P=0.006), fetal distress (OR=0.18, 95% CI; 0.04%, 0.73%, P=0.016), and NICU admission (OR=0.26, 95% CI; 0.08%, 0.78%, P=0.016) with neonatal mortality.

Discussion

In this study, we aimed to determine the factors related to neonatal mortality at discharge among neonates admitted to a tertiary care hospital in Rasht, north of Iran. We found the significant association of fetal sex, gestational age, mode of delivery, five-minute Apgar scores, fetal distress, and NICU admission with neonatal mortality at discharge.



Table 1. Age and obstetric characteristics of mothers with preterm neonates based on outcome

Variables	Total (n=1145)				
Mother's age (y)	<35 ≥35	756(66) 389(34)	715(94.6) 367(94.3)	41(5.4) 22(5.7)	0.892
Infertility	Yes No	210(18.3) 935(81.7)	192(91.4) 890(95.2)	18(8.6) 45(4.8)	0.043
Artificial pregnancy	Yes No	131(11.4) 1014(88.6)	124(94.7) 958(94.5)	7(5.3) 56(5.5)	0.933
History of abortion	Yes No	247(21.6) 898(78.4)	232(93.9) 850(94.7)	15(6.1) 48(5.3)	0.657
History of child death	Yes ath No		73(91.2) 1009(94.7)	7(8.8) 56(5.3)	0.198
Mode of delivery	Vaginal delivery Cesarean section	251(21.9) 882(77.1)	222(88.4) 848(96.1)	29(11.6) 34(3.9)	0.001
	Missing	12(1)	-	-	
History of hypertension	Yes No	303(26.5) 842(73.5)	281(92.7) 801(95.1)	22(7.3) 41(4.9)	0.117
History of preeclampsia	Yes No	109(9.5) 1036(90.5)	97(89) 985(95.1)	12(11) 51(4.9)	0.008
History of diabetes	History of diabetes Yes		331(96.8) 751(93.5)	11(3.2) 52(6.5)	0.027
	Yes	251(21.9)	236(94)	15(6)	
History of hypothyroidism	No	893(78)	845(94.6)	48(5.4)	0.712
	Missing	1(0.1)	-	-	
History of hyperthyroidism	Yes No	6(0.5) 1139(99.5)	6(100) 1076(94.5)	0(0) 63(5.5)	0.999

^{*}Fisher's exact test

The prevalence of neonatal mortality was 5.5% in premature neonates born during the study. A retrospective study in Ethiopia found a neonatal mortality rate of 5.7% in NICU neonates [17]. Considering that the neonatal mortality rate in our study among NICU neonates was 9%, it can be said that it is higher in our study than in Ethiopia, which can be due to the difference in facilities and conditions.

We found that male neonates died more than female neonates. Haghighi et al. did not find a significant difference between the male and female neonates concerning short-term mortality rates [18]. Aghai et al. reported that under the age of 7 days, the risks of stillbirths and mortality were higher among male infants than among

female counterparts [19]. A recent systematic review suggested that few studies maintain a null association between fetal sex and neonatal mortality rate, suggesting that premature male neonates are at a higher risk of mortality after discharge than premature females [20], which should be taken into account by clinical managers in the NICU. In our study, for every one week increase in gestational age, the risk of neonatal mortality decreased. A recent study in Uganda showed that as birth weight increased, the mortality before discharge decreased [21].

We found that cesarean section reduced the risk of neonatal death; however, it may increase maternal deaths. Based on some studies, vaginal childbirth serves



Table 2. Gestational age, sex and clinical characteristics of neonates based on neonate outcome

	_	No.(%)				
Variables	Total (n=1145)	Survived (n=1082)	Died (n=63)	Р		
	≤28	83(7.2)	44(53)	39(47)		
Gestational age (week)	29-32	197(17.2)	185(93.9)	12(6.1)	0.004*	
	≥33	823(71.9)	813(98.8)	10(1.2)	0.001*	
	Missing	42(3.7)				
	Female	510(44.6)	487(95.5)	23(4.5)		
Sex	Male	607(53)	570(93.9)		37(6.1)	
	Missing	28(2.4)				
Birth weight (g)	<2500	58(5.1)	26(44.8)	32(55.2)	0.001*	
Bii tii weigiit (g)	≥2500	1087(94.9)	1056(97.1)	31(2.9)	0.001	
	<7	189(16.5)	139(73.5)	50(26.5)		
One-minute Apgar score	≥7	939(82)	927(98.7)	12(1.3)	0.001*	
	Missing	17(1.5)				
	<7	63(5.5)	28(44.4)	35(55.6)		
Five-minute Apgar score	≥7	1065(93)	1038(97.5)	27(2.5)	0.001*	
	Missing	17(1.5)				
NICU admission	Yes	212(18.5)	193(91)	19(9)	0.019*	
	No Yes	933(81.5) 37(3.2)	889(95.3) 32(85.5)	44(4.7) 5(13.5)		
Any congenital malformation	No	1108(96.8)	1050(94.8)	58(5.2)	0.048*	
	Yes	152(13.3)	137(90.1)	15(9.9)		
Fetal growth restriction	No	993(86.7)	945(95.2)	48(4.8)	0.011*	
	Yes	133(11.6)	121(91)	12(9)		
Fetal distress (according to CTG)	No	1012(88.4)	961(95)	51(5)	0.058*	
	Yes	57(5)	49(86)	8(14)		
Meconium	No	1088(95)	1033(94.9)	55(5.1)	0.01*	
	Yes	75(6.6)	67(89.3)	8(10.7)	0.05*	
Oligohydramnios	No	1070(93.4)	1015(94.9)	55(5.1)	0.06*	
	Yes	27(2.4)	24(88.9)	3(11.1)		
Polyhydramnios	No	1118(97.6)	1058(94.6)	60(5.4)	0.182*	
	Spontaneous	850(74.2)	811(95.4)	39(4.6)		
Preterm birth cause	latrogenic	214(18.7)	194(90.7)	20(9.3)	0.011*	
recenti sii tii taase	Missing	81(7.1)		-	0.011	
	-		256(22.4)			
51	Yes	278(24.3)	256(92.1)	22(7.9)	0.009*	
Electrolyte disorder	No Mississ	807(70.5)	776(96.2)	31(3.8)		
	Missing	60(5.2)				



		No.(%)				
Variables		Total (n=1145)	Survived (n=1082)	Died (n=63)	Р	
	Yes	11(1)	8(72.7)	3(27.3)		
Hyperglycemia	No	807(70.5)	776(96.2)	31(3.8)	0.009*	
	Missing	327(28.6)				
	Yes	37(3.2)	36(97.3)	1(2.7)	0.999*	
Hypoglycemia	No	807(70.5)	776(96.2)	31(3.8)		
	Missing	301(26.3)				
6 ((20)	≤7 days	26(86.7)	21(80.8)	5(19.2)	0.000	
Sepsis (out of 30)	>7 days	4(13.3)	3(75)	1(25)	0.999*	
	Yes	629(54.9)	585(93)	44(7)		
Corticosteroid prescription	No	486(42.4)	467(96.1)	19(3.9)	0.027*	
	Missing	30(2.6)				
	Yes	280(24.5)	255(91.1)	25(8.9)	0.004*``	
Magnesium sulfate prescription	No	865(75.5)	827(95.6)	38(4.4)	0.004*``	
Surfactant prescription	Yes	112(45.3)	92(82.1)	20(17.9)	0.999*	
(for neonates with RDS, n=247)	No	135(45.3)	110(81.5)	25(18.5)		
	No	86(34.8)	62(72.1)	24(27.9)		
Mechanical ventilation (for neonates with RDS, n=247)	NCPAP	130(52.6)	120(92.3)	10(7.7)	0.001**	
(12.1100110100 111011102), 11 2177	IPPV	31(12.6)	20(64.5)	11(35.5)		

Abbreviations: CTG: Cardiotocography; RDS: Respiratory distress syndrome; NCPAP: Nasal continuous positive airway pressure; IPPV: Intermittent positive-pressure ventilation. *Fisher's exact test, **Chi-square test.

As a potential risk for neonatal mortality, and cesarean section serves as a preventive strategy for reducing neonatal mortality [22, 23]. However, a systematic review showed contradictory results [19]. In our study, it can be due to the effect of the gynecologists' decision based on the probability of saving the neonate. In the study center, the risk of a cesarean section was imposed on mothers whose neonates had a higher chance of survival.

Our study demonstrated that higher five-minute Apgar score was associated with neonate survival. This finding is consistent with the findings of Cnattingius et al. [24]. Another study reported that reduced Apgar score may be better predictor of neonatal mortality in very young preterm infants than in older ones [25]. Since in the hospitals of Iran the Apgar score is calculated routinely for all newborns, those with low Apgar scores can be easily identified.

Our results indicated that neonates diagnosed with fetal distress were at higher risk of death compared to neonates without fetal distress. Hussain et al. found that more than two-thirds of patients had normal neonates with an Apgar score of 7 or more, indicating that abnormal cardiotocography alone should not be considered as an indication for cesarean section [26]. Moreover, our results showed that with admission to NICU, the chances of neonatal survival decreases. The fact that very sick neonates are admitted to the NICU can justifies this finding. However, we found that 20.8% of neonates younger than 28 weeks who received NICU care died, while the death rate for those who did not receive NICU care, was 93.3%. In the study center, not all neonates needing intensive care are admitted to the NICU due to the lack of sufficient NICU beds. Perinatal mortality possibly depends on the presence of a NICU, not on the population size or density. The number of NICU beds in Iran is below 500, far from international standards. In



Table 3. Causes of neonatal mortality based on gestational age

Cause of Death	≤28 weeks (n=87)	29-32 Weeks (n=172)	33-36 Weeks (n=394)	Total (n=653)
Total	38 (436 in 1000)	9 (52 in 1000)	4 (10 in 1000)	51 (78 in 1000)
Sepsis	4 (46 in 1000)	1 (6 in live 1000)	1 (3 in 1000)	6 (9 in 1000)
Asphyxia	4 (46 in 1000)	1 (6 in 1000)	0	5 (8 in 1000)
RDS	30 (345 in 1000)	7 (41 in 1000)	3 (8 in 1000)	40 (61 in 1000)

RDS: Respiratory distress syndrome.

addition, there is unequal distribution of NICU beds nationwide [27]. Thus, resources need to be allocated to preventing mortality in premature neonates.

The neonatal mortality rate in our study was higher in neonates with iatrogenic preterm birth than in those with spontaneous preterm birth. This outcome is against the results of Chen et al., who found no difference in mortality between the two groups [28]. This discrepancy may be due to the difference in the ages of neonates. One unexpected finding in our study was that the neonatal mortality rate in neonates of mothers with diabetes was lower than in non-diabetic mothers. However, the effect of this variable was not significant in the regression model. A recent study found that pregestational diabetes was associated with higher odds of neonatal mortality [29].

This study had some limitations. Due to the lack of time, we could not follow the condition of the neonates until 28 days. Therefore, the findings about neonatal mortality rate may not be precise. In addition, some important predictors of neonatal mortality were not explored because of missing data and lack of information. Further studies, such as prospective studies, should be

conducted to explore more maternal, neonatal, and treatment-related factors for neonatal mortality

The present study showed that the frequency of neonatal mortality at discharge among preterm neonates in the study hospital in northern Iran is considerable, indicating a long way to increase child survival rate in Iran and reduce it to a minimum of 12 per 1,000 live births. Clinicians and policymakers in Iran should give special attention to the reported risk factors. The number of NICU beds is key to ensure that all mothers and infants have reasonable access to NICU services in case of emergency. Resources need to be allocated equally to prevent mortality in premature neonates.

Ethical Considerations

Compliance with ethical guidelines

Ethics approval was obtained from the Ethics Committee of Guilan University of Medical Sciences, Rasht, Iran (Code: IR.GUMS.REC.1399.302). Written informed consent for the use of medical data was signed by the neonates' parents.

Table 4. Multivariate logistic regression analysis of factors associated with neonatal mortality at discharge

Variables	0	Standard	d P	OR	95% CI	
	β	Error			Lower Bound	Upper Bound
Fetal sex	-1.395	0.52	0.008	0.24	0.08	0.69
Gestational age	-0.054	0.10	0.001	0.57	0.47	0.71
Mode of delivery (vaginal delivery vs. cesarean section	1.255	0.61	0.042	3.50	1.04	11.78
Five-minute APGAR	-0.897	0.32	0.006	0.40	0.21	0.77
Fetal distress	-1.702	0.70	0.016	0.18	0.04	0.73
NICU admission	-1.332	0.55	0.016	0.26	0.088	0.70

OR: Odds ratio.



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Authors' contributions

Conceptualization: Ali Roshani Tabrizi and Reza Sharafi; Methodology: Seyedeh Hajar Sharami and Mandana Mansour Ghanaei; Formal analysis and investigation: Seyedeh Fatemeh Dalil Heirati and Habib Eslami-Kenarsari; Original draft preparation: Shadi Sabetghadam; Review and editing: Shadi Sabetghadam and Seyedeh Hajar Sharami; Funding acquisition: Seyedeh Hajar Sharami; Supervision: Ali Roshani Tabrizi and Seyedeh Hajar Sharami. Final approval: All authors.

Conflict of interest

The authors declared no conflict of interests.

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