



Causes, Timing, and Factors Related to Neonatal Death: A Descriptive Study

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Abstract

Background: Neonatal and pediatric health have a great share in global health programs. However, the neonatal mortality rate still shows unacceptable figures and statistics worldwide.

Objectives: To investigate the timing and causes of neonatal death.

Methods: In this retrospective descriptive study conducted in neonatal care units of Mahdijeh Hospital in Tehran, Iran, the census sampling method was used to include all the medical records of the expired neonates during 2015-2020. Neonatal and maternal demographics and health complications were recorded. Descriptive statistics such as mean, standard deviation, frequency, and associations were analyzed to compare factors recorded as causes of neonatal death and its timing. A P-value of < 0.05 was considered significant.

Results: Out of 24049 live births, 755 neonates had expired (3.1%). The expired neonates' average birth weight was 1616 ± 905 grams, and 35.9% weighed under 1000 grams. Most (80.8%) expired neonates were preterm (30.9 ± 4.8 gestational weeks), and the most common causes of neonatal death were prematurity (23.6%), congenital anomaly (19.9%), respiratory distress syndrome or RDS (19.5%), sepsis (13.2%), and asphyxia (7%). Most (60.7%) neonates died between the second and seventh days of birth.

The following conditions were associated with an early-period neonatal death rather than a later-period: multiple births (OR = 2.8), normal vaginal delivery (OR = 2.03), low-birth-weight, diabetic mothers, neonatal heart disease, neonatal neurological diseases, RDS, asphyxia, familial marriage, and intrauterine growth restriction (IUGR) ($P < 0.05$).

Being male ($P = 0.005$) or being multiple births ($P < 0.0001$) were associated with a higher risk of death.

While 57% of mothers delivered through Cesarean section, among the expired neonates, 66.9% were delivered through Cesarean section.

In expired neonates, Apgar scores were low in the first (5.71) and fifth (7.27) minutes of birth.

Conclusions: Our study showed that prematurity, congenital anomaly, RDS, sepsis, and asphyxia were the most prevalent causes of death among expired neonates, respectively. Preterm birth and low birth weight were prevalent among expired neonates.

Conducting regular similar studies periodically is important to identify, manage, and reduce neonatal mortality rates as an indicator of health promotion in the country.

Keywords: Neonate, Cause of Death, Neonatal Mortality Rate, Neonatal Death, Newborn.

1. Background

Neonatal and pediatric health have a great share in global health programs. However, the neonatal mortality rate still shows unacceptable figures and statistics

worldwide and remains a complex global challenge (1, 2). Neonatal mortality rate (NMR) is an important health indicator that includes newborns dying during the first 28 days of life. This index is expressed as the number of deaths per 1000 live births per year (3). In this regard, reducing

NMR is one of the goals of the United Nations Sustainable Development (4). Nonetheless, approximately 45% of deaths in children below five years of age occur during the neonatal period (5). As mentioned, NMR is an important indicator of societies' health, culture, and economy (6). Therefore, reducing NMR can significantly reduce mortality in children under five years, and identifying risk factors is the first step (7).

The most common causes of neonatal death based on ICD10, the 10th revision of the International Statistical Classification of Diseases and Related Health Problems, which is a medical classification list used by the World Health Organization, include respiratory distress syndrome, asphyxia, meconium aspiration syndrome, sepsis, seizures, hypoglycemia, air leakage syndrome, intravascular coagulation, pulmonary hemorrhage, cold stress, necrotizing enterocolitis, intracranial hemorrhage, kidney failure, hydrops fetalis, and kernicterus, respectively (8). It is worth noting that the rate and causes of neonatal death vary in different regions (9). In addition, the World Health Organization estimates that about 40% to 60% of neonatal deaths are preventable through low-cost interventions (10).

Naturally, preventing prenatal deaths seems more difficult than during infancy (6). Global statistics suggest a slow trend in reducing neonatal mortality (1). Investigating the causes of neonatal death can lead to improved health care and, thus, reduced neonatal mortality (10). Besides, timely identification of sick neonates and prompt and appropriate intervention to reduce mortality rates are critical (5, 11).

Despite the decreasing trend of neonatal mortality in Iran, which is currently reported at about 2% (3, 12), the risk factors associated with neonatal death in various studies in Iran are very different and sometimes inconsistent (7). Since these causes and factors may vary from region to region, designing context-based policies and planning future interventions is pivotal (1).

One rapid step towards achieving the UN Sustainable Development Goals in resource-constrained countries is identifying risk factors associated with high NMR and developing clinical and prevention programs for those at high risk (4).

2. Objectives

To reduce preventable neonatal death in our country through collecting data for evidence-based planning, this five-year study investigated the causes of neonatal death, the period that neonatal death happened, and the related factors in our referral and central neonatal hospital.

3. Methods

This retrospective descriptive study was conducted in Mahdijeh Hospital, an academic hospital affiliated with Shahid-Beheshti University of Medical Sciences in Tehran, Iran. This maternity hospital has a fertility and perinatology department, approximately 50 NICU beds at level III, and 20 post-NICU beds and has high-tech facilities and instruments for treating hospitalized neonates needing special care. Mahdijeh Hospital receives referrals from different regions and even from other cities. This department works with five neonatologists, one cardiologist, a neonatal ophthalmologist, an immunologist, and a highly-skilled paraclinical team that supports clinicians in diagnostic and management interventions.

The census sampling method was used to include all the medical records of the expired neonates from March 2015 to March 2020 in neonatal wards and neonatal intensive care units (NICUs). Out of 24049 total live births, including patient-transfers, the records of all 755 neonates were included in the study who were born alive after 22 weeks of gestational age (GA) and then died within the first 28 days of life or later due to extended health complications which had started during their neonatal life.

The form proposed by the country's Ministry of Health for recording neonatal and fetal death was used to collect data. This form consists of three parts. The first part includes neonatal demographic information such as gestational age and sex. The second part contains maternal information, including maternal conditions such as gestational diabetes, preeclampsia, etc. The third part includes the neonate's medical records, such as sepsis and congenital heart disease, and the cause of death documented in the neonatal records.

In some cases, the cause of death of the neonate was not recorded according to ICD10; thus, in categorizing the cause of death, the same data recorded in the case were used as the basis for classification. The extracted data were imported into SPSS (Version 19, IBM Corporation), and correlation or association indices such as chi-squared or odds ratio and descriptive statistics such as mean, standard deviation, and frequency were analyzed. P-values less than 0.05 were considered significant. Research ethics were observed.

4. Results

A total of 24049 neonates were hospitalized during the five-year study period, of which 755 (3.1%) died.

Data for those expired neonates showed that their average birth weight was 1616 ± 905 grams and 35.9% of them were under 1000 grams, most (80.8%) of them were preterm, and 66.9% of the expired neonates were born by Cesarean section (while in total 57% of mothers delivered through Cesarean section). In the present study 52% of total neonates and most (57.2%) of expired neonates were male ($P = 0.005$), 98.8% were Iranians (approximately 30% of neonates born in Mahdijeh Hospital were Afghan immigrants), and 97% of neonates had no birth injuries.

While only around 6% of admitted neonates were patient-transfer from other hospitals to Mahdijeh Hospital, 23.2% or 176 expired neonates were patient-transfer (not born in our hospital) and were transferred to our hospital after birth. Moreover, although 90% of total newborns were singleton, only 79.8% of the expired neonates were singleton (chi-squared = 84.3, [95% CI: 7.47% to 13.23%], $DF = 1$, $P < 0.0001$), indicating that multiple births had a higher chance of death.

Among all expired neonates, most were extremely preterm (GA 22-27 weeks) (32.9%) (Appendix 1 in the Supplementary File).

The average Apgar score of the first minute was 5.7, and their fifth-minute Apgar score was 7.3, indicating that the expired neonates had low Apgar scores. Moreover, the average number of hospitalization days was 8.40 (Appendix 2 in the Supplementary File).

The records for the neonate's cause of death showed that 54 different causes of death were recorded in the neonates' files which were matched to the closest ICD10 classifications. Prematurity had the highest prevalence (23.6%), followed by a wide range of congenital anomalies (19.9%), such as heart anomalies, various types of esophageal atresia, diaphragmatic hernias, etc. Other common causes of neonatal death included respiratory distress syndrome (RDS) (19.5%), sepsis (13.2%), and asphyxia (7%) (Table 1 and Appendix 3 in the Supplementary File). Most (60.7%) neonates died between the second and seventh days of birth. Similarly, the most common causes of death mentioned above had their highest prevalence from the second to seventh postnatal days. (Table 2).

Respiratory diseases, RDS, and sepsis were highly prevalent among expired neonates.

In some cases, the causes of death were not recorded according to ICD10. Thus, in categorizing the causes of death, the exact data documented in the neonates' records were used for classification. For instance, in some cases, cyanosis and respiratory difficulties were recorded separately, for which the percentage and frequency were registered similarly.

Of expired neonates: 80.8% were premature, 60.7% died between days two to seven of birth, 66.9% were

Table 1. Most Common Fatal Neonatal Complications Presented in Number and Percent (n = 728)

Fatal Neonatal Problem	No. (%)
IUGR	
Yes	22 (3.0)
No	706 (97.0)
Abnormal presentation	
Yes	20 (2.7)
No	708 (97.3)
Heart diseases	
Yes	264 (36.3)
No	464 (63.7)
Neurologic diseases	
Yes	168 (23.1)
No	560 (76.9)
Seizure of unknown origin	
Yes	113 (15.5)
No	615 (84.5)
Respiratory diseases	
Yes	657 (90.2)
No	71 (9.8)
Cyanosis	
Yes	42 (5.8)
No	686 (94.2)
RDS	
Yes	448 (61.5)
No	280 (38.5)
Asphyxia	
Yes	283 (38.9)
No	445 (61.1)
Diaphragmatic hernia	
Yes	42 (5.8)
No	686 (94.2)
Sepsis	
Yes	301 (41.3)
No	42 (58.7)
Anomalies	
Yes	74 (10.1)
No	654 (89.9)
NEC	
Yes	161 (22.1)
No	567 (77.9)
Metabolic diseases	
Yes	114 (15.6)
No	614 (84.4)
Other diseases	
Yes	591 (81.2)
No	137 (18.8)

Abbreviations: NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome; IUGR, intrauterine growth restriction.

Table 2. Demographic Variables Based on Time of Neonatal Death Presented as Numbers (N) and Presents (n = 755)^a

Variables and Categories	During Day 1	Day 2 to 7	Day 8 to 28	After 28 Days	Total
Gestational age					
Preterm	66 (8.7)	364 (48.2)	22 (20.2)	158 (20.7)	610 (80.8)
Term	17 (2.2)	91 (12.1)	28 (3.7)	2 (0.3)	138 (18.3)
Unknown	4 (0.5)	3 (0.4)	0 (0)	0 (0)	7 (0.9)
Method of delivery					
C/S	54 (7.1)	306 (40.5)	118 (15.7)	27 (3.6)	505 (66.9)
NVD	28 (3.7)	149 (19.8)	62 (8.2)	11 (1.6)	251 (33.1)
Sex					
Female	33 (4.4)	175 (23.2)	91 (12.1)	17 (2.2)	316 (41.9)
Male	48 (6.3)	275 (36.5)	89 (11.8)	20 (2.6)	432 (57.2)
Ambiguous genitalia	3 (0.4)	4 (0.5)	0 (0)	0 (0)	7 (0.9)
Birth weight, g					
< 1000	24 (3.2)	158 (21)	69 (9.1)	20 (2.6)	271 (35.9)
1001-1500	12 (1.6)	84 (11.1)	53 (7)	10 (1.4)	159 (21.1)
1501-2000	13 (1.8)	55 (7.3)	20 (2.6)	2 (0.3)	90 (12)
2001-2500	12 (1.6)	66 (8.7)	11 (1.5)	2 (0.3)	91 (12.1)
2501-3000	13 (1.8)	37 (4.9)	17 (2.2)	3 (0.4)	70 (9.3)
3001-3500	2 (0.3)	37 (4.9)	5 (0.7)	0 (0)	44 (5.9)
3501-4000	4 (0.5)	13 (1.8)	6 (0.8)	0 (0)	23 (3.1)
> 4001	0 (0)	4 (0.6)	0 (0)	0 (0)	4 (0.6)
Multiple births					
Yes	4 (0.6)	98 (13)	41 (5.4)	10 (1.2)	153 (20.2)
No	78 (10.3)	357 (47.3)	140 (18.5)	28 (3.7)	603 (79.8)
Iranian race					
Yes	82 (10.9)	449 (59.5)	177 (23.5)	37 (4.9)	745 (98.8)
No	0 (0)	6 (0.8)	3 (0.4)	0 (0)	9 (1.2)
Referral					
Yes	28 (3.7)	97 (12.8)	41 (5.5)	9 (1.2)	175 (23.2)
No	54 (7.1)	359 (47.5)	139 (18.4)	28 (3.7)	580 (76.8)

Abbreviations: C/S: cesarean section; NVD, normal vaginal delivery.

^a Values are expressed as No. (%).

delivered through C-section, 57.2% were male, and 35.9% weighed less than 1000 grams.

Furthermore, among the mothers of the expired neonates, the most prevalent maternal conditions included maternal diabetes (7.2%), amniotic fluid problems (6.9%, including polyhydramnios, oligohydramnios, and chorioamnionitis), and a history of infertility (5.5%) (Appendix 4 in the Supplementary File).

Neonates with the following conditions died within an earlier period: low-birth-weight classification, multiple deliveries, diabetic mothers, neonatal heart disease,

neonatal neurological diseases, RDS, asphyxia, familial marriage, and intrauterine growth restriction (IUGR) (Appendix 5 in the Supplementary File).

Although most (66.9%) of the expired neonates were delivered through Cesarean section and normal vaginal delivery did not increase neonatal deaths, the former died earlier. Hence, the results of the odds ratio calculation showed that multiple births (OR = 2.8) and normal vaginal delivery (OR = 2.03) were associated with an early-period neonatal death rather than a later-period (P-values < 0.05) (Appendix 6 in the Supplementary File).

Chi-squared test results also showed no association between postnatal age classification and period of neonatal death, type of delivery, neonate's sex, race, and referral from other hospitals.

Additionally, the results of the Spearman correlation demonstrated that the first-minute Apgar score strongly correlated with the Apgar score of the fifth minute. Lower Apgar scores at one minute and five minutes correlated with a longer duration of hospitalization ($P = 0.000$) (Appendix 7).

5. Discussion

This study investigated the causes of neonatal death and showed that more than half of the neonates died between the second and seventh day of birth. Prematurity, congenital anomaly, RDS, sepsis, and asphyxia were the prevalent causes of death. Regarding the time of neonates' death, World Health Organization's reports show that most neonatal mortality occurs within the first day and first week of life, approximately one million neonates die on the first day, and nearly one million die within six days after birth (10). A study by Tietzmann et al. demonstrated that approximately 75% of neonatal deaths occur between 0 to 6 days of birth, and 25% occur within the first 24 hours of birth (2). Contrary to the results of the present study, a study by Eshete and Abiy demonstrated that 64% of neonatal deaths occurred in the second week of life (13). Nonetheless, in a study by Faraji et al., the highest neonatal deaths occurred in the first 24 hours of birth (8). Ashrafzadeh et al. also reported that approximately a quarter of neonatal deaths occurred in the first 24 hours of birth (14). Therefore, regarding the period of death in the present study, it can be concluded that although the main cause of death was prematurity, most of the preterm neonates were alive in the first 24 hours after birth. It can be contended that the relatively better quality of perinatal care, especially the optimal care in the first hour after birth, had allowed even critically ill neonates to live longer. Additionally, questions such as "Why neonates who survived the first 24 hours of life died after 24 hours after surviving the most dangerous hours of transition to extrauterine life?" demand response through investigating more detailed evidence to determine the causes and related factors. The period of neonatal death differed from other care centers in the country, probably influenced by factors such as the number and condition of the preterm and low-birth-weight neonates, or differences between equipment and facilities among different centers, etc. In addition, this difference in neonates' mortality period indicates that the death rate may be reduced by

monitoring and controlling factors related to neonatal mortality.

In the present study, the ratio of expired neonates to all the neonates admitted to our hospital over five years was 3.1%. However, the latest statistics of the country's Ministry of Health have considered the ratio of all the expired neonates to the total number of newborn babies (including non-hospitalized babies) and have reported that the neonatal mortality rate in Iran is about 2% (3). Studies from other parts of Iran showed higher NMRs, including a study by Sabzehei et al. (15) in Hamedan City reported an NMR of 13% in the NICU, and Basiri et al.'s study reported an NMR of 18.52% in NICU (1). In a study by Wang et al. in China, 1.2% of neonates admitted to NICUs expired (16). In all these studies, including ours, the neonatal mortality rates in NICUs have been reported, which may show higher rates than the NMR in the general neonate population. However, in our study, NMR was not that high since it represented the neonates hospitalized in either NICU or the neonatal ward. Also, it may indicate that our hospital provides a successful care and treatment plan.

Our data showed that prematurity and RDS were the most prevalent factors associated with neonatal death. According to the World Health Organization, the cause of about 80% of neonatal deaths includes prematurity, low birth weight, infections, asphyxia, and birth trauma (10). Similar to our study, Alijani Ranani et al. reported that prematurity was the first cause of neonatal death (3).

But other studies identified RDS as the most common cause of neonatal death. Also, inconsistent with our results, Eshete et al. stated that sepsis and low birth weight was the first and second causes of neonatal death (1, 8, 13, 17).

In Wang et al.'s study in China, lung disease was identified as one of the two leading causes of death in neonates admitted to NICUs, with the highest number of deaths due to lung disease occurring in early infancy (16).

Hyaline membrane disease was reported by Orsido et al. as a predictor of neonatal death (18) and by Mohaddesi as the cause of increased death in NICUs (19). Sabzehei's study found a correlation between surfactant use and neonatal death (15). However, surfactant use was done due to prematurity and immaturity of the neonatal lungs (19). Therefore, it seems that the first cause of death of neonates recorded in the present study is slightly different from the first cause of death in those studies. Of course, it should be noted that RDS usually occurs in premature neonates, and these two causes of death are probably not completely separable.

Congenital anomalies were the second cause of neonatal death, where about 19.9% of neonates had congenital anomalies, including cases such as

diaphragmatic hernias and congenital heart disease of neonates. Consistent with the present study, in the study by Zile et al., a significant positive relationship was found between congenital abnormalities and neonatal mortality (20). However, the WHO does not mention congenital anomalies in the category of the most common causes of neonatal death (9). Consistent with a study by Weng et al. that showed congenital malformations were more common in male neonates than female neonates (21), our data demonstrated that most neonates who expired due to congenital anomalies were male. Also, in the Zhao et al. study, congenital anomalies were significantly higher among male twins than female twins (22). Prenatal screening for diagnosis and management of congenital anomalies may reduce mortality due to neonatal anomalies.

Our study showed that about 13.2% of neonates expired due to neonatal sepsis. The recorded diagnosis of sepsis included all cases with clinical signs of neonatal sepsis or positive blood culture. Other studies suggest that among all age groups, the highest incidence of sepsis happens during the neonatal period affecting about three million neonates worldwide (22 per 1000 live births), resulting in 11-19% mortality in neonates. A study by Wang et al. reported that infection was the leading cause of death in the late neonatal period (16). Our study showed a higher incidence of sepsis in the early neonatal period, which demands a more detailed evaluation of infection control methods and the incidence and prevalence of nosocomial infections in neonates.

Asphyxia was another cause of neonatal death in our study. It is one of the most common causes of neonatal mortality and morbidity. According to Gebregziabher et al.'s report, 15-20% of asphyxiated neonates will die in the neonatal period, and around 25% of survivors will have permanent neurological deficits (23).

Our results showed that most of the expired neonates were male. A study by Eshete and Abiy showed that most neonates hospitalized in neonatal intensive care units were male (13). Zhao et al. also pointed out that the mortality and morbidity rate among male twin neonates was higher than among female twins (22). However, studies by Alijani Ranani et al. and Barzilay et al. found no significant relationship between mortality and sex (3, 24).

Similar to the studies by Basiri et al. and Faraji et al., our results showed that Cesarean delivery was the most common delivery method among expired neonates (1, 8). However, Cesarean section was most commonly associated with preexisting prenatal or maternal problems. Moreover, Tietzmann's study showed that Cesarean section provided a better prognosis in neonates with a birth weight of under 2 kg (2). In addition,

Vilanova et al.'s study concluded that Cesarean delivery in very low birth weight neonates reduced the risk of infant death. In contrast, Cesarean section in appropriate weight neonates was considered a risk factor (25). Consequently, due to the high incidence of preterm and low-birth-weight neonates in our study, also a high incidence of maternal problems such as diabetes, preeclampsia, and a history of infertility, our high rate of Cesarean section was justified.

Similar to our results showing higher mortality among multiple births, Zhao et al. found that twin male neonates had a higher chance of dying during infancy (22). A systematic review showed that twin delivery can increase mortality in twins, especially in male neonates (25).

Similar to our results, Zile et al. noted that birth weight was an important indicator of neonates' health and survival (20). However, Mohaddesi et al. observed no significant relationship between NICU neonatal mortality and birth weight (19).

Our data demonstrated that preterm birth was among the most important factors associated with neonatal death. Globally, preterm birth is the most common cause of death in children under five (14, 26). Similar to other studies, the mean gestational age of the neonates in the present study was 30 weeks, indicating that most dead neonates were premature (3, 8). One study has proposed that reducing preterm delivery is the most influential intervention for reducing neonatal mortality (27). However, Mohaddesi et al. found no significant relationship between NICUs neonatal mortality and prematurity (19).

Consistent with other studies, as expected, the Apgar scores of the first and fifth minutes of birth among the expired neonates in our study were low (28, 29). One study concluded that reducing neonatal mortality depends on improving access to health care (30).

5.1. Study's Strengths and Weaknesses

The study's strengths included its moderately large sample size and comprehensive statistical analyses. However, since some causes of death were not precisely recorded according to ICD10 categories, we needed some clarifications during data collection. This can be considered the most prominent limitation of the study.

5.2. Conclusions

Five-year data demonstrated that 3.1% of admitted neonates expired in our hospital. Prematurity, congenital anomaly, RDS, sepsis, and asphyxia were the most common causes of death among expired neonates, respectively. Most expired neonates were male, and low birth weight was an important factor associated with neonatal death.

Multiple births were a risk factor for neonatal death, and the first- and fifth-minute Apgar scores among the expired neonates were low.

Preventing infections and thereby preventing sepsis can be a feasible approach to reducing neonatal mortality. To control and reduce neonatal mortality rates, further investigations are warranted to identify the causes of higher mortality during the second to the seventh day of birth.

Supplementary Material

Supplementary material(s) is available [here](#) [To read supplementary materials, please refer to the journal website and open PDF/HTML].

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Footnotes

Authors' Contribution: Study concept and design: M.V., and F. N.; Analysis and interpretation of data: M.V., and M.M.; Drafting of the manuscript: M.V.; Critical revision of the manuscript for important intellectual content: A.N., N.T., and M.S.; Statistical analysis: F.N, and M.M.

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