# Investigation of Prognosis and Related Factors of Premature Neonates

**Taravat Zohrehvand[1], Maryam Shokouhi Solgi[1], Mohammad Kazem Sabzehei[1], Elham Khanlarzade[2], Behnaz Basiri[1]**

[1] *Department of Pediatrics, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran*

[2] *Department of Community Medicine, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran*

***Received: 11 Jul. 2023; Accepted: 27 Dec. 2023***

**Abstract-** The birth of premature infants remains a challenge in many societies. This cross-sectional study investigates prenatal care and influential factors in preterm infants hospitalized in the Neonatal Intensive Care Unit (NICU) of Fatemieh Educational-Medical Center in Hamadan, Iran, from March 2018 to March 2019. We examined premature infants with a gestational age of less than 37 weeks who were admitted to the NICU. Data on demographic and maternal characteristics, length of hospital stay, maternal underlying diseases, probable causes of preterm birth, neonatal complications, treatment types, treatment-related complications, resuscitation needs, ventilation, and mortality rates were extracted from patient records. Among 388 preterm infants studied, 204 (52.6%) were female. The mean gestational age was 31.8±2.8 weeks, birth weight was 1647.4±625.6 grams, and average hospital stay was 10.2±9.3 days. The most common maternal underlying disease was pregnancy-induced hypertension or preeclampsia (22.2%), respiratory distress syndrome, jaundice, and low birth weight were the leading reasons for hospitalization (84%). Neonatal outcomes included 92 (23.7%) deaths, 25 (6.4%) intraventricular hemorrhages, 39 (10.1%) patent ductus arteriosus cases, 20 (5.2%) bronchopulmonary dysplasia cases, and 41 (10.6%) retinopathy of prematurity cases. Regression analysis revealed significant predictors of neonatal mortality, including male gender, maternal underlying diseases, need for cardiopulmonary resuscitation, low Apgar score at one-minute, lower birth weight, shorter gestational age, and NICU stay duration. This study underscores the high neonatal mortality rate among preterm infants. Implementing preventive measures, particularly addressing maternal underlying diseases and low birth weight, can significantly reduce neonatal mortality.



*Acta Med Iran* 2024;62(Janyary-February):40-45.

**Keywords:** Prematurity; Prognosis; Neonatal intensive care unit

## Introduction

Preterm birth, defined as delivery before 37 completed weeks of gestation, remains a significant challenge in maternal and neonatal health. Approximately 15% of newborns worldwide are born prematurely (1). While some cases have identifiable causes, others remain idiopathic (2). Premature rupture of membranes accounts for 30% of preterm births, while pregnancies that occur earlier than expected due to medical reasons contribute to 15%-20% of cases (3).

Neonatal mortality, particularly within the first 28 days of life, is closely linked to preterm birth (4). The major causes of neonatal death include infections (such as tetanus, sepsis, and pneumonia), diarrhea, prematurity, and birth-related complications (5). These factors underscore the importance of monitoring neonatal mortality rates as a fundamental indicator of community health and hygiene.

Despite advances in perinatal care and specialized neonatal units, surviving premature and low birth weight infants still face significant challenges (6). Complications associated with low birth weight, including severe disabilities, cognitive impairment, cerebral palsy, and sensory deficits, persist even as survival rates improve (7,8).

To address this critical issue, our study investigates predictors and influential factors affecting the survival rate of hospitalized premature infants in the neonatal intensive care unit at Fatemieh Hospital, Hamadan,

**Corresponding Author:** B. Basiri
Department of Pediatrics, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
Tel: +98 918 8121848, E-mail address: b.basiri@umsha.ac .ir

during the period from 2018 to 2019.

## Materials and Methods

This cross-sectional study was conducted from March 2018 to March 2019 at Fatemieh Hospital in Hamadan, western Iran. The Ethics Committee of Hamadan University of Medical Sciences approved the study with the identifier IR.UMSHA.REC.1399.608. The inclusion criteria were infants born before 37 weeks of gestation who required hospitalization. Infants with incomplete study information were excluded. The relevant parameters extracted from patients' medical records included gestational age, birth weight, gender, length of hospital stay, maternal comorbidities, reasons for preterm birth, neonatal morbidity, treatment complications, types of treatment, need for resuscitation and ventilation, antenatal and perinatal care, birthplace, birth order, multiple pregnancies, 1- and 5-minute Apgar scores, IVH (intraventricular hemorrhage), PDA (patent ductus arteriosus), BPD (bronchopulmonary dysplasia), ROP (retinopathy of prematurity), prenatal care, and mode of delivery.

**Sample size and statically analysis**

The sample size was determined based on the study by Shalini and colleagues (9), with a Type I error of 5% and using G-Power software. A total of 388 cases were selected. Data were analyzed using SPSS version 24. Descriptive statistics were used to present qualitative variables as proportions and percentages, while quantitative variables were displayed with mean and standard deviation. For comparing qualitative variables, the chi-squared test was employed. To compare quantitative variables, the t-test was used. Logistic regression (both crude and adjusted) was applied to examine the association between independent variables and the dependent variable (neonatal outcomes) at a significance level of 95%.

## Results

The demographic, maternal, and clinical characteristics of mothers and infants are presented in Table 1. Most infants were female, singleton, delivered by cesarean section, and had non-university-educated mothers. The most common reasons for neonatal hospitalization were respiratory distress syndrome, jaundice, low birth weight, and the average gestational age of infants was 31.8±8.2 weeks, ranging from 25 to 36 weeks. Further details are shown in Table 1.

**Table 1. The demographic, maternal, and clinical characteristics of mothers and infants**

| Variable | | Description |
|---|---|---|
| **Sex, n (%)** | Male | 184 (47.4) |
| | Female | 204 (52.6) |
| **Education of mothers, n (%)** | Under diploma | 149 (38.4) |
| | Diploma | 188 (48.4) |
| | Academic | 51 (13.2) |
| **Underline disease mothers, n (%)** | Non | 234 (60.3) |
| | Hypertriton or Preeclampsia | 86 (22.2) |
| | Premature rupture of membranes | 20 (5.1) |
| | Gestational diabetes | 20 (5.1) |
| | Hypothyroid | 18 (4.6) |
| | Chorioamnionitis | 10 (2.6) |
| **Cause of hospitalization of neonatal** | | 326 (84.0) |
| | | 47 (12.1) |
| | | 15 (4.9) |
| **Type of delivery** | Vaginal delivery | 106 (27.3) |
| | Cesarian section | 282(72.7) |
| **Multifetal pregnancy** | No | 314 (80.9) |
| | Yes | 74 (19.1) |
| **Gestation age(week), mean± SD, (median)** | | 31.8 ±2.8 (32.0) |
| **Duration hospitalization neonatal, mean± SD, (median)** | | 10.2 ± 9.3 (8.0) |
| **Age of mother, (yr.) mean± SD, (median)** | | 32.1 ±5.8 (30.0) |
| **APGAR Score minute one, mean± SD, (median)** | | 5.8 ±1.9 (6.0) |
| **Birth wight (gram), mean± SD, (median)** | | 1647.4±625.6 (1630) |

Out of 388 infants studied, 92 (23.7%) passed away in the hospital. The most common complications observed in the infants were retinopathy of prematurity (10.6%), patent ductus arteriosus (10%), and bronchopulmonary

dysplasia (20%). Additionally, 94 infants (24.2%) required neonatal cardiopulmonary resuscitation. Most of the infants received surfactant administration, nasal continuous positive airway pressure, and were fed with breast milk. Further details are provided in Table 2.

**Table 2. Frequency of outcomes, prematurity complications, and types of care and treatment for neonates**

| Outcome | | Frequency | Percent |
|---|---|---|---|
| **Deth before discharge** | | 92 | 23.7 |
| **Intra ventricular hemorrhage** | | 25 | 6.4 |
| **Patent ductus arteriosus** | | 39 | 10.1 |
| **Bronchopulmonary dysplasia** | | 20 | 5.1 |
| **retinopathy of prematurity** | | 41 | 10.6 |
| **Need CPR** | | 94 | 24.2 |
| **Need surfactant** | | 242 | 62.4 |
| **Nasal continuous positive airway pressure** | | 244 | 62.9 |
| **Need of transfusion blood** | | 57 | 14.7 |
| **ventilation** | **O2** | 64 | 16.5 |
| | **Non invasive** | 227 | 58.5 |
| | **invasive** | 57 | 14.7 |
| **Diet** | **Powder milk** | 136 | 35.1 |
| | **Milk** | 252 | 65.8 |
| **Corticosteroid** | **Non** | 52 | 13.4 |
| | **Yes** | 95 | 24.5 |
| | **Partial** | 77 | 19.8 |
| | **Un known** | 164 | 42.3 |

Logistic regression analysis showed that male neonates born to mothers with underlying diseases, those requiring resuscitation, those with shorter hospital stays, lower gestational age, lower birth weight, delivery mode caesarian section and fewer APGAR scores had a significantly higher risk of mortality. Based on the multivariable regression analysis, the most predictive variables for neonatal mortality were male gender, maternal underlying disease, need for neonatal cardiopulmonary resuscitation, lower gestational age, one- minute APGAR score, lower birth weight, and shorter duration of stay in the intensive care unit. The most significant predictor was the need for resuscitation, with neonates requiring resuscitation having nearly 4.5 times higher odds of mortality. These factors collectively had a 40% predictive ability for neonatal mortality (Table 3).

**Table 3. Association between risk factors (Independent variable) and neonatal outcomes (Dependent variable) using unadjusted regression and adjusted analysis**

| Variable | | Alive | Death | *P* | OR[a] (95 %CI) | *P* | OR[b] (95 %CI) |
|---|---|---|---|---|---|---|---|
| **Sex** | **Female** | 164 (55.4) | 40 (43.5) | 0.045 | 1 | 0.006 | 1 |
| | **Male** | 132(44.6) | 52(56.5) | | 1.6(1.2-1.6) | | 2.79(1.34-5.81) |
| **Delivery** | **Normally** | 92 (31.1) | 14 (15.2) | 0.003 | 1 | 0.087 | 1 |
| | **Caesarian** | 204(68.9) | 78 (84.8) | | 2.5 (1.4-3.7) | | 2.04(0.90-4.63) |
| **Underline disease** | **No** | 204 (68.9) | 30 (32.6) | 0.001 | 1 | 0.038 | 1 |
| | **Yes** | 92 (31.1) | 62 (67.4) | | 4.6(2.7-8.6) | | 1.24(1.01-1.52) |
| **Corticosteroid** | **No** | 129 (43.6) | 43(46.7) | 0.594 | 1 | - | - |
| | **Yes** | 167 (56.4) | 49 (53.3) | | 0.9 (0.1-6.4) | | - |
| **Multifetal pregnancy** | **No** | 234 (79.0) | 80 (87.0) | 0.090 | 1 | 0.936 | 1 |
| | **Yes** | 62 (21.0) | 12 (13.0) | | 0.6(0.1-3.1) | | 0.966(0.41-2.24) |
| **CRP** | **No** | 50 (16.9) | 44 (47.8) | 0.001 | 1 | 0.002 | 1 |
| | **Yes** | 264 (83.1) | 48 (52.2) | | 4.5 (2.7-7.5) | | 4.55(1.53-7.53) |
| **Gestation age(week), mean±SD,** | | 32.2 ±2.1 | 21.4±6.9 | 0.001 | 0.7(0.65-0.78) | 0.001 | 0.71(0.62-0.82) |
| **Duration hospitalization neonatal, mean±SD** | | 12.1±9.7 | 4.0 ±3.4 | 0.001 | 0.70(0.66-.78) | 0.001 | 0.78(0.71-0.86) |
| **Age of mother, (yr.) mean±SD** | | 32.6 ±2.1 | 31.6 ± 4.86 | 0.322 | 0.90(0.94-1.02) | - | - |
| **APGAR Score minute one, mean±SD** | | 6.1 ±2.6 | 4.2 ±8.5 | 0.001 | 0.71(0.63-0.80) | 0.184 | (0.68-1.07) |
| **Birth wight (germ), mean±SD** | | 1739.5±528.3 | 1350.2±801.6 | 0.001 | 0.99(0.99-0.99) | 0.064 | 0.99(0.99-1.01) |

Note: CRP: cardiopulmonary resuscitation, SD: standard devotion, OR: odds ratio, CI: confidence interval, a: crude, b: adjusted

## Discussion

Based on the findings of this cross-sectional study, 24% of infants born before 37 weeks of gestation died within the first 28 days of life before hospital discharge. Male gender, maternal underlying conditions (such as hypertension and preeclampsia), the need for neonatal cardiopulmonary resuscitation, low gestational age, Apgar score less than 5 at one-minute, low birth weight, and shorter hospital stay in the neonatal intensive care unit were significant factors associated with neonatal mortality.

One notable factor highlighted in our study was the high prevalence of maternal education level. Mothers with lower academic education may lack sufficient knowledge for proper antenatal care (10). Conversely, higher maternal education levels may correlate with better living conditions and other factors, such as improved support and care during pregnancy. However, in preterm infants, establishing specialized neonatal care units equipped with advanced facilities, experienced staff, improved intrapartum care, and access to antibiotics is essential for increasing survival rates, as demonstrated in developed countries like England (1).

One of the most significant risk factors in the present study was low gestational age. Research also indicates that with an increase in gestational, the chances of survival in newborns improve (11-12). Currently, one of the remaining challenges in the field of obstetrics and neonatology is preterm birth. Preterm birth refers to any delivery occurring after the 20th week of pregnancy and before the 37th week. The etiology of preterm birth has not yet been fully elucidated. The management of patients diagnosed with preterm birth has always been a focus due to associated complications. In a study by Basiri *et al*., (13) involving 492 infants, it was demonstrated that one of the most critical risk factors for neonatal mortality is low maternal age. In another study by Falahi *et al*., (14), most cases of neonatal mortality occurred between 31 and 28 weeks of gestation. A study conducted over a 3-year period, using data from six Asian countries, revealed that gestational age less than 34 weeks increases the risk of mortality by 3.27 times (15). Khani *et al*., (16) and Abdelrazik *et al*., (17) also identified low maternal age as one of the most significant risk factors for mortality and complications in neonates.

One of the most significant risk factors for preterm birth in the present study was maternal underlying disease, especially hypertension during pregnancy or preeclampsia, which, after adjusting for other variables, increased the risk of neonatal mortality by 1.2 times. According to the definition by the American College of Obstetricians and Gynecologists, preeclampsia is diagnosed in pregnant women who have systolic blood pressure of 140 mmHg or higher or diastolic blood pressure of 90 mmHg or higher after 20 weeks of gestation and no history of high blood pressure (18). The prevalence of this condition varies from 3% to 8% among pregnant women worldwide. Preeclampsia, along with infection and hemorrhage, constitutes one of the triads of maternal mortalities. These diseases are associated with high rates of maternal morbidity and mortality. A population-based study with a large sample size conducted by Davies and colleagues (19) reported a significant positive correlation between preeclampsia and preterm birth. Mothers with preeclampsia had a 4.4 times higher chance of giving birth prematurely. Other studies have also highlighted the association between pregnancy hypertension and neonatal complications, including preterm birth. In our current study, we lacked information on the severity and timing of preeclampsia during pregnancy (20). Some studies have shown that early and severe preeclampsia is linked to certain maternal fetal abnormalities (21). Davies and colleagues (19) found a stronger association between early-onset preeclampsia and cardiac wall disorders. Another study in Turkey demonstrated an association between chronic diseases such as diabetes, anemia, and hypertension with preterm birth, consistent with the findings of our study (22). In another study conducted in the United States, it was determined that the likelihood of preterm delivery was 8.1 times higher in mothers with hypertension during pregnancy, 1.5 times higher in cases of chronic hypertension, and 4.4 times higher in cases of malignant hypertension compared to mothers with normal blood pressure (23).

Based on our findings, the most common reason for hospitalization in neonates, accounting for approximately 85% of cases, was respiratory distress syndrome (RDS), jaundice, and low birth weight. One of the most significant causes of morbidity and mortality due to prematurity is respiratory problems, with RDS being at the forefront. Nearly 55% of infants weighing 501-1500 grams will develop RDS. RDS is characterized by clinical signs of respiratory distress along with specific radiological features in the lungs. Evidence indicates that surfactant deficiency is one of the leading causes of morbidity and mortality in preterm infants (2). The risk of this condition is inversely related to gestational age. Surfactant is naturally produced in the fetal lung tissue

during the third trimester of pregnancy, reducing alveolar surface tension, facilitating alveolar expansion, and decreasing the likelihood of collapse and atelectasis. Consistent with our findings, Basiri *et al*., (13), Faraji *et al*., (24), and Fallahi *et al*., (14) all identified respiratory distress syndrome as the primary cause of mortality in neonates.

Based on the findings of the present study, low birth weight was identified as a risk factor for preterm infants. Birth weight is one of the most important determinants of neonatal survival. In different countries, the rate of low-birth-weight infants has a direct correlation with childhood mortality rates, and the cost of healthcare for low-birth-weight infants is six times higher than that for full-term infants. Birth weight is influenced by various factors, including maternal nutrition status, birth spacing, infant gender, genetics, and prenatal care availability. These factors are interconnected, and it is challenging to pinpoint a single primary factor (25).

In this study, preterm infants were more commonly delivered via cesarean section than through natural childbirth. This difference may be attributed to fetal conditions and maternal health, especially when preterm delivery is planned. Like our study, Mohammadian et al. found that preterm infants were more frequently born via cesarean section. Therefore, understanding the factors contributing to prematurity and implementing appropriate interventions could potentially reduce the prevalence of cesarean deliveries (26).

Our study revealed expected results regarding low Apgar scores in preterm infants at both the first and fifth minutes after birth, compared to those who survived. The greater difference observed at the fifth minute may be due to supportive measures provided to preterm infants. Other studies have also reported lower Apgar scores in preterm infants compared to full-term infants and those who survived (27).

Regarding gender and the risk of preterm birth and its prediction, findings from previous studies are debatable. For instance, Falahi *et al*., (14) reported that male infants had a higher risk of mortality. In our study, out of 60 deceased infants, 40% were female, 55% were male, and 1% had ambiguous sex. Zahed Pasha's (28) study also indicated that female infants were more susceptible to low birth weight (9.6% in females vs. 5.8% in males). Similarly, Hajian *et al*., (29) found a prevalence of low birth weight in 4.54% of male infants and 7.97% of female infants.

Our findings suggest that preterm infants with longer hospital stays had a better chance of survival. This could be because severely ill infants often succumbed in the early days, while increased care in specialized units gradually improved outcomes. However, infants discharged alive from the hospital might still face complications and challenges not explored in this study.

Several limitations were observed in this study, such as the relatively small sample size, absence of long-term follow-up for the infants, the study's cross-sectional design, and incomplete patient information. These factors should be considered when interpreting the study's findings.

The findings of this study indicate a high mortality rate among preterm infants. Considering that maternal health conditions and low birth weight are among the most preventable risk factors for neonatal mortality, adequate prenatal care and postnatal care for infants can significantly reduce mortality rates .

## Acknowledgements

The present study has been approved by the Ethics Committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1399.608). The authors of the article express their gratitude to the Vice-Chancellor of Research of Hamadan University of Medical Sciences for supporting this project.

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