Iran J Public Health, Vol. 54, No.11, Nov 2025, pp.2524-2535

Original Article

Survival and Causes of Death in Infants Admitted in NICU in Iran: A Retrospective Cohort Study 2016-2022

Hosein Dalili [1], ***Mamak Shariat*** [2], ****Leyla Sahebi*** [1]

1. *Maternal-Fetal and Neonatal Research Center, Family Health Research Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*
2. *Reproductive Health Research Center, Family Health Research Institute, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran*

***Corresponding Author:** Email: sahebileila@yahoo.com

(Received 16 Jun 2025; accepted 15 Sep 2025)

Abstract

Background: We aimed to assess neonatal survival and identify predictors of mortality among infants admitted to a tertiary hospital in Iran between 2016 and 2022.

Methods: A retrospective cohort study was conducted on 7,255 neonates admitted to a tertiary hospital in Iran.

Results: Overall neonatal and preterm mortality rates were 6.6% and 9.1%, respectively, with a declining trend across various medical conditions. Multiple Cox regression analysis revealed several predictors of death as gestational age, birth weight, APGAR scores, congenital defects, sepsis, respiratory disorders, intervention treatments, and antibiotic administration history. Implications for Practice: Although survival rates have improved, neonatal mortality in Iran remains a concern. The leading causes of death—congenital anomalies, sepsis, and respiratory disorders—highlight the need for strengthened antimicrobial stewardship and infection control. Managing invasive procedures is essential to prevent hospital-acquired infections.

Conclusion: Further studies are needed to clarify the causal relationship between multiple antibiotic regimens and neonatal survival.

Keywords: Survival; Mortality; Intensive care; Neonatal; Drug therapy, Combination; Kaplan-meier estimate; Respiration disorders; Sepsis

Introduction

Despite significant advancements in neonatal care, neonatal mortality remains a major global public health concern, as documented in multiple studies (1-4).

The global burden of neonatal mortality

Globally, an estimated 2.5 million neonatal deaths occurred within the first month of life in 2022 (5). In low- and middle-income countries, nearly 60% of neonatal deaths occur within the first three days, underscoring the extreme vulnerability of newborns during the early postnatal period (6). A meta-analysis of NICUs in the Eastern Mediterranean reported mortality rates as high as 32% among very low birth weight infants (7). Previous research consistently identifies prematurity, low

birth weight, sepsis, and birth asphyxia as the leading causes of neonatal death in developing countries, accounting for over 75% of cases (2-4, 8, 9).

Iran-Specific Context

Despite improvements in neonatal care, neonatal mortality in Iranian hospitals remains around 11.4%, with 39% of deaths in the first 24 h and over 84% within the first week—highlighting newborns' critical vulnerability (10, 11).

Need for Region-Specific Neonatal Data

Neonatal mortality rates and causes vary significantly across regions and countries due to differences in medical practices, healthcare systems, outcome definitions, and study periods (3, 8, 12). These disparities limit the generalizability of international findings (1).

Most neonatal deaths are preventable, and such variation largely reflects differences in NICU care quality (3). Timely, region-specific survival data are essential for antenatal counseling, NICU management, and the revision of perinatal guidelines and policies (1).

This study aimed to assess neonatal survival and identify clinical and treatment-related predictors of mortality among neonates admitted to a tertiary NICU in Tehran between 2016 and 2022. We hypothesized that care practices and infant characteristics significantly influence survival outcomes.

Methods

Study Design and Setting

This retrospective cohort study evaluated neonatal outcomes at Valiasr Hospital's NICU, a 45-bed tertiary care facility affiliated with Tehran University of Medical Sciences, between Feb 2016 and Dec 2022. Ethical approval was obtained (IR.TUMS.IKHC.REC.1402.090).

Data on neonates and mothers were sourced from a rigorously maintained registry (by the Maternal, Fetal and Neonatal Research Center), with less than 5% missing data across key variables, enabling complete-case analysis without imputation.

Study Population and Eligibility

This survival analysis included all neonates admitted to Valiasr Hospital's tertiary NICU between Jan 2016 and Dec 2022, regardless of birth location or referral source. Neonates were excluded if core outcome data (e.g., survival status at discharge) were missing or if they were transferred to other facilities prior to discharge, due to the absence of systematic follow-up data. Infants discharged alive with complete clinical documentation were included.

The primary outcome was death during NICU hospitalization. Survival was defined as remaining alive throughout the hospital stay and being discharged either with medical advice or following clinical improvement. Time to death was measured from birth to in-hospital death. All data were extracted from the hospital's registry system.

Study Variables

The study examined both neonatal and maternal variables. Neonatal factors included sex, gestational age, birth weight, and APGAR scores (1st and 5th min), as well as clinical conditions such as respiratory disorders, congenital anomalies, gastrointestinal and metabolic disorders, and non-congenital central nervous system defects. Therapeutic interventions were categorized as non-invasive (e.g., total parenteral nutrition [TPN], phototherapy, blood transfusion, probiotics, granulocyte-colony stimulating factor [G-CSF]) and invasive (e.g., chest tube insertion, central venous line, peripherally inserted central catheter [PICC], umbilical vein catheter [UVC], gastric lavage, peritoneal dialysis, and surgery). Additional neonatal variables covered resuscitation status (CPAP, oxygen mask, positive pressure ventilation(PPV); post-intubation: epinephrine, chest compression), antibiotic use and combinations, nosocomial infection history, and admission year (2016–2022). Maternal variables included multiple gestation, prenatal care, chorioamnionitis, hypertension (preexist-

ing/gestational), diabetes (type and gestational), corticosteroid use, premature rupture of membranes, infertility history, reproductive techniques, and HIV status.

Statistical Analysis

Data were summarized as mean ± standard deviation (SD) or frequencies and proportions. Survival analysis was conducted using Kaplan–Meier curves and Cox proportional hazards regression (univariate and multiple) to estimate hazard ratios. Model assumptions were verified using Schoenfeld residuals. Statistical analyses were performed using SPSS ver. 20 (IBM Corp., Armonk, NY, USA) and STATA/MP ver. 14, with significance set at $P \leq 0.05$.

Results

The primary outcome was neonatal survival, focusing on the timing and proportion of NICU deaths. Secondary outcomes included clinical risk factors, survival trends, and treatment effects, aiming to identify mortality predictors and evaluate changes over time.

Population Characteristics

Between Feb 2016 and Dec 2022, 7,255 neonates were admitted to Valiasr Hospital's NICU. Of these, 60.1% were born prematurely (<37 wk), and 45.1% had low birth weight (<2,500 gr). Cesarean delivery accounted for 85.5% of births. Key demographic and baseline comparisons between survivors and non-survivors are detailed in Table 1.

Table 1: Baseline information of neonates admitted by outcome (survived=6773 and expired=482) in NICU at Valiasr hospital, Tehran

Variables	Cofactors(n)	survived; n(%)	expired; n(%)	*P*-value
Gender	Male(3959)	3691(93.2)	268(6.8)	0.544#
	Female(3259)	3050(93.6)	209(6.4)	
	Ambiguous genitalia(11)	7(63.6)	4(36.4)	
Mode of delivery	Vaginal delivery(1048)	979(93.4)	69(6.6)	0.912
	Cessarian section(6172)	5760(93.3)	412(6.7)	
Multiple gestation	No(6308)	5898(93.5)	410(6.5)	0.254
	Yes(948)	875(92.4)	72(7.6)	
Gestational age;weeks(w)+days(d)*	<28w(316)	162(51.3)	154(48.7)	<0.001&
	28w-31w+6d (830)	706(85.1)	124(14.9)	
	32w-36w+6d(3184)	3070(96.4)	114(3.6)	
	37w-41w+6d(2866)	2780(97.0)	86(3.0)	
	≥42w(4)	4(100.0)	0(0.0)	
Birth weight;g*	≤999(398)	208(52.3)	190(47.7)	<0.001^
	1000-1499(661)	572(86.5)	89(13.5)	
	1500-2499(2200)	2106(95.7)	94(4.3)	
	2500-3999(3751)	3650(97.3)	101(2.7)	
	≥4000(216)	210(97.2)	6(2.8)	
APGAR score at minute 1(N=6976)	mean(SD)	7.09(2.11)	3.66(2.51)	
	median(IQR)	8.0(3.0)	3.0(5.0)	<0.001
APGAR score at minute5 (n=6922)	mean(SD)	8.74(1.33)	9.0(2.0)	
	median(IQR)	6.25(2.22)	7.0(3.0)	<0.001

*Gestational age (weeks): <28 extremely preterm, 28w-31w+6d very preterm, 32w-36w+6d moderate to late preterm, 37w-41w+6d normal, ≥42 post-term. Birth weight (g): <1000 extremely low birthweight, <1000-1499 very low birthweight, 1500-2499 low birthweight,2500-3999 normal birth weight, and≥4000 high birth weight

P-value is by comparison of female and male groups,

#Groups ≥42 and 37w-41w+6d weeks has merged in analysis

^ Groups ≥4000 and 2500-3999 g has merged in analysis

Median hospitalization was 11.9 d (IQR: 16.99) for survivors and 5.0 d (IQR: 9.0) for non-survivors (Table 1). Overall neonatal mortality was 6.6% (482 deaths), rising to 9.1% in premature and 11.4% in low-birth-weight infants. Pulmonary hemorrhage, hypoplasia, and pneumothorax were leading causes of death (Table 2).

Table 2: Medical morbidities by outcome (discharge or death) in admitted neonates in NICU

Variables	Cofactos(n)	survived; n(%)	expired; n(%)	*P*-value
Respiratory disorders*	No	6385(95.3)	317(4.7)	<0.001
	Yes	385(70.0)	165(30.0)	
Metabolic system disoreders*	No	6585(93.4)	469(6.6)	0.647
	Yes	82(92.1)	7(7.9)	
Central neurvus system defects(non-congenital)*	No	5754(95.3)	291(4.8)	<0.001
	Yes	913(83.2)	185(16.8)	
Sepsis	No	3111(95.2)	235(7.0)	<0.001
	Yes	404(85.4)	69(14.6)	
Gastrointestinal disorders*	No	1361(83.2)	275(16.8)	<0.001
	Yes	5407(96.3)	206(3.7)	
Congenital conditions	No	4576(97.1)	135(2.9)	<0.001
	Yes	2091(86.0)	341(14.0)	
Troma in birth scalp	No	6738(93.4)	476(6.6)	0.075
	Yes	30(85.7)	5(14.3)	

Respiratory disorders, congenital conditions, gastrointestinal disorders, non-congenital central nervous defects, congenital metabolic system disorders, noninvasive intervention treatment (included total parenteral nutrition(TPN) , phototherapy, blood transfusion, granulocyte-colony stimulating factor(G-CSF), and probiotic nutrition), invasive intervention treatment (included chest tube, central venous (CV)-line, peripherally inserted central catheter (PICC) line, umbilical vein catheters (UVC), surgery, gastric lavage, and peritoneal dialysis), Trauma in birth scalp, antibiotic administration, resuscitation prior to intubation (use of oxygen mask, nasal continuous positive airway pressure (CPAP), and positive pressure ventilation (PPV)), and resuscitation after intubation (epinephrine injection, and chest compression

Neonatal Mortality Rates

From 2016 to 2022, 7,255 neonates were admitted to Valiasr Hospital's NICU (Fig. 1). Prematurity (60.1%) and low birth weight (45.1%) were common, with 85.5% delivered via cesarean section. Mortality was 6.6%, rising to 9.1% in premature and 11.4% in low-birth-weight infants, mainly due to pulmonary conditions.

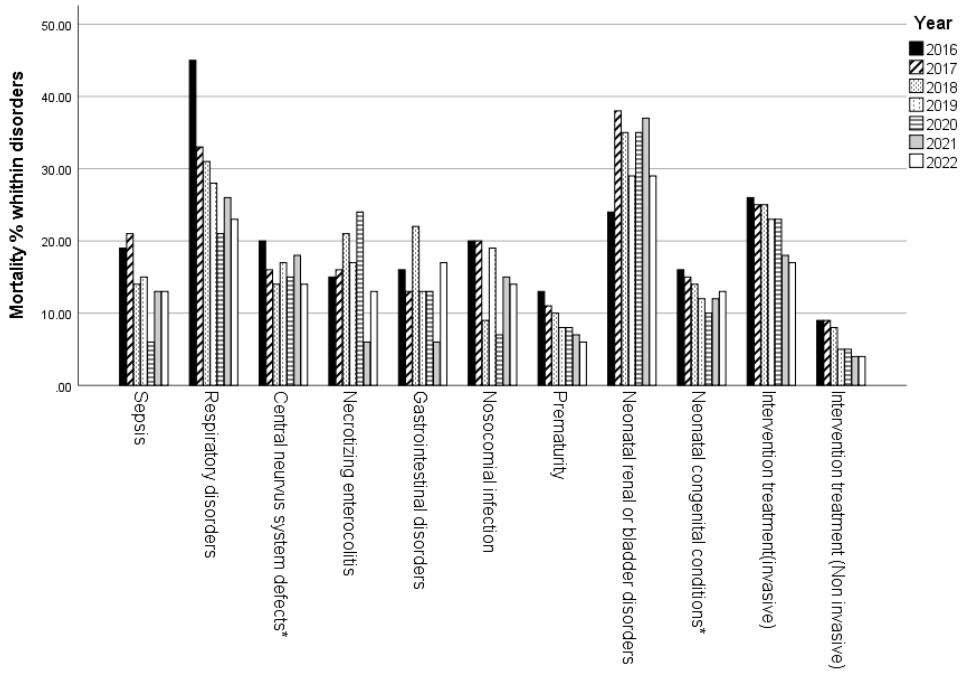

Fig. 1: Neonatal mortality proportion stratified by 2016 to 2022 in various medical morbidities

Temporal Patterns in Survival

Mean survival time was 145.0 d (SE: 4.47), and median was 184.0 d (SE: 30.17). Seventy-five percent of infants survived ≥104 d (Fig. 2). Survival time by key factors is detailed in Table 3.

Table 3: Indices of central tendency of survival time by some neonatal and maternal factors

Variables*	Cofactor	Mean(SE)	Variables	Cofactots	Mean(SE)
Neonatal respiratory disorders	No	156.82(3.39)	Intervention resuscitation(before intubation)	No	161.45(4.48)
	Yes	90.83(4.13)		Yes	135.22(6.368)
Neonatal congenital conditions	No	169.83(3.89)	Intervention resuscitation (after intubation)	No	159.36(5.4)
	Yes	125.86 (6.07)		Yes	106.7(4.79)
Neonatal gastrointestinal disorders	No	146.99(4.99)	Maternal prenatal care	No	158.64(4.93)
	Yes	130.88(8.05)		Yes	137.19(4.39)
Neonatal sepsis	No	141.78(6.52)	Maternal chorioamnionitis	No	147.71(4.49)
	Yes	129.58(6.6)		Yes	108.89(5.07)
Neonatal central neurvus system defects(noncongenital)	No	159.78(3.32)	Maternal pre-exiting blood presure	No	144.05(5.22)
	Yes	123.52(8.68)		Yes	160.63(6.05)
Neonatal metabolic system disorders	No	144.59(4.80)	Maternal gestational blood presure	No	142.98(5.06)
	Yes	140.19(8.86)		Yes	127.22(3.09)
Troma in birth scalp	No	145.25(4.49)	Pre- exiting diabetes	No	145.35(4.83)
	Yes	78.83(7.2)		Yes	151.84(13.64)
Intervention treat-	No	156.20(4.99)	Maternal gestational	No	145.44(4.5)

Table 3: Continued…

ment (non-invasive) in neonate	Yes	138.88(7.31)	diabetes	Yes	110.34(5.09)
Intervention treatment (invasive)	No	162.88(5.72)	Maternal stroid therapy	No	140.49(7.62)
	Yes	110.14(3.78)		Yes	141.27(5.18)
Hopitalization year	2016	152.0(5.53)	Maternal premature rupture of membranes	No	144.12(5.28)
	2017	110.49(5.09)		Yes	137.46(6.54)
	2018	109.85(3.38)	Type of delivery	Vaginal	118.62(10.62)
	2019	127.05(9.96)		Cesarean	149.33(3.12)
	2020	114.26(3.34)	Infertility History	No	147.58(4.54)
	2021	138.85(11.91)		Yes	105.15(5.35)
	2022	122.05(5.85)	Assisted Reproductive Technology	No	146.9(4.52)
	No	146.53(4.59)			
Mutiple gestation	Yes	109.59(4.18)	HIV	Negative	148.39(3.2)
Gender	Female	139.16(4.59)		Positive	124.42(12.01)
	Male	109.59(4.18)	Nosocomial infection in neonate	No	141.73(6.52)
LBW	No	145.24(3.09)		Yes	136.91(8.05)
	Yes	116.02(6.67)	Type of nosocomial infection	Candida	126.89(15.13)
Antibiotic administration in neonate	No	170.62(2.64)		Entrocucus	147.28(10.02)
	Yes	140.77(4.9)		Coagulase negative	98.32(4.47)
				Klebsiella Acinetobacter	109.27(16.02)

Respiratory disorders, congenital conditions, gastrointestinal disorders, non-congenital central nervous defects, congenital metabolic system disorders, noninvasive intervention treatment (included total parenteral nutrition(TPN) , phototherapy, blood transfusion, granulocyte-colony stimulating factor(G-CSF), and probiotic nutrition), invasive intervention treatment (included chest tube, central venous (CV)-line, peripherally inserted central catheter (PICC) line, umbilical vein catheters (UVC), surgery, gastric lavage, and peritoneal dialysis), Trauma in birth scalp, antibiotic administration, resuscitation prior to intubation (use of oxygen mask, nasal continuous positive airway pressure (CPAP), and positive pressure ventilation (PPV)), and resuscitation after intubation (epinephrine injection, and chest compression.

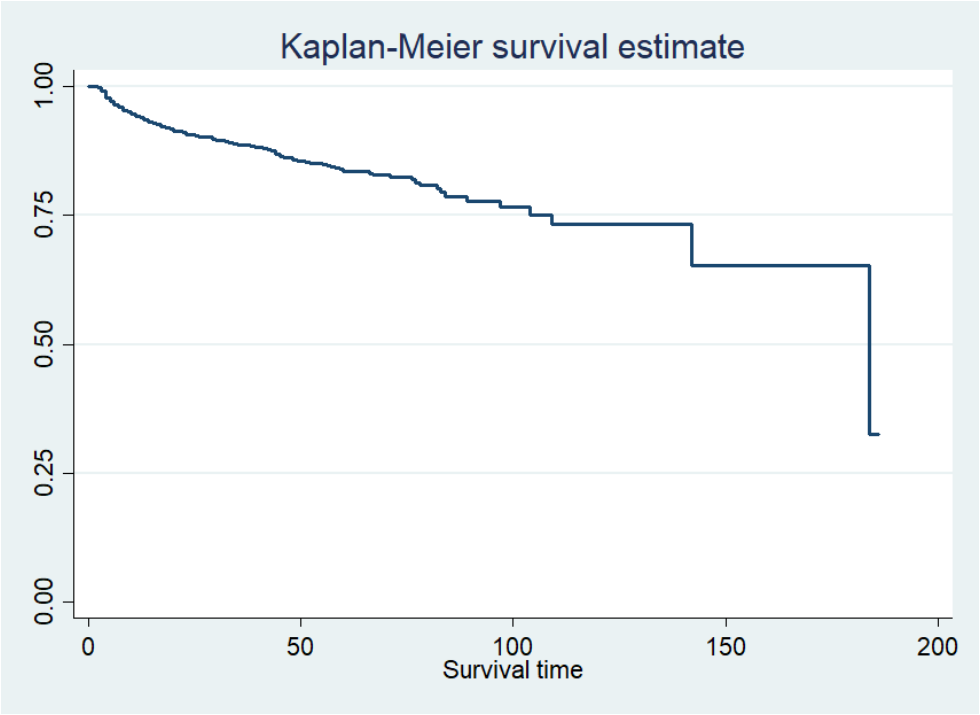

Fig. 2: Kaplan–Meier estimates of cumulative survival probability of neonates in NICU at Valiasr hospital, (in capital of Iran), from 2016 to 2022

Mortality Predictors and Risk Factors

Table 4 summarizes hazard ratios and confidence intervals. Bivariate analysis showed that lower gestational age, birth weight, height, head circumference, and APGAR scores were significantly linked to higher mortality. Although cesarean deliveries accounted for 85.5% of admissions—above global averages—they were not significantly associated with mortality, possibly reflecting national trends. Mortality risk was elevated in neonates with respiratory disorders, CNS defects, invasive procedures, resuscitation history, and antibiotic use. Noninvasive treatments and maternal gestational diabetes were protective. Greater antibiotic use correlated with higher mortality. Admissions in 2021 and 2022 had significantly lower mortality than in 2016 (HR=0.69; 95% CI: 0.48–0.98).

Table 4: crude and adjusted hazard ratio of mortality in neonates admitted to NICU

Variable		Crude analysis			Adjusted analysis		
	Cofactor	B(SE)	HR**(CI95%)	*P*-value	B(SE)	HR(CI95%)	*P*-value
Neonatal Factors							
Gender	Female	-	-	0.87	-	-	-
	Male	-	1.02(0.847,1.22)		-	-	
Height, cm		-0.085(0.005)		≤0.001	-0.052(0.015)		0.001
Head circumference, cm	-	-0.177(0.005)	-	≤0.001	0.001(0.032)	-	0.980
Weight;g	-	-0.001(0.0)	-	≤0.001	-0.01(0.001)	-	≤0.001
Gestational age; day	-	-0.028(0.002)	-	≤0.001	-0.002(0.00)	-	≤0.001
1-minute Apgar	-	-0.405(0.018)	-	≤0.001	-0.104(0.029)	-	0.038

Table 4: Continued…

score							
5-minute Apgar score	-	-.432(0.017)	-	≤0.001	-0.196(0.032)	-	0.004
Body tempra-ture;°C	-	-0.18(0.015)	-	0.234	-	-	-
Respiratory disor-ders*	No	-	-		-	-	
	Yes	-	3.91(3.21, 4.76)	≤0.001	-	1.40(1.05,1.88)	0.023
Congenital condi-tions*	No	-	-		-		
	Yes	-	3.57(2.92, 4.34)	≤0.001	-	2.03(1.51,2.70)	≤0.001
Gastrointestinal disorders*	No	-	-		-	-	-
	Yes	-	1.16(0.86, 1.56)	0.328	-	-	
Sepsis	No	-	-	0.198	-	-	
	Yes	-	1.18(0.821,153)		-	1.63(1.19,2.23)	0.002
Central nervous system de-fects(non-congenital)*	No	-	-	≤0.001	-	-	
	Yes	-	1.98(1.63, 2.39)		-	1.08(0.98,1.34)	0.145
Metabolic system disorders*	No	-	-		-	-	
	Yes	-	1.05(0.875,3.92)	0.217	-	1.05(0.97,1.61)	0.4
Troma in the birth scalp	No	-	-		-	-	
	Yes	-	1.56(0.646,3.77)	0.322	-	-	-
Intervention treat-ment (non-invasive)*	No	-	-		-	-	
	Yes	-	0.52(0.42,0.643)	≤0.001	-	0.318(0.215,0.471)	≤0.001
Intervention treat-ment (invasive)*	No	-	-		-	-	
	Yes	-	3.59(2.98,4.34)	≤0.001	-	1.79(1.34,2.39)	≤0.001
Antibiotic admin-istration	No	-	-		-	-	
	Yes	-	1.695(1.34,2.14)	≤0.001	-	0.577(0.357,0.930)	0.024
Antibiotic number		0.146(0.021)	-	≤0.001	0.107(0.37)	-	0.004
Intervention resus-citation(before intubation)	No	-	-		-	-	
	Yes	-	2.18(1.77,2.69)	≤0.001	-	1.43(0. 884,1.67)	0.242
Intervention resus-citation(after intu-bation)	No				-		
	Yes		10.08(8.26,12.3)	≤0.001	-	2.86(2.06,3.99)	≤0.001
Nosocomial infec-tion	No	-	-		-	-	-
	Yes	-	1.08(0.818,1.42)	0.588	-	-	
Hospitalization year*	2016	-	-		-	-	-
	2017	-	1.28(0.918,1.78)	0.145	-	1.14(0.77,1.66)	0.509
	2018	-	1.04(0.746,1.45)	0.814	-	0.82(0.53,1.23)	0.810
	2019	-	0.804(0.564,1.15)	0.230	-	0.597(0.436,0.867)	0.054
	2020	-	0.737(0.507,1.07)	0.111	-	0.158(0.083,0.3)	≤0.001
	2021	-	0.688(0.482,0.983)	0.04	-	0.306(0.185,0.505)	≤0.001
	2022	-	0.689(0.482,0.984)	0.04	-	0.382(0.224, 0.65)	≤0.001
Maternal Factors							
Multiple gestation	No	-	-		-	-	
	Yes	-	0.832(0.646,1.07)	0.155	-	1.62(1.149,2.28)	0.006
Prenatal care	No	-	-	0.231			-

Table 4: Continued…

	Yes	-	0.843(0.638,1.11)		-	-	
Chorioamnionitis	No	-	-	0.463	-	-	-
	Yes	-	1.265(0.676,2.37)		-	-	
hypertension	No		-	0.992	-	-	-
	Yes	-	0.998(0.66,1.51)		-	-	
Gestational blood pressure	No	-	-	0.38	-	-	-
	Yes	-	1.11(0.88,1.38)		-	-	
Diabetes Mellitus	No	-	-	0.263	-	-	-
	Yes	-	0.881(0.525,0.48)		-	-	
Gestational diabetes	No	-	-	0.022	-	-	
	Yes	-	0.74(0.573,0.975)		-	0.962(0.667,1.39)	0.836
Corticostroid therapy	No	-	-	0.691	-	-	-
	Yes	-	1.04(0.853,1.27)		-	-	
Premature reputation	No	-	-	0.716	-	-	-
	Yes	-	1.05(0.812,1.35)		-	-	
Cesarean Delivery	No	-	-	0.29	-	-	-
	Yes	-	0.87(0.673,1.13)		-	-	
Female infertility	No	-	-	0.017	-	-	
	Yes	-	1.41(1.06,1.87)		-	1.43(0.769,2.65)	0.260
Reproductive technique	No	-	-	0.151	-	-	
	Yes	-	1.28(0.915,1.78)		-	0.783(0.375,1.64)	0.514
Positive HIV in the mother	No	-	-	0.68	-	-	-
	Yes	-	1.23(0.459,3.29)			-	

* Respiratory disorders, congenital conditions, gastrointestinal disorders, non-congenital central nervous defects, congenital metabolic system disorders, noninvasive intervention treatment (included total parenteral nutrition(TPN) , phototherapy, blood transfusion, granulocyte-colony stimulating factor(G-CSF), and probiotic nutrition), invasive intervention treatment (included chest tube, central venous (CV)-line, peripherally inserted central catheter (PICC) line, umbilical vein catheters (UVC), surgery, gastric lavage, and peritoneal dialysis), Trauma in birth scalp, antibiotic administration, resuscitation prior to intubation (use of oxygen mask, nasal continuous positive airway pressure (CPAP), and positive pressure ventilation (PPV)), and resuscitation after intubation (epinephrine injection, and chest compression. ** HR: Hazard Ratio

After adjusting for confounders ($P \leq 0.2$), several factors remained significant predictors of neonatal mortality (Table 4). Significant predictors included neonatal characteristics (gestational age, birth weight, APGAR scores, height), clinical conditions (respiratory disorders, sepsis, congenital anomalies), intervention type, resuscitation history, admission year, and antibiotic use.

In adjusted models, congenital anomalies (AHR 2.20), sepsis (AHR 1.63), and respiratory disorders (AHR 1.40) showed the highest mortality risks. The hazard of death was significantly higher in neonates undergoing invasive procedures (AHR: 1.79) and those resuscitated before or after intubation (AHRs: 1.43 and 2.86, respectively). In contrast, non-invasive interventions were protective (AHR: 0.318; 95% CI: 0.215–0.471). Survival improved over time, with reduced mortality risks in 2020 (AHR: 0.158), 2021 (AHR: 0.306), and 2022 (AHR: 0.382) compared to 2016. Additionally, each unit increase in combination antibiotic use was associated with a measurable rise in mortality risk (AHR: 0.107).

Discussion

Summary of Key Findings

Neonatal mortality was 6.6% overall, rising to 24.3% in very preterm and 26.4% in very low birth weight infants. Mortality declined from over 8.5% in 2016 to under 5.5% in 2022, with sepsis-related deaths falling from 19.4% to 7.7%. Ad-

justed hazard ratios dropped from 6.3 in 2016 to 2.62 in 2022. Invasive interventions increased mortality risk 1.79-fold, while *Acinetobacter baumannii* infections had the highest fatality rate (41.7%). Cesarean delivery (85.47%) showed no impact on survival outcomes.

Comparison with Prior Studies

This study shows measurable improvement in neonatal outcomes at Valiasr Hospital's NICU, with an overall mortality rate of 6.6% and a 26.4% rate among very low birth weight (VLBW) neonates—both notably lower than previous estimates from Iranian NICUs (11.4% overall) and VLBW-specific rates reported across the Eastern Mediterranean Region (32.0%) (9, 11).

Despite a high cesarean rate (85.47%), consistent with Iran's global ranking (5th), and historical rise from 6.7% in 1990 to 60% in 2013, delivery mode showed no significant association with neonatal mortality, echoing concerns about non-standardized delivery protocols (13-18).

Temporal patterns of death aligned with regional and global data: 15.5% occurred on the first day and 64.9% within the first week, consistent with findings from Iran (2010: 39% and 84.3%) (6), Northern Ethiopia (2014: 30% and 80%) (19), and a meta-analysis spanning 2000–2022 (4). Mortality reductions in prematurity and sepsis mirror global improvements reported by Beek et al. (2021, Netherlands), particularly in conditions like necrotizing enterocolitis and respiratory distress syndrome (1).

This study highlights a 41.7% mortality rate from *Acinetobacter baumannii* infections—far higher than other nosocomial pathogens—emphasizing the urgent need for stronger NICU infection control.

Possible Explanations

Between 2016 and 2022, neonatal mortality at Valiasr Hospital's NICU fell markedly, with adjusted HR dropping from 6.3 to 2.62—especially post-2019—reflecting better care and training. Mortality from prematurity and sepsis declined, but invasive treatments remained high-risk, with a 22.3% mortality rate, rising to 41.7% for *Acinetobacter baumannii* infections. Invasive care was strongly linked to nosocomial infections (30.6% vs. 8.5%, $P<0.001$).

Two mechanisms may explain this pattern. First, many invasive interventions are administered during the final hours of life, reflecting the severity of illness in these neonates. This is supported by high rates of ventilator use (95.7%), antibiotics (76.3%), inotropes (58.1%), and sedatives (25.8%) on the final day of life (6). Second, invasive procedures significantly increase the risk of exposure to hospital-acquired pathogens, particularly multidrug-resistant organisms such as Acinetobacter baumannii, strongly associated with poor survival outcomes (20).

Conversely, noninvasive therapies—including TPN, phototherapy, transfusions, G-CSF, and probiotics—were associated with nearly a 50% reduction in mortality risk.

Risk stratification showed elevated HRs for neonates with congenital defects (2.27), sepsis (1.63), and respiratory disorders (1.4), emphasizing the need for early identification and targeted management.

Overall, while therapeutic advances and infection control played key roles, the mortality decline reflects a broader transformation in NICU care, including improved protocols, personnel training, and clinical decision-making.

Implications for Practice

The study emphasizes the importance of noninvasive NICU care, linked to lower mortality, while invasive treatments—especially those involving *Acinetobacter baumannii*—were tied to worse outcomes, highlighting the need for stricter safeguards and stronger infection control.

Antimicrobial stewardship is critical in NICU settings. While broad-spectrum antibiotic combinations are often used for coverage, they can promote resistance and increase infection risk (21-23). Mendelson et al. (24) warned against multi-drug regimens due to their role in fostering untreatable infections and higher ICU mortality. Nayeri et al. (25) further demonstrated a direct link between the number of antibiotics prescribed and nosocomial infections from *A. baumannii* and *S. epidermidis*, both strongly associated with neo-

natal death in this cohort. Neonatal mortality in Iran are declining, but we are still far from the 2030 goal of 12 or fewer newborn deaths per 1000 live births (26).

Reducing neonatal mortality requires institutional stewardship in antibiotic use and infection control, backed by training and diagnostics. National policies should standardize invasive care, refine antibiotic protocols, and boost surveillance through sustained investment in NICU capacity and data systems.

Limitations

This single-center retrospective design limits generalizability and may introduce documentation bias, affecting causal inference. Despite high registry data quality, nosocomial infections may be underreported, especially in neonates undergoing invasive procedures. Unmeasured confounders like socioeconomic status, maternal nutrition, and prenatal care could have influenced outcomes.

Future Research Recommendations

Future research should be multi-center and prospective to confirm mortality trends and long-term outcomes in neonatal sepsis and prematurity. Key priorities include assessing NICU stewardship, tackling *A. baumannii*, and building predictive models for early risk and cesarean drivers.

Conclusion

The main causes of neonatal mortality were congenital defects, sepsis, and respiratory disorders. Managing invasive treatments is essential to prevent hospital-acquired infections. There is need for more studies to determine the causal relationship between multiple antibiotic treatments and neonate survival.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Acknowledgements

We acknowledge the Maternal-Fetal and Neonatal Research Center at Tehran University of Medical Sciences and hospital registry collaborators for their data collection and supervision support.

Conflict of interest

The authors declare that there is no conflict of interests.

References

1. van Beek PE, Groenendaal F, Broeders L, et al (2021). Survival and causes of death in extremely preterm infants in the Netherlands. *Arch Dis Child Fetal Neonatal Ed,* 106 (3):251-257.
2. Gebremariam H, Tesfai B, Tewelde S, et al (2022). Demographic, Clinical Profile and Outcomes of Neonates Admitted to Neonatal Intensive Care Unit of Dekemhare Hospital, Eritrea. *BMC Pediatrics,* 22 (1):716.
3. Tolossa T, Wakuma B, Mengist B, et al (2022). Survival status and predictors of neonatal mortality among neonates admitted to Neonatal Intensive care Unit (NICU) of Wollega University referral hospital (WURH) and Nekemte Specialized hospital, Western Ethiopia: A prospective cohort study. *PLoS One,* 17 (7):e0268744.
4. Dol J, Hughes B, Bonet M, et al (2023). Timing of neonatal mortality and severe morbidity during the postnatal period: a systematic review. *JBI Evid Synth,* 21 (1):98-199.
5. Rosa-Mangeret F, Benski AC, Golaz A, et al (2022). 2.5 Million Annual Deaths-Are Neonates in Low- and Middle-Income Countries Too Small to Be Seen? A Bottom-Up Overview on Neonatal Morbi-Mortality. *Trop Med Infect Dis,* 7(5):64.
6. Sankar MJ, Natarajan CK, Das RR, et al (2016). When do newborns die? A systematic review of timing of overall and cause-specific

neonatal deaths in developing countries. *J Perinatol,* 1(Suppl 1):S1-S11.
7. Nayeri F, Emami Z, Mohammadzadeh Y, et al (2019). Mortality and Morbidity Patterns of Very Low Birth Weight Newborns in Eastern Mediterranean Region: A Meta-Analysis Study. *Journal of Pediatrics Review,* 7 (2):67-76.
8. Lawn JE, Cousens S, Zupan J (2005). 4 million neonatal deaths: when? Where? Why? *Lancet,* 365 (9462):891-900.
9. Dalili H, Shariat M, Nayeri F, et al (2019). Exclusive Breastfeeding Duration and its Effect on the Health of the Children in Iran, a Meta Analysis. *J Pediatr Nurs,* 48:e8-e14.
10. Moura H, Costa V, Rodrigues M, et al (2011). End of life in the neonatal intensive care unit. *Clinics (Sao Paulo),* 66 (9):1569-72.
11. Karimi P, Mahmudi L, Azami M, et al (2019). Mortality in Neonatal Intensive Care Units in Iran: A Systematic Review and Meta-Analysis. *Iranian Journal of Neonatology,* 10 (3):70-80.
12. Lawn JE, Kinney MV, Black RE, et al (2012). Newborn survival: a multi-country analysis of a decade of change. *Health Policy Plan,* 3:iii6-28.
13. Colomar M, Cafferata ML, Aleman A, et al (2014). Mode of childbirth in low-risk pregnancies: Nicaraguan physicians' viewpoints. *Matern Child Health J,* 18 (10):2382-92.
14. Kamal P, Dixon-Woods M, Kurinczuk JJ, et al (2005). Factors influencing repeat caesarean section: qualitative exploratory study of obstetricians' and midwives' accounts. *BJOG,* 112 (8):1054-60.
15. Yazdizadeh B, Nedjat S, Mohammad K, et al (2011). Cesarean section rate in Iran, multidimensional approaches for behavioral change of providers: a qualitative study. *BMC Health Services Research,* 11:159.
16. Bettes BA, Coleman VH, Zinberg S, et al (2007). Cesarean delivery on maternal request: obstetrician-gynecologists' knowledge, perception, and practice patterns. *Obstet Gynecol,* 109 (1):57-66.
17. Cox KJ (2011). Providers' perspectives on the vaginal birth after cesarean guidelines in Florida, United States: a qualitative study. *BMC Pregnancy Childbirth,* 11:72.
18. Sedigheh Hantoosh Z, Mamak S, et al (2024). Obstetricians' Views for Reasons Decision-Making for Cesarean Section in Iran. *Acta Medica Iranica,* doi.org/10.18502/acta.v62i3.17140.
19. Mengesha HG, Sahle BW (2017). Cause of neonatal deaths in Northern Ethiopia: a prospective cohort study. *BMC Public Health,* 17 (1):62.
20. Weinberg SE, Villedieu A, Bagdasarian N, et al (2020). Control and management of multidrug resistant Acinetobacter baumannii: A review of the evidence and proposal of novel approaches. *Infect Prev Pract,* 2 (3):100077.
21. Getabelew A, Aman M, Fantaye E, et al (2018). Prevalence of Neonatal Sepsis and Associated Factors among Neonates in Neonatal Intensive Care Unit at Selected Governmental Hospitals in Shashemene Town, Oromia Regional State, Ethiopia, 2017. *Int J Pediatr,* 2018:7801272.
22. Chen LK, Kuo SC, Chang KC, et al (2017). Clinical Antibiotic-resistant Acinetobacter baumannii Strains with Higher Susceptibility to Environmental Phages than Antibiotic-sensitive Strains. *Sci Rep,* 7 (1):6319.
23. Wang Y, Ren J, Yao Z, et al (2023). Clinical Impact and Risk Factors of Intensive Care Unit-Acquired Nosocomial Infection: A Propensity Score-Matching Study from 2018 to 2020 in a Teaching Hospital in China. *Infect Drug Resist,* 16:569-579.
24. Mendelson M, Whitelaw A, Nicol M, et al (2012). Wake up South Africa! The antibiotic 'horse' has bolted. *S Afr Med J,* 102 (7):607-8.
25. Nayeri F, Dalili H, Shariat M, et al (2023). Epidemiology of nosocomial Staphylococcus epidermidis and Acinetobacter baumannii infections in a neonatal intensive care unit. *Iran J Microbiol,* 15 (3):350-358.
26. Hug L, Alexander M, You D, Alkema L (2019). National, regional, and global levels and trends in neonatal mortality between 1990 and 2017, with scenario-based projections to 2030: a systematic analysis. *Lancet Glob Health,* 7 (6):e710-e720.