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The Iranian Neonatal Registry: Primary Results

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Abstract

Background: Neonatal registry network systems are conducted worldwide in order to improve the quality of neonatal care and also to integrate research into daily practice.

Methods: We designed a neonatal registry system and conducted a pilot study in Vali-Asr Hospital to explore its effectiveness to develop an overview of our neonatal status. This study is a report of three years of data registry (2013–2016) in above mentioned system.

Results: Data were collected from 3360 neonates admitted to level 2 of neonatal ward, and NICU (level 3) of the Vali-Asr Hospital. Among them, 184 (5.5%) neonates didn't survive. The mean ± SD of gestational age (GA) was 35.92 ± 3.352 weeks and the mean ± SD of the birth weight was 2609.23 ± 829.751 g.

Conclusion: This pilot study indicated that the neonatal registry system can help us to have a better overview of the performance of neonatal wards, and also to find new aspects of neonatal disorders.

In addition, this study showed that neonatal registry is an essential tool to improve neonatal care.

Keywords: Infant, newborn, diseases; Intensive care units, neonatal; Patient discharge summaries; Registries

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Introduction

The neonatal mortality rate is 19 deaths per 1000 live births worldwide. In Iran, this rate was 9.6 deaths per 1000 live births in 2016, and reveals the fact that 12731 neonates died in 2016, in Iran. Clearly, progress towards reducing mortality rate has not been satisfactory in our country.[1]

Studies have shown that neonatal registry network systems can provide the necessary data for establishing evidence-based strategies to decrease the complications in high-risk neonates and consequently reduce neonatal mortality rate.[2]

In 2011, Iranian Ministry of Health and Medical Education proposed that the Maternal, Fetal, and Neonatal Research Center should establish a neonatal registry network system to increase awareness and extend knowledge on neonatal health as well as to improve neonatal care in Iran.[3]

This study represents a report of three-year data registry (2013–2016) in above mentioned system.

Materials and Methods

Vali-Asr hospital launched the Iranian Registry System (NRVH) in March 2013 with the aim of collecting data of all neonates admitted to the neonatal ward and neonatal intensive care unit (NICU) in Vali-Asr hospital, one of the teaching hospitals affiliated to Tehran University of Medical Sciences.

Vali-Asr hospital's neonatal ward and NICU has a total of 85 beds available: 32 beds for healthy neonates (level 1), 15 beds for moderately ill neonates (level 2), and 38 beds for neonates who need intensive medical care (level 3).

Case Definition

This registry includes newborns who are admitted to level 2 and 3 of neonatal care and excludes the ones who are admitted to level 2 of care but only for the sake of being observed and do not suffer any clinical and/or para-clinical abnormalities; these neonates are usually born to high risk mothers like preeclamptic mothers or mothers with immune thrombocytopenic purpura (ITP), etc.

Design

In order to design this database, about 10 focus group discussion sessions were conducted with the participation of neonatologists from Vali-Asr hospital and the representatives of the Iranian Ministry of Health and Medical Education. The database in this registry system includes neonatal demographics, diagnosis (the neonatal

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disease coded according to the ICD-10[4]), some laboratory tests, and medical interventions.

ZIGOTEC Co. designed a software program based on this database with SPSS output.

Registry Process

In order to increase the accuracy of data collection, a multiple-choice patient summary sheet (patient discharge data) was designed based on the database required information. The patient summary sheets were completed by pediatric residents; the integrity of which was then checked by an expert registrar on a daily basis by entering data into the software.

Statistical Analysis

We used the $\chi 2$ test and binary logistic regression analysis. Variables were entered in a regression model, based on an expert opinion. *P* values less than 0.05 were considered significant. Data were analyzed using SPSS version 22.

Results

Baseline Characteristics of Neonates

During 3 years of data registry, we collected the data of 3360 neonates admitted to level 2 and level 3 of Vali-Asr hospital. Since a large number of neonates had more than one condition, 5876 diseases or conditions were diagnosed among 3360 neonates. Among them, 184 (5.5%) neonates did not survive. The mean ± SD of the gestational age (GA) was 35.92 ± 3.352 weeks and the mean ± SD of the birth weight was 2609.23 ± 829.751 g. Moreover, 45.5% (1495) of the neonates were girls, 54.3% (1784) were boys, and 0.2% (5) had ambiguous genitalia. The rate of preterm birth (GA < 37 weeks) was 46.6% (1573). The distribution of the neonates based on gestational age and birth weight is shown in Table 1.

Death Pattern

The mortality rate based on birth weight and gestational age is shown in Table 1.

Table 2 presents the association between death and different neonatal characteristics using odds ratio (OR) and 95% CI.

Disease Pattern

According to the results of the present study, 62.2% (2091) of the neonates suffered from gastrointestinal disorders, 25.3% (850) from respiratory disorders, 18.3% (616) from cardiovascular disorders, 18.2% (613) from infectious diseases, 31% (1044) from congenital malformations (except patent ductus arteriosus [PDA] and hydrocephaly), 13.7% (459) from hematological disorders, 11.7% (392) from neuromuscular disorders, 4.6% (155) from urogenital disorders, 2.7% (92) from endocrinopathies, and finally 0.9% (30) from birth trauma.

Gastrointestinal Disorders

Icterus comprised 91% of gastrointestinal disorders. About 59.6% (2004) of all admitted neonates were icteric, and 23.9% (478) of these icteric neonates were term (GA ≥ 37) with no comorbidity. Moreover, 58.2% (1040) of the term neonates and 61.3% (964) of the preterm neonates were icteric.

According to Table 2, icterus and phototherapy had reverse association with death rate. Icterus can be a presentation of many other diseases in neonates. By excluding the icterus with other comorbidities, no correlation was found between icterus and neonatal death.

The rate of GI bleeding was 1.8% (62) and the prevalence of necrotizing enterocolitis (NEC) (including stages 2 and 3 NEC based on Bell Staging Criteria) was 1.4% (46) in the neonates of the present study. NEC distribution based on birth weight and gestational age is shown in Table 1. NEC affected 6% (26) of the neonates with birth weight <1500 g, and 9.4% (12) of the neonates with birth weight <1000 g. The mortality rate of neonates with NEC was 17.4%.

Table 1. The Distribution of Neonates and Their Disorders Based on Birth Weight and Gestational Age

	Total No. (%)	Death No. (%)	NEC No. (%)	RDS No. (%)	Apnea No. (%)	Sepsis No. (%)	PDA No. (%)	IVH No. (%)
Birth weight (g)								
<1000	127 (3.9)	58 (31.5)	12 (26.1)	91 (19.2)	36 (18.2)	37 (9.3)	49 (11.9)	34 (23.4)
1000–1500	240 (7.3)	23 (12.5)	14 (30.4)	118 (24.9)	38 (19.2)	46 (11.6)	74 (18)	47 (32.4)
1500–2500	976 (29.8)	46 (23.6)	14 (30.4)	178 (38.5)	63 (32.5)	138 (35.7)	130 (32.5)	44 (31.2)
≥2500	1927 (58.9)	47 (25.5)	5 (10.9)	73 (15.4)	57 (28.8)	165 (41.6)	146 (35.5)	16 (11)
Gestational age (wk)								
<28	85 (2.6)	45 (24.5)	8 (17.4)	68 (14.4)	27 (13.6)	27 (6.8)	29 (7.1)	24 (16.6)
28–32	279 (8.5)	46 (25)	15 (32.6)	157 (33.2)	54 (27.3)	60 (15.1)	98 (23.8)	65 (44.8)
32–34	300 (9.1)	13 (7.1)	10 (21.7)	94 (19.9)	26 (13.1)	47 (11.8)	55 (13.4)	23 (15.9)
34–37	897 (27.2)	27 (14.7)	7 (15.2)	113 (23.9)	40 (20.2)	108 (27.2)	94 (22.9)	14 (9.7)
≥ 37	1734 (52.6)	52 (28.3)	4 (8.7)	37 (7.8)	51 (25.8)	147 (37)	128 (31.1)	19 (13.1)

Abbreviations: NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome; PDA, patent ductus arteriosus; IVH, Intraventricular Hemorrhage.

Table 2. The Association Between Death and Different Neonatal Characteristics[a]

Characteristics	With[c] No. (%)	Without No. (%)	Unadjusted OR (95% CI)	Adjusted OR[d] (95% CI)
GA <28 weeks	45 (52.9)	139 (4.2)[b]	25.38 (16.04–40.14)	9.23 (2.5–34.09)
GA: 28-32 weeks	46 (16.5)	138 (4.5)[b]	4.21 (2.93–6.03)	3.54 (1.19–10.45)
Hypotonia	12 (11.2)	172 (5.3)[b]	2.26 (1.21–4.2)	3.23 (1.29–8.09)
Pneumothorax	50 (56.8)	134 (4.1)[b]	30.81 (19.53-48.6)	5.27 (2.16–12.85)
Apnea	47 (23.7)	137 (4.3)[b]	6.87 (4.75–9.94)	2.04 (1.11–3.76)
Pulmonary hemorrhage	45 (84.9)	139 (4.2)[b]	128.2 (59.3–277.15)	33.79 (10.59–107.81)
Diaphragmatic hernia	18 (52.9)	166 (5)[b]	21.41 (10.72–42.75)	12.66 (4.51–35.56)
Anemia	37 (13.2)	147 (4.8)[b]	3.02 (2.06–4.43)	0.41 (0.19–0.89)
Icter	58 (2.9)	126 (9.3)[b]	0.29 (0.21–0.4)	0.4 (0.18–0.89)
DIC	31 (79.5)	153 (4.6)[b]	80.23 (36.26-177.49)	13.94 (4.08-47.54)
Asphyxia	26 (28.6)	158 (4.8)[b]	7.87 (4.86–12.75)	4.7 (2.03–10.87)
Intraventricular hemorrhage (IVH)	43 (29.7)	141 (4.4)[b]	9.19 (6.19–13.63)	2.07 (1.01–4.23)
Mechanical ventilation	111 (35.1)	73 (2.4)[b]	22.03 (15.88-30.57)	3.55 (2–6.3)
Phototherapy	59 (3.1)	125 (8.8)[b]	0.32 (0.23–0.45)	0.43 (0.2–0.94)
Intravenous Immunoglobulin (IVIG)	13 (11.5)	171 (5.3)[b]	2.33 (1.28–4.25)	0.08 (0.18-0.41)
Blood Transfusion	111 (21.2)	73 (2.6)[b]	10.20 (7.46–13.94)	3.5 (1.93–6.36)
Pneumonia	17 (12.5)	168 (5.2)[b]	2.61 (1.53–4.45)	0.28 (0.1–0.8)
Congenital malformations of heart (except PDA)	35 (11.5)	149 (4.9)[b]	2.52 (1.71–3.72)	2.5 (1.33–4.69)
Chromosomal syndromes	14 (28)	170 (5.1)[b]	7.18 (3.8–13.57)	11.55 (4.96–26.89)

[a] Variables entered in model: Sex, weight <1000 grams, weight: 1000–1500 grams, weight: 1500–2500 grams, weight ≥2500 grams, GA <28 weeks, GA= 28–32 weeks, GA = 32–34 weeks, GA = 34–37 weeks, GA ≥ 37 weeks, hydrocephaly, seizure, hypotonia, respiratory distress syndrome, apnea, pneumothorax, pulmonary hypertension, pulmonary hemorrhage, diaphragmatic hernia, PDA, neutropenia, thrombocytopenia, anemia, DIC, NEC, GI Bleeding, icter, asphyxia, total parenteral nutrition, blood exchange, phototherapy, chest tube, mechanical ventilation, surfactant injection, antibiotic therapy, GCSF, IVIG, blood transfusion, sepsis, pneumonia, hypoxic ischemic encephalopathy, IVH, neural tube defect, congenital malformations of nervous system (except hydrocephaly and NTD), congenital malformations of heart (except PDA), chromosomal syndromes.
[b] $P < 0.05$; [c] Case-Fatality; [d] ORs calculated from a regression model including all variables.

Respiratory Disorders

Respiratory distress syndrome (RDS) was the most common respiratory disorder in our hospital. About 14% (473) of our neonates suffered from this disorder. The mortality rate of RDS was 17.5% (83). Nearly 61% (288) of neonates with RDS received at least one dose of surfactant injection. About 87% (412) of these infants received antibiotics, and 37.8% (179) of them underwent mechanical ventilation, 25.1% (45) of whom developed a pneumothorax at a later time. A chest tube was inserted in 55.8% (29) of the newborns who developed a pneumothorax.

Table 3 presents the association of RDS with different neonatal characteristics using OR and 95% CI.

Neonatal apnea was the second most common respiratory disorder in our hospital with a prevalence of 5.9% (198). The mortality rate of the neonates with apnea was 23.7% (Table 2). The prevalence of apnea in the neonates with gestational age less than 28 weeks was 31.8% (27). The prevalence of neonatal apnea based on birth weight and gestational age is shown in Table 1.

It should be noted that only 9.4% (316) of our neonates were intubated and underwent mechanical ventilation. The mortality rate of neonates undergoing mechanical ventilation was 35.1% (111).

Infectious Diseases

Neonatal sepsis (suspected sepsis including both early-onset and late-onset) was the most common presentation of infectious diseases (11.8% [397]). Table 1 shows the distribution of sepsis based on gestational age and birth weight. 61.7% (245) of the neonates with sepsis were preterm and 38.3% (152) were term. About 12% (48) of the neonates died due to sepsis. This rate was 15.9% (n = 39) in preterm vs. 5.9% (n = 9) in term neonates. Moreover, 13.1% (52) of the neonates with sepsis had no comorbidities and none of them died. The most common comorbidities among septic neonates were gastrointestinal (71.3% [246]) and respiratory (40.6% [140]) disorders.

Table 4 illustrates the association between sepsis and different neonatal characteristics using OR and 95% CI.

Congenital Malformations and PDA

Congenital malformations included items based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10).

Cardiovascular congenital diseases (CHD), excluding PDA, were the most common congenital malformations. The most prevalent coexisting congenital malformation in neonates with CHD (10.3% [51]) was congenital malformations of the nervous system.

PDA was present in 12.2% (411) of the neonates. The distribution of PDA based on neonatal weight and gestational age is shown in Table 1.

Table 5 shows the association between PDA and different neonatal characteristics using OR and 95% CI.

Table 3. The Association Between RDS and Different Neonatal Characteristics[a]

Characteristics	With No. (%)	Without No. (%)	Unadjusted OR (95% CI)	Adjusted OR[d] (95% CI)
Sex				
Male & other[b]	278 (14.9)	195 (13)[c]	1.02 (0.99–1.05)	1.4 (1.04–1.88)
Female	195 (13)	278 (14.9)[c]	0.93 (0.69–1.26)	0.71 (0.53–0.96)
GA<28 weeks	68 (80)	405 (12.4)[c]	28.34 (16.49–48.71)	2.67 (1.08–6.59)
GA: 28-32 weeks	157 (56.3)	316 (10.3)[c]	11.26 (8.65–14.65)	2 (1.18–3.38)
GA ≥ 37 weeks	37 (2.1)	436 (26.8)[c]	0.06 (0.04–0.08)	0.2 (0.11–0.35)
PDA	153 (37.2)	320 (10.9)[c]	4.87 (3.86–6.14)	1.52 (1.03–2.25)
Mechanical ventilation	179 (56.6)	294 (9.7)[c]	12.22 (9.49–15.73)	1.74 (1.08–2.81)
Surfactant injection	288 (82.3)	185 (6.1)[c]	70.93 (51.91–96.91)	24.74 (16.61–36.85)
Antibiotic therapy	412 (20.9)	61 (4.4)[c]	5.78 (4.37–7.64)	2.19 (1.48–3.24)
Blood exchange	2 (5.9)	471 (14.2)	0.37 (0.09–1.58)	0.02 (0.002–0.171)
Hypocalcemia	70 (11.4)	403 (14.7)[c]	0.75 (0.57–0.98)	0.64 (0.43–0.94)

[a] Variables entered in model: Sex, weight <1000 grams, weight = 1000–1500 grams, weight = 1500–2500 grams, weight ≥2500 grams, GA<28 weeks, GA = 28–32 weeks, GA = 34–37 weeks, GA ≥ 37 weeks, hydrocephaly, seizure, apnea, pneumothorax, pulmonary hypertension, pulmonary hemorrhage, diaphragmatic hernia, chronic lung disease, PDA, neutropenia, thrombocytopenia, anemia, DIC, NEC, hypothyroidism, asphyxia, total parenteral nutrition, chest tube, mechanical ventilation, surfactant injection, antibiotic therapy, GCSF, IVIG, blood transfusion, sepsis, meningitis, pneumonia, blood exchange, phototherapy, hypocalcemia, intraventricular hemorrhage, chromosomal syndromes.
[b] 5 neonates had ambiguous genitalia; [c] $P < 0.05$; [d] ORs calculated from a regression model including all variables.

Table 4. The Association Between Sepsis and Different Neonatal Characteristics[a]

Characteristics	With No. (%)	Without No. (%)	Unadjusted OR (95% CI)	Adjusted OR[c] (95% CI)
Seizure	43 (30.9)	354 (11)[b]	3.69 (2.49–5.28)	2.24 (1.45–3.48)
Anemia	53 (18.9)	344 (11.2)[b]	1.84 (1.34–2.54)	0.52 (0.33–0.82)
Surfactant injection	69 (19.7)	328 (10.9)[b]	2 (1.5–2.67)	0.56 (0.35–0.9)
Antibiotic therapy	370 (18.8)	27 (1.9)[b]	11.72 (7.87–17.44)	9.14 (6.06–13.79)
Transfusion	130 (24.9)	267 (9.4)[b]	3.18 (2.51–4.02)	1.65 (1.14–2.39)
NEC	16 (34.8)	381 (11.5)[b]	4.1 (2.21–7.6)	2.1 (1.05–4.2)
Meningitis	9 (69.2)	388 (11.6)[b]	17.15 (5.25–55.98)	5.93 (1.62–21.74)
Intraventricular hemorrhage	48 (33.1)	349 (10.9)[b]	4.06 (2.82–5.84)	1.66 (1.06–2.59)

[a] Variables entered in model: Sex, weight <1000 grams, weight = 1000–1500 grams, weight = 1500–2500 grams, weight ≥ 2500 grams, GA < 28 weeks, GA = 28–32 weeks, GA = 32–34 weeks, GA ≥ 37 weeks, seizure, respiratory distress syndrome, pneumothorax, pulmonary hypertension, pulmonary hemorrhage, PDA, neutropenia, thrombocytopenia, anemia, DIC, NEC, hypothyroidism, asphyxia, meningitis, total parenteral nutrition, chest tube, mechanical ventilation, surfactant injection, antibiotic therapy, GCSF, IVIG, transfusion, pneumonia, intraventricular hemorrhage.
[b] $P < 0.05$; [c] ORs calculated from a regression model including all variables.

Table 5. The Association Between PDA and Different Neonatal Characteristics

Characteristics	With No. (%)	Without No. (%)	Unadjusted OR (95% CI)	Adjusted OR[c] (95% CI)
Respiratory distress syndrome	153 (32.3)	258 (8.9)[b]	4.87 (3.86–6.13)	1.57 (1.08–2.29)
Pulmonary hypertension	24 (5.8)	387 (11.7)[b]	7.25 (4.1–12.82)	3.1 (1.52–6.3)
Chromosomal syndrome	14 (28)	397 (12)[b]	2.85 (1.52-5.33)	2.75 (1.32–5.73)
Surfactant injection	132 (37.7)	279 (9.3)[b]	5.92 (4.62–7.6)	1.64 (1.09–2.46)
Antibiotic therapy	321 (16.3)	90 (6.5)[b]	2.82 (2.21–3.6)	1.53 (1.15–2.05)
Transfusion	173 (33.1)	238 (8.4)[b]	5.39 (4.3–6.76)	2.01 (1.4–2.88)
Intraventricular Hemorrhage	62 (42.8)	349 (10.9)[b]	6.13 (4.33-8.68)	1.75 (1.13–2.72)

[a] Variables entered in model: Sex, weight <1000 grams, weight: 1000–1500 grams, weight: 1500–2500 grams, weight ≥2500 grams, GA<28 weeks, GA = 28–32 weeks, GA = 32–34 weeks, GA = 34–37 weeks, GA ≥ 37 weeks, hydrocephaly, seizure, respiratory distress syndrome, pneumothorax, pulmonary hypertension, pulmonary hemorrhage, pulmonary hypoplasia, chronic lung disease, neutropenia, thrombocytopenia, anemia, DIC, NEC, GI bleeding, hypothyroidism, asphyxia, sepsis, meningitis, pneumonia, intraventricular hemorrhage, hypoxic ischemic encephalopathy, congenital malformations of nervous system(except hydrocephaly and NTD), chromosomal syndrome, total parenteral nutrition, blood exchange, chest tube, mechanical ventilation, surfactant injection, antibiotic therapy, GCSF, IVIG, blood transfusion.
[b] $P < 0.05$; [c] ORs calculated from a regression model including all variables.

Neuromuscular Disorders

Intraventricular hemorrhage (IVH) was the most common neuromuscular disorder in our neonates. It was seen in 145 (4.3%) neonates of all admitted ones, and in 81 (22.1%) neonates with birth weight <1500 g. Table 1 shows the distribution of IVH based on gestational age and birth weight.

Table 6 presents the association between IVH and different neonatal characteristics using OR and 95% CI.

Discussion

As mentioned earlier, neonatal registry network systems

Table 6. The Association Between IVH and Different Neonatal Characteristics[a]

Characteristics	Yes No. (%)	No No. (%)	Unadjusted OR (95% CI)	Adjusted OR[c] (95% CI)
Birth weight <2500 g	125 (9.3)	20 (1)[b]	10.31 (6.40–16.63)	3.49 (1.84–6.6)
Hydrocephaly	15 (28.8)	130 (3.9)[b]	9.91 (5.30–18.51)	5.63 (2.07–15.27)
Seizure	26 (18.7)	119 (3.7)[b]	5.99 (3.77–9.53)	2.06 (1.06–4.01)
Pneumothorax	27 (3.7)	118 (3.6)[b]	11.83 (7.25–19.29)	2.86 (1.25–6.53)
PDA	62 (15.1)	83 (2.8)[b]	6.13 (4.33–8.64)	2.03 (1.28–3.24)
Transfusion	94 (18)	51 (1.8)[b]	11.97 (8.38–17.08)	3.09 (1.89–5.05)
Sepsis	48 (12.1)	97 (3.3)[b]	4.08 (2.84–5.87)	1.72 (1.09–2.7)
Hypoxic ischemic encephalopathy	7 (31.8)	138 (4.1)[b]	10.86 (4.36–27.08)	6.04 (1.78–20.46)
Congenital malformations of nervous system (except hydrocephaly and NTD)	15 (20.3)	130 (4)[b]	6.19 (3.42–11.22)	4.14 (2.02–8.47)
Congenital malformations of heart (except PDA)	25 (8.2)	120 (3.9)*	2.19 (1.40–3.43)	2.03 (1.16–3.54)

[a] Variables entered in model = weight <2500 grams, GA<37 weeks, hydrocephaly, seizure, respiratory distress syndrome, pneumothorax, pulmonary hypertension, pulmonary hemorrhage, chronic lung disease, PDA, neutropenia, thrombocytopenia, anemia, DIC, hypothyroidism, asphyxia, sepsis, meningitis, pneumonia, hypox-ic ischemic encephalopathy, congenital malformations of nervous system(except hydrocephaly and NTD), congenital malformations of heart (except PDA),blood exchange, chest tube, mechanical ventilation, antibiotic therapy, GCSF, IVIG, blood transfusion.
[b] $P < 0.05$; [c] ORs calculated from a regression model including all variables.

are conducted worldwide in order to improve the quality of neonatal care and also to integrate research into daily practice. Therefore, we conducted a neonatal registry system in our country, and gathered and analyzed the data of 3360 neonates who were admitted to neonatal ward (level 2) and NICU (level 3) of Vali-Asr hospital between 2013 and 2016.

Similar studies have shown that prematurity is the leading cause of neonatal death worldwide.[5]

In the previous study conducted in our hospital during March 2012 and September 2013, the mortality rate in neonates with birth weight ≤1000 g was estimated 46%.[6] In another study in our hospital between 2001 and 2004,[7] the mortality rate was 46.8% in neonates with birth weight ≤1000 g and 33% in neonates with birth weight ≤1500 g. In the current study, these rates decreased to 44.5% and 21.8%, respectively.

Based on a binary logistic regression model, anemia, pneumonia, and IVIG administration had reverse associations with neonatal death. On the other hand, there is some evidence that introduces these items as risk factors of neonatal death (except IVIG),[8,9] while considering them in a model can produce different results. A possible interpretation is that these items may act as interactive risk factors of neonatal death. Statistically, this phenomenon is explained by Simpson's paradox.[10,11] Detecting these interactions requires nested case-control studies with narrow inclusion and exclusion criteria.

In accordance with other studies,[12,13] we found that gastrointestinal disorders and among them icterus, is the most common disorder in our neonates and the phototherapy is a protective intervention against neonatal death. GI bleeding is a rare disorder in neonates and its burden is not well defined in children.[14] A case control study with a sample size of 5180 neonates found that 1.23% (64) of the neonates suffered from upper GI bleeding,[15] this rate is comparable with the results of our study (1.8%).

Our results were consistent with other studies which showed that NEC generally affects about 5% of the neonates with birth weight <1500 g and about 10% of the neonates with birth weight <1000 g, and the overall mortality rate of this disorder is between 10 to 30%.[16,17] A systematic review reported the rate of NEC in high income countries from 2% to 7% in neonates with birth weight <1500 g and 5% to 22% in neonates with a birth weight <1000 g.[18]

Respiratory disorders were the second most common disorders among our neonates, and among them RDS was the most common. RDS mortality rate in our hospital (17.5%) is comparable with the Chinese northwest NICU network (20.1%).[19] But surfactant injection rate in neonates with RDS (60.9%) was higher in our hospital than Chinese NICUs (33.8%).[19] Being term (GA ≥ 37 weeks), blood exchange, and also hypocalcemia had reverse associations with RDS. Hsu and Chen[20] found an association between hypercalcemia and acute respiratory syndrome in adults; but in neonates RDS usually associated with hypocalcemia.[21,22] Calcium can improve the surfactants activity,[23] therefore it seems that calcium gluconate administration in our hypocalcemic neonates could result in protective effect of hypocalcemia against RDS in this study. Further studies should be done in order to clarify the exact effect of calcium levels on RDS management.

Evidence has shown that bilirubin has an inhibitory effect on the surfactants function,[24,25] which may be an explanation for the protective effect of blood exchange against RDS.

According to the literature, the incidence of neonatal apnea is 7%, 15%, and 54% in neonates 34–35 weeks GA, 32–34 weeks GA, and 30–31 weeks GA, respectively.

Neonatal apnea is present in nearly all neonates with gestational age <30 weeks or with a birth weight <1000 g.[26] Nowadays, preventive interventions such as caffeine administration in premature neonates have reduced the incidence of neonatal apnea.[27] The lower rate of neonatal apnea in our neonates (5.9%) may be due to these preventive measures or underestimation of this disorder. Therefore further studies should be done to find out the exact reason for this finding.

The number of mechanically ventilated neonates in our hospital (9.4%) was much lower than Northern California Regional NICU Network (17.2%).[28] Maybe because we included the neonates who were admitted to levels 2 and 3 of neonatal care, while Northern California Regional NICU Network included only level 3 admitted neonates.

The mortality rate of neonates who underwent mechanical ventilation in the current study (35.1%), is comparable with the results of some other studies (40-60%).[29]

In this study we only reported the rate of suspected but not proven sepsis cases. One of the most common diagnoses made in the NICU is suspected sepsis.[30,31] The rate of this disorder in our hospital (11.8%) is comparable with the results of another study in Iran (9.1%),[32] however, much lower than the rate of suspected sepsis in Egypt (45.9%)[33] and Tanzania (39%).[34]

The sepsis mortality rate is mostly reported in proven neonatal sepsis cases; the rates of 19.8%[35] and 27.5%[3] are reported in Iranian studies. In a Tanzanian study,[5] the mortality rate was 28.5% and 19% in neonates with proven sepsis and suspected sepsis, respectively; however, the rate of suspected sepsis diagnosis was very high in their study (39%) which may falsely reduce the mortality rate in these neonates. Accurate diagnosis of neonatal sepsis is a major challenge for neonatologists.[36]

Therefore, it seems more reliable to report the mortality rate in neonates with proven sepsis than neonates with suspected sepsis, but this rate is not the actual mortality rate.

Based on a binary logistic regression model (Table 4), surfactant injection (17.4% [69], $P=0.000$) and anemia (13.4% [53], $P=0.005$) had reverse association with sepsis. As discussed earlier, this phenomenon is explained by the Simpson's paradox.[11,12] Nested case-control studies with narrow inclusion and exclusion criteria should be done in order to clarify the exact effect of anemia and also surfactant injection on neonatal sepsis.

In line with our study, some other studies have also found that PDA is associated with RDS, IVH,[37] blood transfusion,[38] chromosomal syndromes[39] and surfactant injection[40]; but we did not find any evidence on the association between PDA and antibiotic therapy except for prevention of bacterial endocarditis, which is not routine since 2007 based on the American Heart Association modified guidelines.[41] As for the association between PDA and pulmonary hypertension, studies have shown that PDA treatment with ibuprofen can lead to this complication in these patients.[42]

Some studies reported that the incidence of IVH in very low birth weight infant population (<1500 g) has been about 20% from the late 1980s to the last two decades worldwide.[43] Other studies also confirmed our findings based on table 6.[44-49]

Limitations

Since our registry system was not linked to the Health Information System (HIS) in Vali-Asr hospital, we have possibly missed data from some patients who were admitted to our hospital. To solve this problem, we designed a protocol to integrate the registry system to the HIS.

As mentioned earlier, an expert registrar was in charge of entering the data into the software to verify the integrity and completion of the patients' summary sheets filled in by pediatric residents. Unfortunately, in some cases the patients' summary sheets were not filled in completely and thoroughly; therefore, our registrar had to return the sheets to the ward to be revised. Hence, to tackle this problem an accurate policy should be implemented.

In conclusion, neonatal registry networks can help neonatologists to reflect on their practice and performance and also to find new aspects of neonatal disorders.

As mentioned above, compared with other studies, we found lower rates of neonatal apnea and higher rates of surfactant injection in neonates with RDS in our hospital. These findings should be evaluated in future studies.

There are inconsistencies in reporting NEC rates and also suspected neonatal sepsis worldwide. A solution should be found for this problem.

Further nested case-control studies with narrow inclusion and exclusion criteria should be conducted, based on our neonatal registry system, in order to evaluate each category of disorders in detail.

Authors' Contribution

GR: analyzed the data and wrote the article. HD: the neonatologist consultant, MS: consulted on analyzing the data, MF: designed the study protocol, β: gathered the data, FN: administrator and the neonatologist consultant.

Conflict of Interest Disclosures

The authors have no conflicts of interest.

Ethical Statement

This study was approved scientifically and ethically by the Research Deputy of Tehran University of Medical Sciences (Project Code: 88-03-91-9534).

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