

Causes of death in a neonatal intensive care unit in Southeast region of Turkey

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Abstract

Aim: Neonatal mortality rate is a good indicator to show the developmental status of a country. The aim was to assess mortality rate and causes of death in a tertiary level neonatal intensive care unit (NICU) at Sanliurfa Training and Research Hospital.

Material and Methods: All infant deaths occurred in one year period between 2017 and 2018 at Sanliurfa Training and Research Hospital NICU were retrospectively reviewed and causes of death and mortality rate were examined.

A total of 189 (9.4%) infants died in the study period. Most common cause of death was prematurity and associated conditions (49.2%) followed by perinatal asphyxia (16.4%) and congenital anomalies (12.7%). In term infants perinatal asphyxia (36.9%), congenital anomalies (16.9%) and acute bilirubin encephalopathy (12.3%) were the three leading causes of death. The median age of death was 3 (1-240) days. Most of the deaths (73%) occurred in the early neonatal period.

Conclusion: Prematurity, perinatal asphyxia, congenital anomalies and severe hyperbilirubinemia are the leading causes of neonatal mortality in Sanliurfa. Measures for antenatal follow-up, diagnosis of antenatal risk factors, early neonatal follow-up and certification of health staff in delivery room would contribute for reduction of neonatal mortality in southeast region of Turkey.

Keywords: Neonate; Mortality Rate; Prematurity.

INTRODUCTION

Neonatal mortality rate is an important indicator to reflect developmental status of countries. In spite of significant decline in neonatal mortality rates in the last 3 decades, 2.6 million neonatal deaths was reported worldwide in 2015 (1).

In Turkey, during the past 30 years with the improvement in health services especially in obstetric, perinatal, antenatal and neonatal care; neonatal mortality and infant mortality rates have decreased promptly. The neonatal mortality rate was reported as 77.7/1000 in 1988, 17/1000 in 2003, and 10.1/1000 in 2010 according to the results of Ministry of Health of Turkey (2). And by the year 2017, neonatal mortality rate has decreased to 5.8/1000 live births (3).

Despite to efforts of Ministry of Health, great variations in birth rates and infant and neonatal mortality rates are observed in different regions of Turkey currently. The Ministry of Health of Turkey reported the neonatal mortality rate as around 4.7-4.9/1000 in Istanbul and eastern blacksea region contrary to 8.1/1000 in southeast

region of Turkey in 2017 (3). The infant mortality rate was calculated to be 9.1/1000 live births. Majority of the deaths was in neonatal period (64.4%). Sanliurfa was in the fourth order (14.4/1000) for neonatal mortality rate in Turkey. About 7.9% of all infant deaths took place in Sanliurfa province (4). Sanliurfa also has the highest birth rate as 4.29 in Turkey. It is one of the provinces with markedly high neonatal mortality rate above the average of Turkey due to high birth rate, considerably high Syrian refugee population settled in, low education level, some social and cultural beliefs concerning maternal and neonatal care, insufficient obstetric, perinatal and neonatal care.

The aim of the study was to assess mortality rate and causes of mortality in Sanliurfa Training and Research Hospital NICU, to compare it with data from Turkey and other parts of world and highlight the preventable causes of mortality.

MATERIAL and METHODS

Sixty thousands live births occur per year in Sanliurfa. About 50% of all births take place in Sanliurfa Training and

Received: 21.02.2019 Accepted: 17.03.2019 Available online: 05.04.2019

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Research Hospital. The hospital embodies the biggest perinatal service of the 2 perinatal services in Sanliurfa province. The Neonatal intensive care unit (NICU) of the hospital is the most important third level reference center with 107 bed capacity (54 level III and 53 level II) in the city which is in the second order to have highest bed capacity in Turkey. Mostly inborn but also outborn infants are referred to NICU and the NICU accepts over 2000 admissions per year. Majority of the infants hospitalized in the NICU were diagnosed as perinatal asphyxia, multiple congenital anomalies, congenital heart diseases, congenital central nervous system anomalies and extremely low birth weight and prematurity, extreme hyperbilirubinemia and acute bilirubin encephalopathy. So the data of the NICU is thought to reflect the causes of mortality throughout the whole province. But the infants with congenital diaphragmatic hernia and other congenital anomalies of gastrointestinal tract were referred to other third level reference center in the city.

This retrospective cohort study was conducted at Sanliurfa Training and Research Hospital between 1 September 2017 and 31 August 2018. The newborn infants admitted and hospitalized in NICU under 28 days of postnatal age and died before discharge were included in the study. Those that were died in delivery room or operating room or died after discharge and those under viability limits (≤ 22 weeks of gestation and or < 400 g birth weight) were excluded.

The data of total admissions and CRIB scores in defined time period were extracted from hospital and NICU database. Clinical Risk Index for Babies (CRIB) score was used for predicting mortality in the NICU. Expected and observed mortality rates were calculated. Detailed data about maternal and perinatal demographics, infant demographics including gestational age, birth weight, delivery route, gender, intrauterine growth retardation and length of stay, admission diagnosis and causes of death were collected from hospital records and patient files. Infants were defined as preterm with gestational age < 37 weeks and as term with ≥ 37 weeks' gestation. Deaths in first 7 days (0-6) days were defined as early neonatal deaths.

The study was approved by Harran University institutional ethics committee.

Statistical analysis

Categorical data were expressed as frequencies and percentages and continuous data were expressed as means and SDs and medians and minimum-maximum. Student's t-test was used for normally distributed continuous variables and Mann-Whitney U test was used for continuous variables that were not normally distributed. χ^2 test was used to analyze the categorical data, along with Fischer exact test when applicable. All statistics were done using the SPSS for windows software version 17.0 (SPSS Inc., Chicago, IL, USA). A P value < 0.05 was considered significant.

RESULTS

Between 1 September 2017 and 31 August 2018, 2004 infants were admitted to NICU. Of these 189 were died. The expected mortality rate was 11.6% and observed mortality rate was 9.4%. Of the 189 deaths 55.6% were males; 53.4% were delivered by cesarean section and 32.3% were Syrian refugee. Five percent ($n = 10$) were outborn. The antenatal follow-up rate was 65% during pregnancy. The rate of antenatal steroid use was 23.6% (26/110) in preterm infants with ≤ 34 weeks' gestation. The mean CRIB score was 11 ± 4.4 . The median gestational age was 32 weeks (23- 41) and the median birth weight was 1800 g (370-4100). The premature infants accounted for 65.6% of all deaths. About 32% of infants were < 28 weeks' gestation. Very low birth weight infants constituted 44% of neonatal deaths (Table 1).

Table 1. Demographic and antenatal characteristics of infants

	Dead infants (n = 189)
Maternal age, (y)	27.7 \pm 6.8
< 20	23 (12.1)
20-35	125 (66)
≥ 35	34 (17.9)
Gravida, (n)	3 (1-11)
Parity, (n)	2.5 (1-10)
Male sex, n (%)	105 (55.6)
Cesarean delivery, n (%)	101 (53.4)
Birth weight, (g)	1800 (370-4100)
≤ 750	38 (20.1)
751-1500	46 (24.3)
1501-2499	31 (16.4)
≥ 2500	74 (39.2)
Gestational age, (wk)	32 (23-41)
< 28	61 (32.3)
28-32	35 (18.5)
33-36	28 (14.8)
≥ 37	65 (34.3)
Rupture of membranes ≥ 18 hours, n (%)	42 (22.2)
Multiple birth, n (%)	24 (12.7)
Preeclampsia, n (%)	31 (16.4)
Chorioamnionitis, n (%)	20 (10.6)
Polyhydramnios, n (%)	16 (8.5)
Oligohydramnios, n (%)	11 (5.8)
Pregnancy induced hypertension, n (%)	11 (5.8)
Maternal diabetes mellitus, n (%)	5 (2.6)
Intrauterine growth retardation, n (%)	9 (4.8)
Large for gestational age, n (%)	3 (1.6)

Data are presented as n (%), mean \pm SD, median (min-max)

The most common cause of death in whole group was prematurity and associated conditions (49%) followed by perinatal asphyxia (16%) and congenital anomalies (13%) (Table 2). Similarly in Syrian refugees, prematurity and associated conditions were the leading cause of death (46%). But congenital anomalies together with congenital heart disease (21%) were more prevalent in Syrian refugee population constituting the second leading cause of death followed by perinatal asphyxia. Demographic characteristics including maternal age, gravida, parity, antenatal maternal risk factors, delivery type, gestational age and birthweight were similar among refugee and Turkish citizens. In infants ≥ 37 weeks' gestation the most prevalent cause of death was perinatal asphyxia (37%) followed by congenital anomalies (17%) and severe hyperbilirubinemia and associated acute bilirubin encephalopathy (12%) (Table 3). In preterm infants respiratory distress syndrome and respiratory insufficiency was the leading cause of mortality (29%) followed by pulmonary hemorrhage (25%), sepsis (15.3%), congenital anomalies (14.5%), perinatal asphyxia (6.4%), severe intraventricular hemorrhage (4.8%) and necrotizing enterocolitis (4%). Antenatal risk factors including early rupture of membranes (26.6% vs 13.8% $p = 0.04$), pregnancy induced hypertension (8.9% vs 0%, $p = 0.01$), preeclampsia (25% vs 1.5%, $p < 0.01$), chorioamnionitis (15.3% vs 1.5%, $p = 0.003$) were more prevalent in preterm infants compared to terms.

Table 2. Causes of death in whole population

	Dead infants (n = 189)
Prematurity and associated conditions, n (%)	93 (49.2)
Perinatal asphyxia, n (%)	31 (16.4)
Congenital anomalies, n (%)	24 (12.7)
Hyperbilirubinemia and acute bilirubin encephalopathy, n (%)	9 (4.8)
Congenital heart disease, n (%)	8 (4.2)
Meconium aspiration syndrome, n (%)	5 (2.6)
Congenital pneumonia and pulmonary hypertension, n (%)	4 (2.1)
Inborn errors of metabolism, n (%)	4 (2.1)
Sepsis, n (%)	4 (2.1)
Other reasons, n (%)	5 (2.6)

Table 3. Causes of death in term infants (≥ 37 weeks' gestation)

	Term infants (n = 65)
Perinatal asphyxia, n (%)	24 (36.9)
Congenital anomalies, n (%)	11 (16.9)
Hyperbilirubinemia and acute bilirubin encephalopathy, n (%)	8 (12.3)
Congenital heart disease, n (%)	6 (9.2)
Inborn errors of metabolism, n (%)	4 (6.2)
Meconium aspiration syndrome, n (%)	3 (4.6)
Sepsis, n (%)	3 (4.6)
Congenital pneumonia and pulmonary hypertension, n (%)	2 (3)
Other reasons, n (%)	4 (6.2)

The median age of death was 3 (1-240) days. Early neonatal deaths constituted 73% of all deaths. Of the 189 neonatal deaths, 31% (n = 59) occurred within first 24 hours of admission and 46% (n = 87) occurred within first 48 hours. The rate of deaths after 1 month of age was only 7.4% (n = 14). Respiratory distress and respiratory insufficiency were the most common reasons (n = 40) for early neonatal deaths of which 75% (n = 30) took place in the first 48 hours of admission. Pulmonary hemorrhage constituted second common reason for early neonatal deaths (21.7%), followed by perinatal asphyxia (15%), and congenital anomalies (14%). Most prevalent reasons for late neonatal deaths were congenital anomalies (28.6%) and sepsis (20.4%). Nine (18%) of the late neonatal deaths were due to severe asphyxia and associated pulmonary hypertension, five (10%) due to necrotizing enterocolitis and its complications and four (8%) due to severe intraventricular hemorrhage.

DISCUSSION

The overall mortality rate was 9.4% in the study period in the NICU. The premature infants constituted 65% of all deaths. The most common cause of death was prematurity and associated complications. In term infants the leading cause of death was perinatal asphyxia. Severe hyperbilirubinemia and associated acute bilirubin encephalopathy was strikingly an important cause of mortality in term infants being the third most common reason.

Demirel et al. reported the neonatal mortality rate as 10/1000 live births in Turkey in 2009 (5). By the year 2017, the neonatal mortality rate in Sanliurfa was reported to be 14.4/1000 live births (4). Neonatal mortality rates varies in different parts of world even in different regions of a single country (1). While our mortality rate was above the Turkey average it is under the rate throughout the Sanliurfa province.

Prematurity (29%), infections (25%) and asphyxia were the most common three reasons for neonatal mortality in the World (6). In most of the countries prematurity is the leading cause of neonatal mortality (1). In the study of Eventow- Friedman et al. prematurity constituted 76% of all neonatal deaths (7). Deaths due to prematurity and respiratory distress syndrome were reported to increase and deaths due to congenital anomalies decreased in Turkey between the years 2007 and 2012 (8). Recently, Ozdemir et al reported prematurity and respiratory distress as the most common cause of neonatal deaths in Van, located in Eastern Anatolia region of Turkey (9). Preterm birth rate is about 11-12% in Turkey (10). Preterm infants have 13 times greater risk of neonatal mortality than that of term infants (11,12). Prematurity and associated conditions were reported to be the leading cause of mortality in NICUs from different parts of Turkey (13,14). In 2009 72% of all neonatal deaths were reported to be preterm infants (5). Our results were consistent with the results from Turkey.

In the course of time congenital anomalies increasingly became one of the leading causes of neonatal mortality especially in developed countries (15-17). Demirel et al reported congenital anomalies as the second most common reason for early neonatal deaths (17.5%) and third most common reason for late neonatal deaths (13.1%) (5). In our study congenital anomalies (13%) were in the third order for neonatal mortality in all NICU deaths but it was second most common reason in term neonatal deaths. Congenital anomalies were mostly associated with late neonatal deaths. Also in Syrian refugees congenital anomalies were the second most common cause of neonatal mortality. Increased rate of consanguineous marriages and lack of appropriate antenatal follow-up and folic acid supplementation may be a reason for increased rate of deaths due to congenital anomalies in Syrian refugees. In Sanliurfa, termination of pregnancies with congenital/chromosomal anomalies is usually not accepted by the families due to religious and traditional beliefs. So, the rate of mortality due to congenital anomalies was expected to be higher. But, as mentioned previously infants with anomalies of gastrointestinal tract were referred to other referral center in the city. So congenital anomalies having high mortality rate such as congenital diaphragmatic hernia, esophageal atresia and intestinal atresia were not hospitalized in our center. Also cardiovascular surgical procedures could not be done in our center. Infants with congenital heart disease were admitted to NICU and after actual diagnosis they were mostly referred to neonatal cardiovascular surgery centers. Therefore the rate of mortality due to congenital anomalies could be probably underestimated.

Most striking finding is that perinatal asphyxia is the leading cause of neonatal mortality in term infants and second common cause in all NICU deaths. Dilli et al. reported perinatal asphyxia as a decreasing cause of infant mortality between 2007 and 2012 (5.8% vs 3.5%) (8). Perinatal asphyxia was fourth most common cause for early neonatal deaths and fifth most common cause for late neonatal deaths (6.1% vs 3.8%) in the report of Demirel et al. (5). Our results of neonatal mortality due to perinatal asphyxia was significantly above the average of Turkey. One of the reasons for this is that our NICU is the most important center for therapeutic hypothermia in Sanliurfa. We hospitalized 170 neonates with moderate and severe encephalopathy for therapeutic hypothermia consisting 8.4% of all NICU admissions in the study period. Another possible explanation is that about half of the births in Sanliurfa take place in the present hospital and only 10% of health staff was certified with neonatal resuscitation programme. In our study population of neonates with mortality due to perinatal asphyxia 25% of the mothers were < 20 years of age, 38.7% of mothers were having their first pregnancy and giving birth to their first child and 25% were Syrian refugee. This finding is important because perinatal asphyxia and hypoxic ischemic encephalopathy is mostly a preventable cause of mortality.

We think that with prevention of adolescent pregnancies, sufficient education of mothers, appropriate antenatal follow-up and sufficient education of health staff with programmes like neonatal resuscitation program deaths due to perinatal asphyxia will decrease.

Another important finding is neonatal deaths due to severe hyperbilirubinemia and acute bilirubin encephalopathy which constitutes about 5% of all NICU deaths and 12% of term infant deaths being the third most common cause of mortality in infants \geq 37 weeks' gestation. Infants with severe hyperbilirubinemia are mostly referred to Sanliurfa Training and Research Hospital NICU from the city center and districts and the unit serves for about 2/3 of all severe hyperbilirubinemia cases in all around the city. Severe hyperbilirubinemia and acute bilirubin encephalopathy is also a preventable cause of mortality. Prevention of early hospital discharges, close follow-up after early discharge and early recognition of hemolytic risk factors for severe hyperbilirubinemia will probably be significant approaches to reduce mortality due to severe hyperbilirubinemia and associated complications.

Prematurity, perinatal asphyxia, congenital anomalies and severe hyperbilirubinemia are the leading causes of neonatal mortality in Sanliurfa. With appropriate antenatal follow-up, use of antenatal steroids, early recognition and treatment of antenatal maternal infections, increasing number of neonatal resuscitation program certified health staff, avoidance of early hospital discharges after birth and early neonatal visits, neonatal mortality in this southeastern region of Turkey can be reduced to averages of western parts of the country.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports

Ethical approval: Harran University Ethics Committee No:13/07/2018-6180

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