Early and Late Outcome of Premature Newborns with History of Neonatal Intensive Care Units Admission at 6 Years Old in Zanjan, Northwestern Iran

How to Cite This Article: Sadeghzadeh M, Khoshnevisasl P, Parvaneh M, Mousavinasab N. Early and Late outcome of Premature Newborns with history of NICU Admission at 6 years old in Zanjan, Iran. Iran J Child Neurol. Spring 2016; 10(2):67-73.

Abstract

Objective
Premature birth is an important factor for mortality and morbidity of neonates. This study was designed to evaluate the outcome of preterm neonates who needed neonatal intensive care (NICU) hospitalization after 6 yr at their entrance to the school.

Materials & Methods
This cross sectional study was conducted on premature neonates consecutively hospitalized in NICU of Valie Asr Hospital (the Academic Pediatric Hospital, Zanjan, Northwestern Iran) from September 2001 to September 2003. All children with a history of prematurity and NICU treatment were evaluated at their entrance to the school. Demographic findings, clinical examinations, IQ test, hearing and visual acuity exams were recorded.

Results
From 179 neonates, 78 (43.6%) survived and were discharged from hospital. Fifty-four of them were available and entered first grade in primary school. Only one case had severe mental retardation. One case had severe retinopathy of prematurity (ROP). Hearing abnormality was not detected in any case. There was no significant relation between IQ score, visual as well as hearing findings and gestational age.

Conclusion
We did not find significant disability in the outcome of surviving infants. This could be explained by the high mortality rate of neonates during hospitalization.

Keywords: Mortality; NICU; Outcome; Preterm infants; Prematurity

Introduction
Prematurity is defined as a delivery before 37 wk of gestational age (1). The incidence of prematurity has been increased in the USA from 10.6% in 1990 to 12.8% in 2006 (2). Advances in prenatal, obstetric and neonatal care in Neonatal Intensive Care Units (NICU) were responsible for increasing preterm survivors in the last decades (3). Although the mortality rate decreased from 14.3% in 2000 to 12.4% in 2009 (4), it seems that it is associated with increased neonatal morbidity and poor neurodevelopmental outcomes (4-6). On the other hand, prematurity was the most common risk factor in infants with motor developmental delay (7). The neurodevelopmental outcome is a very important index to assess successful treatment in the NICU (3). Although cerebral palsy, mental retardation, blindness and deafness are reported in survived preterm children, more subtle complications...
such as cognitive, sensory, language, visual–perceptual, attention and learning deficits are highlighted (8). The cognitive deficiency depends on biological (antenatal and postnatal) events as well as environmental factors such as socioeconomic status, parental occupation and education, number of siblings, and breastfeeding (9). Although the prevalence of cognitive dysfunction was similar in different cultural environments, it is well recommended to evaluate the cognitive function of these children in a long-term follow up in different populations (10). Some investigations had studied the outcome at 2 yr of age (11), but other surveys have followed the children at the time of school with the conception that longer periods of follow up reveal more disabilities (12). The follow up of these children will improve our knowledge of preterm brain development and treatment strategies (8).

Neonatal morbidities and outcome are different in literature, which could be the result of a discrepancy in sample size or methods of studies, lack of control groups, different inclusion criteria, differences in severity determination and methods of treatment (5, 9). Regarding that similar studies have not been performed in our region, we conducted this study to evaluate the early and late outcome of neonates admitted in NICU at their entrance to the school.

Materials & Methods

The aim of this study was to define the early and late outcome of premature infants surviving the NICU at their entrance to the school. This descriptive study was conducted on premature neonates consecutively hospitalized in NICU of Valie Asr Hospital (academic pediatric hospital) in Zanjan, northwestern Iran from September 2001 to September 2003. All these children were evaluated at their entrance to school, when they were six yr old (2007-2009).

This study was approved by the Ethical Committee of Zanjan University of Medical Sciences.

Parental informed consent was taken prior to enrollment in the study.

The children were assessed by a pediatrician, physically examined, and the history of any underlying disease or taking any medication was investigated. The children’s intelligent quotients (IQ) were determined by Wechsler test. The IQ more than 84 was considered normal. For each child audiometry was performed by a trained audiologist and visual acuity was investigated by an optometrist using Snellen charts.

Meanwhile, their hospital records were evaluated retrospectively. All data, including mortality rate, gestational age, birth weight, sex, Apgar score, history of neonatal diseases, and diagnostic procedures such as intracranial ultrasonography, CT scan and need for ventilators were inserted in prepared questionnaires.

All collected data were analyzed by SPSS software version 16.0 (Chicago, IL, USA). Comparisons for categorical variables were performed by chi-square test. P value less than 0.05 was considered statistically significant.

Results

Overall, of 179 neonates, 101 (56.4%) cases died because of some of common causes of death including hyaline membrane disease or HMD (37.5%), HMD and sepsis (9%), asphyxia (4%), and disseminated intravascular coagulation with IVH (1.7%).

The mortality rate in neonates with a gestational age of 28-34 wk was 50%. There was a significant relation between gestational age and mortality rate (P= 0.001). Seventy-eight (43.6%) newborns survived and enrolled in the study, of them, 53 newborns (68%) had a gestational age of 28-34 wk and 25 (32%) patients had a gestational age of 34-37 wk. Among them, 24 (31%) were female.

The neonatal birth weights varied between 450 gr to 3000 gr with the mean of 1586.21 ±540.53 gr. First minute Apgar scores were less than 7 in 21 (27%), and 7 or more in 57 (73%) cases.

There was a significant relationship between first minute Apgar score <7 and neonatal mortality. (P=0.000). Intracranial ultrasonography was normal in survived patients and approved by brain CT scans. Four (5%) patients were assisted by ventilator. Frequency of neonatal diseases and their mortality have shown in Table 1. There was no significant relationship between mortality rate and some variables, including gender, weight, ventilator assisting, imaging findings and neonatal diseases.

The survived neonates were followed at their entrance...
to school from 2007 to 2009. Twenty-four children were excluded due to immigration, lack of full URL in the file and the lack of information about their new residence.

Finally, 44 patients were evaluated by physical examination, audiometric and optometric assessment and IQ test. None of them had chronic disease, seizure or history of medications.

The audiometric assessment was normal in all of the patients. One of the patients with visual problems had been consulted with an ophthalmologist. Because of retinopathy of prematurity, he was treated with laser therapy. Fifty-one patients (94.4%) had normal IQ and three patients (5.6%) showed mental retardation. One patient had mild, one moderate and the other had severe mental retardation. Two patients with abnormal IQ were in the group of infants with gestational age of 28-33 wk and one patient with abnormal IQ was found in infants with gestational age of 33-37 wk (Table 2). Even though the percentage of the lower IQ was found in the more mature infants, these differences were not statistically significant.

There was not statistically significant relation between GA with IQ, hearing and visual abnormality.

Discussion

The numbers of premature live births are increasing, associated with increased morbidity and mortality (13, 14). In this study, the mortality of 179 premature neonates in NICU was 56.4% compared to 64.4% in a previous study in Iran (15), 80.8% in Alexandria (1) and 86% in Saudi Arabia (16). Although, based on the Vermont Oxford network multicentric study in 33 North American (VON) centers, the mortality rate was 1.4% (11). The mortality of premature neonates weighing 501-1500 gr born in the USA from 2000 to 2009 decreased from 14.3% to 12.9% (4). These differences could be the result of discrepancies in gestational ages and treatment facilities in different studies.

In our study, 54% of survived infants were male and there was no significant difference in mortality rate of two genders. These findings are similar to a study in Turkey (17).

In the present study, there was a significant relationship between gestational age and mortality rate, similar to some other studies (1, 15, 16). The decrease in mortality of tiny neonates (501-750 g) was more than other groups (4). Another study had similar results with a 4.6% decrease in mortality of those premature infants (18). Difference in our results could be due to a lesser prenatal care and maternal factors such as malnutrition and lower treatment facilities in different hospitals.

Our study showed a statistically significant relationship between mortality rate and low first minute Apgar score, similar to previous studies (15, 16). Another study showed that 75% of neonates with a 10 min Apgar score of 0-3 died or suffered a disability compared to 45% of neonates with Apgar scores more than three and incremental in Apgar score was significantly related to a better outcome (19).

We found Hyaline membrane disease (HMD) in 95.3% of our patients, similar to other studies (15, 20). In 38.9% of patients, we found associated complications with HMD that the most frequent was sepsis (18.5%). In previous studies (14, 15, 20), this association was 43.6%, 30.9% and 76%, respectively.

The type of deliveries in our study was through cesarean section at (43%), but previous studies revealed that 59% and 15% of neonates were delivered by this method respectively (2, 16).

Premature rupture of membranes was seen in 10.1% of our neonates similar to another study as 13.4% (2). Intraventricular hemorrhage (IVH) was found in three patients. This complication is reported in 3.5% of neonates (14), besides 8.5% of the evaluated patients had severe IVH (11). Fourteen percent of patients showed IVH grade > II (17). IVH was found in 16% and 9.5% in preterm neonates (13, 21). The lower rate of IVH in our study may be due to the shorter duration of survival in our very low birth weight neonates. Neonates suffering IVH had poorer outcomes (22). Therefore, better outcome of our patients may be related to lesser IVH in our survived neonates.

The weight of 29.6% of our patients was below 5th percentile at school entrance. SGA infants had suboptimal growth until age 5 in Finland (10). Comparing late preterm and term infants, preterm infants are at increased risk of underweight and stunting (23).

Visual disturbance due to retinopathy of prematurity
Since most infants discharged alive in our study had higher gestational age and birth weight, their evaluation at school entering age has been associated with the minimum expected disturbances.

Acknowledgment
This paper is part of a pediatric specialty thesis and has been approved by the Council of Research of Zanjan University of Medical Sciences. We greatly appreciate all patients and their families for their cooperation in conducting the study.

Author’s Contribution:
Mansour Sadeghzadeh, Parisa Khoshnevisasl: Study concept and design;
Mehdi parvaneh, Mansour Sadeghzadeh: Acquisition of data;
Mansour Sadeghzadeh, Parissa Khoshnevisasl, Nooreddin Mousavinasab: Analysis and interpretation of data;
Nooreddin Mousavinasab: Statistical analysis;
Parisa Khoshnevisasl, Mansour Sadeghzadeh, Nooreddin Mousavinasab, Mehdi parvaneh: Drafting of the manuscript;
Parisa Khoshnevisasl, Mansour Sadeghzadeh: Critical revision of the manuscript for important intellectual content;
Parisa Khoshnevisasl, Mansour Sadeghzadeh, Nooreddin Mousavinasab, Mehdi parvaneh: Final approval and agreement for accountability;
Mansour Sadeghzadeh: Study supervision.

Conflict of interest:
The authors declare that there is no conflict of interests.
Table 1. Neonatal Diseases in Survived Cases

| Variable      | Number(%) |
|---------------|-----------|
| HMD           | 47 (60)   |
| Asphyxia      | 1 (1.3)   |
| Sepsis        | 2 (2.6)   |
| HMD+ Sepsis   | 17 (21.8) |
| Hypoglycemia  | 5 (6.5)   |
| NEC           | 1 (1.3)   |
| GIB           | 1 (1.3)   |
| Apnea         | 4 (5.2)   |

HMD = hyaline membrane disease, NEC = Necrotizing Enteroocolitis; GIB = Gastrointestinal Bleeding

Table 2. Relation between Gestational Age and IQ, Auditory and Visual Abnormality

| Variables | Gestational Age(week) | Total | P value |
|-----------|-----------------------|-------|---------|
|           | 28 - 33               | 34 -37|         |
| IQ        | Normal                | 36    | 15      | 51      |
|           | Abnormal              | 2     | 1       | 3       |
|           | Total                 | 38    | 16      | 54      |
| Auditory  | Normal                | 38    | 16      | 54      |
|           | Abnormal              | -     | -       | -       |
|           | Total                 | 38    | 16      | 54      |
| Visual    | Normal                | 37    | 16      | 53      |
|           | Abnormal              | -     | -       | 1       |
|           | Total                 | 38    | 16      | 54      |

NS = not significant

References

1. Fakher M, Shaaban W, Abdel Monein A, Hassan Z, Moustafa Fikry M. Statistical Study of Preterm Infants Admitted to NICU in Fawzy Moaz Hospital For Children. Alex J Pediatr 2005; 19 (1):155-8.

2. Fauth de Araújo B, Zatti H, Madi JM, Coelho MB, Olmi FB, Canabarro CT. Analysis of neonatal morbidity and mortality in late-preterm newborn infants. Jornal de Pediatria 2012; 88 (3): 259-266.

3. Stephens BE, Vohr BR. Neurodevelopmental outcome of the premature infant. Pediatr Clin North Am 2009; 56 (3): 631-46.

4. Horbar JD, Carpenter JH, Badger GJ, Kenny MJ, Soll RF, Morrow KA, Buzas JS. Mortality and neonatal morbidity among infants 501 to 1500 grams from 2000 to 2009. Pediatrics 2012;129 (6): 1019-26.

5. Melamed N, Klinger G, Tenenbaum-Gavish K,
1. Navaei F, Aliabady B, Moghtaderi J, Moghtaderi M, Kelishadi R. Early outcome of preterm infants with birth weight of 1500 g or less and gestational age of 30 weeks or less in Isfahan city, Iran. World J Pediatr 2010; 6 (3): 228-232.

16. Arafa MA, Alshehri MA, Predictors of neonatal mortality in the intensive care unit in Abha, Saudi Arabia. Saudi Med J 2003; 24 (12): 1374-1376.

17. Atalay D, Sahinoglu O, Can E, Beskardes A, Hatipoğlu S. Short-Term Outcomes of Very Low Birth Weight Infants Born at a Tertiary Care Hospital, Istanbul, Turkey. Iran J Pediatr 2013; 23(2): 205-211.

18. Mathews TJ, MacDorman MF. Infant Mortality Statistics From the 2007 Period Linked Birth/Infant Death Data Set. National Vital Statistics Reports. 2011;59(6).

19. Natarajan G, Shankaran S, Laptook AR, Pappas A, Bann CM, McDonald SA, et al. Apgar scores at 10 min and outcomes at 6-7 years following hypoxic-ischaemic encephalopathy. Arch Dis Child Fetal Neonatal Ed 2013;98(6):F473-9.

20. Tommiska V – Heinonen Ikonen S – pokelu ML-Renlund M/Virtanen M-fellman V. A national short-term follow-up study of extremely LBW infants born in Finland in 1996-1997. Pediatrics 2001; 107 (1):1-9.

21. Ahmadpour M, Zahedpasha Y, Khafri S, Pishnamazi N. Short-term outcome of premature neonates admitted to NICU & newborn services at Amirkola children hospital in 2010. IJN 2012; 3(3,4): 10-22.

22. Calisici E, Eras Z, Oncel MY, Oguz SS, Gokce IK, Dilmen U. Neurodevelopmental outcomes of premature infants with severe intraventricular hemorrhage. J Matern Fetal Neonatal Med 2014 ;14(1):6-16.

23. Santos IS, Matijasevich A, Domingues MR, Barros AJD, Victora CG, Barros FC. Late preterm birth is a risk factor for growth faltering in early childhood: a cohort study; BMC Pediatrics 2009; 9:71.

24. Leversen KT, Sommerfelt K, Rønnestad A, Kaalnes P, Farstad T, Skrænes J, et al. Prediction of neurodevelopmental and sensory outcome at 5 years in Norwegian children born extremely preterm. Pediatrics 2011;127(3):e630.
SC, Khatry SK. Associations between preterm birth, small-for gestational age, and neonatal morbidity and cognitive function among school-age children in Nepal. BMC Pediatrics 2014;14:58.

26. Synnes AR, Anson S, Arkesteijn A, Butt A, Grunau RE, Rogers M, Whitfield MF. School entry age outcomes for infants with birth weight≤800 grams. J Pediatr. 2010;157(6):989.

27. van Baar AL, Vermaas J, Knots E, de Kleine MJ, Soons P. Functioning at school age of moderately preterm children born at 32 to 36 weeks’ gestational age. Pediatrics 2009; 124(1): 251.

28. Johnson S, Fawke J, Hennessy E, Rowell V, Thomas S, Wolke D, Marlow N. Neurodevelopmental disability through 11 years of age in children born before 26 weeks of gestation. Pediatrics 2009;124(2):e249.

29. Kerstjens JM, de Winter AF, Bocca-Tjeertes IF, ten Vergert EM, Reijneveld SA, Bos AF. Developmental delay in moderately preterm-born children at school entry. J Pediatr 2011; 159(1):92.

30. Soleimani F, Kazemnejad A, Vameghi R. Risk factor profiles of adverse neuromotor outcome in infants. Iran J Child Neurol 2010; 4 (4): 25-31.