

Neonatal asphyxia: A study of 210 cases

Neonatal asfiksi: 210 vakalık çalışma

Hülya Üzel, Selvi Kelekçi, Celal Devocioğlu, Ali Güneş, İlyas Yolbaş, Velat Şen

Dicle Medical School, Department of Pediatrics, Diyarbakır, Turkey

ABSTRACT

Objectives: Perinatal asphyxia remains an important cause of neonatal morbidity and mortality. The aim of this study was to investigate antenatal, natal, and postnatal risk factors of neonatal asphyxia, relationship with known risk factors and stage of Sarnat and Sarnat scores, the effect of risk factors on hospital discharge and survival for neonates with perinatal asphyxia.

Materials and methods: In this study, we retrospectively analyzed the hospital records of 210 patients diagnosed as perinatal asphyxia. The patients' demographic characteristics, antepartum, intrapartum, and postpartum risk factors and Sarnat and Sarnat clinical staging criteria of newborns were analyzed.

Results: The risk factors for asphyxia were detected antepartum period in 67.7% of newborns, intrapartum in 91% and postpartum in of 29.5% of neonates. When cases were examined according to the studied years, perinatal asphyxia ratio was the most frequent in 2007 as 28.1%. With a decline over the years, frequency dropped to %21 in 2010. The number of patients with stage 3 and mortality rate were significantly decreased over the years ($p < 0.05$).

Conclusions: Less preventable intrapartum causes of birth asphyxia are seen more frequently. Early detection of risk factors together with appropriate prenatal, natal and postnatal care provision, reduced emergency caesarean sections and will decrease considerably decrease frequency of perinatal asphyxia. We think that following up neonates who needed intensive care in neonatal units sufficiently equipped will decrease complications due to asphyxia. *J Clin Exp Invest* 2012; 3(2): 194-198

Key words: Asphyxia, newborn, risk factors, prognosis

INTRODUCTION

Perinatal asphyxia is defined as a clinical condition associated with hypoxemia, hypercapnia and acidosis in a fetus or newborn.¹ Acute brain injury due to asphyxia in the newborn develops due to antepartum (50%), intrapartum (40%) and postpartum

ÖZET

Amaç: Perinatal asfiksi, yenidoğan döneminin önemli mortalite ve morbidite nedenlerinden biridir. Bu çalışmanın amacı yenidoğan asfiksisi için antenatal, natal ve postnatal risk faktörlerini araştırmak, perinatal asfiksili yenidoğanlarda bilinen risk faktörleri ile Sarnat ve Sarnat skorları ilişkisini ve risk faktörlerinin hastanede kalış süresi ve sağkalım ile ilişkisini belirlemektir.

Gereç ve yöntem: Bu çalışmada perinatal asfiksi tanısı alan 210 vakanın dosya kayıtları geriye dönük olarak incelendi. Hastaların demografik özellikleri, risk faktörleri ve Sarnat and Sarnat klinik evreleme özellikleri analiz edildi.

Bulgular: Hastaların %67,7'sinde antepartum, %91'inde intrapartum ve %29,5'inde postpartum risk faktörü bulunmaktaydı. Yıllara göre incelendiğinde perinatal asfiksili olgu %28,1 oranında en fazla 2007 yılında görülürken yıllar içinde bir düşüş ile birlikte %21 oranında 2010 yılında tanı almıştı ve evre 3 olgu sayısı ve mortalite oranı anlamlı şekilde azalmıştı ($p < 0.05$).

Sonuç: Doğum sırasında ki daha az önlenebilir doğum asfiksisi nedenleri daha sık görülmektedir. Risk faktörlerinin erken tespit edilmesi yanında uygun prenatal, natal ve postnatal bakım, düşük APGAR skorlu ve acil sezeryan doğumların azalması perinatal asfiksi sıklığını önemli ölçüde azaltacaktır. Yoğun bakım ihtiyacı ve resüsitasyon yapılan yenidoğanların yeterli donanıma sahip merkezlerde izlenmesi de asfiksiye bağlı komplikasyonları azaltacağını düşünüyoruz.

Anahtar kelimeler: Asfiksi, yenidoğan, risk faktörü, prognoz

(10%) causes that reduce oxygen support or blood flow.² Hypoxic ischemic encephalopathy (HIE) is the most severe result of perinatal asphyxia. Of Patients with hypoxic-ischemic encephalopathy, 15-20% die in the neonatal period, and 25-30% of the survivors develop permanent neurological disorders, such as cerebral palsy (CP) and mental retardation.³ The in-

Correspondence: Dr. Selvi Kelekçi

Dicle University Medical School Department of Pediatrics, Diyarbakır, Turkey Email: selvikelekci@gmail.com

Received: 04.03.2012, Accepted: 30.05.2012

Copyright © JCEI / Journal of Clinical and Experimental Investigations 2012, All rights reserved

cidence of asphyxia has been reported as 1-6/1000 live births, depending on the gestational age and birth weight.^{4,5}

Perinatal asphyxia continues to be a major cause of morbidity and mortality in the neonatal period.⁶ Perinatal asphyxia could be reduced in health centers capable of preventing frequent births, serving high quality antenatal care, closely monitoring high risk pregnancies, providing suitable conditions for giving births, and when needed immediately and correctly intervene to newborn.

In the southeastern part of Turkey, perinatal asphyxia in neonates continues to be a serious problem due to high birth rates, insufficient antenatal follow-up, at-home births, and inadequacy of birth clinics, which must serve more patients than their capacity.

In our study, we aimed to investigate antenatal, natal, and postnatal risk factors of neonatal asphyxia, relationship between known risk factors and stage of Sarnat and Sarnat scores, the effect of risk factors on hospital discharge and survival for patients with perinatal asphyxia who followed-up at our neonatal service between 2007 and 2010.

MATERIALS AND METHODS

In our study, we retrospectively evaluated file records of 210 neonatal patients with perinatal asphyxia who followed up at the neonatal clinic of Dicle University Faculty between January 2007 and December 2010. Newborn babies were diagnosed as perinatal asphyxia if resuscitation was required at birth, an APGAR score below seven at one minute and five minutes after birth, presence of neurological signs (e.g., convulsions) or multisystem dysfunction, requirement of mechanical ventilation within the first hours of life, late onset of breathing, and presence of blood gas acidosis (pH <7.2).

All of these criteria were recorded along with risk factors, demographic characteristics, length of hospitalization, and outcome for each patient.

Patients were investigated the distribution of cases according to risk factors, comparison of risk factors according to the criteria of Sarnat and Sarnat clinical staging and the effect of risk factors on the discharged and over the years.

Accepted risk factors for asphyxia

a) Antepartum risk factors: Multiple gestation, preeclampsia / eclampsia, maternal drug use, oligohydramnios, maternal bleeding, smoking, maternal infection, polyhydramnios, maternal chronic hyper-

tension, maternal age over 35 years, maternal convulsive disease, maternal diabetes.

b) Intrapartum risk factors: cesarean section, premature delivery, amniotic fluid with meconium, cord prolapse, prolonged birth, abruptio placenta, premature rupture of membranes, abnormal presentation, chorioamnionitis, placenta previa, birth trauma, large for gestational age (LGA).

c) Postpartum risk factors: Respiratory distress syndrome (RDS), meconium aspiration syndrome, congenital heart disease, congenital anomaly.

Neonates with asphyxia were classified as stage I (mild), stage II (moderate) and stage III (severe) according to the criteria of Sarnat and Sarnat clinical staging.

Neonates were characterized as preterm (gestational age less than 38 weeks), term (gestational age between 38 and 42 weeks) or post-term (gestational age more than 38 weeks) using the Dubowitz and Ballard classification system. Newborns were designated by weight as either very low birth-weight newborns (less than 1500 grams) or low birth-weight newborns (between 1501 and 2000 grams).

Results were recorded using SPSS version 18.0 for Windows. The chi-square test was used for group comparisons. Results were accepted as significant ($p < 0.05$).

RESULTS

Of the patients admitted to our neonatal service during the four year period, 9.7% (n=210) gave birth to infants diagnosed with asphyxia. Demographical characteristics of children followed up with the diagnosis of asphyxia are given at Table 1.

The number of patients diagnosed each year, and the number of stage III patients, decreased over the four-year period: 28.1% (n=59) were diagnosed as neonatal asphyxia in 2007, 26.7% (n=56) in 2008, 24.3% (n=51) in 2009, and 21% (n=44) in 2010. The distribution of newborns with asphyxia by year is shown in Table 2.

In our cases, 91% of patients had intrapartum risk factors for asphyxia, 67.7% antepartum risk factors and 25.9% postpartum risk factors. Antepartum risk factors included mothers over 35 years of age (20%), presence of preeclampsia/eclampsia (8.6%), presence of maternal diabetes mellitus (15.7%), and maternal cigarette smoking (6.2%). Common intrapartum risk factors were emergency cesarean section (38.1%), premature birth (24.8%) and meconium amniotic fluid (14.3%). The postpartum risk factors were meconium aspiration syndrome

(14.3%), respiratory distress syndrome (8.1%) and congenital anomalies such as hydrocephalus and meningomyelocele (3.8%).

Table 1. Demographic characteristics of newborns with asphyxia

Demographic Data	n (%)
Gender	
Girl	108 (51.4)
Male	102 (48.6)
Birth weight	
<1500 g	10 (4.8)
1500-2000 g	52 (24.8)
>2000 g	148 (70.4)
Gestational age	
Preterm	53 (24.8)
Term	147 (70)
Postterm	10 (4.8)
Delivery	
Spontaneous vaginal	127 (60.5)
Cesarian	80 (38.1)
Multipl Gestation	
Multipl pregnancy	10 (4.8%)
Single pregnancy	200(95.2%)
Birth Center	
Our hospital	174 (82.8%)
Home birth	2 (1%)
Other Hospital	34 (16.2%)

Table 2. Comparison of risk factors according to Sarnat and Sarnat staging

	Stage I	Stage II	Stage III	p
Newborn ratio	42.9%	30%	27.1%	
Gender	→	→	→	NS
APGAR score	↑	→	→	<0.05
Preterm action	↓	↑	→	<0.05
Resuscitation	↓	→	↑	<0.05
Mechanical vent.	↓	→	↑	<0.05
Hospitalization duration	→	→	→	NS
Birth home	→	→	→	NS
Other hospital	→	→	↑	NS
Kinship	→	→	↑	NS
C/S birth	↑	→	→	NS

NS: not significant

According to the Sarnat and Sarnat clinical staging criteria, 42.9% (n=90) of cases were stage I, 30% (n=63) of cases were stage II and 27.1% (n=57) of cases were stage III. The comparison of risk factors according to clinical stage is shown in Table 2. In comparing survivors and non-survivors, non-survivors were found to have lower one- and five-minute APGAR scores. Resuscitation and mechanical ventilation were also more often required for non-survivors (p<0.05). The rate at which the mothers received prenatal care was higher among survivors than non-survivors (p<0.05). The comparison of risk factors between survivors and non-survivors is shown in Table 3.

Table 3. Comparison of risk factors in patients who are survive and nonsurvivor

	Survivor	Nonsurvivor	p
Term delivery	→	↑	NS
<2000gr	→	↑	NS
Hospitalization duration	→	→	NS
APGAR score	↑	↓	<0.05
Gender	→	→	NS
Delivery center	→	→	NS
Spontaneous vaginal	↑	↑	NS
Antenatal care	↑	↓	<0.05
Resuscitation and mechanical ventilation	↓	↓	<0.05
Year	2010↑	2007↓	<0.05

DISCUSSION

Perinatal asphyxia is one of the most important causes of mortality and morbidity, even in developed countries. Despite developments in neonatal care, diagnosis and treatment, perinatal asphyxia has been reported to cause 17% of perinatal deaths and 15-20% of cerebral palsy cases.⁷ It is very important to accurately diagnose perinatal asphyxia as early as possible and to predict the prognosis of the newborn. Given an early diagnosis, it may be possible to minimize unfavorable consequences through prompt application of appropriate treatment and rehabilitation exercises.

No exact statistics are available on perinatal asphyxia and its complications in Turkey. In our study, 9.7% of infants at our neonatal service were diagnosed with asphyxia during the four-year period. This result demonstrated that our country and our region have a higher incidence of asphyctic newborns compared with developed countries.^{6,8}

Our results similarly indicated intrapartum risk factors as prominent risk factors, and emergency cesarean sections were the most frequent risk factor in our study.^{9,10} Negative outcomes due to birth asphyxia can be reduced by preventing intrauterine and postpartum conditions, which may lead to emergency cesarean sections, improving postnatal patient care, and training assistant health staff.

One- and five-minute APGAR score were significantly higher for stage I patients compared to the other stages. One- and five-minute APGAR scores of non-survivors were significantly lower than those of survivors. Similarly, Nagdyman et al. found that one- and five-minute APGAR scores of patients with asphyxia were statistically significantly lower than those of control group.¹¹ The APGAR scoring system has been established as an important predictor of prognosis in asphyxia cases.

Gender ratios in stage I and stage III were similar, while stage II had a large proportion of females. The difference between gender ratios was not statistically significant, as is consistent with the literature. We observed a high frequency of term deliveries and birth weights greater than 2000 g in all stages. Stage II patients had the highest preterm birth rate, while stage I patients had the lowest rate, similar to the results of a previous study.¹⁰ We can conclude from our results that gender and birth weight do not affect asphyxia severity, however, gestational age is important in determining the stage of asphyxia according to Sarnat and Sarnat clinical staging criteria.

Preterm delivery increases the risk of asphyxia. With further investigation of the correlation between preterm deliveries and emergency caesarean sections, we believe the incidence of asphyxia will decline significantly. We think that considerable decreases can be accomplished by performing studies to investigate causes of co-occurrence of preterm delivery and cesarian section. However, in our study the rate of one- and two-degree consanguineous marriages was highest between mothers and fathers of stage III patients. Cesarean section deliveries were most common for stage I patients. Thus, kinship status and type of delivery did not show statistical significance. High asphyxia and mortality rates in our population may be due to a high incidence of consanguineous marriages; further studies on consanguinity and asphyxia are necessary.

In comparing stages by birth location, we observed that no births occurred at home for stage I, but significantly higher rates of hospital deliveries were seen in stage III. A similar study in Turkey reported that home birth rates were still high, and home births were a risk factor for perinatal

asphyxia.¹² These results suggest that births in different centers can cause aggravation in the clinical of asphyxia due to conditions of transport, and home deliveries could be an important risk factor for conditions of our country and other countries. Deterioration in clinical status of newborn may be seen secondary to transportation conditions. Therefore, delivery at home may be an important risk factor for countries resembling to our country. Although, our mortality rate (15.2%) related to asphyxia was near to previous reports.^{13,14} Resuscitation was performed in 94.7% of stage III patients and mechanical ventilation need and mortality were most frequent in stage III.

Stage III cases most often required mechanical ventilation and resuscitation, and had the highest mortality rate. In contrast, stage I cases least often required mechanical ventilation and resuscitation, and had the lowest mortality rate. Some studies have reported similar results.¹⁵ In our study, there was no statistically significant relationship between asphyxia stages and length of hospitalization.

In 2009 and 2010, both the number of stage III patients and the number of patients diagnosed with asphyxia decreased significantly. The causes of these results may be lower number of spontaneous vaginal deliveries, higher rates of C/S, no delivery at home, less number of asphyxia newborns with neurological findings and the least ratio of preterm deliveries at 2009 and 2010 years. The decrease in the incidence of asphyxia patients with neurological evidence and in the number of preterm births during these two years were very also significant.

The most important reason for neonatal convulsions is hypoxic-ischemic encephalopathy.¹⁶ Fifty to 65% of all seizures due to perinatal asphyxia are neonatal convulsions.¹⁷ A significant proportion of neonatal convulsions are seen within the first 12 hours after birth, and the rest occur within 24-48 hours.¹⁸ Ekert et al. reported that the presence of convulsions and the time of occurrence were predictors of a poor prognosis.¹⁹ In our study, stage II and stage III patients had the highest incidences of convulsions at 10.5% and 7.6%, respectively. All convulsions were seen in the first 72 hours. These results support those in the literature.

No significant differences were observed in the ratio of term births with birth weights over 2000 g, the level of consanguinity between the parents, the gender of the newborns, or the birth rate within our hospital between all studied years and the years 2009 and 2010. In our study, the incidence of severe asphyxia (stages II and III) declined from 2.6 out of every 1000 live births to 1.8 out of 1000 over

the four years.²⁰ We have also emphasized that the incidence of neonatal asphyxia in our hospital (9.7 out of every 1000 births) can be reduced over the years; regional and country-level prevalence studies should be implemented to monitor the frequency of neonatal asphyxia and to provide concrete data. We also found the frequency of newborns with asphyxia as 9.7/1000 at our hospital, and showed the gradual decrease in the frequency of asphyxia in our hospital.

The highest incidence of mechanical ventilation and resuscitation, and the highest mortality rate, occurred in 2008; the lowest rate of patients receiving prenatal care occurred in 2007 and 2008. Resuscitation, mechanical ventilation need, asphyxia frequency and mortality rate were found to be highest in 2008; the ratio of patients received perinatal care was the lowest in 2007 and 2008. The frequency of asphyxia could be decreased in countries which perinatal care is performed sufficiently.

Our results showed that we should not forget the importance of prenatal care, the applicability, perinatal asphyxia and important contributions to mortality due to asphyxia. Patients groups that survivors and non-survivors; presence of <2000 grams patients in the non-survivors group, similar gender distributions between stages, occurring delivery in the foreign centers, presence of a high rate of normal vaginal delivery and the rate of full-term cases in the three stage and compared depending on the duration of the hospital stay, showed no statistically significant difference. But low one- and five-min APGAR scores of non-survivors was significant, presence of high rate of the mother's prenatal care of survivors was highly significant. No significant differences were found between babies survive and died in the view point of birth weight, gender distribution and hospitalization duration. However, significantly higher ratios of high APGAR scores at 1st and 5th minutes and sufficient prenatal care were observed in newborns that survive compared with those who died. Non-survivors more often required mechanical ventilation and resuscitation than survivors; the difference between the two groups was very highly significant.

In conclusion, less preventable intrapartum causes of birth asphyxia are seen more frequently. We think the frequency of birth asphyxia can be reduced but neonatal asphyxia cannot be prevented completely. The incidence of asphyxia and related complications can be decreased by identifying risk factors and taking timely precautions against them, providing antenatal care and decreasing the need for emergency caesarian sections. In addition,

newborns with low APGAR scores at birth, requiring resuscitation or mechanical ventilation, and with neurological impairments should be monitored in sufficiently well-equipped neonatal units.

REFERENCES

1. Can G, Neyzi O, Ertuğrul T. Neonatal Asphyxia. *Pediatric 1st Edition Chapter 2002*; 353-6.
2. Dilenge ME, Majnemer A, Shevell MI. Long-term developmental outcome of asphyxiated term neonates. *J Child Neurol* 2001;16 (11): 781-92.
3. Stoll BJ, Kliefman RM. Nervous system disorders. *Nelson Textbook of Pediatrics 17th Edition Chapter 2004*; 88: 561-69.
4. Toet MC, Lemmers PM, van Schelven LJ et al. Cerebral oxygenation and electrical activity after birth asphyxia: their relation to outcome. *Pediatrics*. 2006;117(2):333-9.
5. Shankaran S. Neonatal encephalopathy: treatment with hypothermia. *J Neurotrauma*. 2009;26(3):437-43.
6. Wu YW, Backstrand KH, Zhao S et al. Declining diagnosis of birth asphyxia in California: 1991-2000. *Pediatrics* 2004;114(6):1584-90.
7. Volpe JJ. *Neurology of Newborn*. 3rd ed. WB Saunders Company, 1995; 11-360.
8. Milsom I, Ladfors L, Thiringer K, et al. Influence of maternal, obstetric and fetal risk factors on the prevalence of birth asphyxia at term in a Swedish urban population. *Acta Obstet Gynecol Scand* 2002;81(10):909-17.
9. Buchmann EJ, Pattinson RC. Babies who die from labour-related intrapartum hypoxia: a confidential enquiry in South African public hospitals. *Trop Doct* 2006;36(1):8-10.
10. Gündoğdu M, Retrospective monitoring of patients diagnosed with perinatal asphyxia and hypoxic-ischemic encephalopathy, Van 2010.
11. Nagdyman N, Grimmer I, Scholz T, et al. Predictive value of brain-specific proteins in serum for neurodevelopmental outcome after birth asphyxia. *Pediatr Res*. 2003;54(2):270-5.
12. Katar S, Devocioğlu C, Sucaklı İA, et al. Hypoxic ischemic encephalopathy 80 Evaluation of full-term newborn patient. *Dicle Med J* 2007;34(1): 38-41.
13. Jimmy S, Kemiki AD, Vince JD. Neonatal outcome at Modilon Hospital, Madang: a 5-year review. *P N G Med J* 2003;46(1-2):8-15.
14. Aggarwal R, Deorari AK, Paul VK. Post-resuscitation management of asphyxiated neonates. *Indian J Pediatr* 2001;68(12):1149-53.
15. Gül A, Cömert S, Ağzıkuru T. Retrospective Analysis of the cases of perinatal asphyxia. *J Kartal TR* 2010;21(2):77-83.
16. Tekgul H, Gauvreau K, Soul J, et al. The current etiologic profile and neurodevelopmental outcome of seizures in term newborn infants. *Pediatrics* 2006;117(4):1270-80.
17. Chau V, Farnell K. Neonatal Seizures. *Current Management In Child Neurology Fourth Edition 2009*; Chapter 88; 599-602
18. Sankar MJ, Agarwal R, Aggarwal R et al. Seizures in the newborn. *Indian J Pediatr* 2008;75(2):149-55.
19. Paul E, Max P, Maja S. Predicting the outcome of post asphyxial hypoxic ischemic encephalopathy within 4 hours of birth. *J Pediatr* 1997;131(4): 613-7.
20. Hull J, Dodd KL. Falling incidence of hypoxic-ischaemic encephalopathy in term infants. *Br J Obstet Gynaecol* 1992;99(5):386-91.