Perinatal Asphyxia: Multivariate Analysis of Risk Factors

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Abstract

Perinatal asphyxia contributes greatly to neonatal mortality and morbidity. In developing countries, the need for risk assessment in perinatal asphyxia is obvious because of the high birth rate and limited perinatal resources.

Objective: To determine the incidence and risk factors of perinatal asphyxia in infants who were delivered from mothers with high-risk conditions.

Study Design: A prospective study over a 5-year period from 1993 to 1997 was performed at a tertiary level, referral hospital.

Patients and Method: Nine hundred and sixty-one infants who were delivered from 878 high-risk mothers were recruited. All of the risk factors that might have contributed to asphyxia were identified and recorded. Univariate and stepwise multiple logistic regression analysis was performed to identify significant factors that might have contributed to asphyxia, the odds ratios and 95 per cent confidence interval were computed.

Results: Abnormal fetal heart rate pattern, thick meconium stained amniotic fluid, and premature delivery, were three common risk factors for asphyxia. The mean gestational age was 37.6±3.5 weeks, 10.5 per cent (101/961) were infants less than 33 weeks. The incidence of asphyxia was 9.7 per cent and was highest (26.7%) in infants less than 1000 g. By univariate analysis, significant relationships between perinatal factors and asphyxia were found among birth weight, gestational age, premature and breech delivery but stepwise multiple logistic regression analysis revealed that only birth weight was significantly associated with perinatal asphyxia.

Conclusion: In countries where resources are limited, a neonatal resuscitation team should be available for very low birth weight infants, premature and breech delivery.

Key word : Perinatal Asphyxia, Risk Factors, Neonatal Mortality and Morbidity

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Risk assessment in Perinatology can predict both maternal and neonatal complications. Simple, practical and reliable assessment of risk helps to improve pregnancy outcome. In all countries, perinatal asphyxia contributes greatly to neonatal mortality. Recognition of the fetus at risk is an essential component of neonatal resuscitation if it is to be organized, accurate and successful[1]. The American Academy of Pediatrics (AAP) and the American Heart Association (AHA) indicate that an anticipation of asphyxia, availability of personnel, and resuscitation equipment are requirements for the success of neonatal resuscitation. They also recommend that there should be at least two personnel who can perform all steps of resuscitation well and be available prior to the delivery of a high-risk infant[2]. The objective of this study was to determine the incidence and identify risk factors for asphyxia. If a fetus at risk can be identified before delivery, it will be beneficial to the unit where resources are limited. The asphyxiated infant will have continuing care postnatally if management of a fetus at risk is being organized.

PATIENTS AND METHOD

A prospective study over a 5-year period from 1993 to 1997 was performed in the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital. Eight hundred and seventy-eight high-risk pregnancies resulting in 961 infants were recruited. Stillbirth, congenital malformations and chromosomal abnormalities were excluded from the study. All of the possible factors that place infants at high risk for asphyxia were identified and recorded by the neonatal resuscitation team (Table 1). Following deliveries, the infants were stabilized using guidelines recommended by the AHA and AAP[3]. The Apgar score was assigned at 1 and 5 minutes. If the score was less than 7, it was assigned every 5 minutes until it was greater than 6. Perinatal asphyxia was defined if the Apgar score at 1 minute was less than 4. Complete physical examination including the infant's gestational age assessment was performed by a pediatrician to identify the possible cause and consequences of asphyxia postnatally. The results were expressed as mean and standard deviation. Categorical variables were analyzed by Chi-square and Fisher's Exact test. Continuous variables were analyzed by the Student's *t* test. The odds ratio (OR) and 95 per cent confidence intervals were computed for each variable. Stepwise multiple logistic regression analysis using the maximum likelihood method was used to determine the independent variables that may predispose an infant to asphyxia.

RESULTS

Demographic data of the study population is shown in Table 2. Abnormal fetal heart rate pattern, thick meconium stained amniotic fluid and premature delivery were the most common high-risk conditions (Table 3). Pethidine hydrochloride was prescribed in 96 (12.4%) mothers. Two-thirds of the infants (75%) were delivered by Cesarean section under general (53%), epidural (41%) or spinal anesthesia (6%). The distribution of birth weight and gestational age is shown in Tables 4 and 5. Ninety-nine infants (9.7%) were severely depressed at birth, the incidence being highest (26.1%) among infants less than 29 weeks. Three hundred and

Table 1. Studied demographic data.

Antenatal	duration of membranes ruptured
maternal age	amount and character of amniotic fluid
maternal weight, height	drug administration
pre-existing maternal disease	type of anesthesia and analgesia
gestational age	complication during labor
fetal growth	method of delivery
result of ultrasonography	method of resuscitation
complication during pregnancy	Apgar scores
Delivery	**Postnatal**
fetal presentation	complete physical examination
fetal heart rate pattern	gestational age assessment
evidence of antepartum hemorrhage	consequences of asphyxia

Table 2. Demographic data of the study population.

Factors	Mean ± SD	Median	Mode	Range
maternal age (yr)	27.8 ± 6.0	28	29	14-45
gestational age (wk)	37.6 ± 3.5	39	40	25-44
Apgar score at 1 min.	6.9 ± 2.4	8	9	1-10
Apgar score at 5 min.	9.4 ± 1.2	10	10	1-10
birth weight (g)	2742 ± 771	2830	3100	500-5290

thirty-seven infants (35.1%) required positive pressure ventilation, 2.4 per cent required chest compression accompanied with positive pressure ventilation, and only 1.4 per cent required epinephine administration. Most of the infants responded promptly after resuscitation. The Apgar score at 5 minutes was less than 7 (2.8%) in 27 infants, and of these, 7 infants (25.9%) had a gestational age less than 33 weeks. By univariate analysis, an abnormal fetal heart rate pattern appeared to increase the risk of asphyxia but this was not statistically significant. Relationship between maternal high-risk conditions and asphyxia was found among birth weight, gestational age, prematurity and breech delivery (Tables 6-7). Pethidine hydrochloride and general anesthesia increased the risk but was not statistically significant. Both epidural and spinal anesthesia decreased the risk but epidural anesthesia statistically decreased it by half (OR 0.5). However, when all of the possible risks were computed by multiple logistic regression, perinatal asphyxia was significantly correlated with the infants' birth weight ($P<0.001$).

Table 3. Distribution of high-risk pregnancy.

High-risk conditions	Cases	Per cent
abnormal fetal heart rate	257	26.7
thick meconium stained amniotic fluid	165	17.2
preterm delivery	123	12.8
twin gestation	83	8.6
breech presentation	72	7.5
preeclampsia	41	4.3
placenta previa	57	5.9
maternal diabetes	35	3.6
prolapse cord	16	1.7
IUGR	15	1.6
chorioamnionitis	15	1.6
miscellaneous	82	8.5

DISCUSSION

Perinatal asphyxia remains a significant cause of infant death and neuro-developmental impairment, probably causing 20 per cent of all cases of cerebral palsy[4]. Apparently, because of varying definitions as well as the absence of specific signs, the true incidence of asphyxia is unknown. Although there are criticisms that the Apgar scores are not an accurate predictor of subsequent neuro-

Table 4. Distribution of the birth weight.

Birth weight (g)	Cases	Per cent
≤ 1000	18	1.9
1001 - 1500	56	5.8
1501 - 2000	105	10.9
2001 - 2500	146	15.2
> 2500	636	66.2

Table 5. Distribution of the gestational age.

Gestational age (wk)	Cases	Per cent
≤ 28	23	2.4
29 - 32	78	8.1
33 - 36	188	19.6
37 - 40	519	54.0
41 - 42	131	13.6
> 42	22	2.3

Table 6. Risk factors for neonatal asphyxia.

Factors	Mean ± SD		P value
	cases	controls	
gestational age (wk)	36.3 ± 4.3	37.9 ± 4.4	P< 0.001
birth weight (g)	2377 ± 861	2784 ± 749	P< 0.01

Table 7. Odds ratio for perinatal asphyxia.

Factors	Apgar score at 1 minute< 4	
	OR	95% CI
abnormal fetal heart rate pattern	1.1	0.72, 1.82
thick mec. stained amniotic fluid	0.8	0.47, 1.50
premature delivery	1.8	1.09, 3.17*
normal vaginal delivery	0.8	0.43, 1.83
cesarean section	0.7	0.48, 1.19
forceps delivery	-	-
breech delivery	2.3	1.29, 4.38*
vacuum extraction	1.1	0.49, 2.89
pethidine administration	1.4	0.79, 2.56
general anesthesia	1.5	0.99, 2.28
epidural anesthesia	0.5	0.31, 0.87*
spinal anesthesia	0.4	0.09, 1.68

* statistically significant

developmental outcome of newborn infants,(5,6) this is still the most feasible and practical system to perform in the delivery room. The reported incidence of asphyxia varies from place to place depending on the criteria of diagnosis and population at risk(7-9). In Sweden, it ranged from 2.9 (Apgar score less than 4 at 5 min.) to 17 (Apgar score less than 4 at 1 min. and/or less than 7 at 5 min) per 1000 live-births(9). Chandra reported an incidence of 36.6 per 1000 in 2316 consecutive births(7). When using the Apgar score at 1 minute as an indicator of asphyxia, we found an incidence of 10 per cent. Due to difference in population at risk and one-third being premature infants less than 37 weeks, the incidence of asphyxia in our populatation is higher than in other studies(8). Organ immaturity is responsible for low Apgar scores in premature infants. When using an Apgar score of less than 7 as a definition of asphyxia and infants less than 34 weeks were excluded, Hall found an incidence of 4.6/1000(8).

Factors that place an infant at risk of asphyxia can be categorized into maternal, fetal factors and delivery process. A fetus *in utero* who is suffering from asphyxia usually manifests with an abnormal fetal heart rate (FHR) pattern. Our study revealed that an abnormal FHR is not statistically associated with asphyxia (OR 1.1) because only certain types of FHR pattern are common in a fetus which is suffering from intrauterine asphyxia. Persistent fetal bradycardia or persistent non-reactive fetal heart rate tracing has been shown to be associated with poor outcome(10). Pethidine hydrochloride is commonly prescribed in mothers for pain relief. It may have an influence on respiratory drive of an infant resulting in perinatal asphyia(11). In our population, Pethidine hydrochloride slightly increased the risk (OR 1.4) but this difference was not statistically significant. When comparing the effects of maternal anesthesia on a newborn infant, the infant who was delivered from a mother who received general anesthesia had lower Apgar scores when compared to an infant born with epidural or spinal anesthesia(12). In our study, epidural anesthesia statistically decreased the risk of asphyxia by half. General anesthesia appears to increase the risk but is not statistically significant. Maternal pre-eclampsia with HELLP syndrome and frank umbilical cord prolapse has been shown to be a risk for asphyxia(13,14). But we couldn't find this association because of the small number in our population. Vaginal breech delivery was commonly associated with asphyxia,(7,15,16) the odds ratio in our study was 2.3. In addition to this, we found that premature infants are at risk for asphyxia as in a previous publication,(10) the odds ratio being 1.8.

In conclusion, factors that might place an infant at risk of perinatal asphyxia include premature delivery, vaginal breech delivery, birth weight and gestational age. In countries where perinatal resources are limited, a neonatal resuscitation team should be available at least for those high-risk conditions. If this policy is accepted and is followed, the mortality as well as the morbidity of the asphyxiated infant will be minimized.

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REFERENCES

1. Bloom RS, Cropley C. Textbook of Neonatal Resuscitation. American Academy of Pediatrics and American Heart Association. Texas, Dallas, 1987: 43-364.
2. Bloom RS, Cropley C. Textbook of Neonatal Resuscitation. American Academy of Pediatrics and American Heart Association. IL: Elk Grove Village, 1990: 42-354.
3. Bloom RS, Cropley C. Textbook of Neonatal Resuscitation. American Academy of Pediatrics and American Heart Association. IL: Elk Grove Village, 1994: 40-342.
4. Patel J, Edwards AD. Prediction of outcome after perinatal asphyxia. Curr Opin Pediatr 1997; 9: 128-32.
5. Manganaro R, Mami C, Gemelli M. The validity of the Apgar scores in the assessment of asphyxia at birth. Eur J Obstet Gynecol Reprod Biol 1994; 54: 99-102.
6. American Academy of Pediatrics. Use and abuse of the Apgar score. Pediatrics 1996; 98: 141-2.
7. Chandra S, Ramji S, Thirupuram S. Perinatal asphyxia: multivariate analysis of risk factors in hospital births. Indian Pediatr 1997; 34: 206-12.
8. Hall DR, Smith M, Smith J. Maternal factors contributing to asphyxia neonatorum. J Trop Pediatr 1996; 42: 192-5.
9. Thornberg E, Thiringer K, Odeback A, Milsom I. Birth asphyxia: incidence, clinical course and outcome in a Swedish population. Acta Paediatr 1995; 84: 927-32.
10. Lam BC, Yeung CY. Perinatal features of birth asphyxia and neurologic outcome. Acta Paediatr Jpn 1992; 34: 17-22.
11. Hamza J, Benlabed M, Orhant E, Escourrou P, Curzi-Dascalova L, Gaultier C. Neonatal pattern of breathing during active and quiet sleep after maternal administration of meperidine. Pediatr Res 1992; 32: 412-6.
12. Ratcliffe FM, Evans JM. Neonatal wellbeing after elective caesarean delivery with general, spinal, and epidural anesthesia. Eur J Anaesthesiol 1993; 10: 175-8.
13. Raval DS, Reid MA, Pildes R. Maternal and neonatal outcome of pregnancies complicated with maternal HELLP syndrome. J Perinatol 1997; 17: 266-9.
14. Prabulos AM, Philipson EH, Umbilical cord prolapse. Is the time from diagnosis to delivery critical ? J Reprod Med 1998; 43: 129-32.
15. Koo MR, Dekker GA, van Geijn HP. Perinatal outcome of singleton term breech deliveries. Eur J Obstet Gynecol Reprod Biol 1998; 78: 19-24.
16. Boo NY, Lye MS. Factors associated with clinically significant perinatal asphyxia in the Malaysian neonates: a case-control study. J Trop Pediatr 1991; 38: 284-9.

การศึกษาปัจจัยเสี่ยงของภาวะขาดออกซิเจนระยะปริกำเนิด

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การขาดออกซิเจนเป็นสาเหตุสำคัญที่ทำให้ทารกวัยแรกเกิดเสียชีวิตและมีความพิการทางสมองที่เกิดขึ้นกับทุกประเทศโดยเฉพาะประเทศด้อยพัฒนาหรือกำลังพัฒนา ในประเทศที่กำลังพัฒนา เช่น ประเทศไทย การใช้ทรัพยากรที่มีอยู่ให้ได้ประโยชน์สูงสุดมีความสำคัญเป็นอย่างยิ่ง โดยเฉพาะขณะที่ประเทศกำลังประสบปัญหาทางเศรษฐกิจ และคงมีความสำคัญมากยิ่งขึ้นต่อไปในอนาคต เนื่องจากภาวะขาดออกซิเจนปริกำเนิดสามารถป้องกันได้ถ้าการดูแลมารดาระหว่างตั้งครรภ์และขณะคลอดทำได้อย่างมีประสิทธิภาพ การค้นหาปัจจัยเสี่ยงเป็นสิ่งจำเป็นสำหรับการป้องกันภาวะขาดออกซิเจนปริกำเนิดที่สำคัญประการหนึ่ง คณะผู้วิจัยจึงได้ทำการศึกษาหาปัจจัยเสี่ยงที่ทำให้ทารกซึ่งคลอดจากมารดาตั้งครรภ์เสี่ยงทั้งหมด 961 ราย ทารกตายคลอด ทารกที่มีความพิการแต่กำเนิดและทารกที่มีความผิดปกติของโครโมโซมจะไม่ถูกนำมาศึกษา ปัจจัยเสี่ยงที่ตรวจพบในมารดาและทารกจะถูกบันทึกลงในแบบฟอร์มก่อนคลอด และนำมาวิเคราะห์ทางสถิติด้วยวิธี univariate และ stepwise multiple logistic regression ภาวะตั้งครรภ์เสี่ยงที่พบบ่อย คือ abnormal fetal heart rate pattern, thick meconium stained amniotic fluid และการคลอดก่อนกำหนด ร้อยละ 89.5 ของทารกที่นำมาศึกษามีอายุครรภ์ $\geq$ 34 สัปดาห์ โดยมีอายุครรภ์เฉลี่ย 37.6 $\pm$ 3.5 สัปดาห์ ผลการศึกษาพบอุบัติการณ์ของภาวะขาดออกซิเจนระยะปริกำเนิดร้อยละ 9.7 โดยมีอุบัติการณ์สูงสุด (ร้อยละ 26.7) ในทารกน้ำหนักต่ำกว่า 1,000 กรัม และการวิเคราะห์ทางสถิติพบว่า ภาวะขาดออกซิเจนปริกำเนิดมีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติกับน้ำหนักแรกเกิด อายุครรภ์ การคลอดก่อนกำหนด และการคลอดท่าก้น แต่เมื่อใช้ stepwise multiple logistic regression จะพบว่ามีเพียงน้ำหนักแรกเกิดเท่านั้นที่มีความสัมพันธ์ต่อภาวะขาดออกซิเจนอย่างมีนัยสำคัญทางสถิติ ($P<0.001$)

โดยสรุป เพื่อลดอุบัติการณ์อัตราตาย และอัตราความพิการของทารกที่มีภาวะขาดออกซิเจนระยะปริกำเนิดในประเทศที่มีทรัพยากรจำกัด เช่น ประเทศที่กำลังพัฒนา ทีมช่วยฟื้นคืนชีพควรพร้อมให้การช่วยเหลือทารกน้ำหนักตัวน้อย (very low birthweight infant) ทารกเกิดก่อนกำหนดและทารกคลอดท่าก้น เพราะทารกกลุ่มนี้มีโอกาสเกิดภาวะขาดออกซิเจนได้สูงกว่าทารกกลุ่มอื่น

คำสำคัญ : ภาวะขาดออกซิเจนระยะปริกำเนิด, ปัจจัยเสี่ยง, อัตราป่วย-ตาย

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