

PERINATAL ASPHYXIA: MULTIVARIATE ANALYSIS OF RISK FACTORS IN HOSPITAL BIRTHS

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Objective: To determine risk factors for perinatal asphyxia. **Design:** Cohort study. **Setting:** Teaching hospital. **Methods:** All consecutive hospital births were evaluated during the study period. Asphyxia was defined on intrapartum and neonatal resuscitation criteria. Maternal, intrapartum and neonatal variables were recorded in all births. Data was analyzed after stratifying for live and stillbirths by univariate and logistic regression analyses. **Results:** Amongst 2371 births (55 fetal deaths and 2316 live births), there were 86 cases of perinatal asphyxia (35 fetal deaths and 51 live births), providing an asphyxia rate of 36.3/1000 births. On multivariate analysis, risk factors significantly associated with asphyxia included prolonged second stage labor (OR 9.4), vaginal breech delivery (OR 6.6), elective cesarean delivery (OR 4.6), pregnancy induced hypertension (PIH) (OR 2.7) and fetal growth retardation (SFD) (OR 2.4). Amongst stillborn, the significant univariate factors associated with asphyxia were prolonged second stage labor (RR 1.7) and cord prolapse (RR 1.7). **Conclusions:** There is a need to strengthen intrapartum management and early identification of mothers with PIH or intrauterine growth retardation to reduce asphyxial morbidity and mortality.

Key words: Asphyxia neonatorum, Fetal growth retardation. Perinatal mortality.

PERINATAL asphyxia is an important cause of neonatal morbidity and mortality; and a cause of neurologic handicaps in children. Despite availability of numerous studies, epidemiologists have been unable to quantify the size and distribution of asphyxia with sufficient precision. The major problem in asphyxia epidemiological investigation has been the inability of researchers to universalize its definition and quantification. Asphyxia definitions have included need for assisted ventilation >1 minute, low Apgar scores (<7 at 1 or 5 min), absent or poor respiratory effort at 1 min with or without signs of fetal distress(1-6). Most studies evaluating as-

phyxia risk factors have limited themselves to univariate analysis (without confounder control) and have not included late fetal deaths resulting from intrauterine hypoxia for risk analysis(3,5,6). The present communication attempts to overcome these lacunae and identify risk factors associated with asphyxia, particularly those which may be amenable to interventional strategy.

Subjects and Methods

All consecutive hospital births during the study period formed the cohort. The study population comprised of asphyxiated neonates (as defined below) and the re-

maining served as controls.

Definition of Asphyxia

A. Neonates fulfilling at least one of the intrapartum criteria of fetal distress and one of the neonatal features of asphyxia were defined as having asphyxia. This was done to ensure a reasonable certainty of a perinatal asphyxic insult. The intrapartum criteria of fetal distress included: (a) Fetal Heart Rate (FHR) abnormality: Fetal bradycardia (<100 beats/minute) or fetal tachycardia (>160 beats/minute) or abnormal cardiotocographic findings; and (b) Presence of meconium stained amniotic fluid (MSAF). The neonatal criteria included: (a) Need for assisted ventilation >1 min for establishment of adequate spontaneous respiratory efforts; (b) Apgar score <7 at 1 min of age; and (c) Alteration in both tone (hypo- or hypertonia) and sensorium (obtundation or irritability) during the first day of life not attributable to other causes such as prematurity, sepsis, metabolic disturbances, intracranial hemorrhage, etc.

B. Late fetal deaths accompanied by features of intrapartum fetal distress (FHR abnormalities, MSAF) were also designated as asphyxia.

Infants with lethal or major malformations were excluded from the study. Details of maternal (age, pre-eclampsia, placenta- previa, diabetes mellitus, etc.), intrapartum (duration of labor, use of oxytocin, presence of cord prolapse and abruptio placentae, fetal heart rate abnormalities, fetal presentation, mode of delivery including cesarean section performed as emergency/elective, presence or absence of meconium stained liquor) and neonatal variables (Apgar score, resuscitation need and duration, birth weight, gestation, intrauterine

growth status(7), multiple births) were recorded in all subjects.

Asphyxiated neonates were closely observed for abnormal neurologic signs suggesting hypoxic ischemic encephalopathy (HIE)(8) and development of complications. All neonates were observed for atleast 48 h after birth and morbidities (particularly neurologic) were carefully recorded.

Statistical Analysis

The data was analyzed after stratifying for still births and live birth. Continuous normally distributed data were analyzed by comparing means using the Student-t test. Non parametric data were analyzed using the Mann Whirney-U test. Proportions were analyzed using Chi-square or Fisher's exact test. To adjust for confounders, factors found significant on univariate analyses were analyzed using an unweighted logistic regression model. A probability of 5% was considered significant.

Results

A total of 2371 (55 fetal deaths and 2316 live births) consecutively born infants were enrolled in the study after exclusion of 25 cases (9 fetal deaths and 16 live births) with major congenital malformations (pulmonary agenesis, cyanotic heart disease, hydrocephalus, etc.). There were 86 (35 fetal deaths and 51 live births) cases of perinatal asphyxia, providing a prevalence of 36.3/1000 births. *Table I* provides the profile of asphyxia criteria in liveborn neonates. All asphyxic newborns who had alteration in tone and sensorium were also accompanied by either an Apgar score <7 or needed assisted ventilation at birth.

Table II provides the results of univariate analysis of risk factors for perinatal asphyxia amongst liveborn in-

TABLE I—Profile of Asphyxia Criteria in Liveborn Neonates (%)

Criteria	Asphyxia (n=51)	Control (n=2265)
<i>Intrapartum</i>		
Fetal heart rate abnormality	10 (19.6)	32 (1.4)
Meconium stained amniotic fluid	29 (56.9)	92 (4.1)
FHR + MSAF	12 (23.5)	13 (0.6)
<i>Neonatal</i>		
Apgar <7 (1 min)	21 (41.2)	91 (4.0)
Duration of resuscitation > 1 min	0	3 (0.1)
Altered tone + sensorium	0	1 (0.04)
Apgar <7 + duration of resuscitation >1 min	9 (17.6)	8 (0.4)
Apgar <7 + altered tone & sensorium	3 (5.9)	6 (0.3)
Duration of resuscitation >1 min + altered tone & sensorium	18 (35.3)	11 (0.5)

FHR - Fetal heart rate abnormality
MSAF - Meconium stained amniotic fluid

fants. Those observed to be significantly associated with asphyxia included (in decreasing order of risk) cord prolapse, prolonged second stage of labor, breech vaginal and elective cesareans, pregnancy induced hypertension (PIH), labor induction with oxytocin and lower antenatal visits. The only significant neonatal factor was a small for date (SFD) (<10 centile) birth. Subset analysis of hypertensive mothers did not reveal any difference in the mean systolic or diastolic blood pressures between the groups.

In the case of stillbirths, the variables significantly associated with fetal asphyxia were prolonged second stage labor (RR 1.7) and cord prolapse (RR 1.7) (*Table III*).

All variables observed to be significant on univariate analysis in liveborns were entered into a multiple logistic regression model. Factors that were independently associated with perinatal asphyxia in the reduced model (in decreasing risk order) were prolonged second stage of labor, breech vaginal delivery, elective cesareans, pregnancy induced hypertension (PIH) and SFD births (*Table IV*).

Discussion

Several studies have attempted to evaluate the incidence of asphyxia and its risk factors. The reported incidence of asphyxia amongst live born neonates has varied from 1-10% (1-6). In the present study, the incidence of asphyxia amongst livebirths was 2.2%, but amongst stillbirths it was 63.6%. The variations observed are due to the differing definitions of asphyxia that have been adopted by various authors - Apgar score at 1 or 5 min, duration of resuscitation, breathing effort at 1 min or a combination of features of fetal distress (abnormal fetal heart rates or meconium stained liquor) and one or more of the above criteria. The incidence would also be influenced by the inclusion of late fetal deaths, as has been observed in the present study (they constituted 40% of asphyxiated infants). To the best of our knowledge, none of the earlier studies have included fetal deaths due to perinatal asphyxia in their analysis.

In the present study, it was observed that prolonged second stage of labor, breech vaginal and elective cesareans, pregnancy induced hypertension (PIH) and SFD births had a strong independent association with perinatal asphyxia. A high risk

TABLE II—Univariate Analysis of Risk Factors for Asphyxia Amongst Liveborns

Variables	Asphyxia (n=51)	Controls (n=2265)	RR (95% CI)
<i>Maternal</i>			
* Maternal age (yrs) mean (SD)	23.6 (2.9)	24.3 (3.7)	—
* No. of antenatal visits # median (range)	1 (0-8)	2 (0-9)	
* PIH/Eclampsia (%) ##	8 (15.7)	119 (5.3)	3.2 (1.5,6.7)
—Max. systolic BP (mm Hg) mean (SD)	146.3 (9.1)	144.2 (13.8)]	—
—Max. diastolic BP (mm Hg) mean (SD)	96.5 (7.4)	98.9 (8.4)	—
<i>Intrapartum</i>			
* Oxytocin induction (%) #	25 (49)	740 (32.7)	1.9 (1.1,3.4)
* Prolonged II stage (%) ##	6 (11.8)	27 (1.2)	9.2 (4.2,20.1)
* Abruptio placentae/ placenta previa (%)	2 (3.9)	17 (0.8)	4.9 (1.3,18.8)
* Cord prolapse (%) #	1 (1.9)	1 (.04)	23.1 (5.6,95.1)
<i>* Mode of delivery</i>			
—Breech vaginal (%) #	8 (15.7)	59 (2.6)	6.3 (3.1,12.8)
—Cesarean non-emergency (%) #	10 (19.6)	118 (5.2)	4.2 (2.1,6.1)
—Cesarean emergency (%)	2 (3.9)	66 (2.9)	
—Forceps (%)	2 (3.9)	28 (1.2)	3.1 (0.8,12.2)
<i>Neonatal</i>			
* Birth weight (g) mean (SD)	2554(648)	2668(513)	—
* Gestation (wks) mean (SD)	38.2 (2.9)	38.8 (2.1)	—
* Preterms (%)	3 (5.9)	199 (8.8)	0.7 (0.2,2.1)
* Sex - male (%)	25 (49)	1215(53.6)	
— female (%)	26 (51)	1050(46.4)	0.8 (0.5,1.4)
* Multiple births (%)	1 (1.9)	18 (0.8)	2.4 (0.4,16.6)
<i>Intrauterine growth</i>			
—Small for dates (%) # ¹	14 (27.5)	299 (13.2)	2.5 (1.4,4.6)
—Large for dates (%) ²	4 (7.8)	72 (3.2)	2.5 (0.9,6.7)

p <0.05, ## p <0.001

1 = SFD <10 centile;

2=LFD >90 centile

TABLE III—Univariate Analysis of Risk Factors for Asphyxia Amongst Stillborns

Variables	Asphyxia (n=35)	Controls (n=20)	RR (95% CI)
<i>Maternal</i>			
– Maternal age (yrs) mean (SD)	23.7 (4.4)	25.0 (4.3)	
– No. of antenatal visits # median (range)	1 (0-5)	2 (0-8)	
– PIH/Eclampsia (%) Max. systolic BP (mm Hg) mean (SD)	8 (22.9) 156 (14.8)	5 (25) 147.3 (22.3)	1.2 (0.7,1.9)
– Max. diastolic BP (mm Hg) mean (SD)	109.1 (18.0)	100.3 (16.3)	
<i>Intrapartum</i>			
– Prolonged II stage (%) #	7 (20)	0	1.7 (1.4,2.2)
– Abruptio placentae/ placenta previa (%)	6 (17.1)	1 (5)	1.7 (1.1,2.5)
– Cord prolapse (%) #	7 (20)	1 (5)	1.7 (1.4,2.2)
– Breech vaginal delivery (%)	9 (25.7)	1 (5)	1.6 (1.1,2.2)
<i>Fetal</i>			
– Birth weight (g) mean (SD)	2240 (710)	2088 (688)	
– Gestation (wks) mean (SD)	37.0 (3.5)	37.8 (3.1)	
– Preterms (%)	12 (34.3)	7 (35)	0.9 (0.7,1.5)
– Sex - male (%) - female (%)	23 (65.7) 12 (34.3)	9 (45) 11 (55)	1.4 (0.9,2.2)
– Intrauterine growth Small for dates (%) Large for dates (%)	9 (25.7) 2 (5.7)	10 (50) 1 (5)	0.6 (0.3,1.0) 0.9 (0.3,2.5)

p < 0.05,

of perinatal asphyxia has been reported to be associated with abruptio placentae and cord prolapse(1,3 -6). The reported risk for asphyxia following hemorrhage consequent to abruptio placenta is 5-13 times. The relative risk of asphyxia in these acute obstetrical emergencies has generally been underestimated due to the fact that these

complications have a high risk of fetal mortality and most studies have excluded fetal deaths from their analysis. Earlier studies have also reported a 5 to 12 times risk of asphyxia with toxemia of pregnancy on univariate analysis(5,6). Diastolic blood pressure >85 mm Hg has been reported to be significantly higher in mothers of as-

TABLE IV—Multiple Logistic Regression Analysis of Risk Factors for Perinatal Asphyxia in Liveborns

Predictor variables	Coefficient	SE	Odds Ratio (95% CI)
Prolonged II Stage	2.2458	0.51	9.4 (3.5-25.5)
Vaginal breech delivery	1.8900	0.43	6.6 (2.8-15.4)
Elective cesarean	1.5193	0.39	4.6 (2.1-9.8)
PIH	0.9862	0.42	2.7 (1.2-5.9)
SFD	0.8970	0.34	2.4 (1.3-4.7)

PIH - Pregnancy induced hypertension

SFD - Small for dates (<10 centile)

All factors $p < 0.05$

(All variables coded as present=1 or absent=0)

phyxiated newborns (9). The present study however, did not observe any differences in the maternal blood pressures of asphyxiated and non-asphyxiated neonates. The association of prolonged labor(3,4,9), vaginal breech deliveries(1,2,10-12) and intrauterine growth retardation with increased risk of asphyxia have been well documented by several studies(2,3,5). All these risk factors have not been universally observed to be associated with asphyxia in earlier reports. This may be related to sampling procedures or differing asphyxia definitions as highlighted earlier. The significant association between elective cesarean births and asphyxia is difficult to explain. However, it may reflect non-recognition of risk factors such as fetal growth retardation, or inadequate fetal monitoring in such mothers resulting in non-identification of the presence of fetal distress.

The present study reaffirms the fact that most perinatal asphyxial insults are strongly associated with pregnancy related complications such as hypertension and fetal growth retardation, and intrapartum problems such as prolonged labor, cord prolapse, vaginal breech and cesarean deliveries. If asphyxial incidence and its consequent perinatal mortality and neuro-impairment in the surviving infants are to be

reduced, there is a need to identify mothers at risk, for institutional delivery and also strengthen labor room services with availability of skilled medical personnel at all times to manage complicated labors, including facilities for operative deliveries where required.

REFERENCES

1. Bhargava SK, Batra A, Sen Gupta A, Das SK. Study of asphyxia neonatorum. *J Obstet Gynecol India* 1988, 38:162-166.
2. MacDonald HM, Mulligan JC, Allen AC, Taylor PM. Neonatal asphyxia. I: Relationship of obstetric complications to neonatal mortality in 38,405 consecutive deliveries. *J Pediatr* 1980, 65: 898-902.
3. Boo NY, Lye MS. Factors associated with clinically significant perinatal asphyxia in Malaysian neonates: A case controlled study. *J Trop Pediatr* 1992, 38: 284-289.
4. Nathoo KJ, Chimbra THK, Mtima valve LAR. Mortality and immediate morbidity in term babies with low Apgar scores (Zimbabwe). *Ann Trop Pediatr* 1990, 10: 239-244.
5. Singh M, Paul VK, De orari AK. Epidemiological correlates, early clinical features and sequelae of perinatal hypoxia. Indian Council of Medical Research Report, New Delhi, 1992.
6. Daga AS, Daga SR, Patole SK. Risk assessment in birth asphyxia. *J Trop Pediatr* 1990, 36: 34-39.
7. Singh M, Giri SK, Ramachandran K. Intrauterine growth curves on live born ba-

- bies. *Indian Pediatr* 1974,11: 475-479.
8. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. *Arch Neurol* 1976,33: 696-705.
 9. Alfy AL, Carroll JE, Devarajan LV, Mousaa MAA. Term infant asphyxia in Kuwait. *Ann Trop Pediatr* 1990,10: 355-365.
 10. Bhalerao AR, Nitwe MT, Shah RH, *et al.* Neonatal morbidity and mortality following breech deliveries. *J Obstet Gynecol India* 1987, 37: 406-409.
 11. Chaturvedi P, Shah N. Fetal correlates and mode of delivery in asphyxia neonatorum. *Indian J Pediatr* 1991, 58: 63-67.
 12. Cyr RM, Usher RH, McLean FH. Changing pattern of birth asphyxia and trauma over 20 years. *Am J Obstet Gynecol* 1984, 148:490-498.
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