

## Risk factors for mortality in birth asphyxia of outborn neonates: A prospective observational study

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### Abstract

**Background:** Birth asphyxia accounts for around 23% of annual neonatal deaths in the developing world.

**Objective:** To assess the risk factors for death in outborn neonates with birth asphyxia.

**Method:** A one year prospective observational cohort study was undertaken in a tertiary care teaching government hospital in India. All outborn referral neonates diagnosed with birth asphyxia were included. Demographic, maternal and neonatal factors were included and analysed.

**Results:** Incidence of birth asphyxia was 17.3% with a male: female ratio of 1.3:1. Ninety five percent mothers received antenatal care and 98% were delivered at either primary or secondary health care level institutes. Mean distance travelled by baby was 89.42±69.36 km. One hundred and twenty two (68%) mothers were anaemic, 45 (25%) had systemic hypertension and 75 (42%) had preeclampsia/eclampsia. One hundred and forty (78%) babies were term and 103 (57%) had average birth weights. A history of not crying at birth was available in 95% neonates who were resuscitated by paramedical person and medical officers. Case fatality rate was 40.6%. Average duration of hospital stay of non-survivors was 4.35±2.98 days compared to 9.07±4.85 days in surviving neonates ( $P<0.0001$ ). Most deaths were in HIE stage III. Unbooked mothers ( $p=0.01$ ), maternal anaemia (OR 3.07, CI 1.12-8.41,  $p=0.02$ ), neonates requiring resuscitation (OR 0.26, CI 0.10-0.68,  $p=0.006$ ), neonates presenting with convulsions (OR 4.46, CI 1.46-12.16,  $p=0.003$ ) or cyanosis ( $p<0.008$ ), prolonged capillary refill time (OR 0.32, CI 0.47-0.82,  $p=0.004$ ) and neonates in HIE stage III (OR 1.60, CI

1.04-2.46,  $p=0.03$ ) were the risk factors for mortality in asphyxiated neonates.

**Conclusions:** The case fatality rate was 40.6% among outborn referral neonates with birth asphyxia in this study. Unbooked mothers, maternal anaemia, neonates requiring resuscitation, neonates presenting with convulsions or cyanosis, prolonged capillary refill time and neonates in HIE stage III were risk factors for mortality in asphyxiated outborn neonates.

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(Key Words: Birth asphyxia, risk factors of mortality, outborn neonate, referral neonate)

### Introduction

A correct definition of birth asphyxia requires assessment of cord blood pH, Apgar score, neurological status, and markers of multi-organ function<sup>1</sup>. Thus, accurate assessment of mortality from birth asphyxia is limited in developing countries. WHO defines birth asphyxia as failure to initiate and sustain breathing at one minute<sup>2</sup>. Similarly, National Neonatology Forum of India defines birth asphyxia as gasping and ineffective breathing or lack of breathing at one minute after birth<sup>3</sup>. Birth asphyxia accounts for about 23% of annual neonatal deaths in the developing world<sup>4</sup>. Hospital based studies from India estimate that birth asphyxia accounts for 20-40% of perinatal deaths<sup>5-7</sup>. In India, the burden in rural areas is underestimated due to most deaths occurring at home and being underreported. In rural areas of Uttar Pradesh and Maharashtra, 23% and 25% respectively of neonatal deaths were thought to be due to birth asphyxia<sup>8,9</sup>.

Risk factors for birth asphyxia can be antepartum, intrapartum or fetal/neonatal and include increased or decreased maternal age, prolonged rupture of membranes, meconium stained liquor, multiple births, lack of attendance for antenatal care, low birth weight, malpresentation, induction of labour using oxytocin, antepartum haemorrhage, pre-eclampsia/eclampsia, antepartum and intrapartum anaemia<sup>10,11</sup>. Whilst a great amount of data on perinatal asphyxia in intensive care units is available, data on outborn neonates treated in general paediatric wards are lacking.

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## Objective

To assess the risk factors for death in outborn neonates with birth asphyxia.

## Method

A prospective observational cohort study was undertaken in a tertiary care teaching government referral hospital in central India over a period of one year from May 2016 to April 2017. In the paediatric specialty, there were three wards of 40 beds each and four units working by rotation, a 20-bedded neonatal intensive care unit (NICU) and a 10-bedded paediatric intensive care unit (PICU) functioning effectively. As per policy of the hospital, outborn and referral neonates were not admitted in our NICU and hence were provided level II neonatal care in the general paediatric ward.

All outborn referral neonates, diagnosed with birth asphyxia and admitted through the outpatient or emergency departments, were included in the study after approval from the institutional ethical committee, and after obtaining informed valid consent from the parents. Diagnosis of birth asphyxia was based on the Apgar scores, obtained from available documents, birth information extracted from referral person or estimated from mothers/caretakers based on history of delayed cry, details of activity, colour and respiratory effort of the newborn after birth. History of convulsions in the first 24 hours and documentation of multi-organ failure in the first 72 hours of life were also considered as birth asphyxia. Five minute Apgar scores less than 7 were used to diagnose and grade the degree of perinatal asphyxia on the basis of the Sarnat Scale<sup>12</sup>.

### Exclusion criteria:

1. Babies with birth weight less than 1000g or gestational age less than 36 weeks.
2. Babies with anaesthesia-related low Apgar scores
3. Babies with lethal congenital abnormalities such as hydrops, cyanotic congenital heart disease or congenital infections.
4. Babies of parents who left the hospital against medical advice and babies of parents who did not wish to participate in the study.

Data for the study were collected following admission from either mother or caregiver in a specially designed proforma. The data obtained included maternal age, gravida, parity, previous abortions, availability of health facility, antenatal care provider, booked or unbooked mothers, distance from institute, referral person, maternal disease, obstetric complications, mode of delivery

and place of delivery. Neonatal data included gestational age, gender, age on admission, weight on admission, diagnosis on admission and duration of hospital stay. All neonates were managed as per standard protocol and observed till death or discharge, and outcome was measured as survival and death.

*Statistical analysis:* The data were entered into a Microsoft Excel sheet and analysed utilizing STATA version 14. Continuous variable were expressed as mean  $\pm$  SD. Categorical variables were expressed as frequencies and percentages. Continuous variables were compared between survivors and non-survivors by doing independent "t" test for normalised data and Mann-Whitney test for non-normalised data. Categorical variables were compared by Chi-square test. For small numbers Fischer Exact test was used wherever applicable. Multiple logistic regression was performed to identify significant risk factors for mortality. Adjusted odds ratio (OR) and 95% confidence interval (CI) were calculated. A *p* value of <0.05 was considered statistically significant.

## Results

### Participant characteristics

One thousand and thirty eight outborn neonates were admitted during the study period and 180 of them were diagnosed as having had birth asphyxia. The male: female ratio was 1.3:1 and 108 (60%) were from the rural area and from the lower socioeconomic class. Though healthcare facilities were available to all mothers, 173 (96.1%) mothers received antenatal care at primary, secondary or tertiary centres and 109 (60.6%) from medical officers. One hundred and twenty two (67.8%) mothers were anaemic, 45 (25%) had systemic hypertension and 75 (41.7%) had preeclampsia/eclampsia. One hundred and twenty eight (71.1%) mothers were primigravida. One hundred and seventy six (97.8%) mothers were delivered at primary and secondary care facilities and 155 (86.1%) were delivered vaginally (Table 1).

Mean distance travelled by baby to reach our institute was 89.42 $\pm$ 69.36 km. One hundred and forty (77.8%) babies were term and 103 (57.2%) had average birth weights. History of not crying at birth was available in 95% neonates and they were resuscitated by paramedical person and medical officers. Mean age at admission of non-survivors was 3.14 $\pm$ 4.45 days and of surviving neonates was 3.90 $\pm$ 5.88 days. Average duration of hospital stay of non-survivors was 4.35 $\pm$ 2.98 days compared to 9.07 $\pm$ 4.85 days in surviving neonates (*p*<0.0001). (Table 2)

**Table 1: Maternal variables for mortality in birth asphyxia (Univariate analysis)**

Variable	All patients (n=180)	Survival (n=107)	Non survival (n=73)	p value
<i>Mean age of mother (years) Mean ± SD</i>	22±2.57	23.73±2.77	23.17±2.28	0.13
<i>Gravida</i>				
Primigravida - Number (%)	128 (71.1)	78 (72.9)	50 (68.5)	0.24
Multi Gravida - Number (%)	52 (28.9)	29 (27.1)	23 (31.5)	
<i>Available facilities</i>				
Primary Health Care - Number (%)	50 (27.8)	30 (28.0)	20 (27.4)	0.83
Secondary Health Care - Number (%)	39 (21.7)	21 (19.6)	18 (24.7)	
District Hospital - Number (%)	39 (21.7)	25 (23.4)	14 (19.2)	
Tertiary Teaching Institute - Number (%)	52 (28.9)	31 (29.0)	21 (28.8)	
<i>Service Provider</i>				
Trained Dai - Number (%)	04 (02.2)	02 (01.87)	02 (02.7)	0.45
ASHA Worker - Number (%)	16 (08.9)	08 (07.48)	08 (11.0)	
Medical Officer - Number (%)	109 (60.6)	67 (62.6)	42 (57.5)	
Obstetrician - Number (%)	49 (27.2)	30 (28.0)	19 (26.0)	
Specialist - Number (%)	02(01.1)	0 (0)	02 (02.7)	
<i>ANC Visit</i>				
Booked - Number (%)	173 (96.1)	106 (99.1)	67 (91.8)	0.018
Unbooked - Number (%)	07 (03.9)	01 (0.9)	06 (08.2)	
<i>Referral person of neonate</i>				
Trained Dai - Number (%)	04 (02.2)	03 (02.8)	01 (01.4)	0.61
ASHA worker - Number (%)	36 (20.0)	19 (17.8)	17 (23.3)	
Medical Officer - Number (%)	140 (77.8)	85 (79.4)	55 (75.3)	
<i>Average distance from institute (km) Mean ± SD</i>	89.42±69.36	87.93±67.37	90.43±72.29	0.81
<i>Maternal diseases</i>				
Anaemia - Number (%)	122 (67.8)	66 (61.7)	56 (76.7)	0.03
Diabetes - Number (%)	02 (01.1)	02 (01.9)	0 (0)	0.35
Hypertension - Number (%)	45 (25.0)	28 (26.2)	17 (23.3)	0.66
Sickle cell disease - Number (%)	12 (06.7)	07(06.5)	05 (06.9)	0.93
Hypothyroidism - Number (%)	01 (0.6)	01 (0.9)	0 (0)	1.0
<i>Obstetric complications</i>				
Gestational Diabetes - Number (%)	01 (0.6)	01 (0.9)	0 (0)	1.0
Preeclampsia/Eclampsia - Number (%)	75 (41.7)	43 (40.2)	32 (43.8)	0.62
Antepartum Haemorrhage - Number (%)	02 (01.1)	02 (01.9)	0 (0)	0.35
Intrapartum fever - Number (%)	01 (0.6)	0 (0)	01(01.4)	1.0
<i>Mode of delivery</i>				
Vaginal - Number (%)	155 (86.1)	91 (85.1)	64 (87.7)	0.61
Caesarean Section - Number (%)	25 (13.9)	16 (15.0)	09 (12.3)	
<i>Place of delivery</i>				
Home - Number (%)	04 (02.2)	02 (01.9)	02 (02.7)	1.00
Hospital - Number (%)	176 (97.8)	105 (98.1)	71(97.3)	

*Specialist included cardiologist, endocrinologist and diabetologist; ASHA: Accredited Social Health Activist*

**Table 2: Neonatal variables for mortality in birth asphyxia (Univariate analysis)**

Variable	All patients (n=180)	Survival (n=107)	Non survival (n=73)	p value
Gender (Male) - Number (%)	103 (57.2)	63 (58.9)	40 (54.8)	0.58
Residence (Rural) - Number (%)	108 (60.0)	61(57.0)	47 (64.4)	0.32
Socioeconomic Status				
Lower - Number (%)	100 (55.6)	59(55.14)	41(56.16)	0.89
Middle - Number (%)	80 (44.4)	48(44.86)	32(43.84)	
Mean age at admission (days) Mean ± SD	3.62±5.35	3.90±5.88	3.14±4.45	0.24
Mean duration of stay (days) Mean ± SD	6.71±3.91	9.07±4.85	4.35±2.98	<0.0001
Gestational Age				
Near-term - Number (%)	39 (21.7)	21(19.6)	18 (24.7)	
Term - Number (%)	140 (77.8)	86 (80.4)	54(74.0)	0.46
Post-term - Number (%)	01 (0.6)	0 (0)	01 (01.4)	
Weight on admission				
Average - Number (%)	103 (57.2)	63 (58.9)	40 (54.8)	
LBW - Number (%)	57 (31.7)	34 (31.8)	23 (31.5)	0.68
VLBW - Number (%)	17 (09.4)	07 (06.5)	10 (13.7)	
Above average - Number (%)	03 (01.7)	03(02.8)	0 (0)	
Not cried immediately after birth - Number (%)	171 (95.0)	100 (93.5)	71 (97.3)	0.31
Resuscitation required (Yes) - Number (%)	171 (95.0)	100 (93.5)	71 (97.3)	0.31
Type of resuscitation				
Oxygen - Number (%)	06 (03.3)	06 (05.6)	00	0.083
Bag & Mask - Number (%)	123 (68.3)	82 (76.6)	41 (56.2)	0.004
IPPV - Number (%)	37 (20.6)	09 (8.4)	28 (38.4)	<0.001
Septic screen (Positive) - Number (%)	12 (06.7)	05 (04.7)	07 (09.6)	0.19
Blood sugar Mean ± SD	93.65±24.79	91.01±23.67	97.50±25.86	0.084
Serum calcium Mean ± SD	9.07±0.49	9.13±0.44	9.01±0.56	0.20
HIE staging				
I	40 (22.2)	31(29.0)	09 (12.3)	
II	58 (32.2)	48 (44.9)	10 (13.7)	
III	82 (45.6)	28 (26.2)	54 (74.0)	<0.001

LBW: low birth weight; VLBW: very low birth weight; IPPV: Intermittent positive pressure ventilation; Septic screen included blood culture; HIE: hypoxic ischaemic encephalopathy

### Risk factors for mortality

Out of 180 asphyxiated neonates 73 died giving a case fatality rate of 40.6%. Most deaths were in HIE stage III due to renal failure, shock, convulsions, respiratory distress and sepsis. Healthcare facilities were available for all mothers but neonates whose mothers received inadequate antenatal care (unbooked mothers) had significantly higher mortality compared to mothers who received adequate antenatal care (booked mothers) ( $p=0.01$ ). Factors like service provider or referral person of neonate and antenatal care received either at primary, secondary or tertiary care facility were not statistically significant. Anaemia, the commonest maternal disease, was significantly associated with higher mortality (OR 3.07, CI 1.12-8.41,  $p=0.02$ ) but other maternal conditions like pre-gestational or gestational diabetes, hypertension, hypothyroidism, preeclampsia / eclampsia and antepartum haemorrhage were not significantly associated. Mode of delivery, place of delivery and gravida

status of mother were not significantly associated with mortality (Table 1).

Gender, age on admission, weight on admission and socioeconomic status were not significantly associated with mortality. Average duration of hospital stay of non-survivors was shorter compared to surviving neonates ( $P<0.0001$ ). Neonates who required bag and mask resuscitation and intubations were significantly associated with mortality. As HIE stage increased, mortality increased and 54 (74%) deaths were observed in HIE stage III which was statistically significant ( $p<0.001$ ). Those neonates who presented with convulsions, cyanosis and prolonged capillary filling time were significantly associated with higher mortality (Table 3). The risk factors for mortality in outborn asphyxiated neonates on multivariate analysis are shown in Table 4.

**Table 3: Clinical details of cases (not exclusive)**

Clinical variable	Survivors (n=173)	Non survivors (n=73)	p value
<b>Symptoms</b>			
Lethargy	79 (45.7)	49 (62.1)	0.33
Hypo/Hyperthermia	49 (28.3)	41(56.2)	0.17
Convulsions	57 (33.0)	61(83.6)	<0.001
Respiratory difficulty	97 (56.1)	64 (87.7)	0.52
Cyanosis	12 (06.9)	13 (17.8)	0.21
<b>Signs</b>			
Respiratory distress	104 (60.1)	72 (98.6)	0.65
Apnoea	29 (16.8)	16 (21.9)	0.43
Hypo/Hyperthermia	63 (36.4)	43 (58.9)	0.99
Cyanosis	28(16.2)	33 (45.2)	0.008
Prolonged capillary filling time	52 (30.1)	49 (67.1)	<0.0001

**Table 4: Risk factors of mortality in outborn asphyxiated neonate (multivariate analysis)**

Predictors	Adjusted Odds Ratio	95% Confidence Interval	p value
Duration of hospital stay	0.66	0.57 – 0.76	<0.001
Anaemia	3.07	1.12 – 8.41	0.029
Convulsion	4.46	1.46 – 12.16	0.003
Bags	0.26	0.10 – 0.68	0.006
HIE staging	1.60	1.04 – 2.46	0.033
Prolonged capillary filling time	0.32	0.47 - 0.82	0.004

HIE: hypoxic ischaemic encephalopathy

## Discussion

In the present study, the incidence of birth asphyxia was 17.3% which is lower than that reported by the National Neonatal Perinatal database probably because severely asphyxiated neonates do not reach the hospital but it is comparable to other studies<sup>6,13</sup>. The case fatality rate was 40.6% which is higher than that reported by Padayachee *et al* (27.1%)<sup>14</sup> and Ekwochi *et al* (18%)<sup>15</sup>. However, a higher mortality (70.1%) was reported by Joseph *et al* in outborn neonates<sup>16</sup>. Male to female ratio in our study was 1.3:1 and 60% neonates were from rural areas of low socioeconomic class. The male predominance in this study may be due to gender bias in India where male babies are given more care and the biological vulnerability of the male neonate. Mortality was also more in males. Similar type of gender distribution was observed by various authors<sup>14,15,17</sup>. All neonates were from lower and middle socioeconomic class and the mean age of admission was 3.62±5.35 days. Poverty and lack of transport facilities may be responsible for delayed referral. Average duration of hospital stay of non-survivors was 4.35±2.98 days compared to 9.07±4.85 days in surviving neonates ( $p<0.0001$ ). Similarly, a shorter duration of hospital stay was observed by various researchers<sup>14,18</sup>.

Healthcare facilities were available to all mothers and 95% of mothers received antenatal care, 98% delivered at either primary or secondary health care level, 60.6% received antenatal care from medical officers. The mean distance travelled by the baby was 89.42±69.36km. Adequate and effective

antenatal care for detection of high risk pregnancies, timely referral of high risk mothers, anticipation of prolonged labour, anticipation of development of birth asphyxia and training of birth attendants in resuscitation skills are of vital importance for reducing incidence of birth asphyxia and neonatal deaths.

Amongst the antenatal risk factors, age of mother, gravida status, service provider in antenatal clinic, referral person of neonate, mode and place of delivery were not significantly associated with high mortality but neonates whose mothers received inadequate antenatal care had significantly higher mortality ( $p=0.01$ ). Maternal diabetes, hypertension, hypothyroidism, sickle cell disease, eclampsia, intrapartum fever and antepartum hemorrhage did not significantly increase mortality of birth asphyxia in our study but maternal anaemia had a significant influence on outcome (OR 3.07 CI 1.12-8.41  $p=0.02$ ). A community based study by Lee *et al*<sup>19</sup> in Southern Nepal reported that maternal low literacy, multiple births, maternal infection and low socioeconomic status were strongly associated with birth asphyxia mortality. Aslam *et al*<sup>20</sup> concluded that neonates of primigravida unbooked mothers, prolonged labour, home deliveries, intrapartum fever and pre-eclamptic mothers had a significant risk of development of birth asphyxia while Kiyani *et al*<sup>21</sup> observed that maternal anaemia, maternal fever, instrumental delivery and spontaneous vertex delivery were risk factors for development of birth asphyxia.

Gestational age, birth weight and gender did not significantly influence the outcome of the babies, but babies who required bag and mask ventilation and endotracheal intubation had significantly higher risk of death. Neonates who presented with convulsions, cyanosis and prolonged capillary refill time had a higher mortality and most such neonates were in HIE stage III. Yadav S, *et al*<sup>8</sup> observed that prematurity, shorter hospital stay and presence of shock on admission were risk factors for adverse outcome in asphyxiated newborns while prematurity, low Apgar score at 5 minutes, seizures at admission, need for more than one antiepileptic drug, abnormal neurologic examination and HIE staging were associated with mortality in birth asphyxia and poor neurologic outcome was reported by Trotman *et al*<sup>17</sup>. Place of birth, mode of delivery and bag and mask ventilation were significantly associated with mortality of asphyxiated newborn and duration of stay was significantly longer in survivors in South African studies<sup>14</sup>. Fatality outcome was more correlated with Sarnat staging and similar to our finding, a higher HIE staging increases mortality according to various studies<sup>14,15</sup>. We encourage 100% institutional deliveries, adequate and effective antenatal care, identification of high risk mothers, training of medical and paramedical staff in resuscitation skill, free and safe early transport of sick neonates to be of paramount importance to decrease the incidence and mortality due to birth asphyxia.

Five-minute Apgar scores as described by mother/caretaker and by documentation on referral sheet, and on clinical examination were taken into account. Thus the chance of accurate estimation of Apgar score is less. This is a limitation of the study. Strengthening the maternal health services by availability of obstetricians at primary and secondary health care level and training of birth attendants in neonatal resuscitation skills are recommended. Provision of safe and timely transport in ambulances with warmers, oxygenation, and portable ventilation facility with skilled manpower is essential. Government of India should establish neonatal intensive care facilities for such critically sick neonates in all tertiary care centers as a matter of urgency.

### Conclusions

The case fatality rate was 40.6% among outborn neonates with birth asphyxia in this study. Unbooked mothers, maternal anaemia, neonates requiring resuscitation with bag and mask ventilation and intubation, neonates presenting with convulsions or cyanosis, prolonged capillary refill time and neonates in HIE stage III were risk factors for mortality in asphyxiated outborn neonates.

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