

ORIGINAL ARTICLE

# Predictors of Mortality of Asphyxiated Neonates Admitted in a Tertiary Care Hospital

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## Abstract

**Introduction:** Perinatal asphyxia is a severe condition with significant morbidity and mortality. It is the third leading cause of neonatal mortality in developing countries including Bangladesh. To reduce asphyxia related mortality, it is necessary to find out the responsible factors to reduce the mortality.

**Objectives:** This study was an attempt to find out the risk factors associated with mortality due to birth asphyxia.

**Methods:** This was a cross-sectional observational study, conducted in Department of Neonatal Medicine and NICU of Dhaka Shishu (Children) Hospital during the period of March 2016 to November 2016. Term neonates of within 24 hours of age with diagnosis of perinatal asphyxia were enrolled in this study. Demographic, intrapartum, clinical and laboratory data were recorded. The immediate outcome in terms of expired or survived were also recorded. Statistical analysis was done by SPSS 25 programme. Bivariate and multivariate analyses have been done to find out the associations of risk factors with mortality. P value, <0.05 was taken as statistically significant.

**Results:** A total of 224 asphyxiated term neonates with a mean age of 12.64±6.82 hours were studied. Mean admission weight was 2677.01±407.71gm with male to female ratio of 1.4:1. Among them 51 (22.8%) were expired. In Bivariate analysis, home trial before hospital delivery, obstructed labour, respiratory distress, unconsciousness, abnormal muscle tone, hypothermia, prolonged CRT, SpO<sub>2</sub> <90%, hypoglycemia, and metabolic acidosis at the time of admission were significantly associated with mortality (p<0.05). It was found, home trial before hospital delivery (p=0.009, OR 4.023, 95% CI 1.424-11.366), unconsciousness (p=0.002, OR 4.811, 95% CI 1.773-13.148), hypothermia (p=0.001, OR 4.942, 95% CI 1.858-13.148), prolonged CRT (p=0.009, OR 3.651, 95% CI 1.384-9.630) and metabolic acidosis (p=0.018, OR 3.551, 95% CI 1.243-10.141) at the time of admission were independently affecting the mortality of asphyxiated neonates.

**Conclusion:** This study found that the predictors of mortality of neonates with perinatal asphyxia were home trial before hospital delivery, unconsciousness, hypothermia, prolonged CRT and metabolic acidosis at the time of admission.

**Keywords:** Asphyxia, mortality, neonate, predictors.

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## Introduction

Birth asphyxia is a serious clinical problem worldwide and an important cause of mortality and morbidity in neonatal age.<sup>1-3</sup> World Health Organization (WHO) define birth asphyxia as the failure to initiate and sustain breathing at birth.<sup>4</sup> This failure in the newborn, to initiate and breath normally ultimately leads to hypoxia and increased carbon dioxide accumulation. This hypoxia and ischemia results in biochemical changes, which lead to severe hypoxic ischemic multiorgan cellular damage and systemic dysfunction.<sup>5</sup> The spectrum of disorders to which neonate is exposed as a result of asphyxia include hypoxic ischemic encephalopathy, systemic hypotension, cardiogenic shock, congestive cardiac failure, disseminated intravascular coagulopathy (DIC), meconium aspiration and a wide variety of metabolic problems including hyponatremia, hypoglycemia, hypocalcemia and metabolic acidosis.<sup>6-8</sup>

Globally birth asphyxia is a leading cause of neonatal mortality.<sup>2,9</sup> In the developing countries every year approximately 4 million babies are born asphyxiated of which 1 million die and approximately the same number develop serious sequel.<sup>10</sup> In Bangladesh, under-five mortality and infant mortality rate (IMR) have decreased significantly over the last 3 decades, but neonatal mortality remains high. In the year 2015, out of 3.1 million babies born in Bangladesh,<sup>11</sup> 74,460 babies die in the first 28 days of life.<sup>12</sup> This neonatal mortality (23/1000 live birth)<sup>12</sup> is still high. The main causes of neonatal deaths in 2015 were prematurity, birth asphyxia and sepsis.<sup>13</sup> From Bangladesh very few epidemiological studies searching for causes of neonatal mortality had been reported. Those reports also indicated that birth asphyxia is one of the three leading causes of neonatal death.<sup>1,2</sup>

So, by decreasing birth asphyxia related death we can significantly decrease neonatal mortality and ultimately under five mortality. An effective approach towards the reduction is to identify and timely intervention of risk factors causing mortality in asphyxiated newborn. Therefore, we designed this study to find out the risk factors associated with mortality due to birth asphyxia.

## Materials and Methods

This cross-sectional observational study was conducted in Department of Neonatal Medicine and

NICU of Dhaka Shishu (Children) Hospital for a period of 9 months from March 2016 to November 2016 to find out immediate outcome of neonates with diagnosis of birth asphyxia and its association with risk factors. Dhaka Shishu (Children) Hospital (DSH) is a tertiary care center for children, with no maternity services, which has well equipped Neonatology department including Neonatal Intensive Care Unit (NICU) where out born neonates are admitted.

Term neonates admitted with diagnosis of birth asphyxia within 24 hours of birth were enrolled in this study. Birth asphyxia was labeled as those had APGAR score <7 and/or who had documented history of failure or delay in crying or breathing immediately after birth, whether or not they had neurological symptoms. Preterm neonates, neonates had birth weight <1500gm, and neonates with suspected congenital heart disease or major congenital malformations and those who left against medical advice were excluded from the study.

Neonates were enrolled immediately after admission, and written consent was taken from guardian before enrollment. Data were collected in a questionnaire including demographic and intrapartum variables. On enrollment, clinical examination of all the admitted babies for the study was performed and information including infants' gender, weight on admission, vitals including capillary refilling time (CRT) and oxygen saturation by pulse oximetry (SpO<sub>2</sub>), neurological parameters were documented. At that time, random blood sugar (RBS) done by glucometer and arterial blood was drawn for blood gas analysis (ABG). RBS value and ABG report were also recorded in the questionnaire. We also recorded the immediate outcome of the baby and duration of hospital stay. All patients were managed according to unit protocol for perinatal asphyxia. Babies were categorized into different stages of Hypoxic Ischemic Encephalopathy (HIE) according to Sarnat and Sarnat staging. The immediate outcome was recorded at time of discharge as expired or survived. On the basis of outcome, neonates were divided into two groups, expired and survived.

Data analysis was done by IBM SPSS version 25. Comparative analysis of the variables was done between the "expired" and "survived" groups. Data analysis for associations with mortality was initially

explored with bivariate analyses between mortality and demographic variables, intrapartum variables, infant characteristics, and investigation reports. During bivariate analysis the categorical variables were tested with Chi square ( $\chi^2$ ) test and for continuous variables Student's 't' test was done. Multivariate analysis was done by binary logistic regression for the variables which were found to be significantly related with mortality. P values, <0.05 was taken as statistically significant.

### Results

During the study period, total 224 neonates with perinatal asphyxia admitted within first 24 hours of age with a mean of  $12.64 \pm 6.82$  hours were enrolled in this study. Out of them, 129 (57.6%) were male and 95 (42.4%) were female with male outnumbered female (1.4:1). All were term babies with mean gestation  $38.17 \pm 0.99$  weeks, mean admission weight was  $2677.01 \pm 407.71$  gm and out of them, 72 (32.1%) were low birth weight babies. All included neonates were out born, among them 88 (39.3%) were born at home and the rest 136 (60.7%) were born at different types of hospital facility. More than half of the studied neonates (130, 58.0%) were delivered via normal vaginal delivery and rest (94, 42%) were

delivered by lower uterine cesarean section (LUCS). Out of the 136 hospital born neonates, 59 (43.4%) had history of failed trial of home delivery. Among the 59 neonates who had history of failed home delivery, 33 (55.9%) were delivered at hospital by LUCS and it is statistically significant ( $p=0.011$ ). Out of 224 asphyxiated neonates, 188 (83.9%) developed HIE, of them 28 (12.5%) developed HIE I, 107 (47.7%) developed HIE II and the remaining 53 (23.7%) cases developed HIE III. Amongst the asphyxiated neonates 173 (77.2%) were survived and 51 (22.8%) were expired. Their mean hospital stay was  $5.83 \pm 4.87$  days (with range of minimum 1 day to maximum 23 days) (Table I). Among the expired neonates 25.5% died within first 24 hours of admission.

Table II showed the comparison of demographic, intrapartum, clinical features and investigation variables between expired and survived groups. It was found that home trial before hospital delivery, obstructed labour, respiratory distress, unconsciousness, abnormal muscle tone, hypothermia, prolonged CRT,  $SpO_2 < 90\%$ , hypoglycemia, and metabolic acidosis at the time of admission were significantly associated

**Table I**  
*Characteristics of study population (N=224)*

Variables	Category	Number	Percentage
Gestational age (week)	Range (mean $\pm$ sd)	37-41( $38.17 \pm 0.998$ )	
Weight on admission (gm)	Range (mean $\pm$ sd)	1960-4400 ( $2677.01 \pm 407.71$ )	
Age on admission (hour)	Range (mean $\pm$ sd)	2.50 - 24.00 ( $12.64 \pm 6.82$ )	
Gender	Male	129	57.6
	Female	95	42.4
Socio-economic status	Poor	126	56.3
	average	98	43.7
Residence	Rural	113	50.4
	Urban	111	49.6
Place of delivery	Home	88	39.3
	Hospital	136	60.7
Mode of delivery	Normal	130	58.0
	LUCS	94	42.0
HIE	Present	188	83.9
	Absent	36	16.1
HIE Grade	No	36	16.1
	Grade I	28	12.5
	Grade II	107	47.7
	Grade III	53	23.7
Outcome	Survived	173	77.2
	Expired	51	22.8
Hospital Stay (day)	Range (mean $\pm$ sd)	1-23 ( $5.83 \pm 4.87$ )	

HIE=Hypoxic Ischemic Encephalopathy

**Table II**  
*Comparison of the risk factors among expired and survived groups (N=224)*

Predictor	Category	Expired	Survived	P value
Weight at admission (gm) #	Mean±sd	2670.43±386.15	2678.95±414.90	0.896
Gestational age (week) #	Mean±sd	38.27±0.98	38.14±0.99	0.389
Age at admission (hour) #	Mean±sd	11.23±7.34	13.06±6.62	0.093
Gender†	Male	27	102	0.445
	Female	24	71	
Residence†	Rural	31	82	0.093
	Urban	20	91	
SES†	Poor	30	96	0.673
	Average	21	77	
Place of delivery†	Home	16	72	0.188
	Hospital	35	101	
Mode of delivery†	Normal	29	101	0.847
	LUCS	22	72	
Prolonged labour†	Yes	25	74	0.430
	No	26	99	
Obstructed labour†	Yes	28	62	0.015*
	No	23	111	
Home trial before hospital delivery†	Yes	25	34	0.000*
	No	26	139	
Respiratory distress†	Present	7	51	0.024*
	Absent	44	122	
HIE†	Present	46	142	0.166
	Absent	5	31	
Grading of HIE†	No	5	31	0.060
	Grade I	6	22	
	Grade II	21	86	
	Grade III	19	34	
Convulsions†	Present	25	82	0.839
	Absent	26	91	
Frequency of convulsions†	>3 times	13	39	0.697
	≤3 times	12	43	
Unconsciousness†	Yes	30	24	0.000*
	No	21	149	
Lethargy†	Yes	30	79	0.098
	No	21	94	
Abnormal muscle tone†	Present	41	74	0.000*
	Absent	10	99	
Hypothermia†	Yes	38	43	0.000*
	No	13	130	
Prolonged CRT†	Yes	39	54	0.000*
	No	12	119	
SpO <sub>2</sub> †	<90%	34	65	0.000*
	≥90%	17	108	
Hypoglycemia†	Present	32	68	0.003*
	Absent	19	105	
Metabolic acidosis†	Present	31	16	0.000*
	Absent	20	157	

#Independent 't' test; †Chai square test ( $\chi^2$ ); \*Significant

SES=Socio Economic Status; HIE=Hypoxic Ischemic Encephalopathy; CRT=Capillary Refilling Time;

SpO<sub>2</sub>=Oxygen saturation by pulse oximetry

**Table III**  
*Risk factors for mortality in asphyxiated neonates using multivariate logistic regression*

Risk factor	B	SE	P value	OR	95% CI for OR
Obstructed labour	0.842	0.479	0.079	2.321	0.908 - 5.934
Home trial before hospital delivery	1.392	0.530	0.009	4.023	1.424 - 11.366
Respiratory distress	-0.297	0.629	0.637	0.743	0.217 - 2.550
Unconsciousness	1.571	0.509	0.002	4.811	1.773 - 13.148
Abnormal muscle tone	0.963	0.534	0.071	2.620	0.920 - 7.458
Hypothermia	1.598	0.499	0.001	4.942	1.858 - 13.148
Prolonged CRT	1.295	0.495	0.009	3.651	1.384 - 9.630
SPO <sub>2</sub> <90%	0.704	0.484	0.146	2.021	0.783 - 5.214
Hypoglycemia	0.620	0.483	0.199	1.859	0.721 - 4.794
Metabolic acidosis	1.267	0.535	0.018	3.551	1.243 - 10.141

with mortality ( $p < 0.05$ ). Gender, age and weight on admission of the neonates, place of delivery, mode of delivery, residence, socioeconomic status, lethargy, HIE with its grading, and frequency of convulsions had no significant ( $p > 0.05$ ) effect on mortality.

Significant risk factors on bivariate analysis were introduced into a logistic regression model as independent factors and dependent variable was expired. On logistic regression analysis (Table III), home trial before hospital delivery ( $p = 0.009$ ), unconsciousness ( $p = 0.002$ ), hypothermia ( $p = 0.001$ ), prolonged CRT ( $p = 0.009$ ) and metabolic acidosis ( $p = 0.018$ ) were independently associated with mortality of asphyxiated neonates. Neonates with history of home trial before hospital delivery had 4.02 times risk of being expired compared to those who had no history of home trial before hospital delivery, after adjusting other factors. Similarly, neonates with unconsciousness had 4.8 times, hypothermia had 4.9 times, prolonged CRT had 3.6 times and metabolic acidosis had 3.5 times risk of being expired compared to those who had no sign of unconsciousness, hypothermia, prolonged CRT and metabolic acidosis at the time of admission respectively. There was a tendency for obstructed labour and abnormal muscle tone to be associated with mortality, although those were marginally non-significant ( $p = 0.079$ ,  $0.071$  respectively). However, there were no direct relationship of respiratory distress, hypoglycemia, and SpO<sub>2</sub> <90% with mortality ( $p > 0.05$ ).

### Discussion

This study was conducted to find out the predictor of mortality of asphyxiated neonates admitted in the Department of Neonatal Medicine and NICU of Dhaka Shishu (Children) Hospital. Several studies were reported from Bangladesh in this regard and all were hospital based.<sup>14-16</sup>

Perinatal asphyxia is one of the major causes of neonatal mortality in developing countries including Bangladesh. Studies from Asia<sup>5-7,17</sup> and Africa<sup>8</sup> reported high incidence of asphyxia with high mortality and morbidity among home and hospital born newborn. Mortality rate differs may be due to difference in selection criteria. In this study the rate of mortality was 22.2%. Shireen et al<sup>16</sup> reported 16% mortality in her study conducted in a medical college hospital where they included both inborn and out born neonates. DSH is solely a paediatric hospital and in this study enrolled patients were out born, this was the probable reason of higher mortality found in this study, compared to that of Shireen et al<sup>16</sup>.

This study found 57.6% were male neonates, more than female (1.4:1). Adebami et al<sup>8</sup>, Trotman et al<sup>18</sup> and Padayachee et al<sup>19</sup> reported similar gender distribution but Yadav et al<sup>17</sup> reported that majority (72%) of the study population were male.

In this study all enrolled neonates were of full term and their mean weight was 2677.01±407.71gm and ranged from 1960 to 4400 gm. Similarly, Shireen et al<sup>16</sup> found 49% of asphyxiated baby had normal birth weight, and Saeed et al found 69.7% of the asphyxiated neonates were between 2.1 to 3 Kg.<sup>20</sup> Whereas Afzal et al<sup>21</sup> reported that majority of the

babies were between 1.5 and 2.5 kg. The difference is due to inclusion criteria of the patients for the studies.

This study found, 136 (60.7%) neonates were delivered at hospital, which was much higher than that of hospital delivery rate of Bangladesh.<sup>22</sup> This study done in a tertiary care paediatric hospital where neonates were referred from all category of hospital where deliveries are conducted with or without facility to take care of sick newborns. That is why we found more percentage of hospital delivered neonates in this study. Studies from Nepal<sup>17</sup> and India<sup>23</sup> reported significant association between mortality and place of delivery, but this study found no association between place of delivery and mortality.

In this study, hypoxic ischemic encephalopathy stage I, II and III was found in 12.5%, 47.7% and 23.7% of asphyxiated neonates. These figures were similar to study findings of Yadav et al<sup>17</sup> and Rafique et al.<sup>24</sup> Shireen et al<sup>16</sup> found that mortality was higher in asphyxiated neonates with HIE. Rafique et al<sup>24</sup> and Ekwochi et al<sup>25</sup> reported significant association between HIE stages and mortality but current study documented no such association.

In this study the major contributing factors affecting the mortality in asphyxiated neonate were home trial before hospital delivery, unconsciousness, hypothermia, prolonged CRT and metabolic acidosis at the time of admission.

In developing countries majority of deliveries are conducted at home even without presence of any skilled birth attendant.<sup>17</sup> It is also true for Bangladesh.<sup>22</sup> But in this study, we found 136 (60.7%) neonates were delivered at hospital and out of those hospital delivered neonates 39.1% had history of home trial. We also found that mortality among these neonates was significantly high and this was an independent risk factor of mortality for the asphyxiated neonates. Another reason is due to complications during home delivery, mothers were shifted to hospital and babies were delivered by LUCS. This might be due to unavailability of skilled attendant at the time of delivery at home.<sup>17</sup> So, we should find out the ways to increase the hospital delivery without any trial at home to overcome such risk factor and to reduce mortality among asphyxiated neonates.

Presence of asphyxia was a strong determinant of hypothermia at admission in sick neonates.<sup>26,27</sup> It might be due to inadequate temperature maintenance of babies during resuscitation, moreover, due to hypoxic-ischemic effects of

asphyxia disturb both central and peripheral thermoregulatory mechanisms might cause hypothermia. Although hypothermia is rarely a direct cause of death, it contributes to a substantial proportion of neonatal mortality globally, mostly as a comorbidity of asphyxia, severe neonatal infection and preterm birth.<sup>28</sup> Amritanshu et al<sup>23</sup> reported that hypothermia as a significant factor of mortality in asphyxiated neonates. Similarly, this study found hypothermia was an independent factor related to mortality of asphyxiated neonates.

Neonates with perinatal asphyxia might develop multisystemic or multiorgan adverse effects which can contribute to high mortality. During initial phase of asphyxia cardiac output maintained by physiological mechanisms and subsequently redistributed the blood flow to brain, heart and adrenal glands. With prolonged asphyxia cerebral vascular autoregulation lost and cerebral blood flow becomes dependent on systemic blood pressure. Subsequently reduced cardiac output caused hypotension further causes multiorgan dysfunction in perinatal asphyxia. There may also be cardiac dysfunction caused by transient myocardial ischemia, reduced contractility.<sup>29</sup> Infants with perinatal asphyxia may have transient myocardial ischemia which may present as a shock with prolonged CRT and metabolic acidosis.<sup>30</sup> In a study of moderately to severely asphyxiated newborns, ventricular dysfunction has been demonstrated.<sup>31</sup> Further it has been also showed that that persistently low cardiac output during the first 48 hours of life, in newborns with cardiogenic shock due to perinatal asphyxia was associated with a significantly higher mortality.<sup>32</sup> Like these reports<sup>30-32</sup> the current study found significantly high mortality of asphyxiated newborns who had prolonged CRT and metabolic acidosis at the time of admission. In the present study all newborns were out born, travelled different distances to reach this hospital from home or hospital where they were born. So, delay in reaching the hospital causing further delay in starting the management of shock, might lead to an increase in mortality. Though we did not look for the time taken to reach this hospital, several studies confirmed that delay in hospital arrival was associated with poor outcome.<sup>21,33</sup>

### Conclusion

This study found that the independent factors to predict the mortality of asphyxiated neonates were home trial before hospital delivery, unconsciousness, hypothermia, prolonged CRT and metabolic acidosis at the time of admission. It is the time to intervene

for improvement of perinatal care and taking care of identified risk factors to reduce mortality of perinatal asphyxia which will ultimately contribute to in decreasing neonatal mortality as a whole.

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