



RISK FACTORS ASSOCIATED WITH PERINATAL ASPHYXIA IN LATE PRETERM AND TERM NEWBORNS - AN OBSERVATIONAL STUDY

Pediatrics

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ABSTRACT

BACKGROUND: Perinatal asphyxia is defined as the inability of the newborn to initiate and sustain enough respiration after delivery. It is one of the most common causes of neonatal mortality and morbidity. There are very few studies on perinatal asphyxia in eastern U.P so, this study is aimed at assessing the associated risk factors of perinatal asphyxia in late preterm and term newborns.

METHODS: The present study was retrospective, observational institutional based study was carried out on 400 patients after screening through inclusion & exclusion criteria ranging from 17-40 years of age in the Department of Pediatrics, BRD Medical College, Gorakhpur for a period of 12 months from July 2018 to June 2019 after commencement of Institutional Ethics Committee, BRD Medical College, Gorakhpur Approval. The data was analyzed using SPSS version 20. P values < 0.05 were expressed as associated factors of perinatal asphyxia.

RESULTS: Mean age of the mothers seeking health delivery services was 26.01 ± 3.50 years. The maximum age was 40 years while the minimum age was 19 years. 74% of the mothers were illiterate or below primary level of education. 86.7% mothers who sought delivery services were nonworking. 60.7% mothers were primiparous. 69.7% belonged to stage 3/4/5 of socio-economic status. Male neonates were (64.7%) and Females neonates were 35.3%. 35% of the neonates weighted 1500-2500 gms & 38% of the neonates' weight 2500-3000 gms. 41.5% of the new born had severe hypoxic encephalopathy. 70.75% newborns affected with birth asphyxia improved while 29.25% newborn expired. Maternal age below 25 year were associated with 52.5% of perinatal asphyxia. Lower maternal age was significantly associated with neonatal mortality. 74 % of mother's education level was either upto primary or none. 60.75% mothers were Primiparous and 39.25% mothers were Multiparous. Our study results showed equal distribution of perinatal asphyxia in upper middle and lower socioeconomic status.

CONCLUSION: Our study identifies lower maternal age, Lower maternal education level contributed to increase incidence of perinatal asphyxia. Age of mother, education level, parity, birth interval, and gestation are maternal risk factors. Majority of these factors may be manageable by means of good pre-natal care. Further large scale studies are required to substantiate these findings in different parts of world.

KEYWORDS

Perinatal Asphyxia, Mother, Neonates, Risk factor, Gestation

INTRODUCTION

Birth of a healthy newborn is one of the finest gift of nature, birth process takes only few hours but it is most hazardous period of life since it is associated with largest number of deaths as compared to any other phase of life¹.

Despite the important advances in perinatal care in the past decades, asphyxia remains a severe condition leading to significant mortality and morbidity. The term "asphyxia" is derived from the Greek and means "stopping of the pulse". Perinatal asphyxia is a condition characterized by an impairment of exchange of the respiratory gases (oxygen and carbon dioxide) resulting in hypoxemia and hypercapnia, accompanied by metabolic acidosis.²

Estimates of the incidence of perinatal asphyxia are quite variable from one study to another. De Haan et al. reported an incidence of perinatal asphyxia of 1 to 6 per 1,000 live full-term births and more for those who born preterm.³ Moreover, asphyxia has been shown to be the third most common cause of neonatal death (23%) after preterm birth (28%) and severe infections (26%).⁴

Globally, birth asphyxia is estimated to account for 23% of the 4 million neonatal deaths and 26% of the 3.2 million stillbirths each year. An estimated 1 million children who survive birth asphyxia live with chronic neuro-developmental morbidities, including cerebral palsy, mental retardation, and learning disabilities.⁵

Hypoxic damage can occur to most of the newborn's organs (kidneys, heart, lungs, liver etc) but brain damage is a most serious concern and perhaps the least likely to quickly or completely heal. In term newborns with hypoxic ischemic encephalopathy, defined and acute hypoxic ischemic events before or during birth are usually recognized by the clinician while preterm newborn a sentinel event is rarely recognized and hypoxia-ischemia is generally assumed to have more

complex temporal profile, with intermittent or chronic nature⁶, however it remain challenging to determine the individual contribution of hypoxia ischemia among several coexistent factors such as infection, inflammation, growth restriction, or hypoxia.

As compared to term newborns brain of preterm newborns are more vulnerable to hypoxic ischemia due to anatomical and functional immaturity of periventricular vasculature. Periventricular white matter has lower basal blood flow compared to grey matter regions make it more prone to hypoxia with minor drops in cerebral perfusion.⁷

Perinatal asphyxia in premature newborn is caused by multiple factors with prematurity itself being one of important factor. Despite this high mortality and morbidity associated with perinatal asphyxia, the prevalence and associated factors of perinatal asphyxia are not well studied in North india and there is no report on the prevalence and associated factors of perinatal asphyxia in this study area so far.

In our NICU, perinatal asphyxia contributes to almost 45% to 50% of total admission load and also one of the most common causes of neonatal deaths as contrast to National neonatal mortality data with prematurity being the most common cause of neonatal deaths. In our region it was more prevalent in preterm newborns with higher mortality. Hence the present study was aimed at assessing associated factors of perinatal asphyxia in late preterm and term newborns.

AND OBJECTIVES

1. To observe Demographic profile of patients.
2. To evaluate the risk factors associated with perinatal asphyxia in late preterm newborns (≥ 34 weeks of gestation) and term newborns ($\geq 37-42$ weeks of gestation)
3. To evaluate the risk factors associated with severe HIE & mortality of severe hypoxic encephalopathy in late preterm and term newborns.

MATERIALS & METHODS**Study Design:-**

The present study was retrospective, observational institutional based study. The history of mother and neonates were retrieved by interview of parents, detail proforma designed in a form of preformed questionnaires, from previous medical records and if required by contacting to previous hospitals via telephone.

Study Area:-

The present retrospective observational study was carried out on 400 patients after screening through inclusion & exclusion criteria ranging from 17-40 years of age in the Department of Pediatrics, BRD Medical College, Gorakhpur for a period of 12 months from July 2018 to June 2019 after commencement of Institutional Ethics Committee, BRD Medical College, Gorakhpur Approval. Written consent was taken from parent's by explaining them nature and purpose of study in their language. All these information's were collected in pre-designed structured data collection sheets.

The study took place in maternity unit i.e. labor ward and newborn unit. Deliveries are conducted by trained Doctors who are competent in handling obstetric and neonatal emergencies. The newborn unit was well supplied with necessary equipment for resuscitation for instance like Ambu bag, warm resuscitaire, face mask, oxygen and CPAP machine. Proforma filled on each section constituted four parts:

- **Social demographic data** of the mother that is age, marital status, parity, educational level, socioeconomic status etc.
- **Antepartum details**, it consists of any illness during pregnancy, type of Pregnancy, history of diabetes, preeclampsia, anemia and any previous history of birth Asphyxia etc.
- **Intrapartum status** for presentation of fetus, Mode of delivery, type of assisted vaginal delivery, anesthesia received during C section, History of prolong labor, place of delivery, any emergency complication face by mother and history of sedation.
- **Fetal characteristic**, which consisted of gestational age at birth, history of cry and seizure, about resuscitation, mode of resuscitation and birth weight. Information about the date and time of birth, gender, birth weight.

All the newborns was graded on the basis of levane staging of hypoxic ischemic encephalopathy in severity stage of mild, moderate and severe HIE.

Inclusion Criteria:-

1. All normal neonates born during the study period.

Exclusion Criteria:-

1. Birth weight less than 1500 g pre-maturely.
2. Opium or Anesthesia related Low APGAR score.
3. Babies with lethal anomalies like hydrops, cyanotic congenital heart defects, congenital or chromosomal anomalies and congenital infection.
4. All newborn babies born outside.
5. Incomplete information in files.

In the present study mostly patients belonged to the lower middle class and hence data may not predict the overall situation in the country. Definitions of birth asphyxia designed for use in hospital-based settings require evaluation of neonatal umbilical cord pH, APGAR scores, neurological clinical status and markers of multi-system organ function, which were not feasible in all newborns as most of the patients referred to our center do not have details of all these informations for this clinical definition given by WORLD HEALTH ORGANIZATION was used in this study to determine cases of perinatal asphyxia.

STATISTICAL ANALYSIS

Descriptive statistical analysis has been carried out in the present study. The collected data were analyzed using odds ratio (OR) to determine the risk factors significant for contributing to BA, and modelling were done using logistic regression. P value <0.05 were considered statistically significant.

RESULTS

Following results were obtained from our study.

Table no 1: Demographic information of mother (n=400)

DEMOGRAPHIC FACTORS	FREQUENCY n=400(%)
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MATERNAL AGE GROUP	17-19	30(7.5)
	20-22	70(17.5)
	23-25	110(27.5)
	26-28	56(14)
	29-32	50(12.5)
	33-35	70(17.5)
	>35	14(3.5)
	Total	400 (100)
MEAN AGE 26±3.5 Years		
MINIMUM AGE: 19 Years AND MAXIMUM AGE: 40 Year		
MATERNAL EDUCATION	NONE	150(37.5)
	PRIMARY	146(36.5)
	SECONDRY	82(20.5)
	HIGHER	22(5.5)
PARITY	PRIMIPAROUS	279(69.8)
	MULTIPAROUS	121(30.2)
EMPLOYMENT	HOUSEWIFE/UNEMPLOYED	347(86.8)
	GOVT/PVT JOB	53(13.3)
SOCIOECONOMIC STATUS	1	53(13.3)
	2	68(17)
	3	148(37)
	4	86(21.5)
	5	45(11.3)

- Mean age of the mothers seeking health delivery services was 26.01±3.50 years. The maximum age was 40 years while the minimum age was 19 years. 296 (74%) of the mothers who attended ANC were illiterate or below primary level of education, while 104 (26%) of mothers were with secondary or higher level of education. 347 (86.7%) mothers who sought delivery services were nonworking while 53(13.3%) were working as government employee. This included a proportion of 256(64%) who were housewives. Among all admitted cases 243(60.7%) mothers were primiparous while 121(30.2%) were multiparous. 279(69.7%) belonged to stage 3/4/5 of socio-economic status according modified BG PRASAD SCALE.

Table No 2: Demographic Information Of The Neonates (n=400)

DEMOGRAPHICS		FREQUENCY n=400 (%)
FETAL AGE	PRE-TERM	129(32.25)
	TERM	271(67.75)
SEX	MALE	259(64.75)
	FEMALE	141(35.25)
BIRTH WEIGHT	1500-2500g	140(35)
	2501-3000g	154(38.5)
	>3000g	106(26.5)
GESTATIONAL AGE	SGA	180(45)
	AGA	207(51.75)
	LGA	13(3.25)
ASPHYXIA STATUS (HIE STAGE LEVENE)	MILD	94(23.5)
	MODERATE	140(35)
	SEVERE	166(41.5)

- During the study period among all admission of NICU 400 cases of the new born babies Male neonates were (64.7%) and Females neonates were 35.3%. With regard to birth weight, 35% of the neonates weighted 1500-2500 gms, 38% of the neonates' weight 2500-3000 gms and 27% had weight beyond 3000g. There was a higher proportion of the newborns whose birth ages were term 67.7% compared those who were late pre-term 32.3%. Among all admitted newborns 41.5% of the new born had severe hypoxic encephalopathy while 35% had moderate encephalopathy and rest 23.5% had mild hypoxic encephalopathy according levane staging.

Table No 3: Outcome Of Newborns Affected With Birth Asphyxia

Grade outcome	Mild asphyxia (n=94)	Moderate asphyxia (n=140)	Severe asphyxia (n=166)	Total (n=400)
Improved	92 (97.8%)	110 (78.5%)	81 (48.7%)	283 (70.75%)
Expired	2 (2.2%)	30 (21.5%)	85 (51.3%)	117 (29.25%)

- On analyzing outcome of newborns affected with birth asphyxia, it was observed that among all cases of perinatal asphyxia, 283 (70.75%) newborns improved while 117 (29.25%) newborns expired. Among improved cases 92 newborn had mild asphyxia, 110 newborn had moderate asphyxia while 81 newborn had severe asphyxia. Similarly among expired cases 2 newborn had mild asphyxia, 30 newborn had moderate asphyxia while 85 newborn had severe asphyxia.

Table No 4: Association Of Maternal Age With Severity Of Hie In Newborns

MATERNAL AGE	< 25 YEARS	≥25 Year	P value Odds Ratio (OR) 95%CI
SEVERE HIE	107	59	<0.001 OR 2.3 CI- 1.5-3.4
MILD TO MODERATE HIE	103	131	
TOTAL (400)	210 (52.5%)	190 (47.5%)	

* P Value <0.05 Is Considered Statistically Significant

- It was found that maternal age below 25 year were associated with 52.5% of perinatal asphyxia and mothers with age below 25 year were 2.3 times more likely to give birth to newborns with severe HIE than mothers of elder age group.

Table No 5: Association Of Maternal Age With Outcome Of Newborns With Severe Hie

MATERNAL AGE	<25 YEAR	≥25 Year	P value Odds Ratio (OR) 95%CI
EXPIRED	73	12	<0.0001 OR 8.4CI 3.9-17.8
IMPROVED	34	47	

- Among all newborns of severe encephalopathy, lower maternal age was significantly associated with neonatal mortality, risk of mortality in severe HIE increases 8.4 times if maternal age was found to below 25 years of age as compared to mother of higher age group.

Table No 6: Association Of Perinatal Asphyxia Newborns With Level Of Education

LEVEL OF EDUCATION	PRIMARY OR BELOW	SECONDARY OR HIGHER	P value Odds Ratio (OR) 95%CI
SEVERE HIE	132	34	P=0.0375 OR 1.65 CI 95%=1.03-2.6
MILD TO MODERATE HIE	164	70	
TOTAL (400)	296 (74%)	104 (26%)	

- It was found after the study that out of 400 cases of perinatal asphyxia 74 % of mother's education level was either upto primary or none while 26% had education level upto secondary or higher. Mothers having education level either none or upto primary level are 1.6 times at higher risk of giving birth to new born with severe hypoxic encephalopathy as compared to mothers having higher education group.

Table No 7: Association Of Parity With Severity Of Hie Newborns

CATEGORY	PRIMIPAROUS	MULTIPAROUS	P VALUE ODDS RATIO 95%CI
SEVERE HIE	126	40	P=<0.0001 OR 3.15 95%CI 2.03-4.89
MILD TO MODERATE HIE	117	117	
TOTAL (400)	243 (60.75%)	157 (39.25%)	

* P value <0.05 is considered statistically significant

- On analyzing association of parity with severity of HIE Newborns, it was found among all cases of perinatal asphyxia 60.75% mothers were Primiparous and 39.25% mothers were Multiparous.

Table No 8: Association Of Parity With Mortality Of Severe Hie Newborns

CATEGORY	PRIMIPAROUS	MULTIPAROUS	P VALUE ODDS RATIO 95%CI
EXPIRED	68	17	P=<0.006 OR 2.16 95%CI 1.3-5.2
IMPROVED	49	32	
TOTAL (166)	117	49	

- Above data shows that primiparous mothers are 3.15 times more likely to give birth to severe hypoxic newborn as compared to multiparous mothers and mortality of severe HIE newborns get increased 2.16 times in case of primiparous mothers.

Table No 9: Maternal Employment Association With Severity Of Hie

CATEGORY	HOUSEWIFE/ UNEMPLOYED	EMPLOYED	P VALUE ODDS RATIO 95%CI
SEVERE HIE	143	23	P=0.76 OR 0.98
MILD TO MODERATE HIE	204	30	
TOTAL (400)	347 (86.75%)	53 (13.25%)	

- On analyzing maternal employment association with severity of HIE, 86.75% mothers were Housewife/ Unemployed while 13.25% mothers were Employed. Data shows that maternal employment was not significantly associated with severity of birth asphyxia and mortality of newborns.

Table No 10: Socioeconomic Status Of Mothers

MODIFIED BG PRASAD SCALE	FREQUENCY	%
1	53	13.25
2	68	17
3	148	37
4	86	21.5
5	45	11.25
TOTAL	400	100

- On analyzing socioeconomic status of mothers, our study results showed equal distribution of perinatal asphyxia in upper middle and lower socioeconomic status.

DISCUSSION

The study's objective was to determine the perinatal risk factors associated with Birth asphyxia in late preterm and term newborns and risk factors associated with severe hypoxic encephalopathy and its mortality in Nehru hospital B.R.D Medical College Gorakhpur.

On analyzing maternal demographic factors, the study results showed that maternal age in case of 52.5% neonates of perinatal asphyxia was 24 years and less which suggests that lower maternal age have 2.4 times more risk to develop severe asphyxia while among severe HIE, mothers of age 24 years or less are 8.4 times more likely to have fatal outcome as compared to mother of age 25 years or more which have better outcome (p value<0.0001). It suggests that lower age group is strongly associated with perinatal asphyxia. These results were similar to the findings shown by the study of Lee et al¹ who showed that lower maternal age increases the risk of birth asphyxia mortality. However these findings were contradictory to the findings of chiabi et al who reported that there was no significant association of maternal age with birth asphyxia.⁸ Women's uterus have tough uterine muscle, whereby during labour the uterus contract strongly and vigorously predispose the fetus to lot of asphyxia. Low maternal age also associated with low birth weight and prematurity of newborn that further increase the risk of perinatal asphyxia and mortality.

In our study we found that 74% of the mothers who attended ANC were illiterate or below primary level of education, while 26% of mothers were with secondary or higher level of education. These finding were contradictory to the findings of Erick Kibai et al who reported who reported 52% of mothers were with secondary or higher level of

education.⁹

In our study 86.7% mothers who sought delivery services were nonworking while 13.3% were working as government employee. This included a proportion of 64% who were housewives. These finding were contradictory to the results of Erick Kibai et al.⁹

In our study Male neonates were (64.7%) and Females neonates were 35.3%. With regard to birth weight, 35% of the neonates weighted 1500-2500 gms, 38% of the neonates' weight 2500-3000 gms and 27% had weight beyond 3000g. Among all admitted newborns 41.5% of the new born had severe hypoxic encephalopathy while 35% had moderate encephalopathy and rest 23.5% had mild hypoxic encephalopathy according levane staging which was contradictory to the to the findings of Erick Kibai et al.⁹

In our study on analyzing outcome of newborns affected with birth asphyxia, it was observed that among all cases of perinatal asphyxia, 283 (70.75%) newborns improved while 117 (29.25%) newborns expired. Similarly our study results showed that maternal age below 25 year were associated with 52.5% of perinatal asphyxia and mothers with age below 25 year were 2.3 times more likely to give birth to newborns with severe HIE than mothers of elder age group.

Among all newborns of severe encephalopathy, lower maternal age was significantly associated with neonatal mortality, risk of mortality in severe HIE increases 8.4 times if maternal age was found to below 25 years of age as compared to mother of higher age group. Not much of the study has been reported to compare these parameters.

On analyzing association of perinatal asphyxia newborns with level of education, it was found after the study that out of 400 cases of perinatal asphyxia 74 % of mother's education level was either upto primary or none while 26% had education level upto secondary or higher. Mothers having education level either none or upto primary level are 1.6 times at higher risk of giving birth to new born with severe hypoxic encephalopathy as compared to mothers having higher education group. Similar results were supported by study of Kibai et al shows that mother with no or below primary level of education 4 times more likely to have neonate with PA as compared to higher educated mother.⁹ Similarly Lee et al Nepal shows that maternal education and literacy decreases the risk of PA significantly.⁴

It was found that in 61% of neonates mother were primiparous /nulliparous which was significantly associated with severity of perinatal asphyxia. Mothers with parity 1 or less are 3.1 times more likely to develop severe HIE. It also increases the risk of mortality significantly in severe HIE neonates as compared with severe HIE patient with multiparous mother. Similar results were shown by study of Erick Kibai et al⁹ while study results of Chiabi et al⁸ found no certain association.

Our study findings showed that primiparous mothers are 3.15 times more likely to give birth to severe hypoxic newborn as compared to multiparous mothers and morality of severe HIE newborns get increased 2.16 times in case of primiparous mothers. On analyzing maternal employment association with severity of HIE, 86.75% mothers were Housewife/ Unemployed while 13.25% mothers were Employed. Data shows that maternal employment was not significantly associated with severity of birth asphyxia and mortality of newborns. On analyzing socioeconomic status of mothers, our study results showed equal distribution of perinatal asphyxia in upper middle and lower socioeconomic status.

Maternal illiteracy is a very broad indicator of poor socio-economic conditions associated with consequent malnutrition, frequent pregnancies and also influence care seeking during antepartum period. With good education clients tend to seek health care services early hence improving the outcome during and after delivery.

Reduction of the risk factors of causing birth asphyxia in rural areas of many developing countries may not be an easy task due to certain reasons as uneducated young mothers who are also in most cases are not fast learners and tend to forget a lot the during health education offered in the department. There is also the component of lack of awareness to sensitize the mothers of child bearing age. In order to reduce the burden of birth asphyxia, Women need to be educated from preconception, antenatal, intrapartum and postnatally this would

increase knowledge hence reduction in perinatal asphyxia and its mortality rate.⁹

CONCLUSION

Our study identifies demographic factors such as lower maternal age, Lower maternal education level contributed to increase incidence of perinatal asphyxia and severity of asphyxia in our NICU. Sequence of birth asphyxia varies from no ill effects to multiorgan complications and death. This could vary depending on severity and duration of asphyxia and it may be due to the presence of gaps in the field of research and technology in developing and low income countries. Age of mother, education level, parity, birth interval, and gestation reported as maternal risk factors. Fetal risk factors are low birth weight. Majority of these factors may be manageable by means of good prenatal care. There is an immediate need to develop strategies for identification and management of birth asphyxia by involving all pathways to survival, including women, families, communities, community health workers, health professionals and policy makers. Further large scale studies are required to substantiate these findings in different parts of world.

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