Determinants of outcome in Newborns with Hypoxic-ischemic encephalopathy at Al-Diwaniya Maternity And Children Teaching Hospital

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Abstract

Perinatal asphyxia remain a major cause of neonatal morbidity and mortality , and hypoxic- ischemic encephalopathy is considered a serious clinical condition worldwide, it is an important cause of permanent damage to the central nervous system , it may result in death or manifested later on with cerebral palsy or developmental delay.

Aim of the study

To search for the determinants of outcome (fate) in those newborns with hypoxic-ischemic encephalopathy.

Patient and methods

Total number of patients enrolled in our study were one-hundred twenty one(eighty-five male and thirty-six females). The study was conducted from the first of October 2013 to the thirty of September 2014. All the involved cases were diagnosed with Hypoxic- ischemic encephalopathy by clinical Sarnat classification .

Result

Perinatal asphyxia was more reported among male gender (70.2%) and there is higher association with induced vaginal delivery (38%) , primipara mothers (61.1%) , irregular antenatal care (55.3%) and primary level of education (46.2%).

50.4% were of stage I hypoxic- ischemic encephalopathy, while the reminders were of stage II and III.

Conclusion

Male gender , prim parity ,primary level of education and irregular antenatal care have more association with hypoxic- ischemic encephalopathy . Fate B,C,D were predicted by the clinical staging only , while fate A was predicted by the level of education only.

Key words

Perinatal asphyxia , hypoxic-ischemic encephalopathy , Al-Diwaniya teaching hospital.

Introduction

Perinatal asphyxia is considered as an important cause of preventable cerebral injury in the neonatal period [1]. One of the major obstacles in the collection of accurate data is the absence of standard definition of the condition [2]. The accepted definition is a combination of lack of oxygenation (hypoxia) and lack of perfusion (ischemia) to body organs [3] .

HIE is an important cause of permanent damage to the CNS, it may result in death or manifested later on with C.P. or developmental delay [4]. About 20- 30% of infant with HIE die in neonatal period and 33-50% are left with permanent neurological sequlae [4]. This creates a greater burden to the family and society [5].

Most neonatal encephalopathic or seizure disorder , in the absence of congenital malformation or syndromes, appear to be related to a perinatal event . MRI or autopsy finding in full term neonates with encephalopathy demonstrate that 80% have acute injury , <1% have prenatal and 3% have non-hypoxic ischemic diagnoses [6].

Causes of perinatal asphyxia may be maternal or fetal and it include antepartum , intrapartum and postpartum causes [7] .

According to an estimate by WHO (world health organization), of the 130 million infant born globally each year , approximately 4 million babies die before reaching the age of 1 month [8].

98% of these neonatal death took place in the developing countries . perinatal asphyxia and birth injuries accounting to 29% of these death [8]. Its considerably higher in the developing countries negligible ANC and poor perinatal services [9].

The art of neonatal resuscitation play an essential role in neonatal care of infant with asphyxia [10].

The newborn with perinatal asphyxia can have different clinical courses due to variable involvement of body organs and multi systemic manifestations [11.]

Various techniques have been used to identify whose infant suffering from asphyxia , these include the time required to initiate spontaneous respiration , to start assisted ventilation , to sustain spontaneous respiration and the use of neonatal scoring system developed by virginia apgar [12, 13].

Apgar score remain the standard way to evaluate newborn immediately after birth as well as their response to resuscitative effort [14], but unfortunately there are many factors can influence the apgar score including immaturity , maternal anesthesia , fetal sepsis and neuromuscular abnormalities [15].

For detection of which infant at risk of asphyxia there are many predictors considered important to predict low APGAR score , these are ; fetal movement , Non –stress test(NST) , fetal biophysical profile , fetal scalp PH , fetal heart rate , meconium – stained amniotic fluid , decrease liquor amount [16, 17] .

The clinical determinant of asphyxia are: neonatal depression at birth with low apgar score and acidosis , HIE clinical presentation , multi-organ dysfunction , metabolic abnormalities , a EEG abnormalities (burst suppression ,low voltage or iso-electric ,slow wave abnormalities) , abnormalities on cranial imaging [18].

Ultrasound is used to detect hemorrhage or hypo echogenicity , CT scanning is considered important to detect hypodensities and hemorrhage , but the diffusion weighted MRI is the preferred imaging modality because of sensitivity and specificity early in the process and its ability to outline topography of the lesion [19.]

Selective cerebral or whole(systemic) therapeutic hypothermia play an important role in reducing morbidity and mortality in term and near term infant [21,22]. Infant treated with systemic hypothermia have lower incidence of cortical neuronal injury on MRI [23].

Phenobarbital , is the drug of choice for seizure , there is some clinical evidence that high dose prophylactic phenobarbitone may decrease neuro-developmental impairment in infant with HIE [24]. Other treatment include supportive care directed for management of organ system dysfunction [25].

The outcome of HIE correlate with timing and severity of the insult ranging from complete recovery to death [26].

AIM OF THE STUDY

To search for the determinant of outcome (fate) in those newborn with clinical HIE.

Patients and methods

Total number of patient involved in our study was 121 (85 male and 36 female) , the study was conducted from the first of October 2013 to the end of September 2014 (one year period) .

All newborns involved in this study were term or near term (>35 weeks) , delivered in our hospital or at home and they are admitted to NCU with clinical features of HIE and they were managed , followed up until discharge (for majority of them).

The diagnosis was made for those with fetal distress prior to birth , while after delivery the following criteria were followed ;

-low 1 and 5 minutes APGAR score (0-3) and/or delay first breath > 1 minutes after birth .
-clinical staging of HIE (according to sarnat and sarnat classification)
Exclusion criteria include ; GA (< 35weeks) , lethal congenital and CNS malformation ,syndromes and chromosomal abnormalities , sepsis and congenital infections).
All studied patients were subjected to ;
*maternal history: parity , age , ANC , level of education.
*delivery history : mode and place of delivery , documented history of asphyxia with (low APGAR score and their need for resuscitations)
*neonatal examination : gender ,GA using new Ballard score , B.WT and neurological examination within the first 24 hours using Sarnat and Sarnat classification (1976) as;
- Stage I (MILD) : hyperalert , irritable , normal tone , hyperactive reflexes , strong moro reflexes , mydriasis and no seizure .
-Stage II (MODERATE) : lethargic , hypotonia , hyperactive reflexes , weak moro reflex , miosis and seizure activity .
- Stage III (SEVERE) : comatose , flaccid , negative reflexes ,unequal pupils and seizure activity refractory to treatment .
EEG was not involved in our study as it was not available in our hospital .
We perform MRI to only 26 of those with stage II or III HIE in a time between 14-28days old.
MRI was planned to be involved in our study but unfortunately we have no ability to perform it to all newborn (rejection of parents , discharge on responsibility , un fit for anesthesia) , hence it was excluded .
Statistical analysis

Data obtained in the present study were summarized, presented and analyzed using two software programs; these were statistical package for the social sciences (SPSS) version 16 and Microsoft Office Excel 2010. For purpose of presentation numeric variables were expressed in the form of mean±SD (standard deviation), while categorical variables were expressed in the form of number and percentage. Mean values were compared using independent samples t-test. Chi-square and Fischer Exact tests were used to study association between any two categorical variables. P-value was considered significant when it was equal to or less than 0.05.

Results:

The general characteristics of the study population is shown in table 1 and table 2. The prevalent baby gender was male with a proportion of 70.25%. The main mode of delivery was induced vaginal delivery accounting for 38.02% of the cases.

A minority of pregnant ladies experienced home delivery while the majority of them had delivered in the hospital. According to clinical staging, there were 61 (50.41%) in stage I and the rest of them were in stage II and III. Majority of pregnant ladies were 17-35 years of age (65.29%) .

Table 1: General characteristics of the study sample

Characteristic		No.	%
Gender of baby	Male	85	70.25
	Female	36	29.75
Mode of delivery	Spontaneous vaginal delivery	26	21.49
	Induced vaginal delivery	46	38.02
	Elective CS	21	17.36
	Emergency CS	28	23.14
Place of delivery	Hospital	103	85.12
	Home	18	14.88
Clinical stage	Stage I	61	50.41
	Stage II	35	28.93
	Stage III	25	20.66
Maternal age	<16 years	19	15.70
	17-35 years	79	65.29
	>35 years	23	19.01
Parity	Primipara	74	61.16
	Multipara	47	38.84
ANC	Regular	54	44.63
	Irregular	67	55.37
Education	Illiterate	23	19.01
	Primary	56	46.28
	Secondary and higher	42	34.71
Total		121	100.00

According to parity, 61.16% of cases were primipara and the rest were multipara. Anti-natal care was regular in 44.63% of cases. Mean birth weight was 3.31±0.85 kg and mean gestational age was 38.19±2.53 weeks. Twenty three of mothers (19.01%) were illiterate and the rest were educated.

Table 2: Mean birth weight and gestational age

Characteristic	Mean	SD	Minimum	Maximum
Birth weight	3.31	0.85	1.80	5.20
Gestational age	38.19	2.53	35.00	43.00

According to fate patients were classified into 4 categories, as shown in table 3:

1. Fate A: discharge against medical advice.
2. Fate B: discharge with no apparent neurological sequlae and without AED (antiepileptic drugs).
3. Fate C: discharge with apparent neurological sequlae and with AED.
4. Fate D: death.

Table 3: Fate of patients

Fate	No.	%
A	13	10.74
B	58	47.93
C	30	24.79
D	20	16.53
Total	121	100.00

The only factor that predicts fate B was the sarnat clinical staging (P<0.001), in such a way that all patients with stage I ended up with fate B, as shown below in table 4 and 5 , while other variables (including gender, place and mode of delivery , maternal parity , ANC , level of education B.WT and GA) show no significant association with fate B { p- value was of no statistical significance} .

Characteristic		Others (C,D)	Fate B	Total	P-value
Gender	Male	37	38	75	0.340
	Female	13	20	33	
Mode of delivery	Spontaneous vaginal delivery	12	12	24	0.059
	Induced vaginal delivery	18	21	39	
	Elective CS	4	15	19	
	Emergency CS	16	10	26	
Place of delivery	Hospital	39	53	92	0.051
	Home	11	5	16	
Clinical stage	Stage I	0	52	52	<0.001
	Stage II	27	5	32	
	Stage III	23	1	24	
Parity	Primipara	33	36	69	0.671
	Multipara	17	22	39	
ANC	Regular	23	25	48	0.763
	Irregular	27	33	60	
Education	Illitrate	9	14	23	0.513
	Primary	27	25	52	
	Secondary and higher	14	19	33	
Maternal age	<16 years	9	8	17	0.496
	17-35 years	34	37	71	
	>35 years	7	13	20	

Table 4: Association between general characteristics and Fate B

Table 5: Association between fate B and both birth weight and gestational age of patients

Characteristic	Fate	Mean	SD	P-value
Birth weight	Fate B	3.45	0.81	0.068
	Others **(C,D)**	3.14	0.91	
Gestational age	Fate B	38.31	2.68	0.615
	Others **(C,D)**	38.06	2.44	

Similarly Fate C was predicted by stage of disease in such a way that patients with fate C were either from stage II or stage III (P<0.001), as shown in table 6. No association was found between fate C and other variables as shown in table 6 and table 7.

Characteristic		Others (B,D)	Fate C	Total	P-value
Gender	Male	52	23	75	0.312
	Female	26	7	33	
Mode of delivery	Spontaneous vaginal delivery	19	5	24	0.309
	Induced vaginal delivery	27	12	39	
	Elective CS	16	3	19	
	Emergency CS	16	10	26	
Place of delivery	Hospital	68	24	92	0.372
	Home	10	6	16	
Clinical stage	Stage I	52	0	52	<0.001
	Stage II	7	25	32	
	Stage III	19	5	24	
Maternal age	<16 years	11	6	17	0.581
	17-35 years	51	20	71	
	>35 years	16	4	20	
Parity	Primipara	47	22	69	0.205
	Multipara	31	8	39	
ANC	Regular	38	10	48	0.150
	Irregular	40	20	60	
Education	Illitrate	20	3	23	0.200
	Primary	35	17	52	
	Secondary and higher	23	10	33	

Table 6: Association between general characteristics and Fate C

Table 7: Association between fate C and both birth weight and gestational age of patient

Characteristic		Mean	SD	P-value
Birth weight	Fate C	3.25	0.91	0.630
	Others **(B,D)**	3.34	0.86	
Gestational age	Fate C	38.43	2.47	0.550
	Others **(B,D)**	38.10	2.60	

Fate D showed a highly significant association with clinical stage (P<0.001), in such a way that majority of patients with fate D were of stage III, as shown in table 8. No other variable showed any significant association with fate D as shown in table 8 and table 9.

Table 8: Association between general characteristics and Fate D

Characteristic		Others (B,C)	Fate D	Total	P-value
Gender	Male	61	14	75	0.925
	Female	27	6	33	
Mode of delivery	Spontaneous vaginal delivery	17	7	24	0.201
	Induced vaginal delivery	33	6	39	
	Elective CS	18	1	19	
	Emergency CS	20	6	26	
Place of delivery	Hospital	77	15	92	0.171
	Home	11	5	16	
Clinical stage	Stage I	52	0	52	<0.001
	Stage II	30	2	32	
	Stage III	6	18	24	
Maternal age	<16 years	14	3	17	0.088
	17-35 years	57	14	71	
	>35 years	17	3	20	
Parity	Primipara	58	11	69	0.441
	Multipara	30	9	39	
ANC	Regular	35	13	48	0.04
	Irregular	53	7	60	
Education	Illitrate	17	6	23	0.409
	Primary	42	10	52	
	Secondary and higher	29	4	33	

Table 9: Association between fate D and both birth weight and gestational age of patients

Characteristic	Fate	Mean	SD	P-value
Birth weight	Fate D	3	0.91	0.075
	Others **(B,C)**	3.383	0.85	
Gestational age	Fate D	37.5	2.33	0.180
	Others **(B,C)**	38.35	2.59	

Level of education was the only significant parameter that showed an association with fate A as shown in table 10. There was no significant association between fate A and other variables as shown in table 10 and table 11.

Table 10: Association between general characteristics and Fate A

Characteristic		Others	Fate A	Total	P-value
Gender	Male	75	10	85	0.753
	Female	33	3	36	
mode of delivery	Spontaneous vaginal delivery	24	2	26	0.654
	Induced vaginal delivery	39	7	46	
	Elective CS	19	2	21	
	Emergency CS	26	2	28	
place of delivery	Hospital	92	11	103	1.000
	Home	16	2	18	
Clinical stage	Stage I	52	9	61	0.304
	Stage II	32	3	35	
	Stage III	24	1	25	
Maternal age	<16 years	17	2	19	0.924
	17-35 years	71	8	79	
	>35 years	20	3	23	
Parity	Primipara	69	5	74	0.076
	Multipara	39	8	47	
ANC	Regular	48	6	54	1.000
	Irregular	60	7	67	
Education	Illiterate	23	0	23	0.014
	Primary	52	4	56	
	Secondary and higher	33	9	42	

Table 11: Association between fate A and both birth weight and gestational age of patients

Characteristic	Fate	Mean	SD	P-value
Birth weight	Fate A	3.31	0.77	0.986
	Others	3.31	0.87	
Gestational age	Fate A	38.15	2.38	0.957
	Others	38.19	2.56	

Disscussion

Perinatal asphyxia is considered a global issue especially in the developing countries [27]. It occur worldwide and contribute significantly to neonatal morbidity and mortality [28].

In this study the predominant gender was male with male to female ratio about (2.3:1) . this result was similar to that seen in Ayup medical college, Abbottabad 2010 [29], and in Bangeladesh at Dhaka medical college [30] . This may be explained by the higher birth rate of male . there was no significant difference in gender seen in a study in Nigeria [31].

There is a higher rate of perinatal asphyxia among newborn of primipara mothers (61.6%) which is in agreement to a study done by Myers in 1995 [32] and in a study at Dhaka medical college [30].

Perinatal asphyxia was more reported among mothers with irregular ANC (55.37%). this result was similar to that reported by Brenda [33] but less than reported by Nilofar et al at Dhaka medical college where it was (78%) [30].

While in another study by S. Ibrahim at the national institute of child health karachi [34],the majority of mothers were booked with regular ANC (this may be related to insufficient health services provided to these mothers during their regular visit).

Regarding mode of delivery in our study , the main mode was induced vaginal delivery and the rate of vaginal delivery was slightly higher than that of C/S delivery (Emergency C/S > Elective C/S) .

This result was similar to a study in Karachi [34], but opposite to a study in specialist hospital of Nigeria [31] .

This may be reflected upon the judgment of obstetrician regarding mode of delivery as there should be an effective measures to detect which infant at high risk of perinatal asphyxia.

Majority of deliveries were at hospital (85.1%) while home deliveries was (14.8%) this is about the same result of that of Karachi [34] as hospital delivery was (75.4 %) and in Nigeria where it was (90%) [31]. This is again may reflect that the perinatal services , which may be unsatisfactory in our hospital.

Most of the mothers were 17-35 years old , this may be explained by the higher pregnancy rate in this age group.

We classify the patient according to their fate in to groups and highlighted the character of the patients in each fate group .

Thirteen patient (10.74%) had unknown fate (fate A) because of discharge against medical advice (on parents responsibility) , this rate was less than reported in a study in Karachi [34] where it was 21.7%.

The level of education was the only predictor to this fate , the low rate of fate A may be explained by the low rate of uneducated mothers (illiterate) , as it was 19.1% in our study which is considered lower than reported by other studies { it was 39% in a study at Dhaka medical college hospital [30]}.

The mortality rate (fate D) was (16.53%) in our study which was equal to the study of Bangeladesh where it was (16%) but less than reported by S.Ibrahim et al as it was (26.8%) .

As a fact the mortality rate in our study may be higher than reported as we does not know the fate of infants in group A (they may be died at home or at another hospital).

Infant of group B were (47.93%), it is about the same result by a Bangladesh (40%) [30], while those in group C were 30 (24.79%) are also considered the same result of Bangladesh study where it was 28% [30] .

The clinical staging of HIE was the only determinant factor that predict fate B,C,D.

Study limitations:

The first limitation was in determination of APGAR score to those delivered at home as { we depend in diagnosis on significant history of delayed cry and first breath with history of cyanosis }.

Sometime we relies on data getten from attending staff with possible inadequacy and inaccuracy.

The inability to include the EEG and MRI finding as a predictor of fate because of the unavailability of the first one and the difficulties in performance of the second one for most of newborns.

Conclusion

Male gender , prim parity ,primary level of education and irregular ANC have more association with HIE.

Fate B,C,D were predicted by the clinical staging only , while fate A was predicted by the level of education only.

Recommendations

- Encouragement of all pregnant ladies to follow a regular programs of ANC.
- Accentuation of the effort by obstetrician for early diagnosis of high risk pregnancy and high risk infant.
- More wide programs and training courses of neonatal resuscitation and neonatal care is important .
- Improvement of facilities of EEG and cranial imaging which are considered essential in management plan and prognosis of patient with perinatal asphyxia.

Appreviations

HIE: hypoxic ischemic encephalopathy . , C.P.: cerebral palsy.
MRI : magnetic resonance imaging. , a EEG : amplitude EEG.
GA : gestational age , ANC : antenatal care
B.WT: birth weight , CT : computerized tomography

References

1. McIntosh N, Helms PJ, Smyth LR . The Newborn. In: Forfar & Arneil's Textbook of Pediatrics. 7th edition. Newyork: Churchill Livingstone; 2008. p. 177-392.

2-Costello AM de L . Perinatal health in developing countries. Trans R Soc Tropical Medical Hygiene 1993; 87: 1-2.

3. Niel McIntosh , Ben Stenson . Perinatal Asphyxia & Hypoxic-Ischemic Encephalopathy, Forfor Text book 7th Edition , Churchill Livingstone 2008 ; 12 : p. 204-210.

4. Ambalavanan N, Carlo WA, Shankaran S . : Predicting outcomes of neonates diagnosedwith hypoxic-ischemic encephalopathy pediatrics journal 2006 ; 118: . :2084-2093.

5. State of the World's Children, UNICEF; 2009.

6. Bonifacio SI, Glass HC, Vanderpluym J : Perinatal events and early magnetic resonance imaging in therapeutic hypothermia. *Journal of Pediatr*ics 2011; 158:360-365.
7. BIRTH asphyxia –summery of the past meetings and protocols overview [http://www.curoservice.com 10-09-2007_ birth asphaxia 02.pdf.
8. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: When? Where? Why? *Lancet journal 2005;365: 891-900.*
9. N. Mcintosh. Hypoxic lschaunic encephalopathy (HIE. In Forfar and Arneils text book of paediatncs New York, Churchill Living Stone, 1998, p. 126.
10. Hafizur Rahman Chowdhury, Sandra Thompson, MohammedAli, Nurul Alam, Md. Yunus, Peter Kim Streatfield. Causes of Neonatal Deaths in a Rural Subdistrict of Bangladesh August; pediatrics journals 28(4): 375–382.
11. Renato S. Procianoy, Rita de Cássia Silveira. Hypoxic-ischemicsyndrome. *Journal of Pediaticsr (Rio J) 2001;77(Supl.1):s63-s70.*
12. Apgar V. and James L.S. , further observation of neonatal scoring system . American J. of diseased children 104 ,419-28.
13. Apgar V., Holiday D.A., and James L.S evaluation of the newborn infant J.A.M.A.168 ,1985-8
14. Catlin E.A. , carpenter ,M.W., Branna B.S.IV ,,the apgar score revisited , influence of the gestational age , Journal of pediatrics , 109 ,865-8.
15. Niswarder K.R. AND Gordon M. , collaborative perinatal study of national institute for nourological disease and stroke . the women and their pregnancies , Vol. I Philadelphia: saunders.
16. Russell GA, Cooke RW. Randomised controlled trial of allopurinol prophylaxis in very preterm infants. *Archives of Diseases in Child Fetal Neonatal Ed*. 1995 Jul; **73(1):** F27-31.
17. Jerome Y Yager, Edward Armstrong. The Effect of Brief Post-Ischemic Hypothermia in Combination with Neuroprotective Agents on Hypoxic-Ischemic (H-I) Brain Damage in the Immature Rat. *Perinatal Society of Australia and New Zealand: Annual Congress: 1998*; Poster 1910.
18. Perlman JM, Risser R. Can asphyxiated infants at risk for neonatal seizures be rapidly identified by current high-risk markers? *Pediatrics*. 1996 Apr; **97(4):** 456-62.
19. Gibson-NA; Graham-M; Levene-MI. Somatosensory evoked potentials and outcome in perinatal asphyxia. *Archieves of Dieasesin a Child*. 1992 Apr; **67**(4 Spec No): 393-8.
20. Chau V, Poskitt KJ, Sargent MA, et al : Comparison of computer tomography and magnetic resonance imaging scans on the third day of life in term newborns with neonatal encephalopathy. *Pediatrics* 2009; 123:319-326.
21. Gluckman PD, Wyatt JS, Azzopardi D, et al: Selective head cooling and mild systemic hypothermia after neonatal encephalopathy: multicenter randomized trial. *Lancet* 2005; 365:663-670.
22. Gunn AJ, Wyatt JS, Whitelaw A, et al: Therapeutic hypothermia changes the prognostic value of clinical evaluation of neonatal encephalopathy. *Journal of Pediatr*ics 2008; 152:55-58.
23 . Shankaran S, Pappas A, Laptook AR, et al: Outcomes of safety and effectiveness in a multicenter randomized, controlled trial of whole-body hypothermia for neonatal hypoxic-ischemic encephalopathy. *Pediatrics* 2008; 122:e791-e798.

24. Hall RT, Hall FK, Daily DK: High-dose phenobarbital therapy in term newborn infants with severe perinatal asphyxia: a randomized, prospective study with three-year follow-up. *J Pediatr*ics 1998; 132:345-348.

25. Laptook AR, Shankaran S, Ambalavanan N, et al: Outcome of term infants using Apgar scores at 10 minutes following hypoxic-ischemic encephalopathy. *Pediatrics* 2009; 124:1619-1626.

26. Logitharajah P, Rutherford MA, Cowan FM: Hypoxic-ischemic encephalopathy in preterm infants: antecedent factors, brain imaging, and outcome. *Pediatrics Res*earch 2009; 66:222-229.

27. Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD,

Ferriero DM, *et al*. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicenter randomized trial. Lancet 2005;365:663–70.

28. Airede AI. Birth Asphyxia and hypoxic-ischaemic encephalopathy: incidence and severity. *Ann Trop Paediatrics 1991; 11: 331-5*

29. Azhar Munir Qureshi, Anees ur Rehman, Tahir Saeed Siddiqi Department of Paediatrics, Ayub Medical College, Abbottabad J Ayub Med Coll Abbottabad 2010;22(4)

30. NILUFAR SHIREEN1, NAZMUN NAHAR2, AH MOLLAH 3 Risk Factors and Short-Term Outcome of Birth Asphyxiated Babies in Dhaka Medical College Hospital bangladesh j child health 2009; VOL 33 (3): 83-89

31. West BA Opara PI, Perinatal asphyxia in a specialist hospital in Port Harcourt, Nigeria Nigeria Journal of Paediatrics 2013; 40 (3): 206 - 210

32. Myers RE .Fetal asphyxia due to umbilical cord compression: metabolic and brain pathologic consequences . *Biol Neonate.*1995 ; 26 (1-2):21-43.

33.Brenda Eskenazi, Gaylec , Windhor and shanna LD, Swan AM . Obstetrics and gynecological survey , journal of public health , 1997 ; vol.47 : 81 ,458

34. Ibrahim, J. Parkash S., Birth Asphyxia - Analysis of 235 Cases , National Journal of Medical Research. (National Institute of Child Health Karachi.). 2013; 3(4): 374-37.