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RESEARCH ARTICLE

A CLINICAL STUDY OF HYPOXIC ISCHEMIC ENCEPHALOPATHY AND ITS CORRELATION WITH UMBILICAL CORD BLOOD ANALYSIS

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ABSTRACT

Introduction: Birth asphyxia is the most common cause of mortality and morbidity in new borns. Asphyxia can cause damage to almost every tissue and organ of the new born baby secondary to hypoxia.

Objective: TO study the neurological signs in term neonates with Hypoxic Ischemic Encephalopathy that appear following asphyxia and correlation of conventional umbilical cord blood parameters with seizures and mortality among cases and controls.

Materials and Method of study :A prospective case control study was conducted in term babies from which 60 cases of birth asphyxia and 30 cases of normal newborn delivered in Rajah Muthiah Medical College, and Hospital, Chidambaram over a period of 1 year. Immediately after birth, blood was drawn from clamped umbilical cord, and sent for ABG analysis and parameters like pH, PCo_2, Po_2, HCo_3, Base excess and oxygen saturation were observed.

Results: Increased risk of seizures , mortality was associated with severe birth asphyxia with decreased umbilical arterial pH. Compare to PO_2 value, difference in PCO_2 and base excess values between cases and controls was associated with increased risk of neurological disability.

Conclusion: pH < 7, high PCO_2, base excess values were significantly associated with neurological outcome. Umbilical cord, PCO_2, base excess are better indicators of neonatal mortality and morbidity than PO_2 level.

INTRODUCTION

Birth asphyxia refers to condition of hypoxemia, hypercapnea and insufficient blood perfusion of new born during labour and birth. Birth asphyxia is leading cause of perinatal mortality in our country. It occurs in 9% of new borns less than 36 weeks of gestational age and 0.5% of new borns more than 36 weeks of gestational age and it accounts for about 20% of perinatal deaths.[1] The Fetal tissues that are adapted to low oxygenation during intrauterine development are subjected to a rapid change in an oxygen concentration after delivery. Birth itself is a strong oxidative stress. Oxidative stress, free radicals and its metabolites causes free radical damage in newborns. Consequence of asphyxia is more threatening in preterms as they have immature enzymatic and non-enzymatic antioxidant mechanisms.[2] Asphyxia can damage almost every tissue and organ of newborn baby, the target organs for dysfunction due to asphyxia insult being the brain, heart, lungs, kidneys, liver, GIT. The degree of severity of asphyxia determines the severity of damage to organs involved.

During the past decade umbilical blood gas analysis has increasingly been recognized as the most reliable indicator of fetal oxygenation and acid base condition at birth. The diagnosis of asphyxia mandates the presence of severe cord blood acidemia and normal values refutes the diagnosis. As it can provide important information about past, present and possibly the future condition of infant it is considered as the gold standard objective for the assessment of intrauterine asphyxia.

MATERIALS AND METHOD OF STUDY

A prospective case control study was conducted in term babies from which 60 cases of birth asphyxia and 30 cases of normal newborn delivered in Rajah Muthiah Medical College and Hospital, Chidambaram over a period of 1 year. Immediately after birth, blood was drawn from clamped umbilical cord, and sent for ABG analysis and parameters like pH, PCO_2, PO_2, HCO_3, Base excess and oxygen saturation were observed.

Inclusion criteria

Controls -- Singleton, live born neonates of Gestational age > 37 weeks without evidence of fetal distress and HIE.

1. Cases - Singleton, live born neonates of Gestational age > 37 weeks with Evidence of fetal distress and delayed cry after birth presenting with signs and symptoms of HIE.
2. Those needing resuscitation at birth
3. Low APGAR score <5 after 1 minute or 5 minutes after delivery or well defined episode of fetal distress like,
4. Fetal bradycardia/tachycardia (HR <110 bpm/>150 bpm respectively)

Reduce baseline variability
Decelerations and absence of accelerations on cardiotocogram

Exclusion criteria

1. Evidence of congenital heart disease, traumatic cerebral injuries, hydrocephalus or infection.
2. Those neonates born with major congenital anomaly.

All these infants were graded clinically into stages of hypoxic ischemic encephalopathy based on Sarnat and Sarnat classification without the electro-encephalographic criteria.

METHODOLOGY

Umbilical artery is identified on the cut section of the cord which is doubly clamped. A syringe of 2m1, flushed with l/l000of heparin solution is advanced into the artery and 1ml of blood is collected. Sample is kept air free and transported for analysis in ice packs within thirty minutes of collection. Analysis is done by AVL Compact 3 analyzer

Statistical analysis

Data was analysed by Student t test, Chi square test and p value of <0.05 was considered significant

RESULTS

Table 1 Seizures and umbilical arterial pH in study cases

pH level	SEI				Total	
	Present		Absent			
	N	%	N	%	N	%
<6.80	7	21.9	5	17.9	12	20.0
6.81-6.90	9	28.1	5	17.9	14	23.3
6.91-7.00	9	28.1	6	21.4	15	25.0
7.01-7.10	5	15.6	3	10.7	8	13.3
7.11-7.20	1	3.1	7	25.0	8	13.3
7.21-7.30	1	3.1	2	7.1	3	5.0
Total	32	100.0	28	100.0	60	100.0

X2 – 0.175, p=0.208 Majority of cases with seizures had a pH of <6.9s

Table 2 Seizures and umbilical arterial PCO_2 in study cases

PCO_2 level	SEI				Total	
	Present		Absent			
	N	%	N	%	N	%
<55 mmHg	12	37.5	9	32.1	21	35.0
>55 mmHg	20	62.5	19	67.9	39	65.0
Total	32	100.0	28	100.0	60	100.0

X2 – 0.188, p=0.664 Most of the case with seizures had pco2 levels>55mmhg.

Table 3 Seizures and umbilical arterial PO_2 level in study cases

PO_2 level	SEI				Total	
	Present		Absent			
	N	%	N	%	N	%
<20 mmHg	24	75.0	18	64.3	42	70.0
>20 mmHg	8	25.0	10	35.7	18	30.0
Total	32	100.0	28	100.0	60	100.0

X2 – 0.816, p=0.366 Among cases about 75.0% neonates with seizures had umbilical arterial po2 level of <20mmhg.

Table 4 Seizures and umbilical arterial Pco2, Po2& BE levels in cases

	SEI	N	Mean	Std. Deviation	t	Sig.
Pco2	Present	32	63.0566	23.87463	0.727	0.470
	Absent	28	67.6393	24.89091		
Po2	Present	32	18.7719	5.81224	0.236	0.814
	Absent	28	19.1250	5.75420		
BE	Present	32	-14.2375	4.41177	0.953	0.345
	Absent	28	-17.1179	16.45323		

Between cases with or without seizures there was significant difference in umbilical arterial pco2 and base excess but not for umbilical po2 values.

Table 5 Neonatal mortality and umbilical arterial pH level in study cases

pH level	Death				Total	
	No		Y			
	N	%	N	%	N	%
<6.80	10	17.5	2	66.7	12	20.0
6.81-6.90	14	24.6	0	.0	14	23.3
6.91-7.00	14	24.6	1	33.3	15	25.0
7.01-7.10	8	14.0	0	.0	8	13.3
7.11-7.20	8	14.0	0	.0	8	13.3
7.21-7.30	3	5.3	0	.0	3	5.0
Total	57	100.0	3	100.0	60	100.0

X2 – 5.263, p=0.385
Among the neonates in the case group all those who died has pH of<6.9 among controls there was no death

Table 6 Neonatal mortality and umbilical arterial PCO2 in study cases

PCO2 level	Death				Total	
	No		Y			
	N	%	N	%	N	%
<55 mmHg	21	36.8	0	.0	21	35.0
>55 mmHg	36	63.2	3	100.0	39	65.0
Total	57	100.0	3	100.0	60	100.0

X2 – 1.700, p=0.192
All the neonates who died had PCO2 level of > 55mmhg.

Table 7 Neonatal mortality and umbilical arterial PO2 in study cases

PO2 level	Death				Total	
	No		Y			
	N	%	N	%	N	%
<20 mmHg	41	71.9	1	33.3	42	70.0
>20 mmHg	16	28.1	2	66.7	18	30.0
Total	57	100.0	3	100.0	60	100.0

X2 – 2.022, p=0.155
Among the cases neonate that died had PO_2 >20mmhg.

DISCUSSION

Hypoxic Ischemic Encephalopathy is the common cause of hospital admission in newborn

Different stages of HIE

Study	Stage I	Stage ll	Stage III
Our study n = 60	29**(48.3%)**	21(41.7%)	06(10%)
N.N. Firmer et al[24] n=95	33 **(35%)**	48 (50%)	14(15%)
Sarnat and sarnat etal[54] n=21	7(33%)	9 (43%)	5(24%)

Our study, shows 29 cases (48.3%) in HIE stage I, 21 cases (41.7%)in HIE stage II, 6 cases (10% in HIE stage III ,but in the study of N.N. Finner and C.M.Robertson et al where, in their study of 33 cases (35%) were in stage-1, 50% were in stage II and 15% were in stage III and in the *study* by Sarnat

and Sarnat et al, among 21 cases, 7 (33%) cases were in Stage-1, 9 cases (43%) were in **stage-II** and one (5%) case were in stage-III.

Table 1 Umbilical arterial pH and acidosis

Study	pH value for acidosis
Our study	<7.2
Goldaber3	<7.1
Andres 4	<7.0
Goodwin5	<7.0
Winkler 7	<7.2

In our study, 31% cases had umbilical arterial pH >7.00 and 69% had pH <7.00 similar to the study done by Goldaber and colleagues[3], 28% cases had pH of >7.00 and 72% had pH <7.00. On the contrary Winkler and colleagues[7] found a low incidence of cases with pH <7.00, 6.4% and 93.6% had pH>7.00. This low incidence in their study could be explained on the basis, that cases irrespective of evidence of fetal distress were enrolled in the study

Seizures

Table 2 Incidence of seizures

Study	Incidence of seizures
Our study	53.3%
Andres[6/]	5.2%
Goodwin	1%
Vandenberg [/3]	5.5%

Incidence of seizures in our study was much higher at 53.3% when compared with other studies. Lower incidence was seen in study done by Goodwin and co-workers[5] and a higher incidence (10%) in study done by Sehdev and co-workers[10]

Seizures and umbilical arterial pH

Our results show significantly increase in incidence of seizures with the decrease in umbilical arterial pH <6.9.

In study done by Goodwin and colleagues[5] the incidence of seizures was 9% in pH between 6.90-6.99 and 80% in pH between 6.61-6.70.

Seizures and umbilical arterial PCO2 and base excess levels

There was significant difference in PCO_2 (p=0.664) and base excess (mean -14.23), values between cases with seizures (mean- PCO_2=63.05), BE= (-14.23) and without seizures (mean- PCO_2=67.6, BE = -17.11) which correlated with studies done by Andres and colleagues[4] and Low and co-researchers[6]. On the contrary, Vandenberg and colleagues[9] proposed that PCO_2 values of >75mmHg was not related to seizure. Base excess of >16mmol/l in study done by Sehdev and colleagues and >15mmol/l with pH<7.00 in study done by Vandenberg and colleagues[9] were significantly associated with seizures.

Perlman and Risser in their study found that, there was no significant correlation between seizures and umbilical arterial PCO_2 and base excess, whereas pH was significant.

Belai and colleagues in their study proposed that rather than umbilical arterial PCO_2 and base excess, the arteriovenous differences of PCO_2 >25mm Hg is more significantly associated with the increased incidence of seizures.

Seizures and umbilical arterial PO_2 levels

In our study the differences in PO_2 was not significantly associated so also in other studies[4,6] contradicting the results of the study done by Keith and colleagues where in elevated levels of PO_2 were found to be significantly associated Sehdev and co-workers[10]

Neonatal Mortality

	mortality	
	pH<7.00	pH>7.00
Our study	5%	-
Goldaber3	5%	1.6%
Andres4	4.5%	-
Goodwin5	2.3%	-
Vanderberg9	23%	1.1%
Naegel11	10%	-

Neonatal mortality and umbilical arterial PCO_2 and base excess

In our study neonatal mortality among cases was significantly associated (P=(0.000)-with differences in the PCO_2(p=0.192) and similarly Keith and co-workers[8] found significant association of mortality with high PCO_2 levels but not with pH and base excess.

Our results showed that base excess of >10mmol/l was found to be significantly associated with mortality which agreed on a study done by Goodwin and co-workers[12]. Low and co-workers[6], Sehdev and co-workers[10] found that high base excess values of>-16mmol/l was significantly associated with neonatal mortality.

Neonatal mortality and umbilical arterial PO_2

The low PO_2 values among cases was found to be significant (p=0.155) in predicting neonatal mortality which was similar to study done by Andres and co-workers[4] but in their study statistical significance could not be proved.

Sarnat and Sarnat et al also described convulsions as a pathognomic feature of stage II encephalopathy. In stage I of HIE babies may have weak cry or excessive cry which was seen in 56% and 16.6% cases respectively in our study. In stage II HIE there was always weak cry. Baby having £ shrill cry or cerebral cry was a significant feature of stage III HIE in our study, which was seen in 16.6% of cases. J.K.Brown and J.O. Forfar et al also described cerebral cry in 18% of cases in their study this feature maybe due to severe hypoxia, ischemia to the brain and also cerebral irritation

Neonatal outcome

In our study in stage I, there were 29cases (48.3%), all cases improved. In the study P.E.Eken et al and E.Thornberg et al 100% of the cases in stage I HIE have improved which closely correlates to our study and also the study of Sarnat and Sarnat et al in which all the cases improved.

Table 4 Outcome of cases in different stages of HIE in various studies in neonatal period

Different studies	Stage -I	Improved	Expired	Stage -11	Improved	Expired	Stage-I 11	Improved	Expire d	Total mortality in all the stages
Present study (n=60)	48.3% (29)	100%	0%	41.7% (25)	100%	0%	10% (6)	50%	50%	5%
P.Eken[2]et al (n=34)	32% (ID	100%	0%	21% (7)	. 72%	28%	47% (16)	0	100%	52.9%
E.Thornberg[57] et al (N=65)	55%(33)	100%	0%	26% (17)	94%	6%	19% (12)	8%	92%	18.4%
Sarnat & Sarnat[54] et al 1M=21	33% (7)	100%	0%	43% (9)	100%	0%	24% (5)	80%	20%	4.7%

There were 25 cases 41.7% in stage II in our study of which all cases were clinically improved. In other studies by P.Eken at al among the 7 cases 21% in stage II, 72% of the cases have improved and 28% of the cases have expired.

This is in contrast to study by e. Thomberg et al of the 17 cases 26% in stage II 94% cases improved and only 6% expired. Therefore there was a better prognosis in this study and also the study by sarnat and sarnat et al where all the cases in stage II improved.

In our study stage III HIE had the maximum mortality where in 3 cases (50%) in this stage expired within 3 days of admission. This high mortality may be due to the fact that the much of the brain damage in this stage had already occurred and the value of post partum intervention is probably limited and another contributing factor was severe perinatal asphyxia.

In the study by P.Eken et al out of the 16 cases in stage III all the cases have expired and in the study by E.Thornberg et al of the 12 cases in this stage 92% expired. These studies closely correlates to our findings but is incontrast to Sarnat and Sarnat study where 80% of the cases improved and 20% cases expired.

Total mortality in our study was 5%. Closely comparable to 4.7% in the studies carried out by P.Ekenet and Sarnat and Sarnat et al respectively. In the study by Sudarshan Kumar et al among the total 77 HIE cases Stage I was 28 cases 36.3%, stage II were 22 cases (28.5%) and stage III 27 cases (35%). Total mortality in this study was 18.7%.

When we compare all the above studies the outcome is variable and can conclude that the best prognosis is in stage I, better prognosis in stage II and the worst in Stage III HIE.

CONCLUSION

Hypoxic Ischemic encephalopathy is probably the most important single cause of neurological disability in newborn infants. It is responsible for many neurological changes, mortality and morbidity in infants. Umbilical cord blood parameters like pH <7.00, high PCO_2 and Base excess are significantly associated in predicting the likelihood of seizures, and mortality. This study shows that the "Pathologic acidemia" is indicated by pH <7.00 rather than <7.20, laid down by ACOG[6.] Umbilical arterial PO_2 levels are of little clinical utility.

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