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Umbilical Cord Blood Ph & Base Deficit In Relation To Short Term Neonatal Morbidity & Mortality In Term Asphyxiated Newborns A Prospective Study.

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ABSTRACT

Perinatal asphyxia, all around the world, is one of the commonest causes of neonatal morbidity as well as mortality. objective To study relation of umbilical cord blood pH & base deficit with short term neonatal morbidity & mortality in term asphyxiated newborns.
Materials and Methods: We included full term or post term newborns with APGAR of ≤ 6 at 1min and cord blood sample were taken. Response to resuscitation & outcome parameters were studied in respect to cord blood pH and base deficit. We used MedCalc statistical software version 11.5.0.0. for statistical analysis. Results and conclusions: Out of 93 enrolled neonates, pH was ≤ 7.1 in 67% babies while it was ≤ 7 in36 (38.7%) babies and base deficit was ≥ 20 in 63% babies. Babies with low APGAR at 20 min had significance association with pH ≤ 7 (p=0.0025). Need for ventilator support and risk of developing CNS and CVS complication were significantly higher when the pH was ≤ 7 & when BD was ≥ 16, risk of CNS, electrolyte and metabolic complication and sepsis increased significantly. Base deficit of ≥ 16 was more sensitive in predicting the development of HIE than cord blood pH ≤ 7. There was significant difference in the outcome when the cord blood pH is ≤ 7 (p= 0.0179). Conclusion: Doing cord blood pH and base deficit estimation can be useful in predicting short term neonatal outcome in form of morbidities and mortality.

Keywords : cord blood pH, base deficit, birth asphyxia, neonatal morbidity & mortality

Introduction

Around 4-6% neonates face difficulty in establishment of spontaneous breathing after birth. WHO has estimated around 23% neonatal deaths are due to perinatal asphyxia. Perinatal asphyxia, all around the world, is one of the commonest cause of neonatal deaths and also a major cause of neonatal admission. There are very few epidemiological data on short term out come in asphyxiated neonate in India with respect to cord blood ABG. In these studies investigators used cord blood pH and PaCO2 mainly to compare outcome. Considering these facts this study is was carried out to identify short term out come in asphyxiated newborn and it correlation with cord blood pH and base excess.

Materials and Methods

This was prospective study and was conducted between November 2009 to December 2010, at Department of pediatrics, Medical College & SSG Hospital, Baroda. Inclusion criteria were term or post term asphyxiated newborn having APGAR score of ≤ 6 at one minute of birth. We excluded preterm babies, neonates with APGAR of ≥ 7 at 1 min, babies in which cord blood ABG could not be done, Babies with major congenital malformations, Genetic disorder or syndrome, Inborn errors of metabolism were also excluded from study.

Resuscitation of newborn was carried out as per NRP 2005 protocols. During resuscitation, one person collected cord blood sample from umbilical artery which had been double clamped and was sent to laboratory for blood gas analysis with ice packs. Post-resuscitation management was done as per standard protocols of our nursery which included temperature control, close monitoring of vital signs and continuous monitoring of oxygen saturation, heart rate, blood pressure with anticipation of complication. Blood samples were obtained for laboratory study and blood glucose estimation and subsequent ABG done as per requirement.

Detailed antenatal and perinatal history was taken. All the perinatal events and their course in the NICU were noted in the predesigned Performa.

Babies were examined regarding their weight, length, occipito-frontal circumference, temperature, color and systemic examination with primitive reflex. Gestational age was assessed by menstrual period or by New Ballard scoring system. For discrepancy in gestation, the later was taken. Babies were followed up and note was kept for daily event/s of the baby. The management was given as per the protocol of the unit. Investigations (Hb, S.CRP, Bl. Urea, S.Creatinine, S. Electrolyte) were done at 12 15th HOL and repeated as per the requirement. Blood culture was sent before starting of antibiotics and repeated as and when needed.

During period of NICU stay, morbidities were noted as CNS (apnea, seizures, encephalopathy), pulmonary (pulmonary hypertension, pneumothorax, pneumonia, meconium aspiration syndrome,), cardiovascular (hypotension, Brady/tachycardia), renal (acute tubular necrosis,), gastro-entero (Ileus, necrotizing enterocolitis),

metabolic (hypoglycemia, hyperglycemia, hypocalcemia, hyponatremia) or hematological (anemia, thrombocytopenia) complications. Incidence of sepsis also noted in these babies.

Baby was handed over to the mother once the baby is out of morbidity and when on total breast feeding or katori-spoon feeding or intragastic feeding and did not require O2 or clear fluids (IVF). Discharge was planned when the baby was out of morbidity and mother was confident enough to look after the feeding and routine care of the baby at home. During discharge, babies with abnormal neurological examination were enrolled for regular physiotherapy and early stimulation program advised. All the babies were followed up in the high risk clinic for neurodevelopmental follow up.

Different neonatal morbidities, NICU stay in days, hospital stay in days, and mortalities were analyzed according APGAR score and cord blood ABG analysis.

Statistical Analysis:

Data was recorded on a predesigned detailed Performa & analyzed in Microsoft excel with the help of MedCalc statistical software version 11.5.0.0. χ^2 test was applied wherever required. *P* values of less than 0.05 were considered as statistically significant. Parent's were informed about the need of resuscitation and written informed consent for post resuscitation management and enrolment was taken. Day to day improvement or deterioration in clinical condition was discussed with parents during hospital stay.

Results and Discussion During period of 13 month, from Nov. 2009 to Dec 2010, there were 4589 total deliveries with 4411 live birth. 659 newborns required NICU care during this period. In live birth, 203 babies suffered from perinatal asphyxia of which, 137 were full-term, 61 were pre-term and 5 were post-term. 203 cases of birth asphyxia accounted for 30.8 % of NICU admissions. Out of 142 full term and post-term asphyxiated babies, umbilical artery blood gas analysis was done in 93 babies and these were included in the study. The incidence of birth asphyxia was 46.02 per 1000 live births (4.6%) with male predominance (sex ratio: 1.38:1). Appropriate for date babies were 60.2% which formed a major group, where as small for date were 37.6% and large for date were 2.1%. Blood gas analysis showed linear correlation for cord blood pH and base deficit with coefficient of correlation of 0.499. All patients with a cord blood pH $\leq$ 7 had a base deficit $\geq$ 12. On comparison of cord blood pH and base deficit with APGAR score as shown in table I, response to resuscitation judged by improvement in APGAR at 5 min was not significantly correlating with acidosis (pH $\leq$ 7 or base deficit of > 12.) but the babies who were having 20 min APGAR 7 or less had significant association with pH less or equal 7(p= 0.0025). We did not find such correlation with base deficit of more than 12 and response of resuscitation at 20 min.

Table I. Comparison of cord blood pH and base deficit with APGAR score

Cord blood pH	APGAR score						
	At 1 min		At 5 min			At 20 min	
	0- 3	4 - 6	0-5	6-7	$\geq$8	$\leq$ 7	$\geq$8
pH $\leq$ 7 (n=36)	34	2	27	8	1	16	20
pH > 7 (n=57)	46	11	35	17	5	8	49
BD $\leq$ 12(n=13)	10	3	9	2	2	1	12
BD > 12(n=80)	70	10	53	23	4	23	57
BD $\leq$ 16(n=26)	22	4	16	8	2	3	21
BD > 16(n=67)	58	9	46	17	4	21	48
P value = 0.0025 for cord pH $\leq$ 7 and APGAR score at 20 min 7 or less.							

In our study in asphyxiated babies, HIE was the most common presentation in NICU, being present in 41.94% of asphyxiated babies. Proven sepsis (40.86%), seizures (38.7%), respiratory complications (35.48%) and shock (32.25%) were the next common presentation. CNS complications were the most common and GIT complications were the least common in the study group.

The incidence of each systemic complication with respect to cord blood pH and base deficit is shown in above table. The Incidence of complications was inversely proportional to the cord blood pH and directly proportional to base deficit. This incidence of CNS, RS, CVS, Renal, GIT, Hematological and Electrolyte and metabolic complication was much higher if babies cord blood pH is < 7 as compared to pH > 7 except GI complication. In this observation we noted that the incidence of GI complications does not change with change in pH. Similar observations were made on comparing base deficit. The incidence was higher for CNS, RS, CVS, Renal, GIT, hematological, electrolyte and metabolic complication and culture positive sepsis respectively when base deficit is > 12.

Table II Different systemic complications in study cohort

Systemic complications	%Systemic complications	events in NICU	No.of cases
CNS (n=39)	41.94%	Seizures	36 (92.30%)
		HIE gr. I	3 (7.70%)
		HIE gr. II	20 (51.28%)
		HIE gr. III	16 (41.02%)
Respiratory (n=33)	35.48%	Repeated Apnea	11 (33.34%)
		pulm. HT	4 (12.13%)
		Pulm. Hemorhhage	2 (6.06%)
		Pneumonia	6 (18.18%)
		MAS	18 (54.55%)
		Pneumothorax	2 (6.06%)
CVS/ hemodynamic instability (n=30)	32.25%	Shock within 72 hrs	15 (50%)
		Shock after 72 hrs	15 (50%)
Renal(n=8)	8.60%	ARF	8 (100 %)
GIT (n=3)	3.22%	NEC	3(100%)
Metabolic and electrolyte (n=31)	33.34%	Hyperglycemia	4 (12.90%)
		Hypoglycemia	5 (16.12%)
		Hypocalcemia	21 (67.75%)
		Hyponatremia	20 (64.52%)
Hematological (n=13)	13.98%	Anemia	4 (30.76%)
		Thrombocytopenia	13 (100%)
Sepsis (n=37)	40.86%	Probable sepsis	6 (%)
		Proven sepsis	31 (100%)
		Pyo ME	3 (7.89%)

Table III Comparison of pH and base deficit with different Systemic complications during NICU stay in study cohort. (Table 3)

In this study group we found that if the pH is $\leq$ 7 and BD > 16 then the incidence of CNS and CVS complication increases significantly (p <0.05, RR 1.77 and 2.38 respectively). Incidence of electrolyte and metabolic complications (p=0.0113 RR: 3.622) and culture positive sepsis (p=0.0411 RR: 2.62) were associated with BD > 16, but no such difference was seen with reference to cord blood pH. There was no difference in the occurrence of RS, Renal, GIT and Hematological complication when ph is $\leq$ 7 and BD is > 12 or 16.

In the study cohort, 29 babies required respiratory support of this pH was $\leq$ 7 in 18 babies and base deficit was $\geq$ 12 in 25 babies. Out of 29, 7 babies were discharged and 22 were expired. pH $\leq$ 7 was associated significantly with need of ventilation in asphyxiated baby and it increases by 2.59 times as compare to those having pH > 7. On comparing the mortality in ventilated and non ventilated babies we found that in ventilated babies' mortality increases significantly when cord blood pH is $\leq$ 7. Similar observations were made for BD $\geq$ 12 and 16.

Table IV. Cord blood analysis and outcome in ventilated and nonventilated patient (Table 4)

Occurrence of HIE grade II and III with respect to cord blood pH and base deficit we found that, there was significant increased risk of having HIE grade II and III if pH is $\leq$ 7 or base deficit > 12 or 16. The base deficit of > than 16 was more sensitive (89.74%) than pH $\leq$ 7 (55.56%) in predicting the development of HIE. Similar observation was made by Low et al[4]; but the study done by Williams KP and Singh A[6] found pH less than 7 as more sensitive predictor than base deficit in their study.

Table V Association between HIE and cord blood pH and base deficit. (Table 5)

When the requirement of anticonvulsants was compared with cord blood pH and base deficit, it was noted that out of the 16 cases with HIE grade III, 12 had pH $\leq$ 7and of these 9 required 2 or more anticonvulsant to control seizures, whereas, 15 had base deficit > 12 and of these 12 required 2 or more anticonvulsants to control seizures and none were having BD less than 12.

Similar observation was also noted in HIE gr II. This signifies, that babies with pH ≤ 7 and BD >12 have significant risk of HIE and refractory seizures which require 2 or more anticonvulsants.

There was significant difference in the outcome (in form of discharge or expired) when the cord blood pH is less or equal to 7 (p= 0.0179). No such difference was seen up to base deficit of 20 or more (0.6296) but the base deficit of 30 and more was significantly associated with outcome in the form of death. More the acidic pH, more is the adverse outcome i. e. Death.

On analyzing mortality data with respect to response to resuscitation in labor room, we found that APGAR ≤ 5 at 5 min is significantly associated with mortality; however, on further analyzing, this association became highly significant when APGAR at 20 min is 7 or less.

Conclusion:

Doing cord blood pH and base deficit estimation can be useful in predicting short term neonatal outcome in form of morbidities and mortality.

Table III Comparison of pH and base deficit with different Systemic complications during NICU stay in study cohort.

Systemic complications	Cord blood pH			Cord blood base deficit					
	≤ 7 (n=36)	> 7 (n=57)	X^2 test P value	<12 (n=13)	≥12 (n=80)	X^2 test P value	<16 (n=26)	≥16 (n=67)	X^2 P value
CNS (n=36)	19	17	0.0460	1	35	0.0301	3	33	0.0018
RS (n=33)	14	19	0.7467	4	29	0.9437	8	25	0.726
CVS (n=30)	18	12	0.0073	3	27	0.6573	4	26	0.0547
Renal (n=8)	5	3	0.2867	1	7	0.6839	1	7	0.5439
GIT (n=3)	1	2	0.6832	1	2	0.8914	2	1	0.3872
Heamat (n=1 3)	7	6	0.3675	4	9	0.1467	4	9	0.9286
Electrolyte and Metabolic (n=31))	16	15	0.1140	1	30	0.0723	3	28	0.0113
Culture pos itive sepsis (n=31)	16	15	0.1140	2	29	0.2448	4	27	0.0411

Table IV. Cord blood analysis and outcome in ventilated and nonventilated patient

Cord Blood analysis	No. of cases	Total cohort				
		Ventilated (n=29)		Non ventilated (n=64)		P value
		Expired (n=22)	Discharged (n=7)	Expired (n=60)	Discharged (n=4)	
pH < or = 7	36	15	3	0	18	**<0.0001**
pH > 7	57	7	4	4	42	**0.0002**
BD > or = 12	80	19	6	3	52	**<0.0001**
BD < 12	13	3	1	1	8	0.0984
BD > = 16	69	19	5	2	43	**<0.0001**
BD < 16	24	3	2	2	17	0.0711

Table V Association between HIE and cord blood pH and base deficit.

cord blood analysis	No HIE (n=57)	HIE gr II & III (n=36)	P value (RR)
pH ≤ 7 (n=36)	16	20	0.0150
PH > 7 (n=57)	41	16	(1.9792)
BD ≥ 12 (n=80)	45	35	0.0301
BD < 12 (n=13)	12	1	(5.6875)
BD ≥ 16 (n=69)	36	33	0.0048
BD < 16 (n=24)	21	3	(3.8261)

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