ORIGINAL ARTICLE

Umbilical Cord Blood pH in Intrapartum Hypoxia

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ABSTRACT

Objective: To determine the association of cord arterial blood pH with neonatal outcome in cases of intrapartum fetal hypoxia.

Study Design: Descriptive analytical study.

Place and Duration of Study: Gynaecology Unit-II, Civil Hospital, Karachi, from September 2011 to November 2012.

Methodology: All singleton cephalic fetuses at term gestation were included in the study. Those with any anomaly, malpresentation, medical disorders, maternal age < 18 years, multiple gestation and ruptured membranes were excluded. Patients with abnormal cardiotocography and/or meconium stained liquor were enrolled as index case and immediate next delivery with no such signs as a control. Demographic characteristics, pH level < or > 7.25, neonatal outcome measures (healthy, NICU admission or neonatal death), color of liquor and mode of delivery recorded on predesigned proforma. Statistical analysis performed by SPSS 16 by using independent-t test or chi-square test and ANOVA test as needed.

Results: A total of 204 newborns were evaluated. The mean pH level was found to be significantly different (p=0.007) in two groups. The pH value 7.25 had significant association (p < 0.001) with the neonatal outcome. However, the association of neonatal outcome with severity of acidemia was not found to be significant. Grading of Meconium Stained Liquor (MSL) also did not relate positively with pH levels as 85.7% of grade I, 68.9% of grade II and 59.4% of grade III MSL had pH > 7.25. Majority (63.6%) cases needed caesarean section as compared to 31.4% controls.

Conclusion: There is a significant association of cord arterial blood pH at birth with neonatal outcome at pH < or > 7.25; but below the level of pH 7.25 it is still inconclusive.

Key Words: *Cord arterial blood pH. Hypoxia. Neonatal outcome. Meconium stained liquor.*

INTRODUCTION

Birth asphyxia is a major cause of perinatal morbidity and mortality worldwide. Of the estimated 4 - 9 million cases per year, 1.1 million are still born and a further one million neonates die soon after birth.[1] In the survivors neurodevelopmental disorders have medical, legal, financial and social ramifications to the medical and wider community. Most estimates suggest that labour accounts for only up to 15% of cerebral palsy cases yet these are potentially avoidable and account for much litigation.[2] The National Institute for Health and Clinical Excellence (NICE) states that the monitoring of babies in labour aims to identify hypoxia before it is sufficient to lead to damaging acidosis and long term neurological sequelae for the baby.[3] Metabolic acidosis in arterial cord blood, is considered to be an essential criteria for the diagnosis of birth asphyxia and umbilical cord artery pH at birth provide a sensitive reflection of birth asphyxia with the absence of acidosis excluding the diagnosis.[4] Identification and prevention of fetal acidemia is, therefore, the aim of intrapartum fetal monitoring, the cord arterial blood pH is considered a crucial outcome measure.[2]

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Although cord acid-base assessment provides an objective measure of neonatal condition at delivery, there is a lack of correlation with other measure of neonatal condition and long-term outcome in some studies. Still many investigators believe that universal use of Umbilical Cord Blood Gas (UC - BG) analysis can improve neonatal outcomes, however, no studies have evaluated this contention.[1,5,6] Also till date no local study has been published to evaluate this relationship.

The aim of this study was to detect the significance of cord arterial blood pH in cases of intrapartum hypoxia (fetal distress) as a predictor of neonatal outcome.

METHODOLOGY

This analytical study was conducted prospectively from September 2011 to November 2012 in Civil Hospital Gynae Unit II, Karachi. All women at term gestation (≥ 37 weeks) with singleton, cephalic fetus in labour were included in the study while cases with malpresentation, congenital anomaly, maternal age ≥ 18 years, multiple gestation, medical disorders, rupture membranes > 12 hours and accidental venous blood sampling were excluded. Approval from Ethical and Research Committee of Dow University of Health Sciences was taken (ref. no. IRB-277/DUHS-11).

Cases with evidence of fetal distress (intrapartum hypoxia) during labour (meconium stained liquor or / and abnormal cardiotocographic tracings) were registered as study case and the immediately following delivery with no evidence of fetal distress were taken as control.

Informed consent was taken from eligible women by the duty doctor. Maternal age, parity, gestational age, mode of delivery, birth weight, APGAR score at birth and at 5 minutes, umbilical cord arterial pH results were recorded on predesigned proforma. Colour of liquor was noted and meconium staining was graded subjectively as grade I (green discoloration only), grade II (green particulate suspension) and grade III (pea soup viscosity and appearance). Fetal heart rate patterns on cardiotocography was classified as normal, suspicious and abnormal according to FIGO guidelines.[7]

Acidemia was defined as severe if pH < 7.00, moderate 7.00 to 7.10, mild 7.1 - 7.25 and normal pH was taken as > 7.25. Blood for umbilical cord arterial blood gas analysis was collected at birth by pretrained doctors in labour room. A segment of cord (10 cm) was double clamped immediately after birth before first breath. Three ml blood was drawn from umbilical artery in a pre-heparinized plastic syringe and placed in ice and sent for subsequent analysis to the laboratory immediately. A Ciba corning 248 blood gas analyzer (Chiron Diagnostics, UK) was used for blood gas analysis throughout the study. The primary outcome was to see the relationship of acidemia and neonatal outcome (APGAR score at birth and at 5 minutes, NICU admission and neonatal death). While secondary outcome was to see association of cord blood acidemia with colour of liquor and the frequency of mode of delivery in control and study cases.

Statistical analysis was performed by SPSS version 16. Obstetric and neonatal characteristics were summarized using frequency distributions for categorical data (neonatal outcome, colour of liquor and mode of delivery) and mean and standard deviations for continuous data (maternal age, parity, gestational age, birth weight, APGAR score and pH level). Independent-t-test was used for continuous variables and chi-square test for neonatal outcome. ANOVA test was applied to see the relationship of pH with neonatal outcome. Chi-square trend test was applied to see the Linear-by-Linear association of different pH levels with neonatal outcome. Significant p-value was taken as < 0.05.

RESULTS

A total of 204 cases (102 study cases and 102 controls) were included. The demographic data of control and case groups were statistically insignificant in respect of mean age (26.15 ± 4.68 vs. 27.21 ± 5.17), gestational age (37.82 ± 1.33 vs. 38.27 ± 1.24) and birth weight (2.81 ± 0.38 vs. 2.88 ± 0.45) while parity was found to be significant (p = 0.002, Table I). There was significant difference (p = 0.007) in mean cord blood pH value (7.29 ± 0.08 vs. 7.26 ± 0.10) of control and case groups respectively (Table I). The mean APGAR score at birth and at 5 minutes were found to be significantly low in case group as compared to control group (p = 0.032 and < 0.001 respectively, Table I).

There was statistically significant difference in the neonatal outcome measures among the two groups (p = < 0.001). Out of 33 neonates requiring NICU

Table I: Descriptive data of control and case groups.

	Control Mean ± SD	Case Mean ± SD	p-value
Age (years)	26.15 ± 4.68	27.21 ± 5.17	0.522
Parity (No.)	1.41 ± 1.33	1.48 ± 2.12	0.002
Gestational age (weeks)	37.82 ± 1.33	38.27 ± 1.24	0.547
Birth weight (kg)	2.81 ± 0.38	2.88 ± 0.45	0.064
Cord blood pH	7.29 ± 0.08	7.26 ± 0.10	0.007
APGAR Score at birth	7.24 ± 0.79	6.94 ± 1.013	0.032
APGAR Score at 5 minutes	9.00 ± 0.63	8.65 ± 1.2	0.001

Table II: Comparison of cord blood pH and neonatal outcome between controls and cases (No. 204).

	Total No.	Control No (%)	Cases No No (%)	p-value
pH level				
> 7.25	152	82 (53.9)	70 (46.1)	0.054
≤ 7.25	52	20 (38.5)	32 (61.5)	
A/S at birth				
> 7	173	92 (53.2)	81 (46.8)	0.032
< 7	31	10 (32.3)	21 (67.7)	
A/S at 5 minutes				
> 7	199	102 (51.3)	97 (48.7)	0.030
< 7	5	0 (0)	5 (100)	
Outcome				
Healthy	166	99 (59.6)	67 (40.4)	0.001
NICU admission	33	3 (9.1)	30 (90.9)	
Neonatal death	5	0 (0)	5 (100)	

Table III: Relationship of neonatal outcome and colour of liquor with pH level.

	Total No.	pH level		
		< 7.1 No. (%)	7.1 - 7.25 No. (%)	> 7.25 No. (%)
Neonatal outcome				
Healthy	67	2 (2.98)	15 (22.39)	50 (74.63)
NICU admission	30	7 (22.3)	7 (22.3)	16 (55.3)
NND	5	0 (0)	1 (20)	4 (80)
A/S at birth				
< 7	21	3 (14.3)	6 (28.6)	12 (57.1)
> 7	81	6 (7.4)	17 (21.0)	58 (71.6)
A/S at 5 minutes				
< 7	5	0 (0)	1 (20)	4 (80)
> 7	97	9 (9.3)	22 (22.7)	66 (68)
Colour of liquor				
Clear	4	0 (0)	2 (50)	2 (50)
Meconium stained G-I	21	0 (0)	3 (14.3)	18 (85.7)
Meconium stained G-II	45	5 (11.1)	9 (20)	31 (68.9)
Meconium stained G-III	32	4 (12.5)	9 (28.1)	19 (59.4)

Table IV: Mode of delivery in both groups.

Mode of delivery	Control No. (%)	Case No. (%)	p-value
Normal vaginal delivery	80 (78.4)	32 (31.4)	
Instrumental delivery	4 (3.9)	5 (4.9)	0.001
Caesarean section	18 (17.6)	65 (63.7)	

admission, 90.9% were from hypoxia group while all five neonatal deaths occurred in that group. The APGAR score at birth and at 5 minutes were found to be > 7 in control group (53.2% and 51.3%) as compared to case group (46.8% and 48.7%) respectively (p 0.032 and 0.03 respectively, Table II). Majority of control group patients had pH level > 7.25 as compared to the case group (Table II).

Relationship of neonatal outcome to pH level is depicted in Table-III. When the level of acidemia was correlated with neonatal outcome then the result revealed majority of healthy neonates have pH > 7.25 and 77.8% of neonates with pH < 7.1 needed NICU care (Table III). Linear-by-Linear association was calculated by using chi-square trend test which also showed no association of neonatal outcomes with different pH levels below 7.25 (p= 0.121). Four out of the 5 neonatal deaths occurred in pH group of > 7.25. However, the secondary outcome measure i.e. APGAR score at birth was < 7 in 21 cases and among them only 3 had pH < 7.1 while 6 had pH between 7.1 - 7.25 and 12 had pH > 7.25. Similarly, APGAR score < 7 at 5 minutes present in 5 neonates but again 4 had pH > 7.25 showing no correlation of APGAR score with pH value or severity of acidemia.

Grading of liquor regarding meconium staining also did not show positive relation with pH level as out of 32 patients with grade III and 45 with grade II meconium staining have pH > 7.25 (Table III).

Regarding the mode of delivery there was a significant (p < 0.001) difference between control and case groups as 78.4% of control groups delivered vaginally spontaneously in contrast to 31.4% in case group. Caesarean section rate was high in case group as compared to controls. (63.6% vs. 17.61%, Table IV).

DISCUSSION

The mean umbilical artery cord pH value found in this study is comparable to other international studies.[8,9] There is a significant relationship between umbilical cord pH and the selected neonatal outcomes like APGAR less than 7 at 5 minutes, NICU admission and neonatal death as evident from other studies.[9] Although low cord arterial pH is strongly associated with long-term adverse outcomes like cerebral palsy but it is unclear which pH level is significant as different authors report different threshold. Yeh *et al*. quote that above pH 7.00 the relationship between cord pH and outcome is much less clear.[2] They report pH range of 7.26 to 7.30 as ideal pH range for all outcomes and is, therefore, used for comparison.[2]

Some authors report that although the risks of adverse neurological outcomes start to rise below a pH of 7.10 it rises sharply below an arterial pH of 7.00 as their study revealed a pH below 7.00 accounted for 20 - 24% of adverse neonatal outcome while a further 10 to 15% occurring below 7.11 pH.[2] Even for seizures within the first 24 hours, at least half had a pH > 7.10 whereas 39% had a pH above 7.20.[2] The near-normal cord blood values at which adverse outcome began to increase as reported by others in literature is approximately 7.20 thus supporting a threshold for increasing risk with outcomes.[9]

Consensus for ascribing cerebral palsy to intrapartum hypoxia states that arterial pH must be < 7.00 while other large studies report acidosis is not significant until pH falls to < 7.05.[10] Studies also reveal that neonates without acidemia might still have been hypoxic as they are unable to develop acidemia as a response as we also found 12 out of 21 neonates having pH > 7.25 had < 7 APGAR score at birth and all 5 neonates having < 7 APGAR score at 5 minutes have pH level > 7.1. This observation is made on the basis that neonates with so-called-birth asphyxia often have a normal pH, that catastrophic intrapartum events can occur without acidemia and that neonates with low APGAR score who are that acidemic may do better in long-term than those who are not, for example a very acute insult like shoulder dystocia may cause neurological damage without cord acidemia.[11] The establishment of threshold levels for pathologic acidemia in relation to adverse neonatal outcome depends on the outcome of interest and also on other risk variable as quoted by others. The authors could not evaluate the neonatal neurological morbidity and mortality with umbilical cord pH < 7.00 at birth in this study because of small sample size, although studies concluded 23.1% of neurological morbidity and mortality with this pH.[12] Even some larger studies are reported to be underpowered to detect rare but potentially more serious outcomes such as cerebral palsy and perinatal death caused by intrapartum asphyxia.

White *et al*. suggested introduction of umbilical cord blood gas analysis which is associated with significant improvements in biochemical markers of metabolic acidosis and they argue that this extra biomedical information aids clinical assessment and leads to improved perinatal care.[1] Although guidelines suggest paired umbilical cord sampling but in the case of only one available sample, arterial is preferred.[13] Some studies recommend paired cord blood gas analysis to be ideal and physiological approach to the interpretation of cardiotocographic and fetal blood sampling which is useful in training and education. It also protect against allegations of intrapartum asphyxia. But because of limited facility, the authors only analyzed umbilical cord arterial blood as its pH correlate best with APGAR scores when compared with all other arterial or venous blood gas measurement.[14]

Association of meconium staining of amniotic fluid with acidemia at birth is found to be insignificant as also evident from other studies concluding poor sensitivity

and positive predictive value (< 20%).[15,16] This is because meconium passage during labour may not be a direct response to hypoxia and many risk factors like prolonged labour, epidural analgesia and the use of oxytocin are identified for it while clear liquor is associated with good fetal condition. According to American College of Obstetrics and Gynecology Guidelines abnormal fetal heart rate and meconium staining of amniotic fluid represent physiological response to peripheral hypoxia and are, therefore, not always associated with asphyxia or acidemia.[17] So complimentary methods should support the diagnosis of acute fetal distress. In fact low APGAR score persisting > 5 minutes and acidosis (umbilical cord pH < 7.20) are better prediction of poor outcome.[18]

Regarding the mode of delivery, the study shows significantly higher proportions of cases than controls are delivered by emergency caesarean section but this is primarily because of primary indication rather than the asphyxia.[19]

There were several limitations in this study. First, sample size was small so number of cord blood pH value < 7.00 were few, therefore, effect of severe metabolic acidemia could not be assessed effectively. Secondly, the authors were unable to analyze pCO_2 because it was not recorded in all cases. Thirdly, only arterial pH was analyzed as this is the most commonly used measure although paired venous and arterial sample and base deficit analysis are also important in detecting the relationship of neonatal outcome with acidemia. Finally, long-term follow-up data was lacking. More local studies with larger sample size, are recommended to find the neurological sequelae especially for cord pH < 7.1.

CONCLUSION

Significance of cord arterial blood pH as a predictor of intrapartum hypoxia is considerable in determining neonatal outcome but at pH level > 7.1 the neonatal neurologic morbidity is not so evident. Although moderate degree of acidemia < 7.1 is associated with increased risk of adverse neonatal outcome, the absolute risks are very low and most affected babies have a higher pH than this as evident in this study.

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