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Original article

Neonatal Cord Blood pH versus Eucapnic pH as a Predictor for NICU Admission

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Abstract

Background: For clinicians to determine the possibility for neonate brain damage and guide therapeutic decisions to avoid long-term complications, as cerebral palsy involving umbilical artery cord PH, base deficit(BD), and lactic acid, the majority of biomarkers that are utilized for assessing fetal wellbeing, neonatal metabolic acidosis, and its associated complications in newborns are inaccurate and non-specific. On the other hand, the pH eucap demonstrates that it is the best biomarker and predictor for newborn metabolic acidosis and the obstacles that are associated with it. Aim**:** To evaluate the value of neonatal cord eucapnic PH in prediction of neonatal intensive care unit (NICU) admission in newborn subjected to perinatal asphyxia. **Patients and methods:** This prospective cohort investigation conducted on 40 newborns who subjected to perinatal asphyxia and cord blood pH and eucapnic pH were measured and correlated with parameters of morbidity and mortality. **Results:** there is statistically significant difference between eucapnic pH and NICU admission; as mean of eucapnic pH was higher among neonates admitted to NICU (P=0.03). Also ROC analysis (Receiver operation Curve) showed that eucapnic PH had best prediction for NICU admission with sensitivity (90.91%) and specificity (58.62%) at cut-off point (7.03), while umbilical artery (UA)cord PH had sensitivity (63.64%) and specificity (55.85%)at cut-off point(6.85). a significant positive correlation has been detected between UA cord and pH euc-n and between pH euc-n and UAco2 with(r=0.369, P=0.019). (r=0.789, P<0.001) respectively. **Conclusion:** PH eucapnic is a better marker than Ua cord pH for predicting NICU admission in asphxieted newborns.

Key words: Eucapnic pH; neonatal cord blood pH; NICU.

Introduction

At time of delivery hypoxic ischemic encephalopathy (HIE) is resulted after neonatal metabolic acidosis (NMA) that Occurs at the first day of life and may worsen by acquired brain damage that occur due to reperfusion after attack of initial hypoxia and this can be treated by therapeutic cooling (hypothermia) that prevent long term complication such as

cerebral palsy if applied within the first hours of insult [1].

The recommended criteria that related to occurrence of hypoxic ischemic encephalopathy (HIE) according to **the American College of Obstetricians & Gynecologists and American Academy of Pediatrics 2014 (ACOG- AAP) (pH** less than 7.0 and base deficit [BD] not less than twelve millimole per litter). But this biomarker is inaccurate as the pH affected by CO2 retention disperse when ventilate effectively after delivery, also BD show variation in cases of sever academia [1].

Many studies show that eucapnic pH is the best biomarker for determining NMA **[2 and 3]**.

It is possible for severe neurologic sequelae to occur during neonatal asphyxia per partum, which can ultimately result in the death of the newborn **[4]**.

The absence of a marker that can establish the onset, nature, and time of the insult is an important obstacle that is stopping progress in the therapy of prenatal brain asphyxia **[5]**.

The patient's respiratory exchanges, metabolic rate, and electrolytic status can all be evaluated with the help of the blood gas analysis (BGA) **[6]**. There is a correlation between newborn acidemia and a higher probability of admission to the neonatal intensive care unit, hypoxia ischemic encephalopathy, respiratory distress syndrome (RDS), multi-organ dysfunction, and mortality in newborns **[7]**.

For the purpose of evaluating newborn academia during delivery, umbilical cord blood gas analysis is very essential **[8]**.

In order to diagnose peripartum hypoxia, which might result in hypoxic-ischemic encephalopathy (HIE) and, subsequently, cerebral palsy, metabolic acidosis is widely recognized as an essential marker **[9]**. The condition known as neonatal metabolic acidosis (NMA) is correlated with birth depression and, in more severe situations, hypoxic–ischemic encephalopathy **[10]**.

Despite the fact that the effect of anaerobic metabolism can be determined by evaluation the pH of the blood in the umbilical artery (UA) cord and estimating its metabolic component by assessing the base deficit, the methods that are utilized to quantify base deficit are derived from adult acid–base normal values, such as pH = 7.40 and pCO2 = forty millimeters of mercury, which are not suitable for fetal conditions **[11]**. As a consequence of this, the methods that were utilized to compute base deficit, it elevated concerns about the validity of the findings acquired in neonates. This is due to the fact that the physiological pH of newborns is approximately 7.25–7.28 and the pCO2 is between fifty to fifty-four millimeter of mercury **[12]**.

None of these equations take into consideration the specificity of the acid-base physiology that exists at birth. Fetuses, in comparison to adults, are often profoundly hypoxemic, mildly acidaemic, and moderately hypercapnic. Furthermore, during birth, fetuses may show much higher pCO2 **[13]**.

Neonatal eucapnic pH has been suggested as a means of particularly evaluating the metabolic component of acidosis at birth in order to overcome these physiological variations **[12]**.

This research was conducted with the purpose of determining the role of newborn cord eucapnic PH in the process of predicting admission to the intensive care unit for neonates.

Patients and methods

This prospective cohort investigation has been performed on 40 newborns at time of delivery in Neonatal intensive care unit, department of Pediatrics and neonatology, Benha University Hospitals, Benha, Egypt at attendance of NICU team at time of delivery from 1 March 2023 till 1 March 2024.

Inclusions Criteria: Age: Gestational age ≥ 35 weeks, both genders, born by vaginal delivery or instrumental labor or by caesarean section, PH < 7 and base deficit (BD) ≥ 12 Meq/l

Exclusion Criteria: Parental (Guardian) refusal, preterm neonates and newborns with major congenital malformations of the circulatory, systems, respiratory, digestive congenital metabolic disorders, and congenital malformations or chromosomal abnormalities of the nervous system.

Ethical Consideration

The study protocol was submitted for approval by the ethics committee, faculty of medicine, Benha University {M.S.19.2.2023}.

Informed consent was obtained from each participant in the study after assuring confidentiality.

Sample size: was calculated using Epi Info V.7. A previous investigation by Racinet et al discovered that the sensitivity of Neonatal cord blood eucapnic pH in prediction of NICU was 100% (10). Thus, it was estimated that a minimal sample size of 40 patients is required to achieve a power of 80% to detect expected difference in the sensitivity of 5%, at a significance level of 0.05.

Informed consent and Ethical consideration: An approval from the top managers of the hospital where the research has been carried out was required. The local ethics committee (number Eleven), the Faculty of Medicine at Benha University in Egypt, gave their approval to the research. In agreement with "The Code of Ethics of the World Medical Association" (also known as the Declaration of Helsinki), this work has been performed.

Detailed methodology

All included participants in the study have been subjected to: clinical examination, laboratory investigations and History taking

Cord blood analysis and eucapnic cord pH

During each and every delivery, either nurses or physicians will collect blood samples from the artery umbilical cord. A portion of the umbilical cord measuring between ten and twenty centimeters has been clamped twice, and both samples have been promptly sent to the clinical laboratory for examination at room temperature. Both the pH and pCO2 of the arterial cord have been evaluated, and the standard base defect (cBase extracellular fluid) equations have been utilized in order to describe the findings of the base defect. For the purpose of calculating pH euc-n from umbilical artery cord gasses and pH for each infant, the Charles–Racinet diagram or the application of "neonatal eucapnic pH" has been utilized. The traditional Henderson–Hasselbalch equation has been utilized as the algorithm **(11)**.

Study outcomes:

Primary: Neonatal intensive care unit admission, requirement of invasive ventilation and length of NICU stay.

Secondary: Mortality.

Statistical analysis:

Version 22 of SPSS (Statistical Package for the Social Sciences) for Windows (IBM, Inc., Chicago, states) has been utilized to conduct data analysis. While qualitative data has been presented in the form of numbers and percentages, quantitative data has been reported as the mean ± standard deviation (SD) or the median (range) according to the normality. The nature of the data has been taken into consideration when selecting the suitable statistical tests to utilize. A p-value of less than 0.05 has been regarded as statistically significant.

Results

Table 1 demonstrates that gestational age ranged from 35 to 40 weeks with mean ± slandered deviation of 37.8 ± 1.54. (37.5%) were born by vaginal delivery and (62.5%) were born by caesarian section.

Umbilical artery PH ranged from 6.85 to 6.99 with mean ± SD of 6.95 ± 0.03, while umbilical artery PCO_2 ranged from 57 to 97.6mmHG with mean ± SD of 72.86 ± 10.43, base deficit ranged from 12 to 17.9 millimole per litter with mean ± SD of 14.06 ± 1.62 and calculated neonatal eucapnic PH ranged from 7 to 7.18 with mean ± SD of 7.04 ± 0.04.

Table 2: shows that (72.5%) of the patients had no NICU admission, while (27.5%) of the patients admitted to intensive care unit of newborn. (2.5%) of the patients experienced mortality

Table 3: shows a statistically significant difference between eucapnic pH and NICU admission; as mean of eucapnic pH was higher among neonates admitted to NICU (P=0.03).

Table 4 shows a significant positive correlation among umbilical artery cord pH and pH euc-n (r=0.369, P-value equal to 0.019). Also, a significant positive association has been observed among pH euc-n and UA PCO_2 (r=0.789, P-value less than 0.001).

Figure 1: shows ROC analysis (Receiver operation Curve) to determine the optimal cutoff value to predict NICU admission, analysis showed that UA cord pH had sensitivity (63.64%) and specificity (55.17%) at cut-off point (7.03) with area under the curve was (0.545), while eucapnic PH had highest sensitivity (90.91%) and specificity (58.62%) at cut-off point (6.95) with area under the curve was (0.691).

Table 1: Gestational age, mode of delivery, Cord blood analysis and eucapnic cord PH among studied patients

Variables		**All patients (n=40)**
Gestational age *(weeks)*	*Mean ± SD*	37.8 ± 1.54
	Range	(35 – 40)
Delivery mode *(n. %)*	Vaginal	15 (37.5%)
	Caesarian section	25 (62.5%)
UA cord PH	*Mean ± SD*	6.95 ± 0.03
	Range	(6.85 – 6.99)
UA PCO_2 *(mmhg)*	*Mean ± SD*	72.86 ± 10.43
	Range	(57 – 97.6)
Base Deficit *(mmol/l)*	*Mean ± SD*	14.06 ± 1.62
	Range	(12 – 17.9)
Calculated eucapnic PH	*Mean ± SD*	7.04 ± 0.04
	Range	(7 – 7.18)

Table 2: Outcome among and complication among studied patients

Variables		**All patients (n=40)**
NICU admission *(n. %)*	No	29 (72.5%)
	Yes	11 (27.5%)
Mortality *(n. %)*	No	39 (97.5%)
	Yes	1 (2.5%)

Table 3: Relation between pH-euc-n and different parameters among studied patients

Variables		**pH-euc-n *Mean* ± *SD***	**P Value**
Delivery mode	Vaginal (n=15)	7.06 ± 0.06	
	Cesarian section (n=25)	7.04 ± 0.03	0.14[2]
NICU admission	No (n=29)	7.03 ± 0.03	
	Yes (n=11)	7.07 ± 0.06	**0.03[2]**
Requirement of MV	PCV (n=5)	7.03 ± 0.01	
	SIMV (n=6)	7.05 ± 0.04	0.31[1]
Mortality	No (n=39)	7.05 ± 0.04	
	Yes (n=1)	7.01	0.2[2]

*[1]Student T test, [2]Mann-Whitney U test, Non-significant: P-value higher than 0.05, Significant: P-value equal or less than 0.05

Table 4: Correlation of umbilical artery cord pH and pH euc-n with different parameters among studied patients

Variable	**umbilical artery cord pH**		**pH euc-n**	
	r	***P***	***r***	***P***
Gestational age	0.097	0.551[2]	0.004	0.978[2]
APGAR one minute	0.047	0.775[1]	0.186	0.250[1]
APGAR five minutes	0.234	0.147[1]	0.193	0.233[1]
UA PCO_2	0.271	0.091[2]	0.789	**<0.001[2]**
Base deficit	-0.269	0.093[2]	-0.234	0.145[2]
pH euc-n	0.369	**0.019[1]**	-	-
Period of NICU admission	-0.273	0.416[1]	-0.298	0.374[1]
Creatinine level	0.469	0.145[2]	-0.484	0.131[2]

*[1]Pearson correlation, [2]Spearman rank correlation test

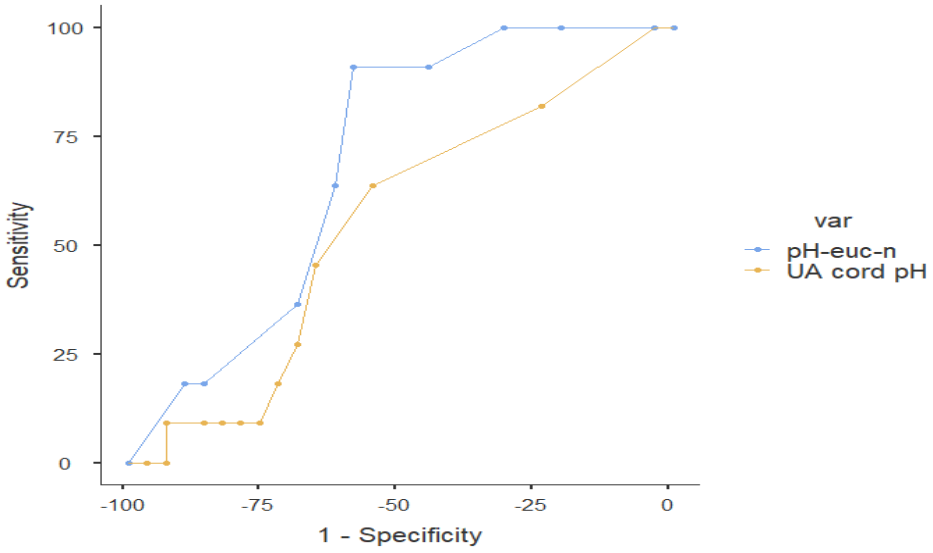

Figure 1: ROC curve analysis of umbilical artery cord pH and eucapnic pH to predict admission to NICU

Discussion

The importance of getting umbilical artery blood gas sample at time of delivery give us chance to determine fetal wellbeing and to make the best decision for therapeutic hypothermia (either head cooling or Whole body) that assured only after delivery by several hours (>6h). So, we should have accurate arterial blood gas based on accurate base deficit and this achieved by calculated eucapnic pH

Gestational age in our research ranged from 35 to 40 weeks with mean ± SD of 37.8 ± 1.54. We select this age as Deep gray matter is nearly functional and influenced and below this age HIE will influence watershed spread of white matter. Sixty two and a half percentages of the cases were born by caesarian section and this in the same line with [3] that identified a group of 32 Cases, of which eighty percent have been born by instrumental delivery or caesarian section.

Umbilical artery pH varied from 6.85 to 6.99 with mean ± standard deviation of 6.95 ± 0.03, while umbilical artery PCO_2 ranged from 57 to 97.6 mmhg with mean ± SD of 72.86 ± 10.43, base defect ranged from 12 to 17.9 mmol/l with mean ± SD of 14.06 ± 1.62 and calculated neonatal eucapnic PH varied from 7 to 7.18 with mean ± standard deviation of 7.04 ± 0.04

While Racinet and colleagues [13] observed that a great pCO2 in all patients with a cord pH o less than 7.0, varying from seventy-three to one hundred and fifteen millimeter of mercury and this near to our study.

Where pHa was always <7.00, ranked from 6.78 to 6.99 **[1].**

(72.5%) of the patients in our research had no NICU admission, while (27.5%) of the patients were admitted to neonatal intensive care unit.

Also, Racinet and colleagues [3] reported that only 5 cases of 32 case (15%) at PH eucap < 7.11, admitted to NICU

Racinet and colleagues [13] recognized a group of thirty patients with umbilical artery cord pH less than 7.0. Among these thirty patients, 4 (thirteen percent) have

been admitted to the intensive care unit of newborn. Our study has higher rate of NICU admission than other studies and, the cause may be that western countries have more follow up and Perinatal Care to pregnant mothers that decrease perinatal and natal asphyxia

Period of NICU admission ranged from 4 to 21 days with mean ± slandered deviation of 8.36 ± 4.67, while creatinine level varied from 0.6 to 1.6 mg/dl with mean ± slandered deviation of 1.1 ± 0.33. As regard requirement of mechanical ventilation, 45.5% of the patients required PCV and 54.5% of the admitted patients required SIMV and mortality rate is (2.5%). Also, Racinet and colleagues [13] observed that other 26 neonates from 30 patients had a normal clinical result with insignificant morbidity.

There was a statistically significant relation between eucapnic pH and NICU admission; as mean of eucapnic pH was higher among neonates admitted to NICU (P-value equal 0.03). Also, a significant positive association has been observed between umbilical artery cord pH and pH euc-n Also, between pH euc-n and UACO2 (r=0.369, P=0.019). (r=0.789, Pvalue less than 0.001) respectively

In their research, **[14]** found that there is an adverse association among pH euc-n and BD euc-n. This finding is in agreement with our own research, which led us to the conclusion that pH euc-n and BD euc-n are both strictly equivalent for diagnosing neonatal metabolic acidosis, and that utilizing both of them simultaneously may be redundant**.**

In their study**,** **[14]** investigated the correlation between the pH and/or BD of the umbilical cord and both short-term and long-term results. Their findings demonstrated that there is still a demand for further research into the commonly accepted cut-off values that are used to identify neonatal metabolic acidosis in relation to newborn complications.

On conducting ROC analysis (Receiver operation Curve) to determine the optimal cutoff value to predict NICU admission, analysis showed that UA cord pH had sensitivity (63.64%) and specificity (55.17%) at cut-off point of 6.85 with area under the curve being 0.545.

In addition**,** Racinet and colleagues **[13]** developed the ROC curve for the pH of the umbilical cord. The ideal cut-off value for the pH of the umbilical cord was 6.96, with a sensitivity of seventy-five percent, a specificity of 38.5 percent, a true-positive rate of 0.750, and a false-positive rate of 0.615. This has the greatest degree of sensitivity and lower specificity than our research, but there is still a bit of distinction between the two. The area under the curve (AUC) for the pH of the umbilical cord is 0.44.

In our study, eucapnic PH had highest sensitivity (90.91%) and specificity (58.62%) at cut-off point of 7.03 with area under the curve being 0.691. Also, Racinet and colleagues **[13]** calculated the pH euc-n. The optimal cut-off value for pH euc-n was 7.11 with a sensitivity of one hundred percent, a specificity of fifty-two percent, a true-positive rate of 1.00 and a false-positive rate of 0.480. The area under the curve for pH euc-n is 0.66. This study is having higher sensitivity and specificity than our study, but the two studies agree that eucap-n PH has higher specificity and sensitivity than UA cord PH.

After applying logistic regression analysis for predictors of admission to NICU; eucapnic pH can be used as independent factors for predicting admission to intensive care unit of newborn and this

agree with Racinet and colleagues [13] that suggested that pH euc-n is a more accurate predictor than pH of umbilical artery for predicting admission to the newborn intensive care unit in neonates who were born with acidemia.

While Kelly and colleagues [14] discovered the relative risk and relation between of value of pH of umbilical artery cord (extent of acidemia) and different outcomes including as seizures, neurodevelopmental follow up, Apgar scores, newborn encephalopathy and admission to intensive care unit of newborn in newborn>35 weeks.

Also, Victory and colleagues [15] show worsening of acidosis at birth that has higher risk and need for assistant ventalion in neonate with perinatal asphyxia.

In their research, Garfinkle and colleagues [16] hypothesized that the pH value of the umbilical cord would be one of the factors that lead clinicians to make incorrect choices regarding whether or not to commence therapeutic hypothermia. Their outcomes provided evidence that a more effective biological marker is required.

Conclusion

In conclusion, pH euc-n is the best biomarker for predicting admission to intensive care unit in neonates. This study supports the value of pH eucap so should be used in hypoxic or acidotic newborns as it improves HIE prediction and outcomes, and prevent harmless intervention when NMA not assured.

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