



## ASSOCIATION BETWEEN NEONATAL ICU ADMISSION AND LOW CORD BLOOD PH

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### ABSTRACT

**Objective:** The assessment of umbilical cord arterial blood provides the foundation for current clinical practice when evaluating a neonate's status. Therefore, the present study aimed to determine the association between neonatal ICU admission and low cord blood pH.

**Methodology:** This was a Prospective cohort study conducted in the Department of Obstetrics & Gynecology, Liaquat National Hospital and Medical College, Karachi from 1<sup>st</sup> July 2023 to 31<sup>st</sup> December 2023 (six months). Detailed history, physical examination, and anthropometric and biochemical measurements were recorded. Patients were followed postoperatively for adverse outcomes.

**Results:** A total of 60 participants, 30 from each group were evaluated. Out of 30 neonates in the unexposed group (pH >7.2) only three were admitted to NICU, the rest of the 27 were not admitted to NICU. However, in the exposed group (pH <7.2) out of 30 neonates 10 were admitted to NICU. Mothers aged between 26 – 30 years from the Exposed Group (Acidotic cord pH) have shown a significant relationship with nine of their infants admitted to NICU (p-value = 0.078).

**Conclusion:** There is a strong association between Neonatal ICU admission and low cord blood pH. This showed that cord blood pH samples can be used to inform clinical management and it is one of the important tools to justify neonatal morbidity and mortality.

**Keywords:** Apgar Score, Low Cord Blood pH, Neonate, NICU admission

### INTRODUCTION

Cardiotocographic (CTG) monitoring is a primary biophysical method of evaluating the condition of a fetus during pregnancy and labor. It includes simultaneous recording and analysis of three signals: fetal heart rate, contractile activity of uterine muscle, and fetal movements <sup>1</sup>.

Intermittent auscultation of Fetal Heart Rate (FHR) and electronic fetal monitoring such as CTG are the most popular methods for intrapartum fetal surveillance. Whereas the former focuses only on the estimation of basal heart rate, the latter also reflects upon other qualities of fetal heart rate such as variability, accelerations, and decelerations. With the reduction in the cost of the equipment, electronic fetal monitoring has become a routine in many labor wards, especially at tertiary-level hospitals. Despite its popularity, CTG is not an ideal monitoring tool. Though a normal trace is predictive of a normal acid-base status at birth in about 98 % of cases, an abnormal trace has a low positive predictive value in terms of fetal pH of < 7.25.6 Even the most ominous fetal heart patterns

are often associated with only 50-65% accuracy for low Appearance, Pulse, Grimace, Activity and Respiration (APGAR) score and fetal acidosis at birth. This is partially due to a lack of agreement on nomenclature and definitions for the interpretation of fetal heart rate and partly due to inter-observer and intra-observer bias. The issue of bias can be solved to some extent through regular audits of CTG tracings against fetal conditions at birth. In this regard, both fetal Apgar score and fetal umbilical cord acid-base status have been used as a Gold standard. The latter is found to have a better correlation with Hypoxic ischemic encephalopathy (HIE) and thus recommended as a better tool for audit<sup>2</sup>. Analyzing the infant's outcome and development may be done quickly and easily by testing for cord blood acidity. Nonetheless, there is an ongoing debate on the potential correlation between the pH of cord blood and the fate of the fetus<sup>3</sup>. In light of this controversy, primarily the current study set out to determine whether low cord blood pH was associated with the number of neonates admitted to the Neonatal Intensive Care Unit (NICU). If so, then secondarily these babies would receive extra care, and attempts would be made to lower the NICU's admission rate, prevent unfavorable outcomes for the neonates, and enhance perinatal care through improved risk assessment and management.

## **METHODOLOGY**

This prospective cohort study was conducted at the obstetrics & Gynecology, Liaquat National Hospital, Karachi, from 1<sup>st</sup> July 2023 to 31<sup>st</sup> December 2023 (6 months). This study was conducted after approval from the College of Physicians & Surgeons Pakistan and the ethical review committee. The sample size was calculated by using the WHO sample size formula and percentages taken from the previous study conducted by Beeby et al<sup>4</sup>. According to NICU admission among the exposed group (acidic pH= 90.9%), NICU admission among the non-exposed group (normal pH=9.1%), Power of test i.e. 99%, and with a Significant level of 5%, the Sample size was 7 in each group. Although the sample size came out to be very small, however, we included 60 patients (30 in each group). A nonprobability consecutive sampling technique was used for data collection.

All women aged between 18-45 years, women either primiparous or multiparous, and all neonates whose cord blood pH < 7.2 (in the exposed group) and pH > 7.2 (in non-exposed group) were included. All multiple pregnancies were diagnosed based on U/S, gestational age < 32 weeks diagnosed based on U/S, and neonates with any congenital anomalies.

A total of 60 participants (30 in each group) were recruited by applying a nonprobability consecutive sampling technique. Permission from the health facility administration was taken before the study. After explaining the procedure informed consent was taken from the parents of study participants. Confidentiality was maintained and parents were accordingly informed about the situation of their babies. After delivery of baby Cord blood about 2ml of paired cord blood was taken in a pre-heparinized syringe by experienced staff or residents conducting delivery and was sent to the laboratory within 10 minutes for assessment of cord blood pH. Each patient's information was entered into a pre-planned study Performa along with the umbilical cord analysis results. After delivery, neonates were observed for two days. Those who were deemed vitally unstable were hospitalized and inspected; otherwise, they were allowed to leave and the result was recorded on an out-of-hospital basis on the seventh day of life.

## **Data analysis procedure**

Data analysis was done by SPSS version 21.0. Mean and standard deviation were calculated for the age of the mother, gestational age, Apgar score, and weight of the neonate. Frequency and percentage were calculated for mode of delivery and NICU admission. The two groups exposed and non-exposed were compared in terms of NICU admission by applying Chi-square. Relative Risk was also calculated. Effective modifiers/ confounders like the age of the mother, gestational age, Apgar score, and weight of the baby were stratified to see the effect of these on NICU admission by applying the Chi-square test. P-value < 0.05 was considered significant.

## **RESULTS**

Sixty patients fulfilling the inclusion criteria were included in this study. The study group consisted

of infants admitted to the NICU. Among those exposed to acidotic cord pH, 10 infants (33.3%) required NICU admission, while among those with normal cord pH (unexposed group), 3 infants (10%) required NICU admission. The p-value associated with the comparison between the two groups was 0.0468. The relative risk of NICU admission for infants with acidotic cord pH compared to those with normal cord pH was calculated as 3.33 (Table 1).

Among individuals aged 20-25 years, those with acidotic cord pH had a NICU admission rate of 33.3%, compared to 18.2% for those with normal cord pH, resulting in a non-significant relative risk of NICU admission of 1.83 (p = 0.55). In the 26-30 years age group, NICU admission rates were notably higher for individuals with acidotic cord pH (34.6%) compared to those with normal cord pH (5.9%), resulting in a significant relative risk of NICU admission of 5.88 (p = 0.078). Conversely, among individuals aged 31-35 years, there were no NICU admissions among those with acidotic cord pH, while 100% of individuals with normal cord pH required NICU admission, yielding a relative risk of NICU admission of 1.5, although this difference was not statistically significant (p = 0.8) (Table 2).

Among infants born at 37 weeks gestation, those with acidotic cord pH had a NICU admission rate of 20%, while none in the normal cord pH group required NICU admission. This yielded a relative risk of NICU admission of 3.00, although the difference was not statistically significant (p=0.472). Similarly, at 38 weeks gestation, NICU admission rates were comparable between acidotic and normal cord pH groups, with a relative risk of 1.25 and no significant difference in p-value (0.77). At 39 weeks gestation, no infants in either group required NICU admission. However, among infants born at 40 weeks gestation, those with acidotic cord pH had a significantly higher NICU admission rate of 55.6% compared to no admissions in the normal cord pH group, resulting in a relative risk of 9.9 (p=0.102) (Table 2).

Infants with APGAR scores of 6/1, 8/5, and 9/10 born with acidotic cord pH had a NICU admission rate of 25%, while those with normal cord pH had a rate of 6.3%, resulting in a relative risk of NICU admission of 4.00, although this difference was not statistically significant (p = 0.19). Similarly, for infants with APGAR scores of 7/1, 9/5, and 10/10, the NICU admission rates were 22.2% for acidotic cord pH and 7.7% for normal cord pH, with a relative risk of 2.88 and a non-significant p-value of 0.354. Furthermore, among infants with APGAR scores of 2/1, 7/5, and 8/10, those with acidotic cord pH had an 80% NICU admission rate compared to 100% for those with normal cord pH, resulting in a relative risk of NICU admission of 0.8, with a p-value of 0.318 (Table 2).

Among neonates weighing 2.1-2.5 kg, none in the acidotic cord pH group required NICU admission, while 12.5% in the normal cord pH group did, resulting in a non-significant relative risk of NICU admission of 3.0 (p = 0.37). For neonates weighing 2.6-3 kg, the NICU admission rate was notably higher in the acidotic cord pH group (22.8%) compared to the normal cord pH group, although the difference was not statistically significant, yielding a relative risk of NICU admission of 8.00 (p = 0.148). Similarly, among neonates weighing over 3 kg, the NICU admission rate was higher in the acidotic cord pH group (55.6%) compared to the normal cord pH group (28.6%), resulting in a relative risk of NICU admission (RR of 1.94, although this difference was not statistically significant (p = 0.319) (Table 2).

**Table 1. Association of Neonatal ICU admission and low cord blood pH (n=60)**

Study Group	NICU Admission (YES)	NICU Admission (NO)	P-Value	Relative Risk
Exposed Group (Acidotic cord pH)	10 (33.3%)	20 (66.7%)	0.0468	3.33
Unexposed Group (Normal cord pH)	3 (10%)	27 (90%)		

**Table 2. Association of Neonatal ICU Admission with Ages of Mother, Gestational Age, APGAR score, and Weight of Neonates (n=60)**

Effect modifiers/Cofounders	Study Group	NICU Admission (YES)	NICU Admission (NO)	P-Value	Relative Risk
Age Group	20-25 years	Exposed Group (Acidotic cord pH)	1 (33.3%)	2 (66.7%)	

		UnexposedGroup (Normal cord pH)	2 (18.2%)	9 (81.8%)	0.55	1.83
	26-30 years	Exposed Group (Acidotic cord pH)	9 (34.6%)	17 (65.4%)	0.078	5.88
		UnexposedGroup (Normal cord pH)	1 (5.9%)	16 (94.1%)		
	31-35 years	Exposed Group (Acidotic cord pH)	0 (0.0%)	1 (100%)	0.8	1.5
UnexposedGroup (Normal cord pH)		0 (0.0%)	2 (100%)			
<b>GestationalAge</b>	37 weeks	ExposedGroup (Acidotic cord pH)	1 (20%)	4 (80%)	0.472	3.00
		UnexposedGroup (Normal cord pH)	0 (0.0%)	5 (100%)		
	38 weeks	ExposedGroup (Acidotic cord pH)	4 (25%)	12 (75%)	0.77	1.25
		UnexposedGroup (Normal cord pH)	2 (20%)	8 (80%)		
	39 weeks	ExposedGroup (Acidotic cord pH)	0 (0.0%)	0 (0.0%)	0.429	2.66
		UnexposedGroup (Normal cord pH)	1 (14.3%)	6 (85.7%)		
	40 weeks	ExposedGroup (Acidotic cord pH)	5 (55.6%)	4 (44.4%)	0.102	9.9
		UnexposedGroup (Normal cord pH)	0 (0.0%)	8 (100%)		
<b>APGAR Score</b>	6/1,8/5,9/10	Exposed Group (Acidotic cord pH)	4 (25%)	12 (75%)	0.19	4.00
		UnexposedGroup (Normal cord pH)	1 (6.3%)	15 (93.8%)		
	7/1,9/5,10/10	Exposed Group (Acidotic cord pH)	2 (22.2%)	7 (77.8%)	0.354	2.88
		UnexposedGroup (Normal cord pH)	1 (7.7%)	12 (92.3%)		
	2/1,7/5,8/10	Exposed Group (Acidotic cord pH)	4 (80%)	1 (20%)	0.318	0.8
		UnexposedGroup (Normal cord pH)	1 (100%)	0 (0.0%)		
<b>Weight of neonates (kg)</b>	2.1-2.5kg	Exposed Group (Acidotic cord pH)	0 (0.0%)	0 (0.0%)	0.37	3.0
		UnexposedGroup (Normal cord pH)	1 (12.5%)	7 (87.5%)		
	2.6-3 kg	Exposed Group (Acidotic cord pH)	5 (22.8%)	16 (76.2%)	0.148	8.00
		UnexposedGroup (Normal cord pH)	0 (0.0%)	15 (100%)		
	>3 kg	Exposed Group (Acidotic cord pH)	5 (55.6%)	4 (44.4%)	0.319	1.94
		UnexposedGroup (Normal cord pH)	2 (28.6%)	5 (71.4%)		

## DISCUSSION

The present study was conducted to explore the relationship between NICU admission and the blood

pH level of the umbilical cord. According to the findings, among those exposed to acidotic cord pH, 10 infants (33.3%) required NICU admission, while among those with normal cord pH (unexposed group), 3 infants (10%) required NICU admission. Acute fetal distress induces asphyxia leading to hypoxia of most of the organs which causes an increase in lactic acid level, along with alteration in pH and HCO<sub>3</sub>. Most of the parameters used for fetal monitoring have good sensitivity but low specificity. Nowadays, umbilical cord vessel acid-base analysis is increasingly employed as an endpoint in the study of antepartum and intrapartum care. It is the most accurate method of quantifying the acid-base status of the fetus at the moment of delivery and is an important adjunct for determining the extent and cause of fetal acidosis at delivery. The cord acid base assessment provides an objective measure of neonatal conditions at delivery. The only scientific, objective means of diagnosis of fetal asphyxia at delivery is through umbilical blood acid-base studies. Umbilical cord blood sampling is regarded as the “gold standard” in the analysis of the biochemical state of the fetus. Umbilical cord blood acid-base analysis has emerged in recent years as a method of assessing the newborn objectively<sup>5</sup>.

A study conducted by Perveen et al (2015) has mentioned poor outcomes in patients with acidotic cord blood. Almost 90.2% required NICU admission as compared to 9.1% in the control group with normal cord blood. Metabolic acidosis in arterial cord blood is considered to be an essential criterion for the diagnosis of birth asphyxia and umbilical cord artery pH at birth provides a sensitive reflection of birth asphyxia with the absence of acidosis excluding the diagnosis. 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<sup>6</sup>.

Fetal acidemia is indicated by an umbilical artery pH <7.00 with a metabolic component. The metabolic component of fetal acidemia (i.e., base deficit and bicarbonate) is the most important variable in subsequent neonatal morbidity<sup>7</sup>. There is a progression of risk in term infants for Apgar less than 7 at 5 minutes, NICU admission, and need for assisted ventilation with worsening acidosis at birth, which begins with cord blood values close to mean values indicating a higher threshold for associated acidemia with these outcomes than is seen for more severe neonatal outcomes<sup>8</sup>. According to previous reports in the literature, the near-normal cord blood levels at which poor outcomes started to increase were about 7.20, suggesting a threshold for rising risk with outcomes<sup>8</sup>.

As acidemic neonates may be at risk for unfavorable outcomes after birth, all neonates with abnormal arterial blood analysis do not always have poor outcomes<sup>9</sup>. Although few studies have shown that even the majority of infants born with pH between 7.000 and 7.100 were asymptomatic and would not have needed immediate admission to the neonatal care unit a regular course without signs of hypoxic damages except in a case of isolated pathological values of cTnI<sup>10</sup>. As per the findings of Yeh et al (2012), the likelihood of negative neurological outcomes begins to increase below a pH of 7.10, it increases quickly below an arterial pH of 7.00. The authors found that 20–24% of unfavorable newborn outcomes occurred below a pH of 7.00, with an additional 10–15% happening below a pH of 7.11<sup>11</sup>.

The risk of severe acidemia is well documented. In a research conducted by Dijkhoorn et al, Indicators of severe asphyxia such as delayed beginning of spontaneous breathing and/or persistently low Apgar scores are associated with either newborn mortality or brain damage in the surviving child<sup>12</sup>. The consensus for ascribing cerebral palsy to intrapartum hypoxia states that the arterial pH must be <7.00. However, a pH of 7.00 in the umbilical artery is very much lower than would be expected following a scalp pH of <7.24, the level considered abnormal by NICE. Above 7.00, the relationship between cord pH and outcome is much less clear<sup>12</sup>.

There were a few limitations in this study. First, the investigators were unable to gather comprehensive data on the long-term outcomes of all neonates in this hospital population, especially those who belonged to the exposed group (Acidotic cord pH). This may have led to an underestimation of the overall prevalence of negative consequences, given the characteristics of a tertiary center where term neonates without NICU admission may not have long-term follow-up. Secondly, the impact of severe metabolic acidemia could not be adequately evaluated due to the short

sample size and the low number of infants with acidotic cord blood. However, to fully examine preterm births and long-term neonatal outcomes, the sample population must be expanded in further research.

## CONCLUSION

There is a strong association between Neonatal ICU admission and low cord blood pH. The majority of afflicted neonates have a higher pH, and while a modest degree of acidemia is linked to an elevated risk of unfavorable neonatal outcomes, the absolute risks are quite low. This suggested that the pH of samples taken from cord blood may be used to guide therapeutic therapy and is a crucial instrument in the defence of newborn morbidity and death.

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## Author's Contribution Statement

Substantial contributions to conception & design, or acquisition of data, and analysis & interpretation of data, drafting the article or revising it critically for important intellectual content, final approval of the version to be published has been made by SA and QA. P, RF and SMY did the drafting of the article and revise it carefully.

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