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Determining the Utility of pH Levels in Predicting Neonatal Outcomes in NICU

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Abstract: ***Background: admission of neonates to NICU has increased over time. The adequate management of neonates demands the serial monitoring of metabolic parameters like pH with arterial blood gas status. Objective: To determine the utility of pH levels in predicting neonatal outcomes. Study design: A prospective observational study. Materials and methods: A total of 121 newborns who were admitted to NICU, were studied during their period of stay. The study period lasted for 12 months, it was carried out after the obtaining an informed consent from parents of every newborn. The arterial blood sample was taken to assess the pH with ABL800 fully automated machine. The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0. A p value of <0.05 was considered statistically significant. Results: In this study, 92.56% got discharged and 7.44% study subjects expired . O2 / MV therapy/ CPAP were required in 83.47% cases. Mean duration of O2/ MV therapy/ CPAP was 2.68 ± 2.09 days. Total mean duration of hospital stay and NICU stay were 12.37 ± 7.02 and 10.87 ± 6.63 days, respectively. For prediction of mortality, pH was a significant predictor at 12, 24 and 48 hours. For the requirement of O2 /MV/CPAP/HFNC, pH was a significant predictor only at 24hours. There was a significant positive correlation of pH at 12 hours (r=0.205, p=0.0241) with hospital stay. Conclusion: It can be concluded that serial estimation of pH may help in determining the outcome of the NICU admitted neonates and their outcomes.***

Keywords: pH, Neonate, Mortality, Arterial Blood Gas(ABG),Respiratory support, Hospital stay

1. Introduction

Blood gas analysis, which allows assessment of patient's acid-base status, involves measurement of the pH and partial pressure of oxygen (pO2) and carbon dioxide (pCO2) in arterial blood. These measurements allow calculation of further parameters that are generated during blood gas analysis, including concentration of plasma bicarbonate [HCO^-] and base excess (BE), and lactate. pH is understood as a number expressing the acidity or alkalinity of a solution on a logarithmic scale on which 7 is neutral, lower values are more acidic and higher values more alkaline. The pH is equal to $-\log_{10} c$, where c is the Hydrogen ion concentration in moles per litre.

Acid–base disorders reflect the seriousness of the underlying disease and also are indicators for morbidity and mortality in sick children.[1] Marked structural and functional differences occur in children in comparison to adults, i.e., children have narrow distal airways, so atelectasis develops quickly resulting in rapid-onset of hypercarbia and hypoxia; chest wall is compliant and respiration is less efficient; the respiratory centre is immature, hypoxia and hypercarbia lead to decreased respiratory drive. In addition, they have reactive vascular beds to maintain their blood pressure until late, so one cannot rely on hypotension to diagnose shock in children as in adults.[2]

Research Question

- To determine the utility of pH levels in first 48 hrs. and their association with neonatal mortality, requirement of respiratory support and hospital stay of the neonate.
- Which will be helpful predict the outcome of newborns especially in developing countries with minimal resources.

[3]

2. Review of Literature

- **Rodríguez-Balderrama I et al[3]** carried out the study in 2016 with an objective to determine the relationship between lactic acid levels and neonatal mortality in the first week of life, in patients admitted to the Neonatal Intensive Care Unit (NICU) of the ''Dr. José E. González'' University Hospital.
- Prospective, observational and diagnostic test performed in the neonatal ward. Study included all live preterm infants on mechanical ventilation who were admitted to the NICU from November 1, 2011 to October 31, 2012. One hundred and fifty-four patients met the inclusion criteria.
- It was found that the pH <7.25 had a sensitivity of 36% and specificity of 91%. So, they concluded that when the pH is greater than 7.25 there is a specificity (to be alive) of 96% on the third day and 91% on the seventh day. 67% of the dead were under 1500 g, and were 61% under 28 gestational weeks
- **Lekhwani S. et al[4]** in 2010 studied acid–base imbalance

neonates. It was observational study was conducted in an emergency room of a tertiary teaching care hospital in Haryana, India. Fifty neonates (from first hour to one month) attending pediatric emergency services with various ailments. Blood gas analysis, electrolytes, plasma lactate, and plasma albumin were estimated in neonates. Metabolic acidosis was the most common acid–base disorder. Birth asphyxia was another common disorder with the highest mortality in neonates followed by bronchopneumonia and sepsis. Significant correlation between mortality and critical values of ph was observed. Plasma lactate concentration measurement provides an invaluable tool to assess type of metabolic acidosis in addition to predicting mortality in these neonates.

- Significant correlation was found between outcome and critical values of pH ($P < 0.01$), pCO2 ($P< 0.05$) Of 50 neonates, 16 neonates died during their hospital stay. Raised blood lactate (>5 mmol/L) and lowest pH (<7.2) were associated with increase in patient mortality Metabolic acidosis (BE ≤ –5mmol/L) was found in 34 patients. Hyperlactatemia was found in 97% and lactic acidosis was present in 35% of those suffering from metabolic acidosis.
- **Ahmed et al**[5] in 2015 carried out observational study was conducted on the samples provided from the neonates with birth asphyxia and sepsis admitted to neonatal intensive care unit (NICU) in the Post Graduate Institute of Medical Education and Research (PGIMER) and Dr Ram ManoharLohia (Dr RML) Hospital, New Delhi, India.
- The blood gas analysis, electrolytes, albumin, lactate levels were compared in the two ailments. The presence of acid base disorders was calculated and the influence of various variables on acid base disorders and outcome were analyzed.
- The metabolic acidosis and alkalosis were seen in 1 and 10 patients as per Boston approach and in 18 and 18 patients with Copenhagen approach. The increased anion gap (AG), and low and high strong ion difference (SID) as measured by Stewart approach were seen in 23,21 and 23 neonates respectively. The acid-base status determined by both Copenhagen and Stewart approach were found to be interrelated.
- For detecting metabolic acidosis, the sensitivity of high for high anion gap (66.67%) and hyponatremia (57.89%), whereas the specificity is high for lactic acidosis (94.74 %), hyperchloraemia (86.99%) and hyponatremia (81.08%). The low PaCO2 (89.4%) and low SID (73.68%) has a high sensitivity for predicting the non-survival
- whereas the lactic acidosis (94.74%) has the high specificity of predicting the non-survival, followed by hyponatremia (81.08%),
- Hence, it was concluded that in neonates with birth asphyxia and sepsis, determining the acid-base status is of vital significance, but in complicated situation strong ion difference and strong ion gap works better in determining acid-base status.

3. Materials and Methods

- **Place of Study:** KVG Medical College Hospital. Sullia
- **Duration of Study:** 12 months
- **Study Population:** The study included all the newborns admitted to NICU in KVG Medical College Hospital over the period of 12 months.

Inclusion Criteria

- All newborns admitted to NICU during the study period

Exclusion Criteria

- Neonates with congenital malformation, and chromosomal abnormalities.
- Neonates with Surgical emergencies.
- Newborn getting discharged prior to 48 hrs from the NICU.

Sample Size and Sampling Technique

- Required sample size was 119.
- Type of Study: Prospective Observational study;
- Methodology: Data collection
- Newborns who were admitted to the NICU were included in the study after obtaining an informed consent from parents of every newborn. They were explained about the study via patient information sheet and data pertaining to Arterial Blood gas analysis and demography were recorded by the study proforma.

Statistical Analysis

- All the data collected was entered in microsoft excel file and further analysed using spss software version 21
- The variables were summarised as percentages, frequencies, mean standerd deviation.

4. Results and Observations

- The prospective observational study was conducted at KVG Medical College Hospital Sullia. The study included all the newborns admitted to NICU. After taking informed consent from parents
- 121 newborns were included in study. Blood sample was collected at 0, 12, 24 and 48 hours. Data pertaining to the pH levels was compared to different outcomes i.e., need for respiratory support, mortality and hospital stay. Following were the results pertaining to the study

Table 1: Distribution of Neonatal complications

Respiratory problems	Frequency	Percentage
Birth asphyxia	22	18.18%
Breathing difficulty at birth	95	78.51%
CPAP	13	10.74%
HFNC	9	7.44%
Mechanical ventilation	54	44.63%
O2	25	20.66%
Surfactant	41	33.88%
Apnea	23	19.01%
Apnea treatment (Caffeine)	22	18.18%
MAS	4	3.31%
PPHN	12	9.92%
Sepsis	23	19.01%

NNJ	67	55.37%
Phototherapy	69	57.02%
E.T	1	0.83%
Hypoglycaemia	11	9.09%
Hypothermia	1	0.83%
Feed Intolerance	16	13.22%
TPN	26	21.49%

Table 2: pH levels at different time intervals

pH	Mean ± Stdev	Median(IQR)	Range
At 0 hour	7.31 ± 0.11	7.31(7.245-7.365)	7.06-7.64
At 12 hours	7.37 ± 0.09	7.38(7.32-7.42)	6.96-7.51
At 24 hours	7.37 ± 0.15	7.4(7.34-7.44)	6.09-7.64
At 48 hours	7.39 ± 0.14	7.41(7.365-7.45)	6.38-7.84

Table 3: Distribution of outcomes

Outcome	Frequency	Percentage
Outcome		
Discharged	112	92.56%
Expired	9	7.44%
Respiratory support requirements		
Yes	101	83.47%
No	20	16.53%
Number of days of respiratory support		
Mean ± Stdev	2.68 ± 2.09	
Median(IQR)	3(2-3)	
Range	0-15	
Total days of hospital stay		
Mean ± Stdev	12.37 ± 7.02	
Median(IQR)	10(7-15)	
Range	2-45	
Number of days of ICU stay		
Mean ± Stdev	10.87 ± 6.63	
Median(IQR)	10(6.5-15)	
Range	2-45	

Table 4: Association of pH with Respiratory support requirement

pH	No (n=20)	Yes (n=101)	Total	P value	Test performed
At 0 hour					
Mean ± Stdev	7.32 ± 0.1	7.31 ± 0.11	7.31 ± 0.11	0.59	Mann Whitney test;933
Median (IQR)	7.32 (7.282-7.378)	7.31(7.25-7.36)	7.31(7.25-7.36)		
Range	7.17-7.54	7.06-7.64	7.06-7.64		
At 12 hours					
Mean ± St dev	7.38 ± 0.05	7.36 ± 0.09	7.37 ± 0.09	0.806	Mann Whitney test;975
Median(IQR)	7.38 (7.328-7.412)	7.37(7.32-7.42)	7.38(7.32-7.42)		
Range	7.24-7.46	6.96-7.51	6.96-7.51		
At 24 hours					
Mean ± St dev	7.42 ± 0.04	7.36 ± 0.16	7.37 ± 0.15	0.005	Mann Whitney test;616.5
Median (IQR)	7.43 (7.4-7.45)	7.39(7.32-7.43)	7.4(7.34-7.44)		
Range	7.33-7.5	6.09-7.64	6.09-7.64		
At 48 hours					
Mean ± St dev	7.42 ± 0.07	7.38 ± 0.15	7.39 ± 0.14	0.11	Mann Whitney test;782
Median(IQR)	7.42(7.41-7.45)	7.4(7.36-7.44)	7.41(7.37-7.45)		
Range	7.3-7.56	6.38-7.84	6.38-7.84		

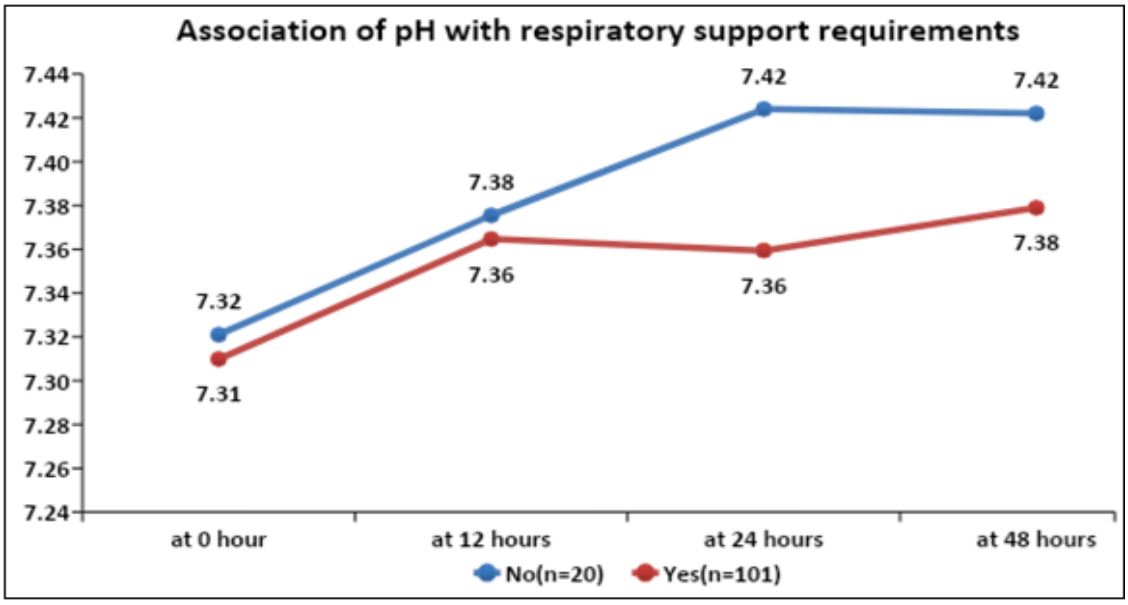

Figure 1: Association of pH with respiratory support requirements.

Table 5: Association of pH with mortality

pH	Discharged (n=112)	Expired (n=9)	Total	P value	Test performed
At 0 hour					
Mean ± Stdev	7.31 ± 0.1	7.29 ± 0.17	7.31 ± 0.11	0.566	Mann Whitney test;446
Median(IQR)	7.31(7.248-7.375)	7.3 (7.26-7.33)	7.31 (7.25-7.36)		
Range	7.09-7.57	7.06-7.64	7.06-7.64		
At 12 hours					
Mean ± Stdev	7.38 ± 0.07	7.24 ± 0.15	7.37 ± 0.09	0.001	Mann Whitney test;184
Median(IQR)	7.38(7.33-7.43)	7.25 (7.2-7.33)	7.38 (7.32-7.42)		
Range	7.2-7.51	6.96-7.39	6.96-7.51		
At 24 hours					
Mean ± Stdev	7.39 ± 0.08	7.11 ± 0.41	7.37 ± 0.15	0.002	Mann Whitney test;192
Median(IQR)	7.4(7.35-7.44)	7.27 (7.02-7.32)	7.4 (7.34-7.44)		
Range	7.18-7.64	6.09-7.45	6.09-7.64		
At 48 hours					
Mean ± Stdev	7.41 ± 0.08	7.11 ± 0.34	7.39 ± 0.14	0.008	Mann Whitney test;238.5
Median(IQR)	7.42 (7.38-7.45)	7.14 (6.96-7.41)	7.41 (7.37-7.45)		
Range	7.13-7.84	6.38-7.45	6.38-7.84		

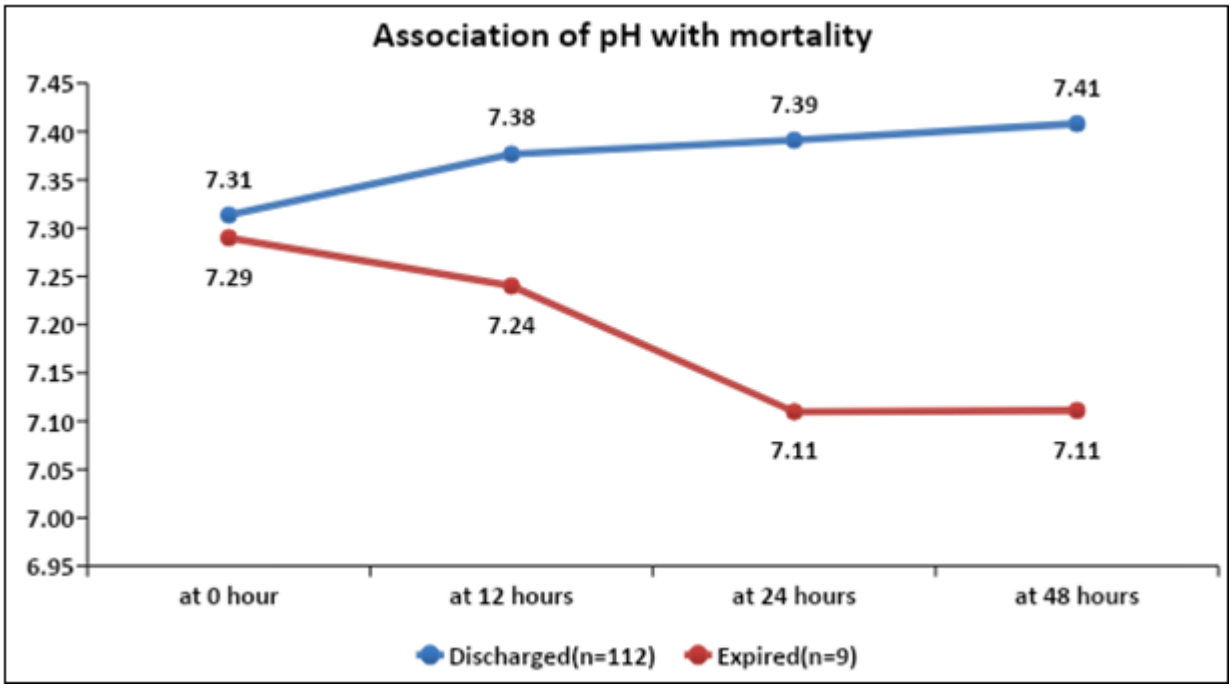

Figure 2: Association of pH with mortality

Table 6: Correlation of pH at different time intervals with Hospital stay

Correlation with hospital stay		pH
At 0 hour	Correlation Coefficient	-0.071
	P value	0.4371
At 12 hours	Correlation Coefficient	0.205
	P value	0.0241
At 24 hours	Correlation Coefficient	0.056
	P value	0.5383
At 48 hours	Correlation Coefficient	0.113
	P value	0.2181

5. Discussion

- Admission of neonates to NICU has increased over time. In our study on 121 neonates who were admitted to the NICU, with various conditions like Birth asphyxia MAS, PPHN, Sepsis, and NNJ, Hypoglycemia, Hypothermia, and feed Intolerance; were analysed in the study. The adequate management of the neonates demanded the serial monitoring of the acid base status. The reason being that the basic acid-base disturbances are the expression of serious mechanisms involved in an increased mortality and morbidity of the NICU patients (6-9)
- pH subserves to determine the acid-base disturbances. We conducted this prospective observational study at KVG Medical college hospital, sullia to determine the serial estimation of Ph at 0, 12, 24 and 48 hours among the NICU neonates and to find its association with different outcomes i.e., need for ventilation, mortality and hospital stay.
- The outcomes determined in our study included the use of respiratory support, hospital stay and mortality. In our study, 7.44% study subjects expired and 92.56% got

discharged. respiratory support was required in 83.47% cases. Mean duration of respiratory support was 2.68 ± 2.09 days. Total mean duration of hospital stay and ICU stay were 12.37 ± 7.02 and 10.87 ± 6.63 days, respectively

- Among the outcome variables, the usage of respiratory support in the form of O2/MV/CPAP/HFNC was seen in 101 out of 121 neonates in the index study.
- The causes for NICU admission among the various studies may be diverse. In our study on 121 newborns who were admitted to NICU, majority of the neonates (43.80%) had respiratory distress syndrome, followed by HIE in 14.05% cases, Septicaemia in 9.92% cases, and NEC in 5.79% cases. BPD, GERD, and HDN were present in 0.83%, 0.83%, and 1.65% cases, respectively.
- Hypernatremia and hypoglycaemia were present in 1 patient (0.83%) each, 43(35.54%) of the neonates were preterm. There was one infant of GDM mother. Laryngomalacia, LV dysfunction, LBW, and subdural hematoma were present in 1 case each. NNJ, RAD, meconium aspiration syndrome, neonatal seizures, and TTNB were present in 4.96%, 4.96%, 3.31%, 2.48%, and 1.65% cases, respectively
- In our study among 121 NICU neonates, Mechanical ventilation and O2 were required in 54(44.63%) and 25(20.66%), respectively and CPAP and HFNC was used in 13(10.74%) and 9(7.44%) patients, respectively.
- The standard treatment for neonatal respiratory distress due to various causes demands respiratory support and the treatment for the underlying disease. At our institute, the management of respiratory distress among the neonates follows a trend of use of respiratory support which is based on case scenario as per protocol. Considering the small fractions of individual respiratory support therapy, we clubbed all the four respiratory support measures (O2 /MV /CPAP /HFNC)as a group, to determine the association of pH levels with the respiratory support as an outcome in the study.

6. Conclusion

- We found that pH of (7.37±0.09, 7.36±0.15, 7.39± 0.14), respectively were a significant predictor of mortality at 12, 24 and 48 hours but not at 0 hours
- For the requirement of respiratory support, pH was a significant predictor only at 24 hours
- There was a significant positive correlation of pH at 12 hours (r=0.205, p=0.0241) with hospital stay.
- Thus, it can be concluded that pH plays a significant role as a predictor of neonatal outcomes among those admitted to NICU.

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