# Value of brain tissue oxygen saturation in neonatal respiratory distress syndrome: a clinical study

Keping Cheng, Huijie Zhu, Zikai Zhou, Weiyuan Chen, Aijuan Yang

*Department of Neonatology, Yongkang Maternal and Child Health Hospital, Yongkang, Zhejiang, China.*



***Abstract***

Neonatal respiratory distress syndrome (NRDS) is one of the major causes of pre-term mortality and morbidity among very-low-birth-weight infants (VLBWI) in low- and middle-income countries (LMIC). Some of the neonates pass away despite admission and care in intensive care units (ICUs). The present clinical trial seeks the application value of elevating oxygen saturation in the brain cells of pre-term neonates born with NRDS. Near-infrared spectroscopy (NIRS) was used to monitor the neonates' microscopic cerebral oxygenation levels do determine hemoglobin concentration in brain tissues, whereas the pulse oximetry was used to measure oxygenation levels among the patients. In statistical analyses, the Analysis of Variance (ANOVA), and descriptive statistics was deployed in the Jupyter Notebook environment using Python language. High saturation of oxygen in the brain tissues result in important biological and physiological processes, including enhanced oxygen supply to cells, reduced severity of NRDS, and balancing oxygen demand and supply. The correlations of oxygen saturation with systemic saturation of oxygen, the saturation of oxygen in brain tissues, the association between brain-specific and systemic saturation, and the impact of these outcomes on clinical practices were deliberated. Also, the pH gas values, the saturation of oxygen in neonates' brain tissues, metabolic acidosis, the effect of acid-base balance and cerebral oxygen supply, and the oxygenation of brain tissues and the pH values emerged as important variables of oxygenation of brain tissues in pre-term neonates. Oxygen saturation in brain cells influence vital physiological and biological processes. Balancing acid-base saturation or levels is needed despite the challenging achievement. Oxygenation of brain tissues improve the brain's overall functioning.

**Key Words**: neonatal; oxygen saturation; neonatal respiratory distress syndrome; very-low-birth-weight infants.

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Neonatal respiratory distress syndrome (NRDS) refers to a common condition among preterm neonates characterized by rapid, sharp, but shallow breathing due to insufficient surfactant production or inactivation.[1,2] NRDS's propensity among neonates, and sometimes among infants, results from lung immaturity.[1,2] A strong association between NRDS and prematurity has been established. The global preterm births are estimated to be about 15, 000, 000, with an approximated neonatal death of 1, 000, 000 per year among infants with >37 gestational weeks.[3] Even though NRDS' risk is high, its fatality and severity vary throughout the gestational period. The 32nd gestational week poses the most significant risk as about 47% of NRDS-related deaths are reported within this period.[4] Despite causing a majority of deaths among infants with <37 gestational weeks, NRDS is known to be a significant contributor to neonatal morbidity and mortality in LMIC. The main indicators of the disease include cyanosis, apnea, grunting, inspiratory stridor, tachypnea > 60 breaths per minute, poor feeding and nasal flaring.[5] In the last 3 decades, a significant reduction in neonatal mortality, within the first 28 days of life, has been reported due to advanced neonatal management, including optimized resuscitation in the delivery room, availability of surfactant and caffeine, alongside the modern techniques of surfactant administration. By 2030, NRDS-related mortality rate is expected to be about 12 per 1, 000 live births.[4] The decreasing mortality and morbidity results from evidence-based interventions like peripartum management, admission of neonates in ICUs, and the management of delivery processes.

One of the previous studies reported the association of brain tissue saturation and ischemia, hypoxia, neurological disorder and cognitive functions among infants with NRDS. Lack of sufficient oxygen in brain tissues results in hypoxia and ischemia, impairing neurological functioning by altering metabolic processes.[6] The benefits of enhancing oxygen saturation in the brain tissues is far reaching and impacts future life of children with NRDS. Increasing oxygen saturation in the brain tissues improves cognitive functions, including attention, memory, alongside problem-resolution.[7]

The present study delves in the implementation of value of brain tissue saturation, focusing on how oxygen saturation in brain tissues benefits neonates with NRDS. The rationale of the present study focuses on the value of improving oxygen saturation in the brain cells of neonates with NRDS, and the need to improve the survival of VLBWI. The outcomes of the present study are a price of oxygenation of brain cells, as an intervention to low oxygen levels among neonates with low oxygen saturation in brain cells.

In this context, this clinical study investigeted three objectives:

i) The dynamics of brain oxygenation, focusing on the level of oxygen saturation in brain tissue to establish NRDS' severity and the oxygenation of brain tissues. As a result, oxygen-demand balance needed to facilitate physiological processes, like neurological functioning, will be established.
ii) The relationship between systemic oxygen saturation and the saturation of oxygen in brain tissues. The outcomes will inform the alignment between systemic oxygen saturation and brain-specific saturation, impacting clinical practices.
iii) pH gas values, with reference to oxygenation of brain cells. This relationship will answers as to whether pH deviations are associated with alterations in brain oxygenation.

The above-stated objectives were examined to answer the following questions:

i) What is the effect of oxygen saturation in brain tissues on the severity of respiratory distress syndrome on physiological processes, and oxygen-demand balance?
ii) What is the relationship between systemic oxygen saturation and the levels of oxygen in brain tissues?
iii) How does it affect brain-specific oxygen saturation?
iv) What is the association between oxygen saturation and pH values in neonates and how does it affect metabolic acidosis?
v) Does it affect cerebral-oxygen supply and acid-base balance?

## Materials and Methods

### *Study Design*

We performed a randomized control study in the neonatology and pediatric department at the Department of Neonatology, Yongkang Maternal and Child Health Hospital, Yongkang, Zhejiang, China. The study focused on pre-term VLBWI born between January 2022 to august 2023. The study contrasted the value of oxygen saturation in brain cells of neonates with a control group. The first assessment was done after 72 hours, after which follow-up was performed after another 4 days and 5 days. First, we monitored the pH gas values within the first 72 hours, 96 hours and 120 hours of the neonates in the study group and contrasted with those in the control group. Also, the NIRS was used to monitor the neonate's oxygenation levels to determine fluctuations of hemoglobin concentration in brain tissues. Secondly, we examined oxygen-demand balance to decipher NRDS' severity and the level of oxygen saturation. The study contrasted the experimental and the control group to inform the overall effect on the neonates' physiological processes. Lastly, we comparatively examined brain tissue oxygen saturation to determine its impacts on clinical practices. This correlation informed brain-specific oxygen saturation and systemic oxygen saturation.

### *Participants*

All procedures performed in this study involving human participants were in accordance with the ethical standards and approved by the Ethics Committee of the Yongkang Maternal and Child Health Hospital (Ethical Code Number:20220207a028) and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written informed consent to participate in this study have been signed by parents or guardians of the neonates. Neonates were randomly selected and include in the present study for a maximum of 5 days. We carried out a clinical study involving premature neonates with respiratory distress syndrome born between January 2022 to august 2023. At first, we included a total of 148 neonates, and later reduced the number based on the eligibility criteria described below. Premature neonates who did not display vital signs of saturation of oxygen in the brain within the first 72 hours were subjected to a follow-up within the following 96 hours. Neonates presenting the implications of oxygen saturation in the brain cells were scrutinized to check for possible reasons to justify their elimination from the study.

### *Eligibility Criteria*

Our study adopted a unique eligibility criterion for the inclusion of premature neonates in the study. The inclusion criteria were as follows:

***Inclusion Criteria***

- Pre-term or premature VLBWI, weighing <1.500 grams.
- Neonates born with less than 32 weeks of gestation.
- Neonates with pH acid-base ranging between 7.35 to 7.45 after oxygen saturation intervention.
- Neonates whose parents or guardians did not issue consent to participantion in the study.
- Neonates born between January 2022 to August 2023.

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***Table 1.*** *Features of the premature very-low-birth-weight infants included in the study.*

| Variables | Average |
|---|---|
| Percentage of brain oxygen saturation (BOS) | 71.15 |
| Gestational period in weeks | 23 |
| pH acid-base balance | 7.25 |

### *Exclusion Criteria*

Neonates would be excluded from the study under the following conditions:

- Neonates with > 32 gestational weeks.
- Neonates with pH acid-base range below the threshold set by the above-stated inclusion criteria.
- Neonates that died of low oxygen supply

### *Statistical Analysis*

Two statistical approaches were used in this trial: the ANOVA tests and the descriptive statistics. These methods were used independently to measure different outcomes pertinent to the collected data.

The ANOVA statistical tool was used to determine statistically significant differences in the mean results or outcomes across the different time intervals in this trial. The tool provided an overall investigation of the value of brain tissue oxygen saturation, whereas the pairwise comparison approach enabled the comparison of different variables. The F-statistic and its related p-value were presented, where a significant p-value indicated outcome differences in two groups or across the comparison groups. The p-value for statistical significance was set at a threshold of ($p \leq 0.05$). Post-hoc analysis indicated the particular differences of the time intervals compared.

Python programing language, using the Jupyter Notebook environment, was used to perform the statistical analyses, and some of the data visualization, including line and bar graphs. In addition to this, raw data collected from the study group was entered into an excel sheet. Two-line graphs were generated using the data entered into the excel sheet.

## Results

We analyzed a total of 98 VLBWI, and contrasted the outcomes against 50 healthy neonates born with January 2022 to august 2023. We focused on the outcomes presented by the 98 neonates for further analysis. The clinical and demographic features of the eligible neonates are tabulated below (Table 1).

The average gestational period of the 98 neonates selected for the study was 23 weeks, which was relatively less than the 28-week threshold. The average BOS was 71.15%, whereas the pH acid-base balance was 7.25 among the VLBWI studied. The level of hemoglobin and the oxygen saturation levels were assessed independently. The NIRS was used to measure the levels of hemoglobin levels among the 98 neonates. The average and mean values of the scores of hemoglobin levels were generated. Equally, pulse oximetry was used to assess the oxygenation concentration among the neonates. The Figure 1 below summarizes the average hemoglobin levels and the oxygen saturation levels at birth (0 hours), 72 hours, 96 hours and 120 hours to represent the application value of brain tissue oxygen saturation among the neonates (Table 2).

While Table 1 shows a trend in hemoglobin levels and tissue oxygen saturation ($STO_2$) levels, the trends in hemoglobin levels and oxygen concentration were assessed independently. To begin with, the mean and average of hemoglobin levels at the time of pre-term birth was 15.04 and 15.02, respectively. At the 72$^{nd}$ hour, the average and mean of the hemoglobin levels increased to 15.94 and 15.95, respectively (Figure 1). The mean and the average levels increased at the 96$^{th}$ and 120$^{th}$ hour, suggesting a consistent increase in hemoglobin levels with the brain tissue oxygen saturation intervention. However, the difference in the mean was relatively small across the time intervals. Similarly, the difference in averages of hemoglobin levels were small across the time intervals. The Figure 2 below shows a consistent increase in the mean and average levels of hemoglobin among the neonates.

At the beginning of the assessment (0 hours), the average and mean oxygen saturation in the brain tissues was 62.68 and 62.67, respectively. The mean and average oxygen saturation would increase among the neonates after 72 hours, 96 hours and 120 hours (Figure 2). Although the increase in oxygen saturation was constant

***Table 2.*** *Hemoglobin levels and oxygen saturation levels.*

| | Hemoglobin levels | | | | $STO_2$ | | | |
|---|---|---|---|---|---|---|---|---|
| Time in hours | 0 | 72 | 96 | 120 | 0 | 72 | 96 | 120 |
| Average | 15.02 | 15.94 | 16.02 | 16.94 | 62.68 | 66.06 | 68.13 | 71.15 |
| Mean | 15.04 | 15.95 | 16 | 16.95 | 62.72 | 66.1 | 68.3 | 70.94 |

*$STO_2$ - oxygen tissue saturation*

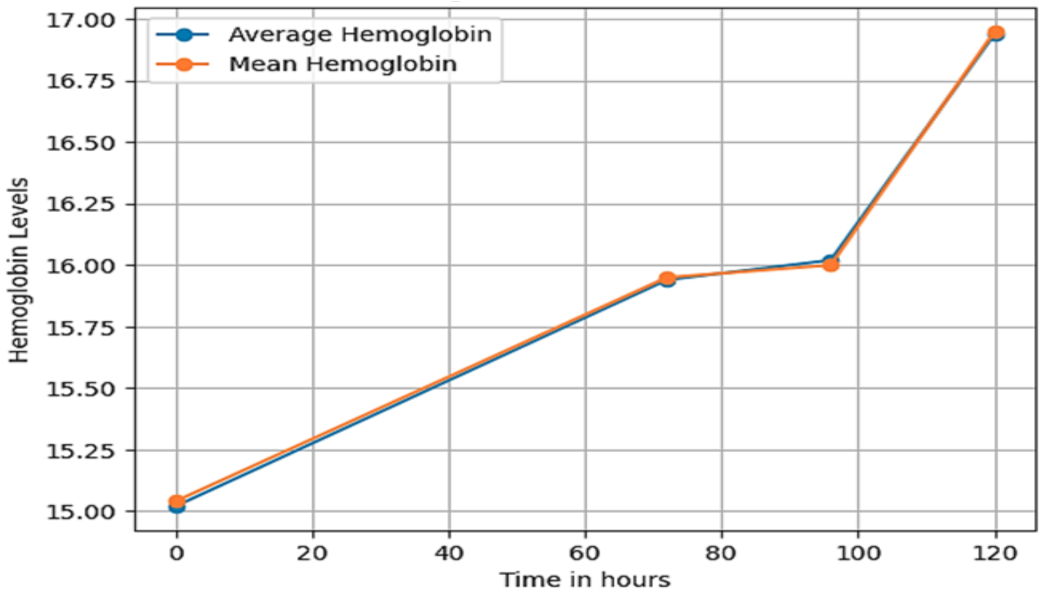


***Fig 1.*** *Trend of hemoglobin levels.*

throughout the study, the difference or magnitude of the increase was relatively small.

We collected data to represent the percentage of Blood Oxygen Saturation among the pre-term neonates at birth (0 hours), 72 hours, 96 hours and 120 hours. A preliminary analysis of the data indicates that BOS started at 60% thereabout in most cases. The percentage of oxygen saturation increases with the time interval, suggesting that the value of oxygen saturation in the brain cells yielded positive results regarding oxygen concentration. After 72 hours, notable increase in BOS percentages were observed, most of which exceeded 80%. The BOS percentages were in the 90s after 96 hours, and after 120 hours, the highest percentage of BOS was reported, in the range of 90% to 99%. A line graph was drawn to represent the trend in the increase in BOS percentages over time intervals of the study (Figure 3).

The descriptive statistics summarized BOS percentages among the VLBW pre-term neonates at the different intervals. summarily, the statistics indicated the distribution of BOS at every time interval, with the mean BOS percentages progressively increasing with the

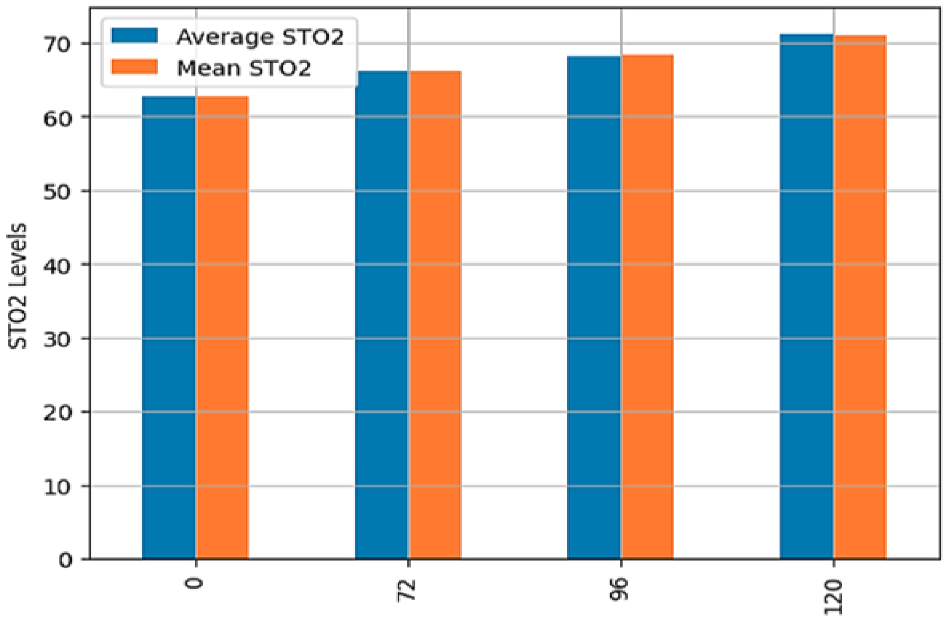


***Fig 2.*** *Trend of hemoglobin levels. $STO_2$ - oxygen tissue saturation*

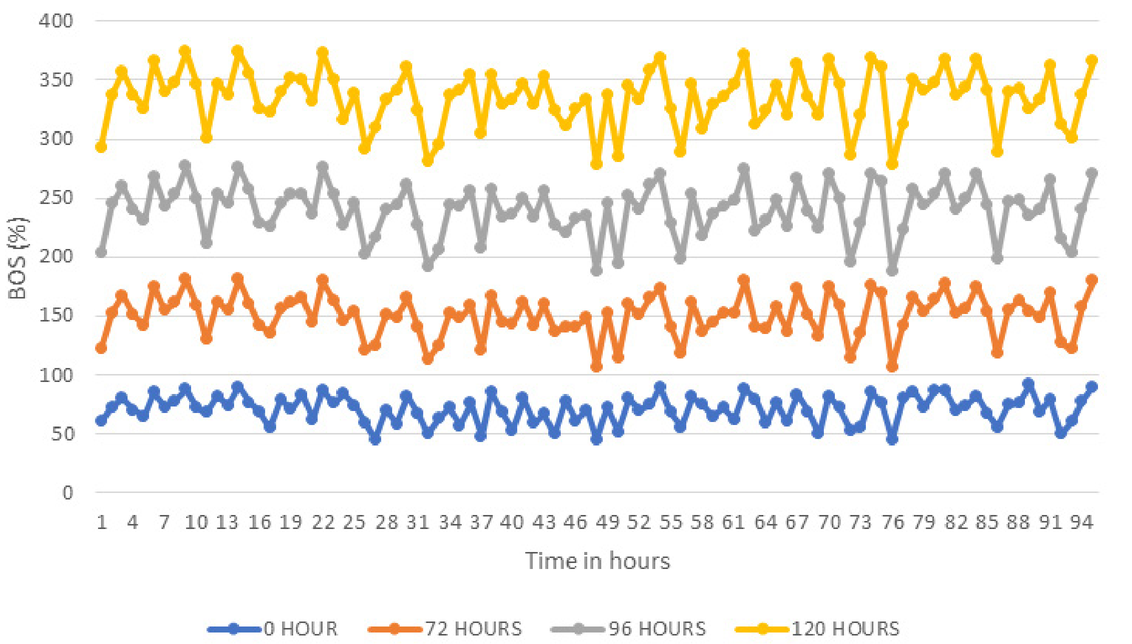


***Fig 3.*** *A line graph of brain oxygen saturation over time. BOS – obrain oxygen saturation*

increase in time or at every time interval. The mean increased from 70.78% at birth or 0 hours to 94.95% at 120$^{th}$ hour. On the other hand, the standard deviation showed a gradual decrease across the time interval. Notably, these outcomes emphasize the dynamics of BOS percentages, reflecting the dynamics of brain oxygenation among pre-term neonates with low birth weights. The descriptive statistics are summarized in Table 3.

Additionally, ANOVA repeated measures test results on saturation of oxygen in blood revealed BOS at the different intervals. The outcomes showed that time significantly impacts on BOS percentages as there was a significant variation in BOS percentages at 0 hours, 72 hours, 96 hours, and 120 hours. Statistically, the effect of time on the percentage of brain oxygen saturation was (F-statistic = 3, 282) = 158.86, $p < 0.001$.

A post-hoc pairwise t-test explored and reported the differences in BOS according to the time intervals. Table 4 presents the outcomes of the post-hoc analysis that suggest that BOS percentage increased with time. The pairwise t-test suggests a significant difference in the percentages of brain oxygen saturation at all the time intervals, with a standard $p<0.001$ across the 6 comparison which emphasized statistical significance. Notably, the highest difference in BOS percentage in this comparison was observed at 0 hours, and the following time intervals of 72 hours, 96 hours, 120 hours.

We documented the dynamics of oxygenation of brain tissues, where a high incidence of oxygen saturation levels of 90% emerged and indicated a positive trend. This outcome suggested a steady supply of sufficient oxygen to the pre-term neonates. On the other hand, the low incidence of severity NRDS among the pre-term neonates (10%) indicated better outcomes as the respiratory distress syndrome decreased (Table 5).

As for the correlations of oxygen saturation, our assessment established a high level of oxygen saturation (95%), with a relatively high level of oxygen saturation in brain tissues (91%). These outcomes indicated the

***Table 3.*** *Descriptive statistics of brain oxygen saturation outcomes.*

| Time interval | Count | Mean | Standard deviation | Minimum | 25$^{th}$ percentile | Median | 75$^{th}$ percentile | Maximum |
|---|---|---|---|---|---|---|---|---|
| 0 hours | 95 | 70.78 | 12.03 | 45.00 | 61.50 | 80.00 | 80.00 | 92.00 |
| 72 hours | 95 | 79.47 | 9.82 | 62.00 | 77.00 | 87.00 | 87.00 | 93.00 |
| 96 hours | 95 | 89.51 | 5.01 | 79.00 | 87.00 | 92.50 | 92.50 | 97.00 |
| 120 hours | 95 | 94.94 | 2.96 | 89.00 | 93.00 | 97.00 | 97.00 | 99.00 |

***Table 4.*** *A pairwise comparison of BOS percentages at different time intervals.*

| Comparison | t-statistic | p-value |
|---|---|---|
| 0 hours vs. 72 hours | -6.77 | $1.08^{-09}$ |
| 0 hours vs. 96 hours | -16.08 | $1.00^{-28}$ |
| 0 hours vs. 120 hours | -20.38 | $2.93^{36}$ |
| 72 hours vs. 96 hours | -16.99 | $2.03^{30}$ |
| 72 hours vs. 120 hours | -19.51 | $8.00^{-35}$ |
| 96 hours vs. 120 hours | -14.56 | $8.07^{-26}$ |

alignment between brain-specific oxygen saturation and systemic saturation. This association was supported by a high percentage of incidence (99%), underscoring and emphasizing that systemic oxygenation influences the oxygenation of brain tissues.
The pH gas values of 7.35, alongside the oxygenation of neonatal brain tissues (with an incidence rate of 88%), represented a balanced acid-base status. This outcome indicates stable pH levels and oxygenation of brain tissues, suggesting a conducive environment for physiological processes. This outcome extends to metabolic acidosis where a moderate incidence of 50% was established. Notably, this percentage suggests the need to monitor the neonates and an intervention as the probability of altered acid-base balance prominently arose. By extension, acid-base balance effected cerebral oxygen supply, where we found an incidence rate of 50%. Further, we examined the distribution of pH values across the intervals. we summarized the distribution of the pH values to represent the acid-base balance among the pre-term neonates (Table 6). The descriptive analytic approach reveals a gradual increase in the pH values from 0 hours (pH = 7.25) to the 120$^{th}$ hour (pH = 7.33), and this observation cut across the 96 observations. A notable upward trend in pH values is evident, and this suggests potential effects on the pre-term neonatal improvement. The analysis processed the central tendencies, the distribution of pH values for the different time intervals and the variability. A slight increase in the standard deviations of the pH values was observed from 0 hours

***Table 5.*** *The variables of the oxygenation of brain tissues.*

| Variable | Incidence (%) |
|---|---|
| The dynamics of oxygenation of brain tissues | |
| Oxygenation saturation levels | 90 |
| NRDS’ severity | 10 |
| Oxygen-demand balance | 55 |
| Neurological functioning | 70 |
| Correlations of oxygen saturation | |
| Systemic saturation of oxygen | 95 |
| Saturation of oxygen in brain tissues | 91 |
| The association between brain-specific saturation and systemic saturation | 99 |
| Impact on clinical practices | 100 |
| pH gas values (oxygenation of brain tissues) | |
| pH gas values | 7.35 |
| Saturation of oxygen in neonatal brain tissues | 88 |
| The association between oxygenation of brain tissues and pH values | 89 |
| Metabolic acidosis | 50 |
| Effects on acid-base balance and cerebral oxygen supply | 50 |

***Table 6.*** *A summary of the descriptive statistics of the acid-base balance.*

| Time interval | 0 hours | 72 hours | 96 hours | 120 hours |
|---|---|---|---|---|
| Count | 96 | 96 | 96 | 96 |
| Mean | 7.25 | 7.33 | 7.36 | 7.41 |
| Standard deviation | 0.11 | 0.22 | 0.05 | 7.41 |
| Minimum | 7.01 | 7.16 | 7.23 | 0.04 |
| $25^{th}$ percentile | 7.18 | 7.27 | 7.32 | 7.40 |
| Median ($50^{th}$ percentile) | 7.28 | 7.33 | 7.38 | 7.42 |
| $75^{th}$ percentile | 7.33 | 7.37 | 7.4 | 7.44 |
| Maximum | 7.42 | 9.31 | 7.44 | 7.45 |

(STDV=0.11) to 72 hours (STDV = 22), after which a slight decline in the standard deviations were observed at 96 hours and 120 hours, STDV = 0.05 and STDV = 0.04, respectively. We proceeded with the statistical analysis by deploying the ANOVA test. This analysis was based on the assumption that the data was equally distributed throughout the set, with equal variance across the dataset. The ANOVA test established a significance of p-value of 0.05, which is greater or less than the threshold of the significance level. This led to the rejection of the null hypothesis. We carried out a pairwise T-test and ANOVA measurements for the variation of pH values across the time intervals to get an insight of the importance of the changes in pH values over time. The outcome would suggest differences of the pH values at specific intervals. We found a statistically significant F-statistic of 28.08, and a low p-value of $2.01^{-16}$. Our outcomes suggested statistically significant variation in the pH values across the time interval, justifying the inference that pH values are significantly influenced by time holds. The pairwise yield more data to unmask the effect of time and the specific time intervals (Table 7). The pairwise T-tests revealed significant pH differences at 0 hours and the rest of the time intervals, including 72 hours, 96 hours and 120- hours. Also, the p-values were tremendously low. On the other hand, there was no statistical significance in the pH values in the pairwise comparison at 72 hours vs. 120 hours, and 72 hours vs. 96 hours. The p-values of these two caparisons exceeded the threshold p-value (0.05). The greatest impact of the brain tissue oxygen saturation was witnessed by the examination of acid-base balance, where the pH values increased significantly and differed with the different time intervals. The Figure 4 below shows a tremendous increase in the pH values, with a clear distinction of the acid-base profile across the time intervals.

## Discussion

Pre-term neonates are at high risk of low hemoglobin levels and anemia due to immature production of red blood cells, blood loss, physiological stress, low nutrient supply, and most importantly, inadequate oxygen supply. Immature bone marrow is a common incidence among pre-term neonates with low birth weights. In connection to this, immature bone marrow results in low oxygen supply than demand.[8,9] In a bid to establish the value of oxygen saturation in brain tissues, the present delved in an in-depth examination of oxygen-need balance, acid-base balance and brain-specific aspects of oxygen among pre-term neonates.

The clinical trial yielded substantial evidence regarding a stead and increase in oxygen saturation and hemoglobin levels among neonates from the period of pre-term birth to the $120^{th}$ hour. A characteristic trend is observable in the increase in oxygen saturation levels in the brain cells and hemoglobin levels in the blood after 72 hours, 96 hours and 120 hours. A small and consistent change in hemoglobin levels and oxygen levels was noted. Even though the small difference in the mean and average changes, the stead increases in oxygen saturation in the brain cells and hemoglobin levels suggest significant

***Table 7.*** *ANOVA measurements for the variation of PH values.*

| Interval comparison | T-statistic | p-value | Degree of freedom |
|---|---|---|---|
| 0 vs. 72 hours | -3.79 | 0 | 95 |
| 0 vs. 96 hours | -15.43 | $1,29^{-27}$ | 95 |
| 0 vs. 120 hours | 17.21 | $5.97^{-31}$ | 95 |
| 72 vs. 96 hours | -1.48 | 0.14 | 95 |
| 72 vs. 120 hours | -3.78 | 0 | 95 |
| 96 vs. 120 hours | -12.24 | $3.05^{-21}$ | 95 |

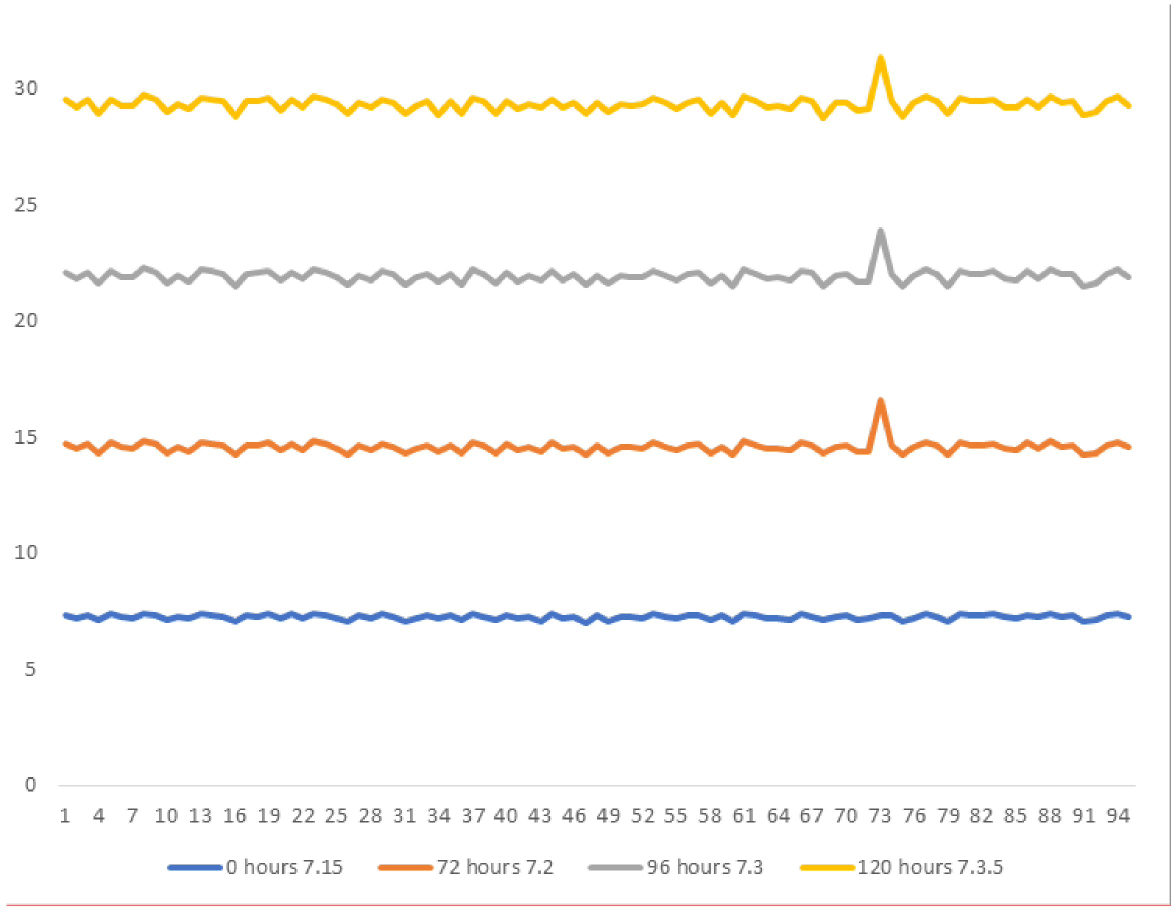


***Fig 4.*** *A line graph of pH acid-base balance.*

developments in health-related functions, including physiological processes and functions in the specimen.

The consistent and stead elevation of oxygen saturation and hemoglobin levels is a crucial clinical outcome as it suggests positive growth or improvement of the neonates. The increasing oxygen saturation indicates an increase in oxygen-hemoglobin affinity.[10,11] The bonding between oxygen and hemoglobin facilitates oxygen transportation to the brain cells, and other organs. By extension, this effect implies high oxygen transportation to other body's cells and organs, implying improved cellular activity or functions.[12] This account is supported by previous studies where NIRS assessment outcomes reported improved physical activity among male and neonates with improved oxygenation of cerebral cells. High oxygenation of cerebral cells enhances cellular metabolism, improves hemodynamics, and maximizes physical activity.[13]

An upward trend in BOS percentages over the time intervals of the study was strong evidence of the positive change and improvement among the preterm neonates. High BOS percentages indicate increased oxygenation of brain tissues, which is crucial for brain functions and the overall body's physiology. This implies that the pre-term neonates would grow and gain full physiological and biological functions. Data collected from the pre-term neonates suggests that there was a certain degree of oxygen saturation among the participants at birth (60%), which is quite low considering that full-term infants are born with oxygen saturation of 90% to 97% range.[14] Notably, some of the pre-term neonates displayed even lower oxygen saturation levels, which poses danger to overall health and general growth.

The observable rise in the percentages of oxygen saturation in brain tissues concur with the physiological maturation of the respiratory systems of the pre-term neonates. Our findings concur with previous studies and literature that pre-term neonates' respiratory systems develop significantly after delivery. Hillman et al. found that pre-term neonates undergo multi-organ transition and adapt to overcome abnormalities like poor pulmonary vasodilation and changes in blood flow.[15] This success spells improved oxygenation of the body's tissues, including the brain cells. Our study replicates a similar perspective, especially the gradual increase percentages of brain oxygen saturation at the 120$^{th}$ hour mark.

The decrease in standard deviations is a fundamental indicator of BOS' convergence to the central value, which aligns our findings with the literature and previous findings. The common takeaway from our findings and the literature regards stabilization of BOS in the neonates cardiovascular and respiratory systems to adaptation to extrauterine survival.[15,16] The maturing of the neonates' brain tissues and lungs benefits saturation of oxygen in brain tissues and breathing, respectively. Nonetheless, the decrease in the variation of BOS percentages is noteworthy.

We observed an achievement of the ideal oxygen saturation among the pre-term neonates after 72 hours and 96 hours. At these intervals, the pre-term neonates achieved oxygen saturation >80% and reached the 90%, especially after 96 hours. The ability to achieve near-optimal saturation levels indicates oxygenation of brain cells, which would implicate better functioning. Additionally, there is a steady rise in BOS from 90% to 99% after 120 hours. This trend underscores a steady improvement and change and suggests that the neonates consistently achieved remarkable oxygenation at the end of the trial period.

The clinical significance of the increasing percentages of oxygen saturation is reflected by the physiological processes constrained by oxygen, including overall cell functions, growth, brain development and general growth. Knowledge borrowed from the literature of human physiology suggests that oxygen is crucial for brain functions, cellular growth and functions, alongside overall growth and development of the human body.[17,18] Based on these outcomes, neonatal care experts should be aware of the variations. Hence, oxygenation should be tailored to pre-term neonates accordingly. Early interventions like neonatal screening or monitoring are vital during the initial hours, after pre-term birth, as BOS percentages or oxygen saturation, could be too low to sustain optimum biological processes.[19,20] However, the significant improvement in oxygenation stability as the neonates grow reduce the need for admission in ICUs. Therefore, the ANOVA test results are key information to neonatal care providers.

Our evaluation on pH gas acid-base balance established a balanced acid-base status through the pH of 7.35, which was relatively stable and favoring physiological processes. We found that the incidence of oxygenation of neonatal brain tissues was 88%, which was a key step to maintaining ideal oxygen levels. These findings implicate on the concept of metabolic acidosis where we found an incidence of 50%. At 50%, the pre-term neonates should be monitored for possible adverse effects of metabolic acidosis. Often, altered acid-base equilibrium affects cerebral oxygenation. Hyperventilation enhances oxygenation of brain tissues, with many factors like brain hemorrhage, and physico-chemical properties standing out as factors that can alter acid-base equilibrium.[21] Our study found that the acid-base equilibrium disrupted the supply of oxygen to the cerebral tissue, with an incidence rate of 50%. The relatively high disruption of the supply of oxygen to brain tissues indicates the relationship between cerebral oxygenation and acid-base equilibrium. The clinical relevance of this outcome regards the need to maintain or ensure a steady supply of oxygen to the brain tissues among pre-term neonates. This will prevent neurological complications.

Oxygenation of the brain cells span to the aspect of acid-base levels and the pH of the anatomical environment. Low oxygen saturation destabilizes the acid-base balance by enabling high carbon dioxide concentration, and the converse is true.[22,23] We delved into an examination of the acid-base balance among the pre-term neonates and found an increase in the minimum pH values at 0 hours (pH = 7.01) to 72 hours (pH = 7.19). The increase of the minimum pH values indicates a shift basicity to acidity. However, this trend does not implicate health issues as the resulting pH values is still within the ideal homeostatic limits suitable for physiological function. The ideal pH value of a stable internal environment ranges between 7.35 to 7.45.[23,24] After 72 hours, an unusual pH value of 9.31 was observed, and regarded as an outlier.

As for the central tendency, the 50$^{th}$ percentile of the median pH value indicated a steady elevation of pH value from 0 hours (pH = 7.28), 72 hours (pH = 7.33), 96 hours (pH = 7.38), and 120 hours (pH = 7.42). this finding concurs with the increasing mean values, hence asserting the trend regarding the temporal increase in the pH values. Even though these findings point at our study objective, it is ideal to consider the fact that pH is subject to the influence of many factors, including environmental changes, biological systems or physiological processes, alongside chemical reactions.[23,24] The examination of the acid-base profile of the pre-term neonates across the time intervals revealed a remarkable finding regarding pH value changes. Despite the steady increase in pH values, the values did not exceed the range of pH of 7.35 to 7.45. There was a consistent increase in the pH values, without a significant variation across the time intervals.

The pairwise T-test outcomes and the repeated ANOVA measurements conferred the importance of time in regards to pH changes. In ANOVA analysis, the overall differences of p-value changes across the time intervals were notable. On the other hand, the pairwise T-test outcomes revealed unique interval comparisons as the levels of the significance varied across the time intervals. Our findings guide the interpretation of temporal variations of the levels of pH, and give in-depth information regarding possible trends or changes that could influence various domains within the biological and chemical perspectives.

In conclusion, the importance of brain tissue oxygen saturation emerged among pre-term neonates with low birth weights. The importance of oxygen saturation on brain tissues is implied by the weight of the physiological and biological impacts felt on the pre-term neonates under care.

Increasing oxygen saturation in the brain tissues stabilized the pH values, and hence the acid-base balance. The study pursued evidence concerning the dynamics of oxygen saturation in brain tissues, with the data obtained from the sample group informing brain-specific aspects of oxygen levels among pre-term neonates. The importance of the outcomes of this study regards clinical practice where caregivers develop a care plan based on evidence-based approaches.

## List of acronyms

ANOVA - analysis of variance
BOS - blood oxygen saturation
ICUs - intensive care units
LMIC - low- and middle-income countries
NIRS - near-infrared spectroscopy
NRDS - neonatal respiratory distress syndrome
STO2 - tissue oxygen saturation
VLBWI -very-low-birth-weight infants

## Contributions of Authors

Authors contributed equally to this work in design, draft, analysis and writing the manuscript. All authors read and approved the final edited typescript.

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## Conflict of Interest

The authors declare they have no financial, personal, or other conflicts of interest.

## Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

## Corresponding Author

Keping Cheng, Department of Neonatology, Yongkang Maternal and Child Health Hospital, Yongkang, Zhejiang, 321300. China.
ORCID iD: 0009-0009-3976-9494
Email: chengke012@mailfence.com

*E-mails and ORCID iD of co-authors*

*Huijie Zhu: 1385798352@163.com*
*ORCID iD:  009-0003-4870-3068*
*Zikai Zhou: Zhouzikaiqq@163.com*
*ORCID iD: 0009-0002-8868-0858*
*Weiyuan Chen: 270413914@qq.com*
*ORCID iD: 0009-0002-6374-2469*
*Aijuan Yang:: 55724110@qq.com*
*ORCID iD: 0009-0005-8345-9232*

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