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Preductal postductal oxygen saturation gradient in preterm infants immediately after birth: Effect of gestational age on achievement of target saturation

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ABSTRACT

Background: The delivery room oxygen saturation (SpO_2) monitoring in neonates is based on studies in term infants. Study of preductal-postductal SpO_2 gradient in healthy preterms immediately after birth will help in follow-up of an abnormal gradient, rationalizing oxygen therapy, and early identification of congenital cyanotic heart disease. **Aims and Objectives:** SpO_2 is initially low and gradually increases to normal in healthy term newborns postnatally. Postductal SpO_2 is lower than preductal, but their difference gradually decreases postnatally. Our study aims to find out the preductal-postductal SpO_2 gradient in healthy preterms and the correlation between gestational age and SpO_2. In preterms, gradient may persist longer due to patent ductus arteriosus and higher pulmonary vascular resistance. **Materials and Methods:** This observational cross-sectional study has been conducted over 1 year with 80 preterms immediately after birth, after the Institutional Ethics Committee approval and parental informed consent. Preductal and postductal SpO_2 were recorded by probes on right hand and left foot respectively for 20 min after birth. Data were analyzed by SPSS software. **Results:** This study shows that preductal-postductal SpO_2 gradient is significant in the first 20 min of life in preterms, and there is significant positive correlation of gestational age with preductal SpO_2 at 1 min and negative correlation of gestational age with time taken to achieve 90% SpO_2. **Conclusion:** This study concludes that significant preductal-postductal SpO_2 gradient persists for first 20 min of life in preterms and preductal SpO_2 at 1 min decreases and time taken to reach SpO_2 90% increases significantly with decreasing gestational age.

Key words: Oxygen saturation; Pulse oximeter; Preterm neonate

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INTRODUCTION

Studies of postnatal transition in healthy term and near term infants have shown that oxygen saturation (SpO_2) in the first few minutes can be as low as 60–70% and it takes more than 5 min to reach a stable SpO_2.[1-3] Many healthy newborns have an SpO_2 < 90% during the first five minutes of life.[4] These studies aim to identify term or near term infants taking longer time to attain stable SpO_2. SpO_2 monitoring also guides FiO_2 adjustment during resuscitation. Studies show that most healthy term infants born through vaginal delivery attain SpO_2 >90% at 10 min. Postductal SpO_2 is consistently 7–10% less than preductal SpO_2 in term newborns.[3,5] There are only a few studies on SpO_2 trends in preterms. These mainly include late preterm infants (gestational age >34 and <37 completed weeks).

SpO_2 trends in term infants may not be generalized for preterms.[1] Data on preductal-postductal SpO_2 gradient in preterms are insufficient. Available data show that preductal-postductal SpO_2 gradient in preterms with congenital heart disease is more than 25%. The previous studies show that preductal-postductal SpO_2 gradient monitoring can help in identifying congenital cyanotic heart

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disease and persistent pulmonary hypertension (PPHN) early.[6] Our study looks for a trend in preductal-postductal SpO_2 gradient in healthy preterms immediately after birth so that an abnormal gradient may be followed up for development of cyanotic heart disease or PPHN.

The American Academy of Pediatrics has stated standard SpO_2 range in the early minutes of life for a term infant. Preductal SpO_2 values have been stated as these reflect brain oxygenation. No such standard SpO_2 ranges for preterms have been stated. Studies show that following the first 10 min of life, a saturation target of 91–95% in preterms reduces morbidity (chronic lung disease and retinopathy of prematurity) without increasing mortality.[6] Pulse oximetry screening can identify asymptomatic infants with critical congenital heart disease before acute collapse during ductal closure.[6] Our aim here is to look for the usual preductal-postductal SpO_2 trend in healthy preterms. This can guide future studies for determination of standard ranges in preductal-postductal SpO_2 trends in the 1st min of life in preterms. Past studies also show that differences in achievement of target saturation level in preterms were influenced by multiple factors such as probe location, maternal smoking, birth way, and umbilical blood gas pH.[7] These factors may act as confounders while identifying infants at risk for cyanotic congenital heart diseases by SpO_2 monitoring in an asymptomatic preterm. Other studies show that not reaching the SpO_2 target of 80% at 5 min is associated with adverse outcomes in preterms.[8] This further stresses the importance of having standard delivery room minute by minute SpO_2 values for preterm infants.

Aims and objectives

The primary objective of this study is to understand if the preductal postductal SpO_2 gradient in preterm infants persists longer. This will help in identifying infants with congenital cyanotic heart disease or persistent pulmonary hypertension before acute collapse.

The other objectives are to see how gestational age affects the preductal saturation and the time taken to achieve target saturation in preterm infants. This will help in further understanding whether the target delivery room oxygen saturation values for preterm babies should be different from term babies.

MATERIALS AND METHODS

This observational cross-sectional study has been conducted over a period of 1 year (February 1, 2019-January 31, 2020) in the labor room and operation theater of Department of Gynecology and Obstetrics, and Neonatology division of Department of Pediatric Medicine, KPC Medical College and Hospital, Kolkata. The study population includes 80 preterm infants (gestational age <37 weeks) immediately after birth who did not need resuscitation. The infants were selected by simple random sampling. Sample size calculation based on the institutional preterm delivery rate of 5% (prevalence proportion) shows that sample size should be 73. The considered confidence interval in sample size calculation was 95% and absolute error/precision was 5%. It was difficult to recruit many preterm infants, especially the early preterms fulfilling the inclusion criteria, as many required resuscitation, some developed respiratory distress and had to be excluded from the study. Hence, we had to proceed with a small sample of 80 preterms. The resuscitation team posted in labor room and obstetric operation theater was informed 15 min before delivery. Preterms with central cyanosis, perinatal asphyxia, requiring resuscitation, multiple gestation, congenital anomalies, maternal medical or obstetric complications, and maternal addictions were not eligible. Institutional ethics committee approval and prior parental informed consent were taken. Data collection was done according to predesigned pro forma which includes variables such as gestational age, mode of delivery, and maternal medications (anesthesia and analgesia). Assessment of gestational age was done using the New Ballard scoring system.[9] Babies delivered by spontaneous vaginal delivery and cesarean section were included in the study. Immediately after delivery, the baby was placed on mother's abdomen or chest. After drying and initial assessment, cord clamping and cutting was done at around 30 s after birth. The baby was then transferred under a radiant warmer and SpO_2 monitoring was done from 1 min after birth. Two such pulse oximeters were set at their highest sensitivity. One sensor was connected to the right hand of the baby (preductal SpO_2) and another to the left foot (postductal SpO_2), and both were secured with adhesive tapes.[10] Two such pulse oximeters were set at their highest sensitivity. One sensor was connected to the right hand of the baby (preductal SpO_2) and another to the left foot (postductal SpO_2), and both were secured with adhesive tapes. The sensors were then connected to the two pulse oximeters which continuously recorded SpO_2. The data were recorded from 1 min after birth at intervals of 1 min for the first 20 min, irrespective of at what time the infant reached SpO_2 of 90%. The SpO_2 data was transferred to a Microsoft Excel spreadsheet for further analysis by the SPSS software. Data have been represented in terms of mean and standard deviation (SD) or as median and interquartile range (IQR). Data represented as mean and standard deviation were analyzed using independent (unpaired) t-tests.[8] The difference between the mean preductal and postductal SpO_2 at each minute after birth was taken to be the mean preductal-postductal SpO_2 gradient. The mean preductal and postductal SpO_2

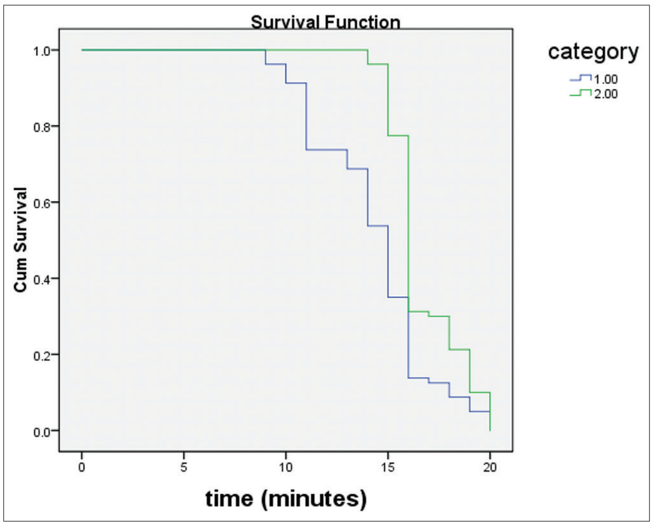

Figure 1: Survival function

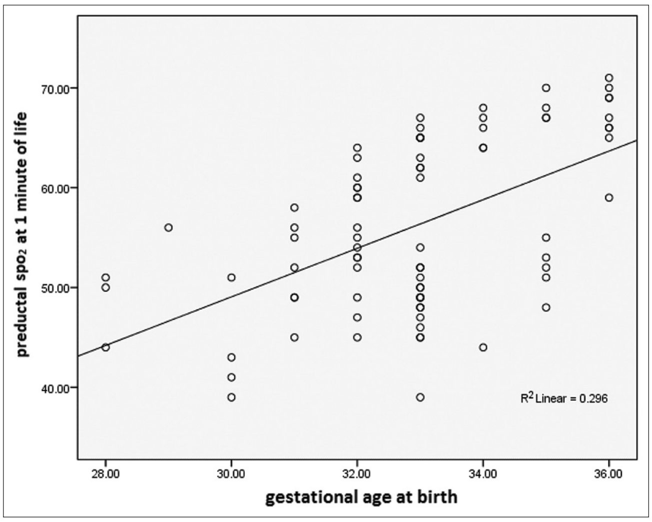

Figure 2: A scatter diagram showing correlation between the gestational age and preductal SpO_2 values at 1 min of life

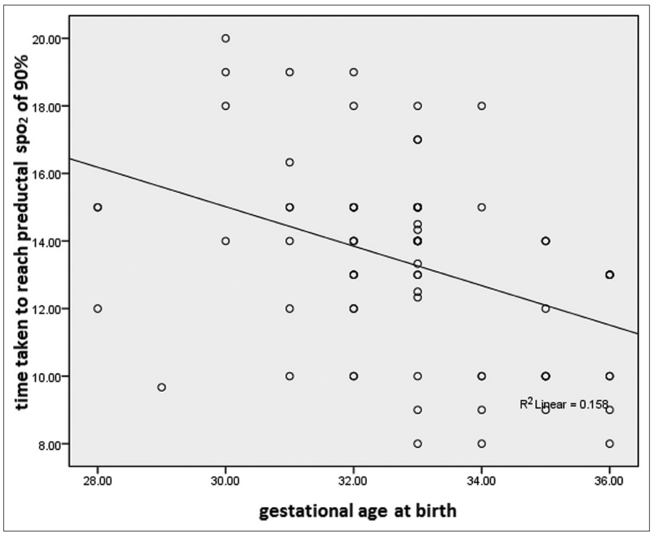

Figure 3: A scatter diagram showing correlation between the gestational age and time taken to achieve a preductal SpO_2 of 90%

values at 1, 5, 10, 15, and 20 min of life were analyzed using independent t-tests. Everywhere, the 95% confidence interval was used and P<0.05 was taken to be significant. Life table analysis was done to test the null hypothesis. The Pearson correlation coefficient was used to test linear association of gestational age and preductal SpO_2 at 1 min and association of gestational age and time taken to achieve 90% SpO_2 target.

RESULTS

The mean gestational age of infants included was 32.88 weeks and their mean body weight was 1665.56 g. Of these 36 (45%) were male and 44 (55%) female, 56 (70%) were early preterm (gestational age <34 weeks) and 24 (30%) late preterm (gestational age 34–36 weeks), 44 (55%) were born by spontaneous vaginal delivery, and 36 (45%) by caesarean section. The median 1 and 5 min

Table 1: The mean and SD of pre and postductal SpO_2 of all preterm infants during first 20 min of life

Minutes after birth	Mean preductal SpO_2 (%)	SD	Mean postductal SpO_2 (%)	SD
1	56.06	8.62	46.89	8.32
2	62.09	7.83	53.56	7.65
3	69.56	7.81	59.35	7.40
4	72.90	7.31	62.54	7.09
5	78.80	6.37	72.49	6.03
6	80.19	5.98	74.05	5.84
7	81.61	5.70	75.71	5.51
8	83.03	5.49	77.23	5.39
9	84.3	5.30	78.83	5.35
10	85.99	5.23	80.15	5.19
11	87.00	4.21	82.15	4.35
12	87.99	3.41	84.21	3.39
13	89.26	2.66	86.20	2.65
14	90.29	2.45	88.04	2.20
15	91.54	2.24	89.72	2.14
16	91.91	2.06	90.08	1.78
17	92.48	1.81	90.60	1.83
18	92.95	1.75	91.30	1.77
19	93.65	1.44	92.25	1.57
20	94.39	0.94	94.04	0.99

SpO_2: Oxygen saturation

Table 2: The mean preductal-postductal SpO_2 gradient at 1, 5, 10, 15, and 20 min of life

Minutes after birth	Preductal-postductal SpO_2 gradient (%)
1	9.2
5	6.3
10	5.5
15	1.9
20	0.4

SpO_2: Oxygen saturation

Apgar score for all subjects included in the study were 8 (IQR 1) and 10 (IQR 0.00), respectively.

Table 1 shows that both the pre and postductal SpO_2 of preterm infants increase from 1 to 20 minutes after birth. The mean preductal SpO_2 is always more than the mean postductal SpO_2 and the difference gradually decreases from 1 to 20 min after birth. A mean preductal SpO_2 of 90% is achieved between 13 and 14 min after birth.

The preductal-postductal SpO_2 gradient in all preterm infants in the first 20 min after birth is shown in Table 2. The gradient gradually decreases from 1 to 20 min. For all preterms, at no point of time is the preductal-postductal SpO_2 gradient more than 17%. It was found during data collection that the maximum difference detected between pre- and postductal SpO_2 was 17%.

Life table analysis was done after observing all the cases for 20 min. Time for obtaining 90% SpO_2 for each of the participants was noted and considered as "time variable." The 90% SpO_2 was considered as the "event of interest" and coded as "1" and there were no censored (right) cases, which would have been coded as "0," as all the participants obtained the "event of interest" within the specified period of observation. Preductal SpO_2 and postductal SpO_2 values were considered as "category variables" and were coded as "1" and "2."

The difference between the occurrence of the preductal and postductal specimens is statistically robust as reflected by the high value Wilcoxon (Gehan) Statistic of 33.910 (df 1, Sig. 0.000). It means that at different points of time, the observed occurrence of "event of interest" was significantly higher than the expected occurrence if there was no difference in occurrence of events between the groups, that is, the actual "Null hypothesis." The log rank in the life table analysis is 15.85. The test statistic is 6.65 and P=0.0001, leading to the conclusion that the null hypothesis is rejected. The figure depicts that survival function in terms of non-occurrence of the target events is higher in category 2. The median survival times in category 1 and 2 were, respectively, 14.2000 and 15.5946.

Table 3 shows the results of independent t-tests done comparing the pre and postductal SpO_2 values of all preterm infants at 1, 5, 10, 15, and 20 min after birth. These t-tests show that the difference between the pre and postductal SpO_2 values for all preterm infants during the first 20 min of life is significant (P<0.001).[11]

Figure 2 shows that there is significant positive correlation between gestational age and the preductal SpO_2 at 1 minute of life (Pearson Correlation Coefficient 0.544, P<0.001), indicating that preterm babies will have a lower preductal SpO_2 at 1 minute of life.

Figure 3 shows that there is significant negative correlation between gestational age and the time taken to reach a preductal SpO_2 of 90% (Pearson Correlation Coefficient -0.397, P<0.001), indicating that preterm babies will take longer time to reach a preductal SpO_2 of 90%.

DISCUSSION

Our study shows that the preductal SpO_2 is significantly higher than the postductal SpO_2 up to 20 min after birth in preterm babies. The preductal-postductal SpO_2 gradient gradually decreases from 1 to 20 min. Existing studies show that preductal SpO_2 may be significantly higher than postductal SpO_2 up to 15 min after birth. Meier-Strauss et al., showed that SpO_2 from hand was always higher than that from foot and there was no significant difference between the two after 17 min of life in term babies.[12] Moller mentions that for healthy newborn infants, the preductal and postductal SpO_2 gradually decrease and both reach a value of 95% at 60 min after birth.[13] Dawson et al., showed that SpO_2 at 5 min of life was significantly less for preterm

Table 3: Comparison of pre- and postductal SpO_2 values of all preterm infants at 1, 5, 10, 15, and 20 min of life

Preductal and postductal SpO_2 at 1, 5, 10,15 and 20 min after birth	Mean (standard deviation) (%)	95% confidence interval	P-value*
Preductal SpO_2 at 1 min after birth	56.06 (8.62)	6.53–11.82	<0.001
Postductal SpO_2 at 1 min after birth	46.89 (8.32)		
Preductal SpO_2 at 5 min after birth	78.80 (6.37)	4.38–8.25	<0.001
Postductal SpO_2 at 5 min after birth	72.49 (6.03)		
Preductal SpO_2 at 10 min after birth	85.99 (5.23)	4.21–7.46	<0.001
Postductal SpO_2 at 10 min after birth	80.15 (5.19)		
Preductal SpO_2 at 15 min after birth	91.56 (2.23)	1.21–2.57	<0.001
Postductal SpO_2 at 15 min after birth	89.68 (2.12)		
Preductal SpO_2 at 20 min after birth	94.39 (0.94)	0.25–0.63	0.034
Postductal SpO_2 at 20 min after birth	94.06 (0.99)		

*P derived by independent t-test. SpO_2: Oxygen saturation compared to term infants.[14] Our study likewise shows a positive correlation between gestational age and preductal SpO_2 at 1 min. On the contrary, Nuntnarumit et al., showed that there was no significant difference in SpO_2 of infants born at ≤33 weeks and >33 weeks.[2] McVea et al., mention that in preterm, following the first 10 min of life, a saturation target of 91–95% reduces morbidity (chronic lung disease and retinopathy of prematurity) without elevating mortality.[6] Tiwari et al., show that SpO_2 at 10 min reaches >90% in most term neonates born through vaginal delivery.[15] Hence, the question remains, whether the same preductal SpO_2 values should be used as target for delivery room resuscitation of both term and preterm infants, as is the current practice. McVea states that a saturation gradient of >5% in the sick neonate warrants assessment for PPHN and congenital heart disease.[6] In our study, we looked for the normal saturation gradient in the first few minutes of life in preterm so that well preterms who have an abnormal gradient can be screened for congenital cyanotic heart disease, before acute collapse. Binder-Heschl et al., concluded that preterms needing respiratory support, and not reaching SpO_2 target of 80% at 5 min after birth, show significantly diminished cerebral oxygenation compared to neonates reaching the target.[8] In our study, we see that healthy preterm neonates, not requiring respiratory support, reach a saturation of 80% between 10 and 15 min of life. This warrants further studies to understand the target saturation level in apparently healthy preterms, below which cerebral oxygenation maybe compromised and oxygen therapy should be started. Oei et al., state that not reaching SpO_2 80% at 5 min is associated with adverse outcomes including intraventricular hemorrhage in preterm babies.[16] Whether this is due to illness or oxygen therapy which is uncertain. This study includes sick babies. Our study includes healthy preterm babies who reach SpO_2 80% between 10 and 15 min. This tells us that we need more studies to understand what should be the target SpO_2 at what time after birth in apparently healthy preterm babies to wisely titrate their oxygen requirement and identify babies at risk of cerebral hypoxia or congenital heart disease before they become symptomatic without increasing the risk of complications like intraventricular hemorrhage.

This study shows that infants with lower gestational age had significantly lower 1 min SpO_2 and took significantly more time to reach a preductal SpO_2 of 90% compared to those having a higher gestational age. The mean time taken to reach a preductal and postductal SpO_2 of 90% is 13.34 and 15 min, respectively, which is more than other available studies. Kamlin et al., found that the mean time to reach SpO_2 >90% was 5.8 min.[3] Their study included infants ≥31 weeks of gestation. Mariani et al., showed that the mean time to reach a preductal SpO_2 of 90% was 5.5 min in term babies.[5] Toth et al., mention in his study that SpO_2 >95% was reached after 12 min preductally and 14 min postductally in term infants.[17] Our study includes predominantly early preterm infants, who have an immature respiratory system and this explains the difference.

The drawbacks of this study are small sample size, movement artifacts, manual data recording, and data collection only up to 20 min after birth and lack of follow-up. Problem encountered while fixing the probe due to the presence of vernix may have influenced the first few readings. This study indicates that future studies may be conducted on the same issue with a larger sample size. Studies of SpO_2 in the first few minutes of life in preterm infants, particularly early preterm infants, are lacking. Those available are mainly on late preterm infants. So further, studies need to be carried out in the early preterm infants so that target SpO_2 in the first few minutes of life can be determined and oxygen therapy rationalized. The preterm infants who take longer time to achieve preductal SpO_2 90% or have abnormal SpO_2 gradient may be followed up for development of congenital heart disease and to study the detrimental effects of delayed brain oxygenation.

Limitations of the study

The sample size used in this study is small, as many preterm infants could not be recruited due to requirement of resuscitation and development of respiratory distress. Movement artefacts may have influenced some of the readings, particularly in late preterm babies. Problem encountered while fixing the probe due to the presence of vernix may have influenced the first few readings. Data was recorded manually and only upto the first 20 minutes after birth. The babies with a prolonged persistent saturation gradient were not followed up for the development of congenital heart disease.

CONCLUSION

From this study, it can be concluded that there is a significant preductal-postductal SpO_2 gradient in preterm infants in the first 20 min of life which gradually decreases from 1 to 20 min. It can also be concluded that preterm babies have a lesser preductal SpO_2 at 1 min and take longer time to reach 90% SpO_2. Further studies are required to comment whether a different target SpO_2 is required for delivery room management of preterm infants and an abnormal gradient will require early investigations for detection of congenital heart disease.

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SM- Literature review, concept, design, data collection, and review; **AM**- Planning statistical analysis, data analysis, and drawing conclusions.

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