

Effect of Optimizing Oxygen Saturation Targets on the Incidence of Retinopathy of Prematurity in a Quaternary NICU

Naveed Ur Rehman Durrani^{a, b} Sanoj Karayil Mohammad Ali^a Ghaniya Ede^a
Amr Moussa Mahmoud Khalil^c Pedro Mattar Neri^d Mai Al Qubaisi^c
Samir Gupta^{a, e}

^aDepartment of Pediatrics, NICU, Sidra Medicine, Doha, Qatar; ^bDepartment of Pediatrics, Weill Cornell Medicine, Doha, Qatar; ^c Department of Pediatrics, NICU, Women Wellness and Research Center, Doha, Qatar; ^dOphthalmology Division, Department of Surgery, Sidra Medicine, Doha, Qatar; ^eNeonatology Department, Durham University, Durham, UK

Keywords

Retinopathy of prematurity · Oxygen · Oxygen saturation

Abstract

Introduction: Retinopathy of prematurity (ROP) is a multifactorial disease and a preventable cause of blindness in childhood. Hyperoxia and hypoxia can cause retinal neovascularization resulting in retinal detachment and blindness if left untreated. Besides oxygen treatment, other reasons for ROP development are well known. We prospectively adopt various strategies to keep oxygen saturation (SpO₂) within targets' between 91 and 95% for those on supplemental oxygen. By adapting this, we postulated that the incidence of severe ROP might be reduced. **Methods:** 2018–2019 provided pre-intervention and 2020 post-intervention data for the project. For all babies (≤32 weeks, ≤1,500 g with FiO₂ >0.21), target SpO₂ between 91 and 95% was measured as a percentage of time spent within and outside target SpO₂ during 1–4 weeks of life. **Results:** 112 and 60 preterm neonates were screened for ROP during the pre- and post-intervention phase. Twenty neonates (18.3%) during pre-intervention and 16 (26.7%) in the post-intervention phase developed severe ROP requiring treatment. Despite a statistically signifi-

cant increase of 10 percent points in time spent within target SpO₂ (91–95%) in the post-intervention phase ($p < 0.05$), the incidence of severe ROP did not decline. Using a multivariate model, odds of ROP development decreased with gestational age (25%) while increasing with PDA requiring treatment (4.33 times) and glucose ≥10 mg/dL (4.15 times), considering one variable at a time, keeping others constant. **Conclusion:** Our QI project showed successful attainment of maximum time; the SpO₂ remained within targets during supplemental oxygen; however, the incidence of severe ROP had not declined. Factors other than SpO₂ might be responsible for a high incidence of ROP in our neonatal intensive care unit.

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Introduction

Retinopathy of prematurity (ROP), first described in 1942 [1], is multifactorial proliferative retinopathy of preterm infants, and currently represents the most common preventable cause of childhood blindness worldwide [2, 3]. ROP prevalence varies with geographical location but is approximately 10–25% [4–6]. It has been reported that 40–50% of babies born ≤31 weeks gestational age develop

some stage of ROP, while 7–8% develop severe ROP and 5–6% require treatment [7].

Many risk factors are associated with ROP development [8], which varies among units or countries; however, the most significant are prematurity, low birth weight, and the need for supplemental oxygen. In view of this substantial variability, there is a potential for modifying certain risk factors associated with ROP and decreasing its incidence [9].

The relationship between oxygen and ROP development was initially described in the 1950s [10] when the use of unregulated oxygen therapy was found to be a significant risk factor. However, ROP remained a substantial cause of significant morbidity and blindness even under controlled oxygen delivery. Both hyperoxia and hypoxia lead to neovascular proliferation, resulting in retinal damage [11, 12].

In its two-stage development, initial triggers are abnormal oxygenation and lack of growth factors [11, 12], leading to arrest or loss of retinal blood vessels. This leads to incomplete vascularization of the retina by causing increasing hypoxia to the high metabolic demand of the retina. The second stage is characterized by the appearance of vascular endothelial growth factor. If left untreated, this promotes unorganized neovascularization and progresses to retinal detachment and blindness [11, 12].

Despite the fact that the well-established deleterious effects of hypoxia and hyperoxia on the retina and multiple large collaborative trials, the ideal oxygen target range for preterm babies is still contentious [13]. A systematic review, combining data from nearly 5,000 extremely preterm infants enrolled in oxygen targeting studies across five countries, Neonatal Oxygen Prospective Meta-analysis (NeOProM) reported that targeting higher (91–95%) compared with lower (85–89%) oxygen saturations (SpO_2) had no significant effect on the composite outcome of death or major disability or disability alone. However, when mortality was assessed in isolation, there was significantly increased survival in the high SpO_2 target group. Even though there was an increase in ROP incidence in the high SpO_2 target group, there was no significant increase in blindness, likely due to efficient screening protocols and effective early treatment in this study population. This has resulted in most guidelines recommending the higher SpO_2 target range as used in the NeOProM collaboration [13–15].

The current standard for monitoring oxygenation noninvasively in preterm infants in neonatal intensive care unit (NICU) is via pulse oximetry (SpO_2). The American Academy of Pediatrics recently suggested a target

SpO_2 of 90–95% [16], while European guidelines recommend a 90–94% SpO_2 target in preterm infants [17]. The present quality improvement (QI) study, Avoid Variations of Oxygenation in Decreasing (AVOID)-ROP, was undertaken to assess whether the incidence of severe ROP requiring treatment could be reduced by improving the time spent in the prescribed target SpO_2 range.

A lack of consistency and guidance regarding SpO_2 targeting in our NICU was a key clinical issue identified before commencing this project. There was also a concurrent increase in the rates of severe ROP warranting intervention. All babies born <36 weeks and <3 months corrected age on respiratory support were evaluated for their alarm limits set on the bedside monitor and nurses' knowledge about SpO_2 targets. The audit showed that only 12% of alarm limits were set correctly, and 37% of bedside staff members were aware of their patients' appropriate SpO_2 targets.

The “Oxygen With Love” (OWL) QI project was implemented to tackle this critical issue regarding poor awareness of SpO_2 targets and suboptimal time spent in the prescribed target range. After extensive discussions and literature reviews [18], a consensus uniform SpO_2 target range and alarm limit of 91–95% was agreed by all team members, including physicians, respiratory therapists (RTs), and nurses. This was the platform for commencing prospective data collection for the “AVOID-ROP” study. This study aimed to identify risk factors for ROP development among the infants screened (<32 weeks and <1,500 g) and whether the incidence of severe ROP could be reduced by optimizing the time spent within the target SpO_2 of 91–95%.

Materials and Methods

This QI project was conducted at a quaternary level 54 bed, NICU at Sidra medicine, Qatar. The NICU at Sidra Medicine is a referral center for all infants in the state of Qatar requiring surgical and subspecialty medical care. Hence, relevant pre-transfer data from the primary perinatal care referral NICU in Qatar with 20,000 deliveries per annum, the Women's Wellness and Research Center (WWRC), were also included in the study. The project consisted of a retrospective chart review (pre-intervention phase), implementing a change of target SpO_2 range of 91–95% (intervention phase), and finally prospective observational data collection of infants (post-intervention phase) as described below.

The retrospective chart review was done for the cohorts of babies cared for at Sidra medicine NICU and those born at WWRC, subsequently transferred to Sidra Medicine for quaternary care. The study was approved by Institutional Review Board (IRB) at Sidra Medicine.

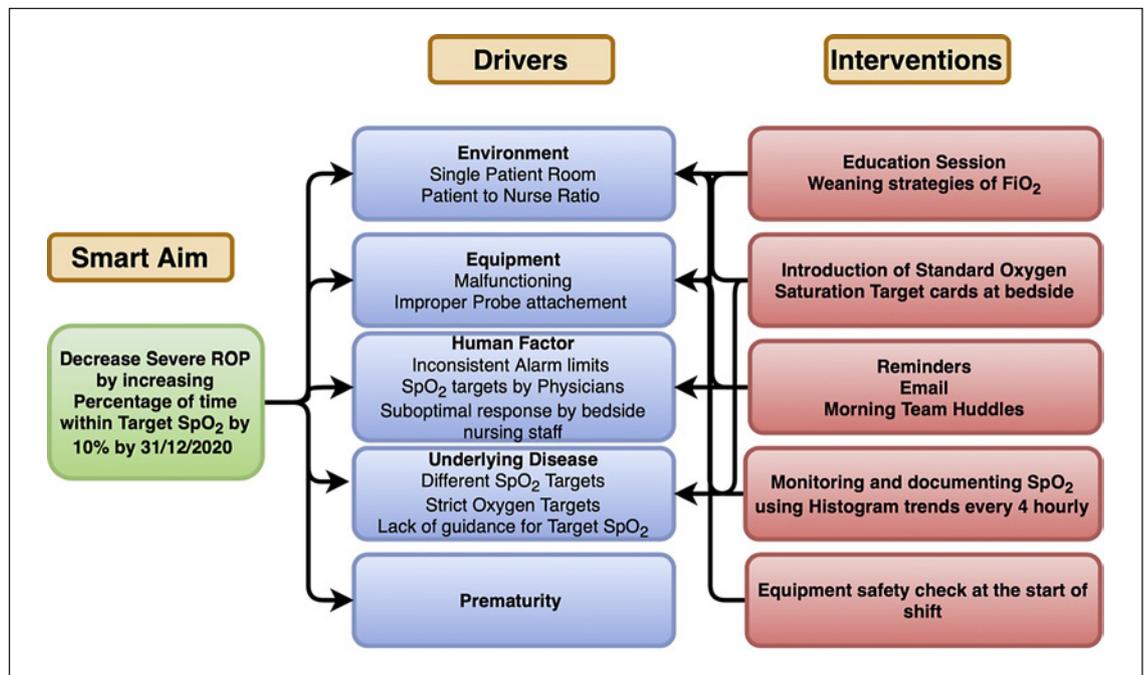


Fig. 1. Key driver diagram.

Process measures included SpO₂ and a fraction of inspired oxygen (FiO₂) exposure calculated as described below for the patient cohort after 3 months of the intervention phase. Interventions included periodic bedside histogram assessments every 4 h and documentation in a log sheet to serially monitor oxygenation trends, random audits for correctly set alarm limits on the monitors and positive reinforcement rewards, and regular appreciation for staff achieving improved time within the SpO₂ target range.

We identified various barriers to SpO₂ targeting in our NICU. To mitigate these, multiple strategies were utilized to increase the time spent within the target SpO₂, as shown in Figure 1.

Pre-Intervention Phase (January 1, 2018 to December 31, 2019)

In the pre-intervention phase, a retrospective review of the electronic medical records (EMRs) was performed on all preterm infants born before 32 weeks gestational age or birth weight less than 1,500 g and were screened for ROP. Data regarding gestational age, gender, birth weight, and z score at 4 weeks; delivery details; inborn or out born; Apgar score at 1 and 5 min; nationality; respiratory distress syndrome requiring surfactant; bronchopulmonary dysplasia defined as oxygen requirement at 36 weeks corrected age [19]; hemodynamically significant patent ductus arteriosus (PDA) requiring medical or surgical/device closure; severe intraventricular hemorrhage defined as grade III-IV according to Papile classification [20]; surgical necrotizing enterocolitis; hyperglycemia defined as blood glucose ≥ 10 mmol/L; sepsis episodes defined as blood culture positive for bacteria significant in neonates and required antibiotics; hypotension requiring inotropes; red blood cell transfusion; and days on a mechanical ventilator and/or nasal continuous positive airway pressure.

ROP screening results were obtained from ophthalmology records documented in the EMR, including the day of life treatment given as applicable. Data were also collected regarding the commencement and discontinuation of oxygen therapy. The highest FiO₂ for each day was averaged to less and greater than 0.30 for the time baby remained on respiratory support, defined as either on mechanical ventilation, nasal continuous positive airway pressure, nasal intermittent positive pressure ventilation, heated humidified high flow nasal cannula, or low flow nasal cannula. Low flow oxygen is defined for this study as the oxygen flow rate < 2 L/min. FiO₂ ($\geq 22\%$) and SpO₂ values used in this study were based on hourly readings documented by the nursing and RT in the EMR of the neonate for weeks 1, 2, 3, 4, or till 32 weeks postmenstrual age (PMA) if still on oxygen therapy. These data points were averaged to calculate the percentage of time per week; each infant remained either.

- Below target saturation range ($< 91\%$).
- Within target saturation range (91–95%).
- Above target saturation range ($> 95\%$).

If the infant was weaned down to 0.21 FiO₂ before 32 weeks PMA or earlier than 4 weeks, while still on respiratory support, data for FiO₂ and SpO₂ were recorded up to the day when the baby was on FiO₂ ≥ 0.22 . These values were then compared with the severity of ROP. Severe ROP was defined as the need for diode laser therapy, ranibizumab injection, or both during a stay in NICU.

Intervention Phase (December 1, 2019 to February 28, 2020)

All NICU nursing staff, RTs, neonatal nurse practitioners, and physicians at Sidra medicine were educated about the consensus saturation target of 91–95% and the role of oxygen in contributing to ROP via lectures and reminders sent via emails. A multidisciplinary team consisting of physicians, RTs, and nurses coordinated

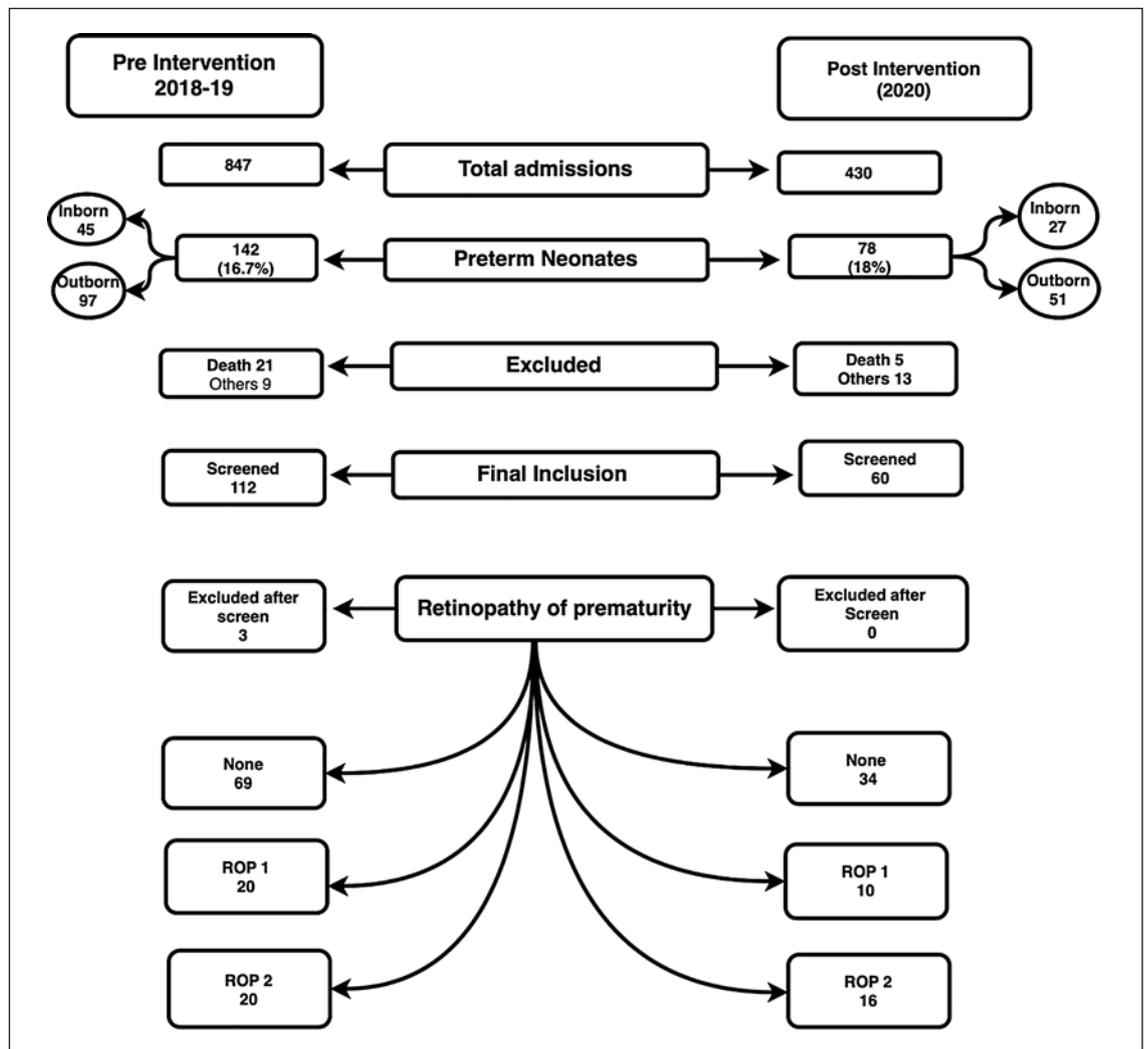


Fig. 2. Flowchart.

and oversaw the oxygen management protocol in the NICU. A laminated card showing set alarm limits and target saturations were displayed at the bedside to improve compliance. Furthermore, this education included standardized guidance on weaning and escalating FiO_2 support based on the degree of SpO_2 outside the target range.

Post-Interventional Phase (March 1, 2020 to December 31, 2020)

The same data mentioned above in the pre-intervention phase were recorded from the EMR of babies undergoing ROP screening.

Retinal Screening and Degree of ROP Severity Classification

All retinal screenings were done using a binocular indirect ophthalmoscope and a +20D lens by an ophthalmologist experienced in ROP screening after 4 weeks of age or at 31 weeks of PMA, whichever was later. Examinations were repeated according to international guidelines at every 1–2 week-intervals depending on

the underlying stage of ROP and continued till the retina was fully vascularized to the periphery. The findings were documented in the EMR on neonates on the stage and zone of any ROP and the presence or absence of plus disease in each eye at each examination. When the severity of the disease was anticipated, the interval examination was individually adjusted by an ophthalmologist according to the findings and severity. For the study purposes, the severity of ROP was grouped as follows:

- Incomplete retinal vasculature or no ROP (ROP 0).
- Stage 1 or 2 without the plus disease (ROP 1).
- Stage 2 with plus disease and aggressive posterior ROP, stage 3 with or without plus disease, or stage 4 or 5 disease (ROP 2).

Exclusion Criteria

- All preterm infants referred to Sidra Medicine after 4 weeks of age.
- Unavailable data (FiO_2 and SpO_2) for preterm infants.
- Death or transferred before the first retinal examination.

Table 1. Baseline demographics

	Pre-intervention (N = 112), n (%)	Post-intervention (N = 60), n (%)	Total (N = 172), n (%)
GA in weeks*	28.7±0.3	28.7±0.3	28.4±0.2
Birth weight			
<1,000 g	44 (39.3)	28 (46.7)	72 (41.9)
1,000 to <1,500 g	55 (49.1)	20 (33.3)	75 (43.6)
≥1,500 g	12 (11.6)	12 (20.0)	25 (14.5)
APGAR score			
1 min*	5.9±0.2	5.6±0.3	5.8±0.2
5 min**	8.0 (7.0–9.0)	8.0 (7.0–9.0)	8.0 (7.0–9.0)
10 min**	9.0 (7.0–10.0)	8.0 (7.0–8.8)	8.0 (7.0–9.5)
Twins	25 (22)	10 (16)	35 (20)
Triplets	2 (1.8)	4 (6.6)	6 (3.5)
Place of birth			
Inborn	32 (28.6)	19 (31.7)	51 (29.7)
Outborn	80 (71.4)	41 (68.3)	121 (70.3)
Gender			
Male	61 (54.5)	31 (51.7)	92 (53.5)
Female	51 (45.5)	29 (48.3)	80 (46.5)
Nationality			
Qatari	48 (42.9)	22 (36.7)	70 (40.7)
Non-Qatari	64 (57.1)	38 (63.3)	102 (59.3)

* Mean ± standard deviation. ** Median (IQR).

- Eye examinations were done for other reasons (microphthalmia, trisomy 21, cataract, workup for syndromes, etc.).

Statistical Analysis

Data were entered and analyzed using Stata v16.0. Descriptive statistics were reported for baseline variables. After normality assessment, normally distributed continuous variables were expressed as means ± standard deviations, whereas median and interquartile ranges were reported for non-normal continuous variables. Categorical data were expressed as frequency and percentages. A Student's *t* test or a Mann-Whitney U test was used for comparison of the groups in respect to continuous data accordingly.

In contrast, the χ^2 test was used to compare the groups in relation to categorical data. The parameters were evaluated by univariate logistic regression analysis to show ROP severity (in other words, significant difference between the groups). Parameters with $p \leq 0.25$ in the univariate logistic regression analysis were considered significant, and a multivariable logistic regression analysis was performed. For the multivariable model, p value <0.05 was considered to be statistically significant. Effect estimates were expressed as odds ratio with likelihood-based 95% confidence limits.

Results

During the study period, there were two cohorts: pre-intervention cohort 2018–2019 and post-intervention cohort 2020. There were 142 (17%) and 78 (18%) preterm neonates admitted to NICU in pre- and post-intervention

cohorts, respectively. After excluding non-eligible infants (death, inaccessible medical records, >32 weeks, $>1,500$ g, duplicate entries), there were 112 and 60 eligible preterm infants (<32 weeks and $<1,500$ g) that were screened for ROP (Fig. 2). Three babies were excluded after screening (one with microphthalmia and two with incomplete data).

Baseline characteristics of neonates between two cohorts are shown in Table 1. There was no difference between pre- and post-intervention periods for gestational age, birth weight, and Apgar score. The majority of the study population were male and referred to our center for surgical management and medical reasons, and about 70% were non-Qatari Nationals.

In the pre-intervention phase, a total of 40 babies (35.7%) developed any stage ROP, of which 20 (50%) progressed to severe ROP (ROP 2). In contrast, during the post-intervention period, 26 babies (43%) developed any stage ROP, of which 16 (61%) required treatment (ROP 2). 3 (2.8%) babies in pre-intervention and 1 (1.7%) in post-intervention phase developed retinal detachment (Table 2). The median age for diagnosis of severe ROP and treatment was around 80 days of life, ranging between 239 and 280 days among the study cohort.

The time spent within the target SpO₂ range (91–95%) was significantly higher in the post-intervention period

Table 2. ROP distribution and time of diagnosis

	Pre-intervention (N = 112), n (%)	Post-intervention (N = 60), n (%)	Total, n (%)
No ROP			
Yes	69 (63.3)	34 (56.7)	103 (60.9)
No	40 (36.7)	26 (43.3)	66 (39.1)
ROP 1			
Yes	20 (18.3)	10 (16.7)	30 (17.8)
No	89 (81.7)	50 (83.3)	139 (82.2)
ROP 2 and laser treatment			
Yes	20 (18.3)	16 (26.7)	36 (21.3)
No	89 (81.7)	44 (73.3)	133 (78.7)
Retinal detachment			
Yes	3 (2.8)	1 (1.7)	4 (2.4)
No	106 (97.2)	59 (98.3)	165 (97.6)
Age at diagnosis**	265.5 (239.5–277.3)	254.0 (239.0–280.0)	260.0 (239.0–277.5)
Day of life ROP diagnosis**	78.0 (70.5–98.0)	82.0 (63.0–90.0)	80.0 (65.0–93.5)

** Median (IQR).

Table 3. Univariate and multivariable binary logistic regression showing a risk for ROP development

	Univariable model			Multivariable model		
	crude OR	95% CI	p value	adjusted OR	95% CI	p value
Gestational age, weeks	0.65	0.55–0.77	<0.0001	0.75	0.62–0.92	0.005
PDA requiring treatment	9.18	4.09–20.60	<0.0001	4.33	1.69–11.04	0.002
Glucose levels ≥10 mg/dL	5.25	1.69–16.24	0.004	4.15	1.01–17.05	0.049
Birth weight						
Extremely low birth weight	13.5	1.71–106.0	0.013			
Very low birth weight	4.26	0.52–34.67	0.176			
APGAR at 5 minutes	0.79	0.63–0.99	0.046			
Z-score at birth	1.32	0.93–1.89	0.125			
Z-score at 4 weeks	1.38	0.92–2.08	0.12			
SpO ₂ 91–95%						
Week 1	1.03	1.01–1.04	0.002			
Week 2	1.02	1.01–1.04	0.002			
Week 3	1.02	1.01–1.04	0.003			
Week 4	1.03	1.01–1.05	<0.0001			
CPAP days	1.02	1.00–1.04	0.007			
HFNC days	1.02	1.00–1.05	0.095			
Place of birth (referrals)	2.02	0.86–4.77	0.107			
Nationality (not locals)	1.87	0.88–4.01	0.106			
Sepsis (culture proven)	2.39	0.98–5.86	0.056			
Severe IVH	1.88	0.6905.09	0.216			
Hypotension (required inotropes)	2.04	0.88–4.72	0.097			
Antenatal steroids (not given)	1.87	0.80–4.34	0.147			
Received surfactant	4.37	1.46–13.14	0.009			
Received TPN	1.84	0.84–4.04	0.128			
BPD	5.94	2.65–13.32	<0.0001			
Ventilator days						
7–14	4.58	1.29–16.25	0.018			
≥15	7.29	2.21–24.03	0.001			

Cutoffs: crude OR = 0.25, adjusted OR = 0.05. BPD, bronchopulmonary dysplasia; IVH, intraventricular hemorrhage; OR, odds ratio.

Table 4. Time spent at different categories of SpO₂ levels for 4 weeks with an interquartile range

Time spent	Pre-intervention			Post-intervention			Total		
	median	25th percentile	75th percentile	median	25th percentile	75th percentile	median	25th percentile	75th percentile
Week 1									
Below 91%	2	0	6	3.2	1	5.7	2.3	0.5	6
On 91–95%	30.5	11	58	45.5	20.8	67.9	38	16.7	59.9
Above 95%	66	35	88	50.3	25.7	78.7	58.9	30.1	82.8
Week 2									
Below 91%	1	0	7.8	3.4	1.1	7.9	2	0	7.9
On 91–95%	29.5	6	57.8	45.3	15.1	69.4	38	9	61
Above 95%	67	30	93.5	50.9	20.8	84.9	59	26.1	91
Week 3									
Below 91%	2	0	10	3.5	0.6	8.1	2.8	0	9
On 91–95%	32	6	55	35.7	19.4	67	33.9	7.8	60
Above 95%	63	30	93	61	24.7	78.2	61.8	27.9	90.8
Week 4									
Below 91%	2	0	10	3.1	1	7.5	2.4	0	9
On 91–95%	22.5	5	50	28.9	10	60.4	23	7	55.7
Above 95%	75	35.3	94	67.9	28.6	86.2	74	33	92

than in the pre-intervention period. This was significantly higher in all 4 weeks in the post-intervention cohort with a *p* value of 0.018, 0.010, 0.023, and 0.07, respectively, as shown in Table 3, their respective interquartile range shown in Table 4 and shown in Figure 3. In univariate logistic regression, a statistically significant difference (*p* < 0.05) was noted between various risk factors for ROP; however, in the multivariate model, only three factors show an independent risk for developing ROP, as shown in Table 3.

Discussion

The purpose of this project was to evaluate the effect of changes in SpO₂ on the incidence and severity of ROP in our NICU over two epochs, with the rationale being the increase in severe ROP cases. We hypothesized that this might be due to inconsistent SpO₂ alarm settings and a lack of awareness regarding the importance of maintaining SpO₂ within the prescribed target range. Optimizing time spent in the target SpO₂ in the first few weeks is vital in preventing severe ROP and reducing mortality [21]. In our study, a statistically significant increase in target SpO₂ by 10% point (*p* < 0.05) and at the same time, a 15% point decrease in SpO₂ >95% in the post-intervention phase was achieved. This clearly shows that babies during the first 4 weeks of life spent increasing time in the target range and less exposure to hyperoxia. However, despite

being in optimal SpO₂ target range for about 60–70% of the time in the first 4 weeks of life following the implementation of the OWL project, education of physicians and nursing providers, and reminders about keeping target oxygen ranges in the post-intervention phase, there was no significant reduction in the incidence of severe ROP requiring intervention. This is probably reflective of the complexity of the predominantly surgical preterm infants cared at our center with multisystem issues and other contributing factors such as sepsis, multiple blood transfusions, higher rates of malnutrition, and prolonged periods of invasive mechanical ventilation. ROP being a multifactorial disease, addressing issues with oxygenation alone may not reduce the incidence and severity of this condition.

Our results on time spent in the SpO₂ target range are consistent with other studies that have reported challenges in SpO₂ targeting in preterm neonates [21–23], both for physiological and nursing reasons. Physiologically the sigmoid-shaped oxyhemoglobin dissociation curve is almost vertical at 90% SpO₂. Therefore, even a slight change in inspired oxygen pressure at this point results in a significant shift in SpO₂ presenting clinically in variable SpO₂ values [24]. From a nursing perspective, a low nurse-to-patient ratio is associated with improved time spent in the target SpO₂ range [25]; however, a 1:1 staffing ratio changes with increasing postnatal age as the infant becomes more stable and requires less time invasive respiratory support. At this point, the time spent outside

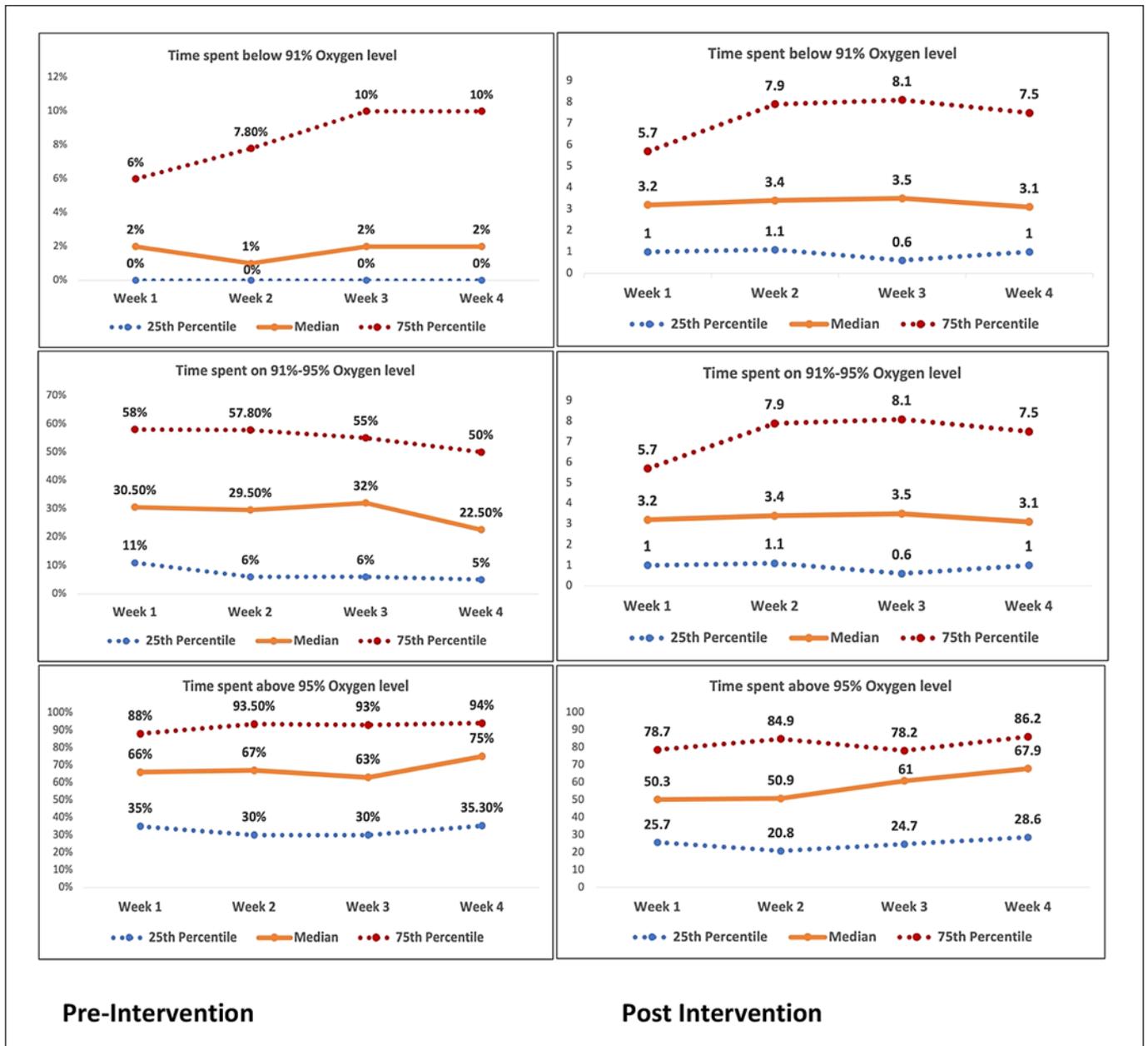


Fig. 3. Median (interquartile range) for time spent below, on, and above target oxygen level.

the target range increases, and there is a high risk for developing ROP. However, maintaining SpO₂ in the target range from 33 weeks PMA onward is less concerning due to studies supporting the association of higher SpO₂ targets during the second phase of ROP and decreasing progression to severe ROP [26–28].

Although the trend of maintaining SpO₂ in preterm neonates by the American Academy of Pediatrics (90–

95%) [29], WHO (88–95%) [30], and European guidelines (90–94%) [31] have increased, ophthalmologists everywhere in the world doing screening examinations anticipate higher trends of ROP. Our study reflected this observation that despite spending increased time in target SpO₂, the incidence of ROP remained high. Thus, we explored other associated risk factors and found that gestational age, the presence of a hemodynamically significant

PDA, and hyperglycemia are independently related to the development of severe ROP.

Our study showed that the odds of developing severe ROP is 4.3 times (95% CI: 1.69–11.04, $p = 0.002$) in neonates with hemodynamically significant PDA requiring treatment for same gestational age and serum glucose is <10 mmol/L. Similar to our study, the association of PDA and ROP has been reported previously [32], reflecting a possible alteration in retinal perfusion and oxygenation [33, 34].

With a one-unit increase in gestational age in weeks, we showed that the odds of developing ROP decrease by 25% when PDA requires treatment and glucose level is less than 10 mmol/L. Gestational age is a significant risk factor for ROP, as similarly reported in other studies [35, 36], and a lower GA increases the likelihood of developing ROP.

The odds of ROP developing are 4.15 times in neonates with glucose levels more than 10 mmol/L, keeping other variables constant. There are conflicting data about the association between hyperglycemia and ROP in extreme preterm neonates, likely corresponding to cutoff values used for hyperglycemia and treatment threshold [37].

Limitations to our study include small sample size, inter-physicians, and inter-hospital treatment variability since 70% of neonates were out born and referred to our center for subspecialty medical and surgical care. Our analysis was strictly based on data available during the NICU stay at WWRC and at Sidra Medicine. We did not have access to data pertaining to SpO₂ and FiO₂ during resuscitation, during transportation from the referral hospital, and during surgical or other radiological procedures that warranted transfer to the operating room and other areas within the hospital and during general anesthesia.

Another limitation is averaging the SpO₂ over 1 h. It might be possible that the infant's SpO₂ remains less than 91% for 30 minutes and more than 95% for next 30 min; the single averaged data point may fall within the target range of 91–95 percent. This bias might be due to averaging data taken at wide intervals. By taking these points at shorter averaging times of 2–15 minutes might have eliminated such bias. The strength includes comparing data between two epochs on either side of the successful implementation of a bundle of interventions (OWL project) and a statistically significant improvement in SpO₂ targeting in the post-intervention phase.

Conclusion and Recommendations

Our QI project achieved a 10% increase in time spent within the SpO₂ target range above the baseline in the post-intervention phase via successful implementation of the OWL project. Though we were unable to reduce the incidence of severe ROP, we found that PDA and hyperglycemia were independently associated with a higher incidence of severe ROP along with the universal risk of prematurity, lower gestation age, and time spent in targeted oxygenation.

Understanding risk factors and associated comorbidities of prematurity are essential to developing future QI projects related to preterm neonates. Differences in guidelines and neonatal care at various institutions and health care settings also need to be considered before designing future projects.

Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board (IRB) of Sidra Medicine, approval number: 1566589. The IRB of Sidra Medicine also granted a waiver of consent as infants continued to receive standard of care irrespective of inclusion within the QI study and had any effect on the plan of care.

Conflict of Interest Statement

None of the authors have any conflict of interest.

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Not relevant.

Author Contributions

Naveed Ur Rehman Durrani contributed to concept designs, analysis, and interpretation; drafted the manuscript; critically revised the manuscript; and gave final approval. Sanoj Karayil Mohammad Ali contributed to analysis and interpretation, critically revised the manuscript with expert advice, and gave final approval. Ghaniya Ede contributed to data collection, analysis, and interpretation; critically revised the manuscript; and gave final approval. Amr Moussa Mahmoud Khalil contributed to data collection, analysis, and interpretation from WWRC; critically revised the manuscript; and gave final approval. Pedro Mattar Neri screened for ROP, provided data for ROP and expert opinion on ophthalmological aspects of the manuscript, critically revised the manuscript, and gave final approval. Mai Al Qubaisi provided data from WWRC, contributed to analysis and interpretation, critically re-

vised the manuscript, and gave final approval. Samir Gupta contributed to analysis and interpretation, provided expert advice on the manuscript, critically revised the manuscript, and gave final approval.

Data Availability Statement

Data are not available publicly nor can be shared.

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