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EVALUATION OF OXYGEN SATURATION INDEX (OSI) AS NON-INVASIVE TOOL AND COMPARISON WITH OXYGENATION INDEX (OI) IN HYPOXEMIC RESPIRATORY FAILURE IN NEONATES: A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

INTRODUCTION

Oxygenation index (OI) is routinely used as a marker of severity of hypoxemic respiratory failure in neonates and to decide management in these babies. But it is an invasive procedure requiring Vascular puncture and also confers cost, cumbersome for continuous monitoring.

IMPORTANCE OF STUDY

As Oxygen saturation Index (OSI) is a non-invasive method of monitoring, evaluating it's efficacy with OI which requires frequent ABG sampling, will provide a better tool for monitoring of these babies specially in resource limited set up where ABG is not available. It is more cost effective and provide continuous monitoring of hypoxemia.

OBJECTIVES *:To determine the correlation between OSI and OI and to validate the values of OSI against defined severity of OI as mild, moderate and severe 10-15, 15-20 and above 20 respectively.*

METHODOLOGY

The Study design was Prospective Observational cross-sectional Study conducted at Dept of Neonatology, Chengalpattu Medical College and Hospital (CMCH) Chengalpattu, Tamil Nadu from May 2022 – April 2023 (1 year) and include 41 ***Neonates with Hypoxemic Respiratory Failure***

RESULT

A total of 257 paired OI and OSI measurements from 41 infants median gestational age 37 weeks; mean birth weight 2.8 kg were recorded during the study. The median (interquartile range) number of samples was 5 (4-7) per patient. Overall, OSI values showed strong correlation (r = 0.91) with OI.

The predictive derivative equation showed a strong linear association and good agreement in both derivation and validation data sets, with strong accuracy measures of OSI for OI cutoffs of 10- 15,16- 20, 21-25 and >25.

Conclusion

A strong correlation of OSI with OI was found. OSI was strongly predictive of severity of HRF in the ventilated neonates and was in agreement with the OI values which correlated with modification in treatment like change in mode of

ventilation, need for Sildenafil and iNO

KEYWORDS: *Is Oxygen saturation index (OSI) is a valid and reliable marker of Neonatal hypoxemic respiratory failure as compared to Oxygenation index (OI) and can it add in taking decision in the Management of illness ?*

What is Already Known?

Oxygenation Index (OI) is the usual standard method for assessment of severity of Hypoxic Respiratory failure (HRF)/PPHN in Neonates which is a invasive, costly method and required skill.

What this Study will Add ?

Oxygen saturation Index (OSI) can be used reliably as surrogate marker of HRF/PPHN in neonates which does not require vascular puncture, cost effective and easily monitored continuously.

We have also taken steps in correlation of OSI in need of modification of treatment like change of ventilator mode, requirement of sildenafil and iNO and correlation with the corresponding OI values in HRF babies on ventilatory support.

Article History

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INTRODUCTION

After birth, rapid postnatal rise in oxygenation occurs during the normal fetal to neonatal transition. Preductal and postductal levels measured by way of pulse oximetry showed significantly lower postductal than preductal levels at 3, 4, 5, 10, and 15 minutes. (12)

Neonatal hypoxic respiratory failure (HRF) is a severe respiratory illness that affects 2% of all live births and is responsible for >33% of all neonatal mortality.[1]

About 15% of term infants and 29% of late-preterm infants admitted in a neonatal intensive care unit (NICU) develop respiratory morbidity. (2)

Respiratory failure in these newborns is often associated with persistent pulmonary hypertension of the newborn (PPHN), which contributes to hypoxemia. (3)

PPHN Persistent pulmonary hypertension, also called persistent fetal circulation, occurs due to an abnormal transition from fetal to extrauterine circulation. It can also result from poor lung vascularization in conditions such as congenital diaphragmatic hernia. Newborns with this diagnosis present with significant hypoxemia and respiratory failure. (8)

PPHN further complicates the course of respiratory failure in these infants and is a source of increased burden associated with health care costs as well as the indirect burden to these patients' families and caregivers.

The etiology of neonatal HRF/PPHN includes aspiration of meconium, respiratory distress syndrome, pneumonia, congenital diaphragmatic hernia, and oligohydramnios. Additionally, exposure to specific drugs—including non-steroidal

anti-inflammatory drugs (NSAIDs) and anti-depressants—during pregnancy is associated with increased prevalence of PPHN among neonates. Each condition may cause an increase in pulmonary shunting, limited lung volume, decreased compliance, or a combination of all three of these pathogeneses, resulting in hypoxemia, hypercarbia, and acidosis, all of which increase the morbidity in neonates with HRF. (4) Humoral mediators such as endothelin-1, and arachidonic acid metabolites such as leukotrienes and thromboxane and lack of vasodilators such as nitric oxide (NO) and prostacyclin (PGI_2) contribute to high Pulmonary vascular resistance (PVR) (10,11)

The standard treatment for neonatal HRF/PPHN includes conventional mechanical ventilation, respiratory alkalosis, ionotropic support, systemic infusion of vasodilators, neuromuscular blockade, and sedation. Traditional neonatal HRF therapies, including mechanical ventilation, have failed to reduce the mortality rate and often resulted in the use of more invasive procedures, including extracorporeal membrane oxygenation (ECMO). New and advanced treatments including administration of exogenous surfactant, inhaled nitric oxide, high-frequency ventilation, and ECMO have improved survival rates among neonates with HRF.(5) The approval of inhaled nitric oxide has dramatically changed treatment for PPHN, although it has not reduced mortality. (9)

Severity of HRF/PPHN

Oxygenation index is more commonly used during medical management of PPHN since it also takes into the consideration of ventilator support.

Oxygenation index is calculated as:

OI = MAP×FiO2×100/PaO2

MAP is the mean airway pressure provided by the ventilator.

OI below 10 is usually considered to be normal, OI between 10 -15 is considered to be mild PPHN, whereas OI of 15-20 is considered to be moderate PPH, OI >20 is severe PPHN.

Although both, the SNAP (Score of Neonatal acute physiology) score and highest OI, are useful and similar in predicting outcome of HRF, OI is preferable because of its ease of use.(13)

OI has traditionally been the assessment tool for acute lung disease in newborn and need for arterial sampling is its major limitation.

Continuous monitoring of these babies is done by measuring oxygen saturation with pulse oximeter (SpO2). SpO2 is linearly related to partial pressure of oxygen in the middle portion of oxygen dissociation curve. Most of the sick children on ventilatory support fall in this range.

Hence noninvasive Oxygen saturation index (OSI) can be used in lieu of OI. OSI is calculated by dividing the product of mean airway pressure (MAP) and FiO2 with SpO2, and has been validated in pediatric population [6]. However, there are no prospective studies have been done exclusively in neonates.

METHODS

Data Source

This was a Prospective cross-sectional cohort study conducted in Government medical College, TamilNadu from March 2022 to February 2023. The institute has an administrative patient-level database which includes inpatient in Level 3 NICU.

The data include patient demographic information (age, sex, admit source, admit type, discharge status, etc), procedural and diagnosis codes with procedure date, detailed insurance plan with financial class information, patient-level costs, and hospital reimbursement.

Study Population

The study population was All neonates who had a diagnosis of HRF/PPHN (idiopathic PPHN [ICD-9-CM code: 747.83; ICD-10-CM code: P29.3] with or without meconium aspiration [ICD-9-CM codes 770.11, 770.12; ICD-10-CM codes: P24.00, P24.01]) in the inpatient setting during the identification period (March 2022 to February 2023)

The first hospitalization (from admission date to discharge date) during this period which included an HRF/ PPHN diagnosis was defined as the index hospitalization.

Study variables

Patient characteristics including sex, most common comorbid condition were examined for the hospitalization period. To depict clinical care for hospitalized infants with HRF/PPHN, clinical procedure and treatments (like antibiotics, surfactants, inhaled nitric oxide, and sildenafil) were also examined

Study Outcome

Primary outcome

- number of neonates requiring change to invasive ventilation from non invasive ventilation
- number of infants requiring change in mode of ventilation

Secondary outcome

- duration of ventilation
- need for initiation of iv sildenafil
- need for iNO
- requiring reintubation within 24 hours.

Statistical Analysis

All study variables including demographics and outcomes were analyzed descriptively among the overall infant population and among preterm and T/NT infants in the study sample. Linear correlation between OI and OSI were analysed and Pearson correlation coefficient was calculated along with p-Value. Means were provided for continuous variables. Numbers and percentages were provided for categorical variables. All analysis were conducted using Statistical software SPSS 2.0

Results

Demographic and Clinical characteristics

The study included a total of 41 infants with HRF/PPHN during index hospitalization, including 53(99%) term and 1 Late preterm. Additionally, the prevalence of HRF/PPHN was 52% among Term and 2% among preterm infants in the NICU. Overall, most infants were male22 (53.6%) and 2 patients had respiratory distress syndrome (5.0%), followed by 3 patients having patent ductus arteriosus (7.3%). Mean birth weight of enrolled babies was 2.990 Kg. Table 1

Most common cause of PPHN /HRF in our study was Meconium aspiration syndrome(36.5%) followed by Post natal hypoxia(21.9%), Black PPHN and Sepsis(14.6%each). Pneumonia and RDS was cause for PPHN in 7.3% and 4.8% respectively.

Table 1

SEX	Frequency	percent
Male	22	53.5
Female	19	46.5
Cause of PPHN		
Black PPHN	6	14.6
MAS	15	36.5
Pneumonia	3	7.3
Post natal hypoxia	9	21.9
RDS	2	4.8
Sepsis	6	14.6
Total	41	100.00

Table 2: Treatment Patterns during Index Hospitalization

Mode of Ventilation	Frequency	Percent
TCPL	24	57.5
TCPL then HFOV	17	42.5
Total	41	100
	Mean	Std. Deviation
No Of Days of Ventilation	5.00	1.43

41 Babies with HRF/PPHN received adequate ventilation during hospital stay out of which 17 patients(42.5%) were initially put on TCPL mode (time cycled pressure-limited) which later required HFOV (High frequency oscillatory ventilation) while 24 patients required TCPL ventilation only.

Mean duration of ventilation was 5.00 days with standard deviation 1.43 (Table 2)

Number of babies requiring Reintubation for extubation failure were 7 (17.0%).Most common reason for extubation failure was ET tube induced subglottic stenosis (upper airway obstruction) which was treated with periextubation IV Dexamethasone and Adrenaline nebulisation.

Most infants with HRF/PPHN received antibiotics (95.9%) 16 patients (39.0%) required inhaled nitric oxide, 28(68.2%) babies also required Sildenafil infusion and 4 babies received surfactants. (Table 3)

Table 3

	Frequency	Percent
Inhaled NO	16	39.0
Sildenafil	28	68.2
Reintubation	7	17.0

OSI vs OI

Table 4 and 5 showing severity of PPHN/HRF according to OI and OSI respectively.

Table 4

Oxygenation Index	Frequency	Percent
<10 (Normal)	9	21.9
10-15 (Mild)	13	31.7
16-20 (Moderate)	10	24.3
21-25 (Severe)	5	12.1
>25 (Very severe)	4	9.7
Total	41	

Table 5: Showing Frequency of a Particular Value of OSI in Neonates

Oxygen Saturation Index	Frequency	Percent
<5(Normal)	5	12.1
5-10 (Mild)	14	34.1
11-15 (Moderate)	13	31.7
16-20 (Severe)	6	17.0
>20 (Very Severe)	3	7.3
Total	41	

Table 6 :Correlation between OSI and OI is depicted in table 6

	Pearson correlation coefficient (r)	p- Value
OI and OSI	0.919	0.001

Graphic representation of Correlation is sown in figure 1

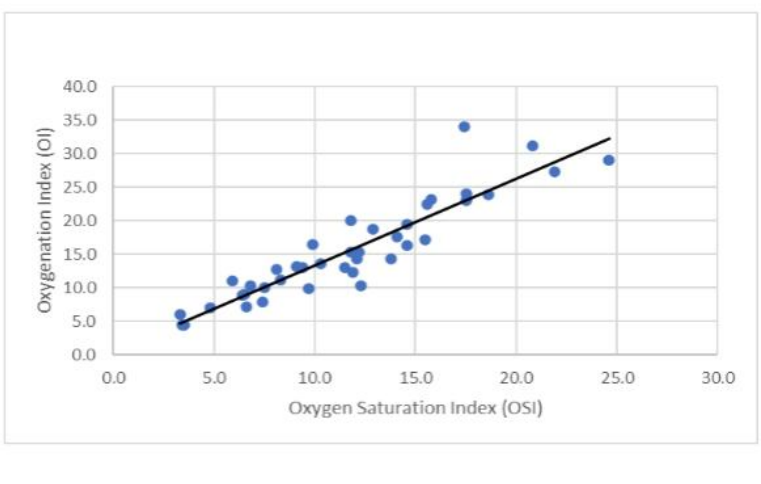


Figure 1: Sensitivity and Specificity of OSI As Compared To Different Values of OI Have Been Depicted In Figure 2

Oxygen Saturation Index cut off for different Oxygenation Index

Oxygenation Index	Cut off value	Sensitivity	Specificity
<10 (Normal)	6.15	55.6%	3.2%
10-15 (Mild)	6.7	92.3%	25.9%
16-20 (Moderate)	11.65	88.9%	58.1%
21-25 (Severe)	15.7	80.0%	88.6%
>25 (Very severe)	17.45	75.0%	91.7%

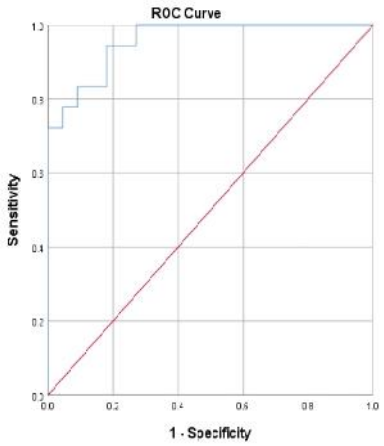
Figure 2:

Figure 3 depicts ROC analysis.

ROC analysis shown in graph depicted high sensitivity and specificity of OSI at various cut-offs of OI with area under curve (AUC) depicting that OSI very well predict the severity of HRF/PPHN.

ROC analysis

Cut off value for OSI	Area	Asymptotic 95% Confidence Interval		Sensitivity	Specificity	P value
		Lower Bound	Upper Bound			
11.55	0.957	.904	1.000	94.44%	81.8%	0.0001



Out of 41 babies, 13 babies expired and mortality rate was 31.7%.

DISCUSSION

Persistent pulmonary hypertension of the newborn (PPHN), previously referred to as persistent fetal circulation, is a syndrome of impaired circulatory adaptation at birth (14). The hallmark of PPHN physiology is sustained elevation of pulmonary vascular resistance (PVR) and persistent hypoxemia after birth (15). Despite advances in understanding of perinatal pathophysiology and neonatal management strategies, its prevalence (2 per 1000 live births) has not changed significantly (15). The vast majority of infants with PPHN are born at term or near term, although around 2% cases are born prematurely (16). Mortality has not changed (5–10%) and PPHN remains as one of the leading causes of critical illness in the neonatal intensive care unit (NICU)(17)

PPHN is secondary to impaired or delayed relaxation of the pulmonary vasculature associated with a diverse group of cardiopulmonary pathologies such as meconium aspiration syndrome (MAS), congenital diaphragmatic hernia

(CDH), congenital pneumonia, hypoxic ischemic encephalopathy (HIE / perinatal asphyxia), premature prolonged rupture of membranes (pPROM), respiratory distress syndrome (RDS) and underlying or associated congenital heart disease (CHD) (18)

Hypoxemic respiratory failure is associated with increased risk of mortality, morbidity, and worse neurological outcomes.[19,20] Oxygenation index (OI) is routinely used as an indicator of severity of HRF in neonates, with an arbitrary cutoff of 15 or less for mild HRF, between 16 and 25 for moderate HRF, between 26 and 40 for severe HRF, and more than 40 for very severe HRF.[21]

Oxygenation index (OI) has been used as a marker in clinical management and clinical trials for initiating therapies including inhaled nitric oxide in infants with HRF and pulmonary hypertension (22) and for administering and evaluating response to surfactant therapy.[23] Oxygenation index higher than 40 is used as a criterion for consideration of extracorporeal membrane oxygenation.[24] Oxygenation index has also been proposed as a predictive marker for neonatal outcomes, including mortality. Limitations of OI include the need for an indwelling arterial catheter for frequent sampling and that it is an intermittent measurement of oxygenation status by nature.

The advantages of OSI include that it is noninvasive and allows continuous monitoring of oxygenation status. Oxygen saturation index has been validated in pediatric intensive care unit patients as a reliable index for assessing severity of respiratory failure and lung injury (25)

To our knowledge, there are very few conclusive studies in world and more so in India, which compare and correlate OSI and OI in HRF in neonates. It is evident that HRF/PPHN has higher mortality rate and need prolonged cardiopulmonary support in the surviving neonates, it is important to evaluate the noninvasive methods of monitoring the severity of PPHN instead of ABG which is costly, invasive and requires skills.

In our study, we found a good linear association of OSI, with OI,with pearson correlation coefficient of 0.919 and P-value of 0.001.

In ROC analysis, area under curve was 0.957 with asymptomatic 95%confidence interval of 0.904 to 1.000 and P-value of 0.001

Table 7: Accuracy Measures Based on Derived Values of OI

Cutoff AUC (Area under Curve)
Derived OI ≥10 Derivation (n=125) 0.91 Validation (n=40) 0.86
Derived OI ≥15 Derivation (n=108) 0.92 Validation (n=38) 0.89
Derived OI ≥ 20 Derivation (n=27) 0.92 Validation (n=21) 0.90

The above table 7 prepared after using regression equation for deriving the OI from OSI and shown strong discriminative ability of our derived OI value to rule in those neonates with HRF, within the OI cutoffs from 10 to >20.

Considering that HRF/PPHN can vary from mild hypoxemia with minimal respiratory distress to severe hypoxemia and cardiopulmonary instability, the overall goal of treatment is to improve oxygen levels in the blood with various vasodilators including inhaled nitric oxide.

OSI shown a good correlation with OI for monitoring the severity of HRF/PPHN and help in deciding the escalation and de-escalation of treatment plan.

The results or our study were comparable to the findings of Ramnathan et al (7)

Strength and Limitation of the study

Strength of the study – Most of the neonates were term neonates in whom HRF/PPHN were significant as compared to preterm because of which we found more significant correlation of OSI with OI. We have not included more preterm neonates as there are less evidence for use of HFOV and iNO in these preterm groups.

This study has certain limitations. One of those is that timing of vascular puncture to measure ABG were purely at clinician's discretion. We have tried our best to match the timing of ABG sampling with SpO2 recording from pulse oximeter (MASIMO,Rad7 with Signal Extraction Technology).. Maximum efforts taken to control some variables which can affect the association of OSI with OI like temperature, pH, pCO2 which can affect Oxygen dissociation curve. Certain other factors like effect of duration of antibiotics, blood transfusion, hypothermia were not studied.

CONCLUSION

A strong correlation of OSI with OI was found in our study. OSI was strongly predictive of severity of HRF in the ventilated neonates and was in agreement with the OI values which correlated with modification in treatment like change in mode of ventilation, need for Sildenafil and iNO

We found Oxygenation saturation index (OSI) as a useful non-invasive tool for assessment of severity of hypoxemic respiratory failure in neonates and also to monitor the response to therapy on a continuous basis.

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