Original Article

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Paediatrics Section

# Correlation of Oxygen Saturation Index and Oxygenation Index in Hypoxaemic Respiratory Failure among Neonates

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## ABSTRACT

**Introduction:** Hypoxaemic Respiratory Failure (HRF) is severe arterial hypoxaemia that is refractory to supplemental oxygen. Oxygen Saturation Index (OSI) can be an alternate method of diagnosing and assessing the severity of HRF as it uses Oxygen Saturation ($SpO_2$) in place of Partial Pressure of Oxygen ($PaO_2$) and may be utilised with reasonable sensitivity and specificity.

**Aim:** To evaluate the correlation between OSI and Oxygenation Index (OI) in HRF in neonates.

**Materials and Methods:** The prospective observational study was conducted in Kempegowda Institute of Medical Sciences and Hospital, Bengaluru, Karnataka, India, from December 2016 to July 2018. Fifty neonates who were admitted to Neonatal Intensive Care Unit (NICU) and conventionally ventilated in view of HRF were included. Arterial blood gases in the first 24 hours of life and corresponding oxygen saturations and ventilator settings were recorded. OI and OSI was calculated using the standard formula and their correlation was analysed.

**Results:** The neonates were all on first day of life at admission to NICU and were invasively ventilated due to HRF. The mean birth weight was 1.89±0.84 kg. Of the 50 neonates, 22 (44%) were preterm babies (<34 weeks), 17 (34%) belonged to late preterm group (34 weeks to 36 weeks +6 days), 9 (18%) were term babies (>37 weeks), two neonates were extremely preterm (less than 28 weeks). In this study, OSI and OI significantly associated and correlated (p-value <0.01) with a correlation coefficient r=0.727. Area under the Receiver Operating Characteristic (ROC) curve for OSI was 0.912 which indicates that OSI is an excellent test to assess the severity of HRF.

**Conclusion:** That OSI can be used to diagnose and assess the severity of lung disease in neonates having HRF.

**Keywords:** Arterial hypoxemia, Arterial blood gases, Neonatal intensive care unit, Pulse oximetry

## INTRODUCTION

The HRF is a relative deficiency of oxygenation, often associated with insufficient ventilation. This deficiency is reflected by progressive respiratory and metabolic acidosis and remains a persistent challenge in the management. The overall scope of the problem was described in a large cohort study by Angus DC et al., who found that the overall incidence of HRF in very low, low, and normal birth weight infants, as measured by the overall rate of mechanical ventilation, was 18 per 1000 live births [1]. In a study conducted by Eriksen V et al., babies treated for Persistent Pulmonary Hypertension (PPHN) of the newborn were followed up 5-11 years of age and had found a higher frequency of learning disabilities, higher rates of sensorineural hearing loss than a matched control group [2]. Other morbidities include neurodevelopmental abnormalities, cognitive delay, and a high rate of chronic childhood diseases. The incidence of Acute Lung Injury (ALI) has been described recently in the adult population, with the estimate that, each year in the United States, there are >190,000 cases of ALI, with a mortality rate of almost 40% [3].

In 1994, the American-European Consensus Conference on Acute Respiratory Distress Syndrome (ARDS) agreed to standardised definitions in adults that continue to be used presently [4]. These well accepted definitions require: a) an acute onset of the process; b) bilateral infiltrates on chest radiograph; c) no evidence of left atrial hypertension; and d) a defined degree of hypoxia. The extent of hypoxia is defined by a partial pressure of oxygen/fraction of inspired oxygen, or $PaO_2/FiO_2$ (P/F) ratio, of ≤300 to meet the definitions of ALI, and a P/F ratio of ≤200 to meet the definition of ARDS. Many clinicians consider (OI) {$FiO_2 \times Paw/PaO_2$} to be a better indicator of lung injury. Though, both $PaO_2/FiO_2$ ratio and OI have been used frequently to diagnose ALI and ARDS, it is difficult in critically ill newborns of NICU in view of serial arterial punctures for arterial blood sampling.

The HRF is a clinical syndrome that occurs in diverse settings. HRF can occur in infants with Meconium Aspiration Syndrome (MAS), Respiratory Distress Syndrome (RDS), idiopathic PPHN of the newborn, and congenital diaphragmatic hernia [5].

The OI is used to assess the severity of hypoxic respiratory failure and the intensity of ventilator support required to maintain oxygenation. As it uses Mean Airway Pressure (MAP) it is the better indicator than $PaO_2/FiO_2$ ratio. But it is invasive, requires an indwelling arterial line or arterial puncture to obtain a blood gas sample. Oxygenation can be continuously and non invasively assessed using pulse oximetry. The use of OSI can be an alternate method of assessing severity of HRF [6]. It uses saturation instead of $PaO_2$ which can be measured by a simple pulse oximetry thereby avoiding painful arterial punctures in sick neonates.

Hence, this study aimed to correlate OI with OSI in neonates with HRF thereby invasive technique can be avoided for further management purposes.

## MATERIALS AND METHODS

The prospective observational study was conducted in Kempegowda Institute of Medical Sciences and Hospital, Bengaluru, Karnataka, India, from December 2016 to July 2018. Ethical clearance was obtained from Institutional Ethical Committee with reference letter no. KIMS/IEC/D-56/2016. Fifty newborn who were admitted to KIMS NICU in the Department of Paediatrics were chosen. This study included both term and preterm neonates who had respiratory distress and mechanically ventilated in view of respiratory failure and who were continuously and serially monitored by arterial blood gases and pulse oximetry. Sample size of 50 was considered with purposive sampling with 95% confidence level and margin of error of ±15%.

**Inclusion criteria:** Term and preterm newborn intubated and mechanically ventilated due to HRF were included in this study.

**Exclusion criteria:** Newborn on ventilator due to apnoea of prematurity, congenital heart disease, congenital lung malformations were excluded in this study.

### Study Procedure

Postductal arterial blood gases in the first 24 hours of life and corresponding oxygen saturations were collected in neonates. Blood samples of around 0.5 mL each neonate was drawn by standard technique and sampling errors were avoided. Samples were sent at ideal temperature and blood gas analysis was done. Corresponding saturation was recorded by pulse oximetry.

Neonates were mechanically ventilated by dragger ventilator and before starting the therapeutic measures ventilator settings was recorded. Ventilator settings taken were Peak Inspiratory Pressure (PIP), Positive End Expiratory Pressure (PEEP), Fraction of Inspired Oxygen ($FIO_2$), Mean Arterial Pressure (MAP):

OI was calculated by the formula:

$$OI=MAP\ (in\ cmH_2O)\times FiO_2\times 100/PaO_2.$$

OSI was calculated by the formula:

$$OSI=(MAP)\times(FiO_2))/(SpO_2).$$

## STATISTICAL ANALYSIS

Descriptive and inferential statistical analysis was carried out in the present study Significance was assessed at 5% level of significance. Analysis of variance (ANOVA) was used to find the significance of study parameters between $PaO_2/FiO_2$, OI and OSI. Chi-square/ Fisher-Exact test was used to find the significance of study parameters on categorical scale like $PaO_2/FiO_2$, PIP, $FiO_2$ and OI with OSI. Pearson correlation between study variables was performed to find the degree of relationship between OI and OSI with oxygen saturation, PIP and $PaO_2/FiO_2$. The p-value of <0.05 <p<0.10 was suggestive of significance. Receiver Operating Characteristic (ROC) curve analysis was performed to find the predictability of study variables for predicting the outcome. The statistical software namely Statistical Package for the Social Sciences (SPSS) version 18.0, and R environment version 3.2.2

## RESULTS

The neonates were all on first day of life at admission to NICU and were invasively ventilated due to HRF. The mean birth weight was 1.89±0.84 kg. Of the 50 neonates, 22 (44%) were preterm babies (<34 weeks), 17 (34%) belonged to late preterm group (34 weeks to 36 weeks +6 days), 9 (18%) were term babies (>37 weeks), two neonates were extremely preterm (<28 weeks).

The most common cause for HRF in neonates was RDS which comprised of Hyaline Membrane Disease (HMD) and congenital pneumonia. Other causes were MAS (10%) and PPHN of newborn (4%). An 86% of neonates admitted for HRF had HMD.

Postductal $SpO_2$ was between 90-94% in 16 (32%) neonates, 23 (46%) neonates had $SpO_2$ between 75-89%, 11 (22%) neonates had $SpO_2$ between 95-97%. $PaO_2$ observed in this study was >80 mmHg in 34 (64%) neonates, 60-79 mmHg in 15 (30%) neonates, and 40-59 mmHg in 1 (2%) neonate.

Partial pressure of oxygen/Fraction of inspired oxygen ($PaO_2/FiO_2$) ratio, which indicates the severity of HRF, were calculated. Mild hypoxemia ($PaO_2/FiO_2$ 200 to ≤300 mmHg) was seen in 1 (2%) patient, moderate ($PaO_2/FiO_2$ 100 to ≤200 mmHg) in 33 (33%), and severe ($PaO_2/FiO_2$ ≤100 mmHg) in 16 (32%).

The OI observed was ≤5 in 13 neonates (26%), 5.1-15 in 37 (74%) neonates and >15 in none. The OSI was ≤3 in 2 (4%) neonates, 3.1 to 6.5 in 26 (52%) neonates, >6.5 in 22 (44%) neonates.

In this study, four neonates who had $PaO_2/FiO_2$ of <100 mmHg had a OSI between 3.1 to 6.5 and 12 had OSI more than 6.5. Only two neonates with $PaO_2/FiO_2$ of 100-200 mmHg had OSI <than 3, 22 neonates had OSI between 3.1-6.5 and 9 had OSI of more than 6.5 [Table/Fig-1].

| $PaO_2/FiO_2$ | Oxygen saturation index | | | Total (n=50) | p-value |
|---|---|---|---|---|---|
| | ≤3 (n=2) | 3.1-6.5 (n=27) | >6.5 (n=21) | | |
| <100 | 0 (0%) | 4 (14.8%) | 12 (57.1%) | 16 (32%) | 0.006 |
| 100≤200 | 2 (100%) | 22 (81.4%) | 9 (42.8%) | 33 (66%) | |
| 200≤300 | 0 (0%) | 1 (3.7%) | 0 (0%) | 1 (2%) | |
| Mean $PaO_2/FiO_2$ | 177.00±16.50 | 148.01±39.79 | 105.05±40.15 | 130.26±45.23 | 0.001 |

**[Table/Fig-1]:** Comparison of $PaO_2/FiO_2$ with oxygen saturation index.
Chi-square test; p-value <0.05 is considered as significant

Only one neonate had $PaO_2/FiO_2$ between 200-300 and the corresponding OSI was between 3.1-6.5. From the above data it was observed that there is a significant association between $PaO_2/FiO_2$ and OSI with p-value of 0.006. The [Table/Fig-2] showed a significant association between OI and OSI with p-value of 0.007.

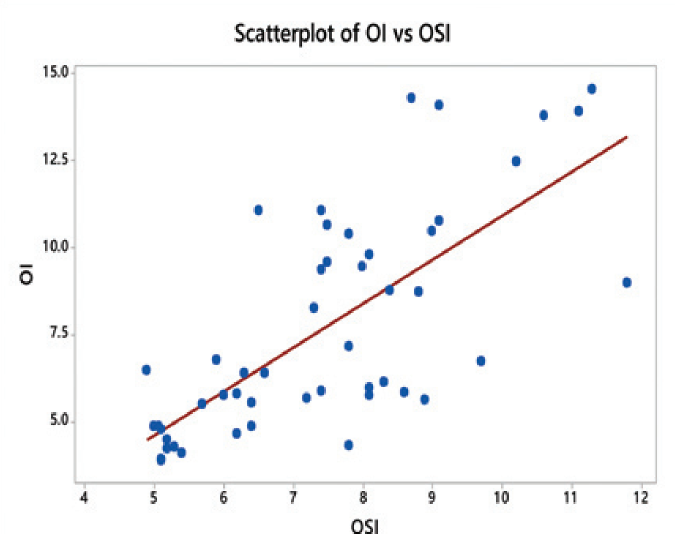
| Oxygenation index | Oxygen saturation index | | | Total | p-value |
|---|---|---|---|---|---|
| | ≤3 | 3.1-6.5 | >6.5 | | |
| ≤5.0 | 1 (50%) | 11 (40.7%) | 1 (4.7%) | 13 (26%) | 0.007 |
| 5.1-15.0 | 1 (50%) | 16 (59.25%) | 20 (95.23%) | 37 (74%) | |
| >15.0 | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | |
| Mean±SD Oxygenation index | 5.66±1.16 | 6.26±2.27 | 9.44±3.29 | 7.64±3.15 | 0.001 |
| Pearson correlation | | | | | |
| | r value | p-value | | | |
| Oxygen saturation index vs Oxygenation index | 0.727 | <0.001 | | | |

**[Table/Fig-2]:** Comparison of OI with OSI.
Chi-square; p-value <0.05 is considered as significant

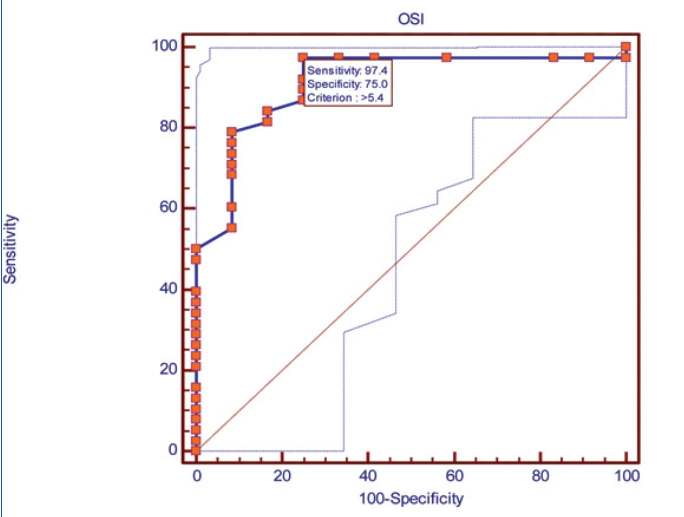
Pearson correlation coefficient was calculated to find correlation between OI and OSI which showed a positive correlation with r value of 0.727 [Table/Fig-3]. ROC curve analysis was done for OSI which showed a high sensitivity of 97.37% and a specificity of 75.00%. The area under the ROC curve was 0.912 which implies the overall accuracy of the test is good and hence OSI can be used with good accuracy in place OI in neonates with HRF [Table/Fig-4,5].

| Variables | ROC results to predict severity | | | | Cut-off | AUROC | SE | p-value |
|---|---|---|---|---|---|---|---|---|
| | Sensitivity | Specificity | LR+ | LR- | | | | |
| OSI | 97.37 | 75.00 | 3.89 | 0.035 | >5.4 | 0.912 | 0.05 | <0.001** |

**[Table/Fig-3]:** ROC curve analysis between OI and OSI.
ROC: Receiver operator curve; LR: Linear regression; AUROC: Area under the ROC curve; **p-value <0.05 is considered as significant




**[Table/Fig-4]:** Pearson correlation between OI and OSI by scatter plot.




**[Table/Fig-5]:** Receiver Operating Characteristic (ROC) curve analysis for OSI.

# DISCUSSION

Hypoxemic respiratory failure remains an important cause of morbidity and mortality in neonates of NICU. As there is only a few studies on HRF among neonates as it requires an invasive procedure to calculate $PaO_2$. The authors hope this study might bring out the importance of using OSI in place of OI as it is non invasive.

In a study by Gnanaratnem J and Finer NN hypoxic respiratory failure was the most common problem seen in the infants admitted to NICU units [7]. In preterms, the most common condition observed was RDS due to HMD caused by surfactant deficiency. In term and near term infants it is usually the result of MAS, sepsis, pulmonary hypoplasia, and primary pulmonary hypertension of the newborn. The present study had a similar result that RDS being the most common in preterm neonates.

In this study, RDS was more common in preterm then in late preterm which is similar to the study by Stoelhorst GMJ et al., and Ventolini G et al., where the incidence of RDS decreases with advancing gestational age. A 60-80% occurs in infants born at 26-28 weeks to approximately 15-30% in those born at 32-36 weeks [8,9].

As $O_2$ saturation varies non linearly with the $PaO_2$, $SpO_2$ can be used in place of $PaO_2$ for specific saturation ranges because at extreme values oxygen saturation does not correlate well with $Pao_2$. Sarkar M et al., studied the relation between $SpO_2$ and $PaO_2$ [10]. The sigmoid shape of the oxyhaemoglobin (Hb) dissociation curve reflects this co-operative interaction.

A study by Thomas NJ et al., on defining acute lung disease in children with the OSI, the correlation coefficient observed between OSI: P/F ratio <200 was 0.84 and OSI: P/F ratio <300 was 0.84 again which is more towards positive correlation [6]. It is similar to the present study where OI and OSI were positively correlated with correlation coefficient of 0.727.

This was similar to the study done by Doreswamy SM et al., where the Pearson product moment correlation (r) for OSI and OI was 0.91; which in the present study was 0.727 both being a positive correlation [11]. In another study by Rawat M et al., OSI was used to define severity of HRF; the mean values of OSI and OI showed a correlation coefficient of 0.952 in neonates [12].

Similarly, in the study by Doreswamy SM et al., OSI had a sensitivity of 89.4% and specificity of 93.6% with moderate severity of OI value 5-15 [11]. OSI had a sensitivity of 100% and specificity of 93.7% with OI value of more than 15. In the same study, OSI of 3 and 6.5 corresponded to OI of 5 and 15, respectively with high sensitivity and specificity whereas in present study sensitivity was 97.37% and specificity was 75%.

## Limitation(s)

Movement of the limb during the technique of pulse oximetry may interrupt reading. Due to non linear correlation of $PaO_2$ and $SpO_2$ in oxygen haemoglobin dissociation curve OSI can only be utilised in patients <98% saturated.

# CONCLUSION(S)

In this study, OSI and OI are significantly associated with positive correlation by Pearson correlation test. Oxygen saturation has been used to assess the severity of HRF previous studies, in this study, ROC analysis was done for OSI which showed the area under the ROC of 0.912 which again indicates that OSI is an excellent test to assess the severity of HRF. Hence, it was concluded that OSI has more of positive correlation with OI in neonates with HRF, and it can be used to diagnose and quantify the severity of lung disease.

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