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Original Research Article

The utility value of ROX index and modified ROX index in determining the efficiency of HFNC in children admitted with respiratory distress

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ABSTRACT

Background: The ROX index is defined as the ratio of SpO_2/FiO_2 to respiratory rate. The modified ROX index or ROX-HR index is defined as the ratio of ROX index/heart rate×100. The aim of the study was to determine the utility of the ROX index and the modified ROX index as predictors of initiation and efficiency of HFNC in children admitted with respiratory distress.

Methods: This prospective observational study included 133 children with respiratory distress, who received HFNC. The ROX index, and modified ROX index were measured, and outcomes were recorded.

Results: Total number of study subjects were 133. Statistically significant increase was seen in ROX index and modified ROX index at follow up (p value<0.05). Interpretation of the area under the ROC curve showed that the performance of ROX index and modified ROX index at '0' hour was outstanding. ROX Index and modified ROX Index at a Cut-off of ≤4.7959 and ≤2.5579 respectively at initiation i. e.; at '0' hour predicted HFNC requirement. In prediction of HFNC requirement ROX index at '0' hour had a sensitivity, specificity, positive predictive value, and negative predictive value of 88.24%, 87.84%, 93%, and 80.2% respectively, and modified ROX index had 78.68%, 93.24%, 95.5%, and 70.4% respectively. Low ROX and modified ROX indices at '0' hour predicted prolonged ICU and hospital stays, as well as extended HFNC duration.

Conclusions: Both ROX index, and modified ROX index were good predictors of HFNC requirement.

Keywords: Heart rate, Respiratory rate, High flow nasal cannula, Respiratory distress

INTRODUCTION

Recently, heated humidified high flow nasal cannula (HFNC) has gained popularity and is used as standard respiratory support in pediatric patients with acute respiratory distress. Several studies have shown the benefits of HFNC, such as good outcomes, improvement in physiologic parameters, and decreased intubation rates.[1-3] Understanding and predicting the outcomes of HFNC treatment are crucial for improving bedside patient care and monitoring.[4-8] Additionally, the pediatric population has a varied range of vital signs. Heart rate and respiratory rates are commonly measured vital signs, and incorporation of these vital signs into oxygen indices will evaluate the clinical progress.

Roca et al evaluated the utility of SpO_2/FiO_2 (SF) ratio in pneumonia patients with hypoxemic respiratory failure and described the respiratory rate oxygenation (ROX) index, which is the ratio of SF to the respiratory rate (RR).[9,10] A subsequent study was conducted to validate the ROX index in adults with pneumonia requiring HFNC treatment.[11] But, studies are scanty on the usefulness of the ROX index in pediatric patients.

Heart rate is a commonly measured vital sign, and incorporation into the ROX index may improve the diagnostic accuracy of the index. One such index is ROX-HR index or Modified ROX index. ROX-HR index was defined as the ratio of ROX index over HR (beats/min), multiplied by a factor of 100. In his study by Ken Junyang Goh validated the ROX-HR index as a promising tool in the early identification of patients who are at high risk of HFNC failure. Tachycardia recorded as early as 1 hour into HFNC therapy has been found to be associated with HFNC failure.[12,13]

Therefore, the study of such bedside indices for prediction of HFNC outcomes could guide clinical decision making. The aim of the study was to assess the utility of the ROX index and modified ROX index in initiation of HFNC therapy, and evaluating its efficiency in pediatric patients with respiratory distress.

Aim and objective

The aim and objective of this study was to determine the utility of the ROX index and the modified ROX index as predictors of initiation and efficiency of HFNC in children admitted with respiratory distress.

METHODS

This study was a prospective observational study conducted during January 2022 to October 2022 at Sri Ramachandra Children's and Dental Hospital, Guntur, Andhra Pradesh, India.

Patients aged 1 month to 14 years with respiratory distress of any etiology and who received HFNC were included in the study.

Demographic data, vital parameters, ROX index, modified ROX index, and outcome parameters were taken. The ROX index, and modified ROX index were measured at 0, 1, 12, and 24 h after commencement of HFNC therapy. Primary outcomes like whether the child discharged or diseased were noted. Secondary outcomes like total duration of HFNC days, total duration of ICU stay, and total duration of hospital stay were recorded

Inclusion criteria

Children aged 1 month to 14 years, who were admitted to PICU with respiratory distress of any etiology, and treated with HFNC therapy were included in the study

Exclusion criteria

Children under the age of 1 month and over 14 years old, along with surgical cases involving congenital malformations and acute abdomen, trauma cases such as road traffic accidents and head injuries, children with congenital abnormalities, chronic lung disease, heart disease, chronic renal disease, and those with cerebral palsy were excluded from the study.

Ethical approval

This study was approved by Hospital ethics committee and written informed consents were obtained from the parents before inclusion in the study.

Statistical analysis

The presentation of the categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data with normal distribution were presented as the means±SD and the data with non-normal distribution as median with 25th and 75th percentiles (interquartile range). The comparison of the variables which were quantitative and not normally distributed in nature were analysed using Mann-Whitney Test. The comparison of the variables which were qualitative in nature were analysed using Chi-square test. Spearman rank correlation coefficient was used for correlation of duration of ICU stay (days), hospital stay, oxygen requirement, HFNC requirement with ROX index, and Modified ROX index. Receiver operating characteristic curve was used to find cut of point, sensitivity, specificity, positive predictive value and negative predictive value of ROX index, and Modified ROX index for predicting HFNC requirement.

The data entry was done in the Microsoft excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 25.0. For statistical significance, p value of less than 0.05 was considered statistically significant.

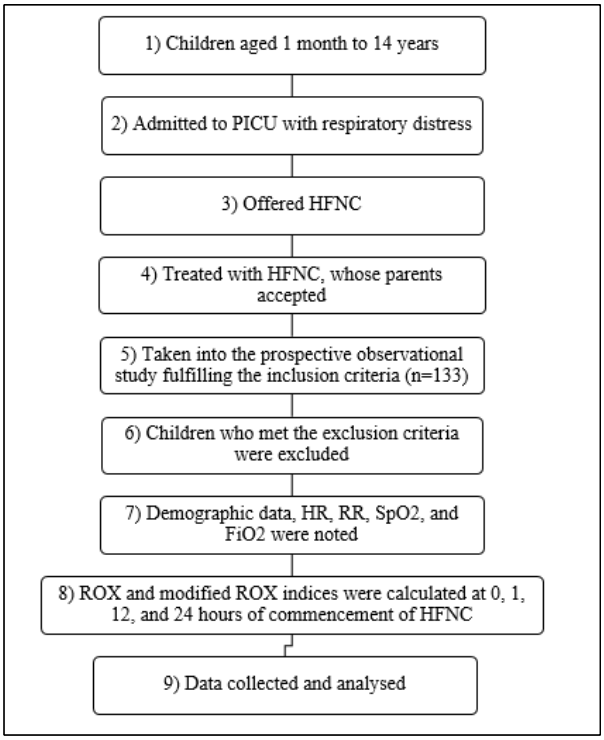

Figure 1: Study flow chart 1.

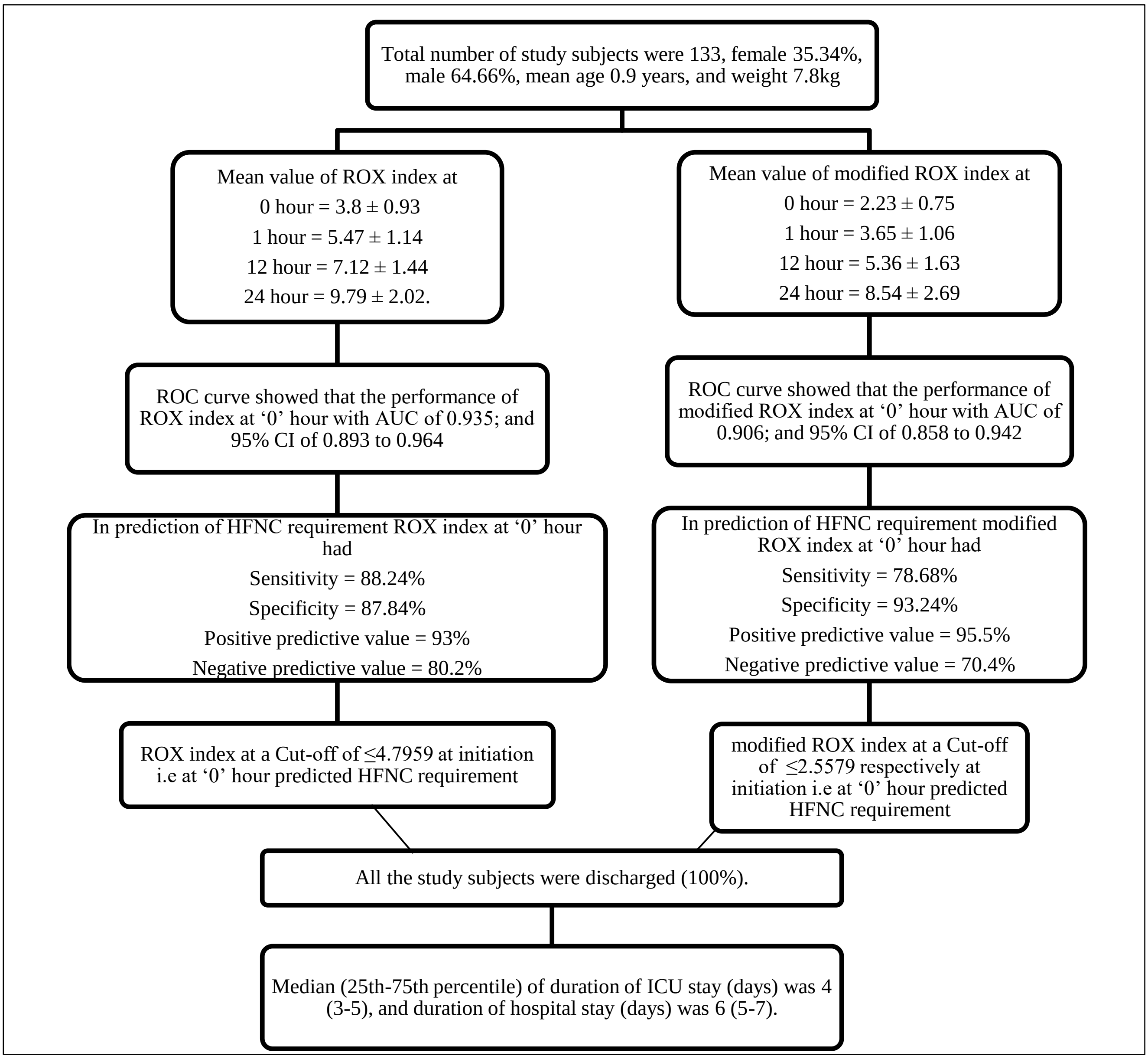

Figure 2: Study flow chart 2.

RESULTS

Total number of study subjects were 133. Distribution of gender was female 35.34%, male 64.66%, mean age (in years) was 0.9 (0.3-3), and weight (in kg) was 7.8 (4.7-11.8) (Table 1).

Table 1: Comparison of demographic characteristics of HFNC.

Demographic characteristics	HFNC (n=133)
Gender	
Female	47 (35.34%)
Male	86 (64.66%)
Age (years)	0.9 (0.3-3)
Weight (kg)	7.8 (4.7-11.8)

Mean value of heart rate (per minute) at 0, 1, 12, and 24 hours of study subjects was 175.19±19.8, 153.85±17.22, 136.84±16.63, and 118.56±14.61 respectively. Respiratory rate (per minute) at 0, 1, 12, and 24 hours of study subjects was 68.06±8.79, 53.98±7.42, 44.54±6.64, and 36.37±5.58, respectively.

Statistically significant reduction was seen in heart rate, and respiratory rate at follow up as compared to baseline value (p value<0.05) (Table 2). Mean value of ROX index at 0, 1, 12, and 24 hours of study subjects was 3.8±0.93, 5.47±1.14, 7.12±1.44, and 9.79±2.02 respectively. Mean value of modified ROX index at 0, 1, 12, and 24 hours of study subjects was 2.23±0.75, 3.65±1.06, 5.36±1.63 and 8.54±2.69 respectively. Statistically significant increase was seen in ROX index and modified ROX index at follow up as compared to baseline value (p value<0.05) (Table 3). ROC curves that extend above the diagonal line are regarded as demonstrating reasonable discriminatory ability in predicting the need for HFNC therapy. The parameters exhibited significant discriminatory power in predicting the requirement for HFNC, emphasizing their effectiveness in this regard. Interpretation of the area under the ROC curve showed that the performance of ROX index at '0' hour with AUC of 0.935; and 95% CI of 0.893 to 0.964 and modified ROX index at '0' hour with AUC of 0.906; and 95% CI of 0.858 to 0.942 was outstanding. In prediction of HFNC requirement ROX index at '0' hour had a sensitivity, specificity, positive predictive value, and negative predictive value of 88.24%, 87.84%, 93%, and 80.2% respectively. In prediction of HFNC requirement modified ROX index at '0' hour had a sensitivity, specificity, positive predictive value, and negative predictive value of 78.68%, 93.24%, 95.5%, and 70.4% respectively (Table 4). ROX index and modified ROX index at a Cut-off of ≤4.7959 and ≤2.5579 respectively at initiation i. e.; at '0' hour predicted HFNC requirement. Increasing trend of the above parameters was observed suggestive of clinical improvement. There is always a trade-off between sensitivity and specificity (any increase in sensitivity will be accompanied by a decrease in specificity). So we chose that variable as best in which combination of sensitivity and specificity gives the maximum predictive value i.e. maximum area under curve. So the above cut-offs were achieved. So overall both ROX index, and modified ROX index were good predictors of HFNC requirement (Table 4).

Table 2: Descriptive statistics of vitals of HFNC group.

Vitals	Mean±SD	Median (25th-75th percentile)	Range	P value
Heart rate (per minute) at 0 hour	175.19±19.8	176 (164-188)	110-210	-
Heart rate (per minute) at 1 hour	153.85±17.22	156 (142-168)	102-188	<0.0001
Heart rate (per minute) at 12 hours	136.84±16.63	140 (126-148)	94-188	<0.0001
Heart rate (per minute) at 24 hours	118.56±14.61	120 (108-130)	88-156	<0.0001
Respiratory rate (per minute) at 0 hour	68.06±8.79	68 (64-72)	44-96	-
Respiratory rate (per minute) at 1 hour	53.98±7.42	52 (50-58)	36-72	<0.0001
Respiratory rate (per minute) at 12 hours	44.54±6.64	44 (40-48)	30-68	<0.0001
Respiratory rate (per minute) at 24 hours	36.37±5.58	36 (32-38)	24-70	<0.0001

Table 3: Descriptive statistics of ROX and modified ROX indices of HFNC group.

Other parameters	Mean±SD	Median (25th-75th percentile)	Range	P value
ROX index at 0 hour	3.8±0.93	3.77 (3.333-4.332)	1.4-6.97	-
ROX index at 1 hour	5.47±1.14	5.52 (4.714-6.282)	2.61-8.6	<0.0001
ROX index at 12 hours	7.12±1.44	7.17 (6.149-8.167)	3.53-11	<0.0001
ROX index at 24 hours	9.79±2.02	9.26 (8.684-11)	3.43-16.5	<0.0001
Modified ROX index at 0 hour	2.23±0.75	2.16 (1.793-2.53)	0.74-5.03	-
Modified ROX index at 1 hour	3.65±1.06	3.5 (2.956-4.107)	1.61-7.63	<0.0001
Modified ROX index at 12 hours	5.36±1.63	5.1 (4.33-6.138)	1.91-11.58	<0.0001
Modified ROX index at 24 hours	8.54±2.69	7.85 (6.74-9.549)	2.2-17.31	<0.0001

Note: Paired t-test.

Table 4: Receiver operating characteristic curve of ROX index, modified ROX index for predicting HFNC requirement.

Variables	ROX index at 0 hour	Modified ROX index at 0 hour
Area under the ROC curve (AUC)	0.935	0.906
Standard error	0.016	0.0201
95% CI	0.893 to 0.964	0.858 to 0.942
P value	<0.0001	<0.0001
Cut off	≤4.7959	≤2.5579
Sensitivity (95% CI)	88.24% (81.6-93.1%)	78.68% (70.8-85.2%)
Specificity (95%CI)	87.84% (78.2-94.3%)	93.24% (84.9-97.8%)
PPV (95% CI)	93% (87.2-96.8%)	95.5% (89.9-98.5%)
NPV (95% CI)	80.2% (69.9-88.3%)	70.4% (60.3-79.2%)
Diagnostic accuracy	87.62%	83.33%

All the study subjects were discharged (100%). Median (25th-75th percentile) of duration of ICU stay (days) was 4 (3-5), and duration of hospital stay (days) was 6 (5-7) (Table 5). Significant negative correlation was seen between duration of ICU stay (days) with ROX index at '0' hour, and modified ROX index at '0' hour with correlation coefficient of -0.266, and -0.212 respectively. Significant negative correlation was seen between duration of hospital stay (days) with ROX index at ‘0’ hour, and modified ROX index at ‘0’ hour with correlation coefficient of -0.25, and -0.196 respectively. Significant negative correlation was seen between duration of HFNC requirement(days) with ROX index at ‘0’ hour, and modified ROX index at ‘0’ hour with correlation coefficient of -0.344, and -0.29 respectively. So low ROX and modified ROX indices at ‘0’ hour predicted prolonged ICU and hospital stay, as well as extended HFNC duration (Table 6).

Table 5: Outcome distribution of HFNC group.

Outcomes	HFNC
Discharged	133 (100%)
Duration of ICU stay (days)	4 (3-5)
Duration of hospital stay (days)	6 (5-7)
Duration of HFNC requirement (days)	2 (2-3)

Table 6: Correlation of duration of ICU stay (days), hospital stay, oxygen requirement, HFNC requirement with ROX index, modified ROX index in HFNC.

Variables	ROX index at 0 hour	Modified ROX index at 0 hour
Duration of ICU stay (days)		
Correlation coefficient	-0.266	-0.212
P value	0.002	0.015
Duration of hospital stay (days)		
Correlation coefficient	-0.250	-0.196
P value	0.004	0.024
Duration of HFNC requirement (days)		
Correlation coefficient	-0.344	-0.290
P value	0.0001	0.001

Note: Spearman rank correlation coefficient.

DISCUSSION

Our study aimed to determine the utility of the ROX and modified ROX indices as predictors of initiation and efficiency of HFNC in children admitted with respiratory distress to PICU. Total number of study subjects were 133, of which female 35.34%, male 64.66%, with a mean age (in years) was 0.9, and weight (in kg) was 7.8.

In our study the mean value of heart rate (per minute) at 0, 1, 12, and 24 hours of study subjects was 175.19±19.8, 153.85±17.22, 136.84±16.63, and 118.56±14.61 respectively, and respiratory rate (per minute) was 68.06±8.79, 53.98±7.42, 44.54±6.64, and 36.37±5.58, respectively. Indicating statistically significant reduction was seen in heart rate, and respiratory rate after initiation of HFNC, that to in 1st hour after initiation of HFNC, and continued to improve over the next hours as compared to baseline value (p value<0.05). When compared to previous studies, our study showed good correlation. In the study by Chang CC et al, there were significant improvements in heart rate, respiratory rate, pulse oximetry (SpO_2), S/F ratio, and ROX index score in the early HFNC period (0.5-8 h) and late HFNC period (8-24 h).[14]

In our study the mean value of ROX index at 0, 1, 12, and 24 hours of study subjects was 3.8±0.93, 5.47±1.14, 7.12±1.44, and 9.79±2.02 respectively, and modified ROX index was 2.23±0.75, 3.65±1.06, 5.36±1.63 and 8.54±2.69 respectively. There was a statistically significant increase seen in ROX index and modified ROX index after initiation of HFNC, as compared to baseline value (p value<0.05), suggesting clinical improvement. When compared to the study by Goh et al patients with HFNC failure had a significantly lower ROX and ROX-HR index and a significantly higher heart rates observed at 1, 2, 4, 10 and 12 hours of HFNC indicating HFNC failure.[15] In our study improvement of the indices after initiation of HFNC suggested clinical improvement, whereas in Goh et al study worsening of indices suggested HFNC failure. In line with our study, a study by Mustafa et al was also highlighted good utility of ROX index in predicting HFNC success as gradually improving ROX index predicted HFNC success or vice versa.[16]

In our study the interpretation of the area under the ROC curve showed that the performance of ROX index at ‘0’ hour with AUC of 0.935; and 95% CI of 0.893 to 0.964 and modified ROX index at ‘0’ hour with AUC of 0.906; and 95% CI of 0.858 to 0.942 was outstanding. In prediction of HFNC requirement ROX index at ‘0’ hour had a sensitivity, specificity, positive predictive value, and negative predictive value of 88.24%, 87.84%, 93%, and 80.2% respectively, and modified ROX index had 78.68%, 93.24%, 95.5%, and 70.4% respectively. When compared to study by Goh et al ROX and modified ROX indices appeared to have the highest diagnostic accuracy at 10 hours with an AUROC of 0.723 [95% confidence interval (CI) 0.605-0.862] and 0.739 [95% CI 0.626-0.853] for the ROX index and ROX-HR index, respectively.[15] Our study looked at the indices performance at ‘0’ hour to predict the requirement of HFNC and the above study looked at the ‘10’ hour performance to assess HFNC success/failure.

A study by Karim et al showed the mean ROX versus mROX at baseline and six-hour values was 59.81 versus 70.68 and 67.42 versus 74.88, respectively (all p>0.05) for predicting failure of HFNC. The AUC for ROX and mROX at baseline and at six hours were statistically indifferent. Only an mROX of 4.05 (mean value) and 3.34 (Youden’s J cut-off) had a sensitivity plus specificity at 156% and 163%, respectively. [17] Our study looked at the indices performance at ‘0’ hour to predict the requirement of HFNC and the above study looked at the base line and ‘6’ hour performance to assess HFNC failure. According to Li et al, Chen et al, both the ROX and mROX indices at 2 h after HFNC initiation can predict the risk of intubation after HFNC. Two hours after HFNC initiation, the mROX index had a higher area under the receiver operating characteristic curve (AUROC) for predicting HFNC success than the ROX index. Besides, baseline mROX index of greater than 7.1 showed a specificity of 100% for HFNC success.[18] Our study looked at the indices performance at ‘0’ hour to predict the requirement of HFNC and the above study looked at 2 hours after initiation of HFNC to predict the risk of intubation.

In our study ROX index and modified ROX index at a Cut-off of ≤4.7959 and ≤2.5579 respectively at initiation i. e.; at ‘0’ hour predicted HFNC requirement. Increasing trend of the above parameters was observed suggestive of clinical improvement. When compared to study by Goh et al using the ROC curve at 10 hours into HFNC therapy, cutoffs for the ROX and ROX-HR were determined to be 5.80 and 6.80, respectively, for the prediction of HFNC success.[15]

In line with our study, Roca et al examined the use of the ROX index for patients with acute respiratory failure from pneumonia and documented a best cutoff of 4.88 at 2, 6 and 12 hrs.[11] Whereas Yildizdas et al evaluated pediatric respiratory rate-oxygenation index (p-ROXI) and variation in p-ROXI (p-ROXV) as objective markers in children with high-flow nasal cannula (HFNC) failure. At 24 h, if both p-ROXI and p-ROXV values were above the cutoff point (≥66.7 and ≥24.0, respectively), HFNC failure was 1.9%. if both were below their values HFNC failure was and 40.6% ($p < 0.001$). At 48 h of HFNC initiation, if both p-ROXI and p-ROXV values were above the cutoff point (≥65.1 and ≥24.6, respectively), HFNC failure was 0.0%; if both were below these values, HFNC failure was 100% ($p<0.001$).[19]

According to Irene Yuniar et al there are significant differences in the ROX index between the successful and failed HFNC group therapy ($p<0.05$). This study suggests that mP-ROX index is not useful as predictor of HFNC therapy in pediatrics. While ROX index <5.52 at 60 min and <5.68 at 90 min after HFNC initiation have a sensitivity of 90% and specificity of 71%, sensitivity of 78% and specificity of 76%, respectively.[20]

All the study subjects were discharged (100%). Median (25th-75th percentile) of duration of ICU stay (days) was 4 (3-5), and duration of hospital stay (days) was 6 (5-7). Low ROX and modified ROX indices at ‘0’ hour predicted Prolonged ICU and hospital stay, as well as extended HFNC duration.

Strengths of the study

Simple bedside indices like ROX index, and modified ROX index (which are incorporated with vital parameters like respiratory rate, heart rate, $Sp0_2$, and FiO2) are good predictors of HFNC requirement. These findings have the potential to enhance clinical decision-making and improve patient outcomes in this specific population.

Limitations

This study is subject to certain limitations. Specifically, it focused solely on children receiving HFNC therapy, thus lacking a comparison with patients utilizing low-flow devices such as prongs or masks. Conducting comparative studies to observe the behaviour of these indices among patients on different respiratory support modalities could enhance the robustness of the findings. Consequently, further research and validation are necessary to strengthen these conclusions and enhance the precision of these indices application in pediatric respiratory care.

What this study adds

Simple bedside indices like ROX index, and modified ROX index (which are incorporated with vital parameters like respiratory rate, heart rate, Sp02, and FiO2) are good predictors of HFNC requirement.

CONCLUSION

ROX and modified ROX indices were good predictors of HFNC requirement. ROX index at a Cut-off of ≤4.7959, and modified ROX index at a Cut-off 0f ≤2.5579 at commencement of HFNC (i. e.; at ‘0’ hour) predicted HFNC requirement. Increasing trend was seen in ROX index and modified ROX index, and significant increase was seen at follow up as compared to baseline value, with a p value of <0.05, suggestive of clinical improvement and efficacy of HFNC. Low ROX and modified ROX indices at ‘0’ hour was associated with prolonged ICU and hospital stays, as well as extended HFNC duration.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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