MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.10.170.175

A Study of Comparison of SPO2/FIO2 Ratio with PAO2/FIO2 Ratio in Patients with Acute Respiratory Distress Syndrome and Acute Lung Injury

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ABSTRACT

ALI and ARDS are two of the most severe respiratory syndromes. In line with the AECC in 1994, PaO2/FiO2 ratios of ≤300 and ≤200 are used to define ARDS and ALI respectively. ABG is an invasive investigation used to obtain PaO2 values from arterial blood. ABG is not easily available in resource poor settings. SpO2 is a non-invasive measurement of blood oxygen content. SpO2/FiO2 ratio has been proposed as a surrogate for PaO2/FiO2 for diagnosis of ARDS and ALI. This study was undertaken to assess correlation between SpO2/FiO2 and PaO2/FiO2 in critically ill patients with ALI and ARDS and to determine the efficacy of SpO2/FiO2 in diagnosing ALI or ARDS. To study the correlation between SpO2/FiO2 and PaO2/FiO2 in critically ill patients with ALI and ARDS and to determine the efficacy of SpO2/FiO2 ratio compared to PaO2/FiO2 ratio in diagnosing ALI and ARDS in critically ill patients.150 patients diagnosed as ARDS and ALI were included in the study after applying inclusion, exclusion criteria. History, clinical examination and relevant investigations were done. Data was entered in excel sheet and statistical analysis done using SPSS software. In critically ill patients who are getting admitted in MICU of KIMS hospital, SpO2/FiO2 and PaO2/FiO2 ratios have good positive correlation (r-0.995, p<0.001) and SpO2/FiO2 can be used for the diagnosis of ALI (sensitivity and specificity of 100%) and ARDS (sensitivity of 100%, specificity of 97.6%). SpO2/FiO2 can be used as a surrogate for PaO2/FiO2 ratio for the diagnosis of ARDS and ALI with high sensitivity and specificity in critically ill patients who are getting admitted in MICU of KIMS hospital. However, this was a monocentric study with a study population of 150. More studies are needed for a definitive conclusion.

OPEN ACCESS

Key Words
ARDS, ALI SpO_2/FiO_2, PaO_2

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Received: 30 July 2024
Accepted: 05 September 2024
Published: 12 September 2024

Citation: Arjun Krishnakumar, Shivanaik Rayanaikar, Ishwara C. Havaragi, Akshath A. Hegde and Niranjan Gangoor, 2024. A Study of Comparison of SPO2/FIO2 Ratio with PAO2/FIO2 Ratio in Patients with Acute Respiratory Distress Syndrome and Acute Lung Injury. Res. J. Med. Sci., 18: 170-175, doi: 10.36478/makrjms.2024.10.170.175

INTRODUCTION

ALI and ARDS are two of the most severe syndromes associated with respiratory illnesses and both of them amounts to high morbidity and mortality. Studies show that 25% of ICU patients suffer from ALI and 5-10% from ARDS. It is found that the mortality and morbidity associated with these syndromes can be brought down with lung protective ventilation. PaO_2/FiO_2 ratios $\leq$200 and $\leq$300 are one among the criteria developed by AECC in 1995 for diagnosis of ALI and ARDS respectively[1]. ABG is not easily available in resource poor settings and this might lead to underdiagnosis of the condition and delayed initiation of necessary treatment strategies[2]. The SpO_2/FiO_2 ratio has been proposed as a non-invasive surrogate for the PaO_2/FiO_2 ratio[3]. The percentage of oxygenated and deoxygenated hemoglobin can be measures using pulse oximetry using their differences in light absorption wavelengths, ie, 660nm for oxygenated and 940nm for deoxyhemoglobin[4]. Pulse oximetry is commonly used in hospital set up to detect hypoxia in patients and is cost effective and non-invasive compared to Arterial blood gas analysis. So, it is more feasible to use SpO_2 instead of PaO_2 for the diagnosis of these respiratory conditions[9]. So, SpO_2/FiO_2 can be considered as a cost effective and non-invasive alternative of PaO_2/FiO_2 for the diagnosis of ARDS and ALI[5].

MATERIAL AND METHODS

Single Centre Randomized Prospective Observational Study was among cases were selected from patients admitted to KIMS hospital MICU excluding those mentioned in exclusion criteria, randomly. Duration of study was 2 years-October 2020-October 2022

Methods of Collection of Data: 1032 cases were admitted in MICU during the study period out of which, 150 patients were selected and distributed into 3 groups of 50 each.

Group 1 patients with ARDS (PaO_2/FiO_2 </=200mmHg)
Group 2 patients with ALI (PaO_2/FiO_2 </=300mmHg)
Group 3 patients without ARDS or ALI (PaO_2/FiO_2 >300mmHg)

They were subjected to detailed history, clinical examination and relevant investigations and the data obtained was recorded in predesigned proformas and were analyzed in SPSS software using Pearson's correlation and Area Under the Curve from ROC analysis.

Sample Size:

- Sample size was calculated to be 98.6 and was rounded to 99.
- A total of 150 samples were collected.

Inclusion Criteria:

- All critically ill patients who were admitted in MICU.
- All patients who gave consent to be a part of the study.

Exclusion Criteria:

Patients who:

- were on long term oxygen therapy or non-invasive ventilation at home.
- were pregnant.
- were revived after cardiac arrest and admitted in MICU.
- had traumatic brain injury or cranial hypertension as the reason for ICU hospitalization.
- had sickle cell disease.
- had hemoptysis with embolization or surgery.
- had organophosphorus poisoning.
- had COPD, with oxygen or non-invasive ventilation.
- had indications for hyperbaric oxygenation: carbon monoxide poisoning, gas embolism, necrotizing fasciitis.
- had methemoglobinemia.
- had untreated pneumothorax.
- underwent lung transplant.

All the selected patients were subjected to detailed history, clinical examination and investigations.

Statistical Analysis: The data so collected was recorded in a predesigned proforma and was subjected to relevant statistical analysis in SPSS software using Pearson's correlation and Area Under the Curve from ROC analysis.

RESULTS AND DISCUSSIONS

Maximum patients, among ARDS group, belonged to the age group of >60 years followed by 46-60 years, 31-45 years, while least being in age group of $\leq$30 years. Maximum patients, among ALI group, belonged to the age group of 31-45 years followed by 46-60 years, $\leq$30 years and the least being in age group of >60 years. Maximum patients, among patients without ARDS or ALI group, belonged to the age group of >60 years followed by 31-45 years, 46-60 years, while the least being in age group of $\leq$30 years.

Table 1: Distribution of the Study Population as Per Mean Age Group.

Age	ARDS		ALI		Patients without ARDS or ALI		Total	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
	56.8	16.6	46.6	15.9	53.3	16.1	52.8	16.6

The mean age of the patients included in the study among various (3) groups was found to be-ARDS-56.8 +/-16.6 years, ALI-46.6+/-15.9 years.

Patients without ARDS or ALI-52.8+/-16.6 years. Male predominance was observed compared to female population in all 3 study groups. Among all the 3 groups studied, majority of patients had breathlessness as presenting complaint. However, on comparing individual study groups, it was observed that almost equal number of patients had cough as their presenting complaint in the ALI group and the group without ALI and ARDS. Patients who presented with fever were found to be more in the ARDS group as compared to the other two groups. Maximum number of patients who presented with chest pain were observed in the ALI group, followed by ARDS group and the group without ARDS and ALI. Almost equal number of patients who presented with Myalgia were observed in all 3 groups. Apart from the above presenting complaints (breathlessness, fever, cough, myalgia and chest pain), other presenting complaints were maximum in the ALI group of patients.

Table 2: Distribution of Study Population as Per in Terms of Comorbidities.

Comorbidities	ARDS		ALI		Patients without ARDS or ALI		Total	
	n	%	n	%	n	%	n	%
T2DM	11	18.6	12	29.3	9	18.0	32	21.3
HTN	21	35.6	11	26.8	16	32.0	48	32.0
IHD	3	5.1	4	9.8	1	2.0	8	5.3
CVA	3	5.1	0	0	1	2.0	4	2.6
Total	59	100.0	41	100.0	50	100.0	150	100.0

Among the study population, the most common comorbidity observed was hypertension (48) followed by type 2 diabetes mellitus (32), ischemia heart disease (8) and cerebrovascular accident (4). However, among the ALI group, type 2 diabetes mellitus (12) was the most common comorbidity as compared to hypertension (11) and none had cerebrovascular accident.

Table 3: Distribution of Study Population as Per Risk Factors.

Habits	ARDS		ALI		Patients without ARDS or ALI		Total	
	n	%	n	%	n	%	n	%
Alcohol	8	13.6	6	14.6	9	18.0	23	15.3
Smoking	9	15.3	4	9.8	7	14.0	20	13.3
Tobacco	9	15.3	9	22.0	9	18.0	27	18.0
Total	59	100.0	41	100.0	50	100.0	150	100.0

The most common habit among entire study population was tobacco chewing followed by alcohol and smoking. However, smoking as a habit was observed to be slightly less among patients with ALI.

Table 4: Distribution of Study Population as Per Etiology.

Aetiology	ARDS		ALI		Patients without ARDS or ALI		Total	
	n	%	n	%	n	%	n	%
Bronchopneumonia	23	39.0	16	39.0	13	26.0	54	36.0
Pneumonia	11	18.6	8	19.5	7	14.0	35	23.3
Viral fever	8	13.6	6	14.6	7	14.0	20	13.3
Sepsis	10	16.9	5	12.2	13	26.0	23	15.3
Others	7	11.9	6	14.6	10	20.0	18	12.0
Total	59		41		50		150	

*Others include-traumatic ARDS, acute pancreatitis, unknown compound consumption, drowning.

Among all the 3 groups studied, majority of patients had bronchopneumonia as the cause of illness. However, on comparing individual study groups, it was observed that almost equal number of patients of lobar pneumonia were observed in ARDS and ALI group. Almost equal no of patients of viral fever were observed in all the 3 groups. Patients with sepsis were found to be more in the group without ARDS or ALI, as compared to other groups.

Apart from the above four causes (Bronchopneumonia, Lobar Pneumonia, Viral Fever and Sepsis) other causes were found more in the group without ARDS or ALI compared to ARDS and ALI groups.

The no of quadrants involved increased as the respiratory status deteriorated from patients without ARDS or ALI to ALI to ARDS in that order. Chest x-ray of majority of patients with ARDS showed involvement of all 4 quadrants whereas in patients with ALI and in patients without ALI or ARDS showed involvement of 3 or <3 quadrants. As seen with quadrants involved in chest x-ray, CORADS value of HRCT chest increased as respiratory status of the patients deteriorated from group of patients without ALI or ARDS, to ALI group, to ARDS group. Almost 100% of patients without ARDS or ALI had a CORADS value of 1 in HRCT chest.

Table 5: Distribution of Respiratory Parameters of Study Population.

Parameters	ARDS		ALI		Patients without ARDS or ALI		Total	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
SpO2/FiO2	139.8	41.7	271.8	30.1	421	33	269.6	125.1
PaO2/FiO2	108	34.5	229.5	27.9	375	33	230.2	118.2
Respiratory rate	26.5	8.3	23.6	5.1	24.8	4.9	25.2	6.5
PCO2	35.6	13.7	31.9	8.2	32.1	11	33.4	11.5
Arterial pH	7.3	0.1	7.4	0.1	7.3	0.1	7.4	0.1

Respiratory rate values and mean pH values were almost equal among all the 3 study groups Both PaO_2/FiO_2 and SpO_2/FiO_2 values were highest in the group of patients without ARDS or ALI followed by ALI group and ARDS group in that order. Mean PCO_2 values were highest in ARDS group and were almost equal in ALI group and group of patients without ARDS and ALI. Correlation between SpO_2/FiO_2 and PaO_2/FiO_2 of the patients included in the study.

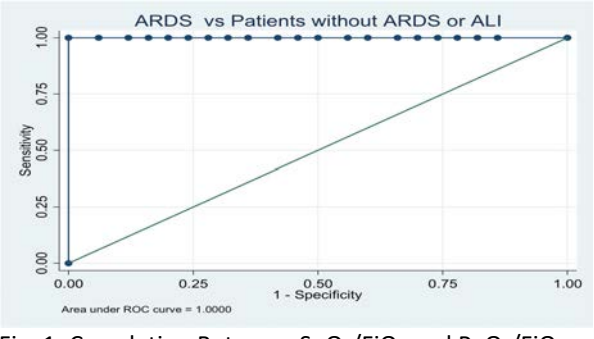

Fig. 1: Correlation Between SpO_2/FiO_2 and PaO_2/FiO_2

SpO_2/FiO_2 and PaO_2/FiO_2 ratios have a correlation coefficient of 0.995 with a p<0.001, with mean

SpO_2/FiO_2 ratio of 269.6 and mean PaO_2/FiO_2 ratio of 230.2 mm of Hg, ie, significant positive correlation is present between the two. SpO_2/FiO_2 ratio was found to increase in a linear fashion as PaO_2/FiO_2 ratio increases. From the above graph, SpO_2/FiO_2 values corresponding to PaO_2/FiO_2 values of 200 and 300 were calculated and were found to be 237 and 343 respectively. ROC analysis-area under the curve.

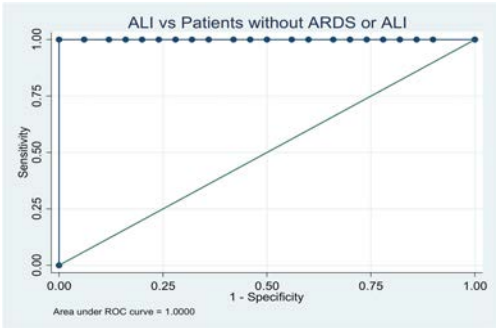

Fig 2: ROC Analysis-Area Under the Curve for ARDS vs Patients without ARDS or ALI

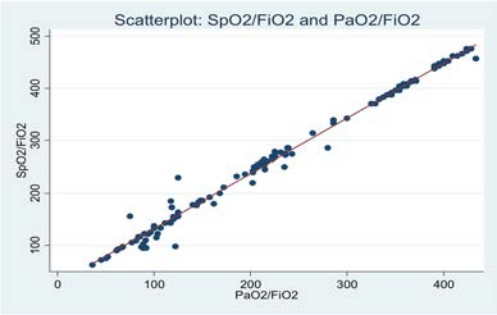

Fig 3: ROC Analysis-Area Under the Curve for ALI vs Patients without ARDS or ALI

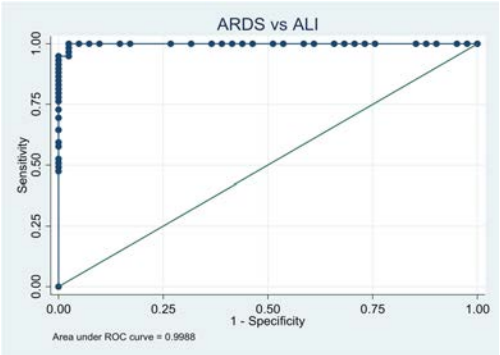

Fig 4: ROC Analysis-Area Under the Curve for ARDS vs ALI

The ability of SpO_2/FiO2 to differentiate between different groups in the study was calculated by plotting the ROC graph of false positivity rate (1-specificity) against test positivity rate (sensitivity) and calculating the area under the curve for the same.

The ROC Curves of SpO2/FiO2 Ratio for:

- Patients with ARDS vs patients without ARDS or ALI shows an AUC of 1.0 with p value of <0.001 indicating good ability to differentiate between the two.
- Patients with ALI vs patients without ARDS or ALI shows an AUC of 1.0 with p value of <0.001 indicating good ability to differentiate between the two.
- Patients with ARDS vs patients with ALI shows an AUC of 0.998 with p value of <0.001 indicating good ability to differentiate between the two.

Table 6: Diagnostic Accuracy of SpO2/FiO2 in Patients with ARDS Against Patients without ARDS or ALI

SpO2/FiO2	PaO2/FiO2≤200		PaO2/FiO2 >300	
	n	%	n	%
≤237	59	100.0	0	0
>237	0	0	50	1000
Total	59		50	

Table 6: Diagnostic Accuracy of SpO2/FiO2 in Patients with ARDS Against Patients without ARDS or ALI

Parameter	Point estimate	95 % Confidence limit
Sensitivity	100.0	93.9-100.0
Specificity	100.0	92.9-100.0
Positive predictive value	100.0	93.9-100.0
Negative predictive value	100.0	92.9-100.0

The sensitivity and specificity of SpO_2/FiO_2 ratio of 237 for differentiating between patients with ARDS and patients without ARDS or ALI are 100 each, with positive and negative predictive values also being 100.

Table 7: Diagnostic Accuracy of SpO_2/FiO_2 in Patients with ALI Against Patients without ARDS or ALI

SpO_2/FiO_2	PaO_2/FiO_2>200-300		PaO_2/FiO_2 >300	
	n	%	n	%
≤343	41	100.0	0	0
>343	0	0	50	100.0
Total	41		50	

The sensitivity and specificity of SpO_2/FiO_2 ratio of 343 to differentiate between patients with ALI and patients without ARDS or ALI are 100 each, with positive and negative predictive values also being 100.

Table 8: Diagnostic Accuracy of SpO_2/FiO_2 in Patients with ARDS Against Patients with ALI

SpO_2/FiO_2	PaO_2/FiO_2≤200		PaO_2/FiO_2>200-300	
	n	%	n	%
≤237	59	100.0	1	2.4
>237	0	0	40	97.6
Total	59		41	

The sensitivity and specificity of the SpO_2/FiO_2 ratio of 237 were 100 and 97.6 respectively, with positive and negative predictive values being 98.3 and 100 respectively

The mean age of subjects in our study is comparable to that of Rice[6] and Festic[7], but different from Janipalli[8]. The study conducted by Janipalli[8] was conducted during COVID-19 PANDEMIC, between May 2019-January 2020, when younger patients were affected and admitted more as compared to elderly population, which probably was the cause of the mean age of their study group being low 34.08 as compared to ours and other studies.

On analysis of gender distribution among the study population, we observed that majority of the study subjects in our study were male, which was comparable with most of the studies except that of Janipalli[8]. in which females were affected more than males.

According to the study conducted by Baik *et al,* the risk for community acquired pneumonia among men increases as age increases, but age was not found to be a risk factor for women.

As the mean age of the population in the study conducted by Janipalli[8] was lower and as pneumonia was the most common aetiology among them, the proportion of males in the population might have reduced compared to females as against our study.

While analysing the Prevalence of Comorbidities among the study population we found that the most common comorbidity among our study population was Systemic hypertension (32%), followed by Type 2 diabetes mellitus (21.3%), ischemic heart disease (5.3%) and Cerebrovascular Accident (2.6%).

On analysing the prevalence of risk factors among our study population, it was found that tobacco consumption was the most prevalent risk factor (31.3%), followed by alcoholism (15.3%). On comparing with other studies, it was found out that in the study conducted by Festic[7], too, tobacco consumption was the most common risk factor (50%) followed by alcoholism (10%) Other studies did not mention about risk factors.

While analysing the aetiologies of the underlying diseases leading to ARDS and ALI in our study group we observed that Bronchopneumonia was the most common aetiology, followed by Lobar Pneumonia, Viral Fever and Sepsis, in that order. Other aetiologies in our study included Traumatic ARDS, Acute Pancreatitis, Unknown Compound Consumption and Drowning.

In the study conducted by Janipalli[8], other aetiologies like Malaria, Dengue and H1N1 were also included, which were neither observed in our study nor other studies 145,146.

Analysis was done using the data from our study population on the number of quadrants involved in chest x ray among the affected patients. Majority of patients in our study had involvement of all 4 quadrants in chest x ray, followed by involvement of 2 quadrants. Janippalli[8], reported similar observations in their study where majority of the patients had involvement of 4 and 2 quadrants in chest x ray147. But the proportion of patients with involvement of 3 quadrants in chest x ray was higher than that seen in our study.

In the present study we recorded and compared SpO2/FiO2 ratio with PaO2/FiO2 ratio in all the patients, including patients with ARDS and ALI.

The data obtained from the study population was analysed for the mean SpO2/FiO2 and mean PaO2/FiO2 ratio and the same was compared with other studies.

In the present study, the mean SpO2/FiO2 ratio of the entire study population was 269.9 and the mean PaO2/FiO2 ratio of the study population was 230.2. These values were on the higher side as expected, because of inclusion of more number of patients of younger age and also mainly because of the inclusion of group of patients without ARDS or ALI, whose mean SpO2/FiO2 ratio was 421 and PaO2/FiO2 ratio was 325, raising the Mean Values of our entire study population to be Higher. Hence our values were relatively higher with that of other studies.

On deleting the values of patients without ARDS or ALI, the mean SpO2/FiO2 and PaO2/FiO2 ratios reduced to 193.92 and 157.81 respectively, which was more comparable to other studies than the initial value.

Additionally, we also recorded the PCO2 values of our study group patients and on calculating, it's mean value was found to be 33.4mm of Hg .

On comparison with other studies we found that the our mean PCO2 values were comparable to one of the Indian study by Janippali[8] while it was observed to be slightly lower than that of a western study conducted by Rice *et al* (42.9) 145. As the SpO2/FiO2 ratio increases proportionately to PaO2/FiO2 ratio, a linear graph can be plotted between the two. From the linear graph obtained between SpO2/FiO2 and PaO2/FiO2 ratios, SpO2/FiO2 values corresponding to PaO2/FiO2 ratios of 200 and 300 were determined (237 and 343 respectively).

On comparing this with other studies, we found that the SpO2/FiO2 ratios corresponding to PaO2/FiO2 ratios of 200 and 300 in our study, to be tested for its efficacy for diagnosis of ARDS and ALI, are comparable to that of other studies.

A Receiver Operating Characteristic curve (ROC curve) is a graph showing the performance of a classification model at different thresholds. True Positivity Rate and False Positivity rates are plotted on the y and x axis respectively and Area Under the Curve (AUC) thus formed is assessed. Closer the AUC is to 1, the higher the ability of the threshold value for classifying the parameter under consideration.

ROC analysis of data set to determine the ability of SpO2/FiO2 ratio to distinguish patients with ALI and patients without ARDS or ALI revealed an Area Under the Curve of 1.0 ($p<0.001$) which indicates good efficacy of SpO2/FiO2 ratio to distinguish between patients of ALI and patients without ARDS or ALI.

On comparison with other studies, it was seen that our study shows similar, or even higher efficacy for diagnosis of ALI, with Area Under the Curve values of other studies varying between 0.74-0.92.

The higher efficacy can be attributed to the refinement brought about by the division of the study population in our study into 3 groups, as there is a clear definition and comparable numbers of patients in all the three groups, while other studies did not do the same and considered them as a whole.

ROC analysis of data set to determine the ability of SpO2/FiO2 ratio to distinguish patients with ALI and patients with ARDS revealed an Area under the curve of 0.998 (p<0.001) which indicates good efficacy for diagnosis of ALI and ARDS and to distinguish between the two.

On comparison with other studies, it was seen that Area under the curve of our study was similar to that of other studies, the p values of all the studies measuring above 0.9[6,7,8].

For PaO2/FiO2 of 200: The sensitivity and specificity of the SpO2/FiO2 ratio of 237, corresponding to the PaO2/FiO2 ratio of 200 was calculated using the above formula and was found to be 100 and 97.6 respectively.

On comparing with other studies, it was seen that the values were similar to those seen in Janipalli[8] (sensitivity 92.30, specificity-90.90), but difference was seen with the studies conducted by Rice *et al* (sensitivity-85, specificity-85)[6] and Festic *et al* (sensitivity-42, specificity-88)[7].

As explained by Festic *et al* in his study, because of the study being multi-centric, the accuracy with which SpO2 and PaO2 values were measured might be variable at different centres. Also, the procedure dictated that if >1 value is available, the worst values from the first six hours were collected. This could have led to the low sensitivity and specificity seen with the two multicentric studies.

For PaO2/FiO2 of 300: The sensitivity and specificity of the SpO2/FiO2 ratio of 343, corresponding to the PaO2/FiO2 ratio of 300 was calculated using the above formula and was found to be 100 and 100 respectively. These values, when compared with that of other studies, were found to be comparable and sometimes way more sensitive and specific. The study conducted by Janippalli[8] showed a sensitivity of 97.82 and specificity of 75, Rice *et al,* a sensitivity of 91 and specificity of 57 and Festic[7], a sensitivity of 53 and specificity of 78.

Hence, SpO2/FiO2 ratio might be able to replace PaO2/FiO2 for diagnosis of ARDS and ALI in the population of patients getting admitted in MICU of KIMS hospital, Hubli. But the study we conducted was a monocentric study with a small sample size of 150. More studies are needed on the topic for a definitive conclusion.

CONCLUSION

We were able to infer that SpO_2/FiO_2, has a significant positive correlation with PaO_2/FiO_2 (r-0.995, p<0.001), and high sensitivity and specificity for the diagnosis of ARDS (Sensitivity of 100 and specificity of 97.6) and ALI (sensitivity of 100 and specificity of 100), comparable to or even higher than those of the reference studies. Hence, SpO_2/FiO_2 ratio might be able to replace PaO_2/FiO_2 for diagnosis of ARDS and ALI in the population of patients getting admitted in MICU of KIMS hospital, Hubli. But the study we conducted was a monocentric study with a small sample size of 150. More studies are needed on the topic for a definitive conclusion.

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