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Correlation Of SpO2/FiO2 To PaO2/FiO2 In Patients With Acute Hypoxemic Respiratory Failure.

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Abstract

Acute hypoxemic respiratory failure (AHRF) is very common presentation with high risk of mortality and morbidity. Acute respiratory distress is one of the main causes of AHRF, it is often difficult to differentiate between ARDS and non-ARDS hypoxemia cases. The definition of ARDS requires the partial pressure of arterial oxygen (PaO2) from the invasive arterial sample to calculate the PaO2/FiO2 according to Berlin criteria which may be difficult to apply in limited resource settings and lead to underestimation of the patients with ARDS. The SpO2/FiO2 ratio has been recently used as a measure for oxygenation status. We proposed a correlation between the non-invasive SPO2/FiO2 (S/F) ratio and the invasive PaO2/FiO2 (P/F) ratio in both non-invasive and invasive ventilation and the SpO2/FiO2 can be used instead of PaO2/FiO2. All attempts globally to change the definition of ARDS according to berlin criteria by suing the non-invasive SpO2/FiO2 as well as the new trend of using ultrasound of the lung and the use of non-invasive high flow nasal canula. To study the correlation between the SpO2/FiO2 and the PaO2/FiO2 and determine the cutoff values of SpO2/FiO2 that correlate with PaO2/FiO2 in patient with acute hypoxemic respiratory failure. Patients with hypoxemia and acute respiratory failure and treated in the ICU by invasive and non-invasive measures enrolled in this single center observational cross-sectional study which was conducted from August 2023 to March 2024 in the ICU department of Ghazi Alhariri hospital. Fractional inspired oxygen (FiO2), partial pressure of arterial oxygen (PaO2) and oxygen saturation of hemoglobin (SpO2) were recorded from blood gas analysis reports and monitoring of the patients simultaneously, the S/F and P/F ratios calculated, the correlation between the ratios were noted by scatter plot with line of fit, The degree of correlation was determined using Spearman Pearson equation and the cutoff values of S/F ratio determined by linear regression equation. A total of 100 sample data were collected. The mean age of the patients in the study was57.38 year, the PaO2 mean was 100.81, the SpO2 mean was 96.32%, the mean of calculated P/F ratio was 258.77 while the mean of calculated SpO2/FiO2 ratio was 244.75.

Keywords: Arterial blood gas analysis (ABG), Intensive, acute hypoxemic respiratory failure (AHRF), acute respiratory distress syndrome (ARDS), PaO2/FiO2 ratio, SpO2/FiO2 ratio.

Introduction

Respiratory failure occurs when there is either failure in ventilation and hence the removal of CO_2 (hypercapnic) type 2 which is determined by blood gas abnormalities $PaCO_2$ above 45 mmHg e.g. opioid overdose, Guillain Barre or increased work of breathing (decreased CO_2 elimination), or lung dysfunction hence impairment of oxygen transfer in the lung (hypoxemic) type I which is determined by blood gas abnormalities PaO_2 below 60 mmHg which is caused by either ventilation/perfusion (V/Q) mismatch, shunt impaired diffusion or low inspired oxygen fraction [1].

Acute respiratory distress syndrome (ARDS) was described in 1967 by [2] as the main cause of acute hypoxemic respiratory failure type I, it accounts for about 10% of total ICU admission and 23% of cases with mechanical ventilation [3], with still high mortality rate of 30-50% despite medical development, However the epidemiology for patients with ARDS in low income countries not reported [4].

It is a syndrome of lung inflammation with increased pulmonary capillary permeability because of injury to the endothelium [5], ARDS has high mortality rate depending on its severity while the early diagnosis with continuous monitoring some necessary medical adjustments like FiO_2 and ventilator settings, prompt management which include supportive measures and treatment of precipitating events help to lessen the morbidity and mortality, this require more easily diagnostic approach and a system for easy classification for early recognition of respiratory failure, implementing at times, measures such as early intubation and lung protective mechanism [6].

There are few researches showing categorizing and risk stratification of patients with non ARDS hypoxemic respiratory failure vs ARDS hypoxemic respiratory failure but have the same mortality rates in similar level of hypoxemia [7].

ARDS definition by Berlin criteria in 2012 (Table1) include acute onset (within 1 week of a known cause) or new worsening respiratory symptoms, bilateral opacities by CXR, pulmonary oedema not fully explained by heart failure or fluid overload and lastly the PaO_2/FiO_2 which is required for diagnosis and determining the severity of ARDS [8].

PaO_2/FiO_2 200-300 mmHg is mild ARDS

PaO_2/FiO_2 100-200 mmHg is moderate ARDS

PaO_2/FiO_2 below 100 mmHg is severe ARDS

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The 1st 3 criteria can be obtained by clinical history or non-invasive tools such as CXR or echocardiography, while the use of parameters such as PaO_2 and positive end expiratory pressure PEEP which reflect the lung function and oxygenation, have some limitations.

Table 1: Berlin criteria for the diagnosis of ARDS [9].

Acute onset within 1 week of known insult
Bilateral opacities on CXR or CT chest
3 severity categories defined by P/F ratio
Requirement for invasive and non-invasive MV such as PEEP ≥ 5

The PaO_2/FiO_2 ratio have some limitations because need special tools like arterial catheter and transducers, etc. or need trained staff for arterial gas sampling, all these sometime unavailable in limited resources conditions, also additional concerns about its cost, invasiveness, anemia, thrombosis, bleeding, etc. has led to fewer ABG measurement in critically ill patients which lead to under diagnosis of ARDS [10].

The Oxygen saturation change with the PaO_2 in non-linear correlation and affected by PH, $PaCO_2$, temperature and 2,3 diphosphoglycerate [11], in this curve the upper flat part the PaO_2 decrease to 60 mmHg while the SpO_2 decrease to just 90% the next part the drop in PaO_2 is more with decrease in SPO_2 to 80% after that the steeper part of the curve start after PaO_2 45 mmHg and corresponding SPO_2 is 80% so that in healthy subjects, changes in PaO_2 correlate well with changes SPO_2 if SPO_2 in the range of 80-100 % So the calculation of less invasive SPO_2/FiO_2 ratio can be easily calculated at the bedside using the SpO_2 by pulse oximeter and the FiO_2 delivered at that time also to see its correlation with the more invasive PaO_2/FiO_2 ratio to be used in place of it for determine the degree of hypoxemia and the diagnosis and classification of ARDS without the need of arterial blood sampling and frequent puncture make it more useful in resource limited conditions [12].

2. Aim of the study

- Study the relationship between SPO_2/FiO_2 and PaO_2/FiO_2 ratios in patients with acute hypoxemic respiratory failure.
- Calculate the SPO_2/FiO_2 ratio cutoff values that correlates with PaO_2/FiO_2 ratio in patient with acute hypoxemic respiratory failure.

3. Patients and methods

This observational cross section study was conducted in patients admitted to the ICU department of Ghazi Alhariri hospital from August 2023 to March 2024.
The study included 140 patients that were admitted to the ICU after fulfilling the inclusion criteria, 10 cases discarded because the data were incomplete and 30 cases excluded after exposed to the excluded criteria, the eligible cases were 100 cases.
Excluded criteria

- Age ≤18 years old.
- Severe shock.
- Hypothermia (body temperature < 35° c).
- Unreliable pulse oximetry waveform.
- Severe congenital heart disease.
- Congestive heart failure (EF < 50%).

- Peripheral vascular disease.
- Severe jaundice.
- $SPO_2 < 80\%$.

Patient demographics, Ventilator setting, mode of oxygen supplementation, CXR finding, SPO_2, PaO_2 and FiO_2. The PaO_2, SpO_2 and FiO_2 recorded at the same moment. These measures recorded once per patient i.e. not repeated for same patient. PaO_2 taken from ABG recorded by radiometer machine after arterial sample confirmed.FiO_2 values for oxygen therapy with nasal cannula regarded as follows: 0.24for 1L,0.28 for 2 L,0.32 for 3L,0.36 for 5L while FiO_2 delivered with standard face mask regarded as 0.45 with 5 L/min flow of oxygen, 0.50 with 6 L/min,0.55 with 7 L/min, with non-rebreathing mask as 0.80 for 10 L/min and 0.90 for 12 L/min, while FiO_2 setting on HFNC or NIV device as patient requirement recorded [13]. ABG samples usually but not always under the protocol of taken twice daily, there is no protocol for decision regarding putting arterial catheter, regarding the FiO_2 the trend usually tapering till reaching 40% when the SpO_2 in 90s but not restrict to below or equal 97%.

The following precautions was taken for the precise reading of SpO_2:

- Regular SPO_2 waveform.
- The right position of probe.
- Ensure clearness from skin rash at place of probe.
- Ensure cleanliness of probe and finger.
- No positional change.
- No airway suctioning for at least 10 min before the recording.
- No bronchoscopy or change ventilator setting for at least 30 min before recording.
- Waiting for 1 min before taking SPO_2 recording.

Sample size calculate by using confidence level 90%, power of 0.8 and SD of previous study by [7] was 3.3, so the sample size was 100 after exposed to exclusive criteria.

Statistical analyses done by using the Statistical Package for Social Sciences (IBM SPSS version 26), the variables were PaO_2, SPO_2 and FiO_2, the P/F and S/F ratio calculated. Continuous data were presented as mean ± Standard deviation SD, while qualitative data were presented as frequencies and percentage correlation between P/F and S/F ratio were studied by scatter diagram and plot, Pearson correlation coefficient were calculated, we defined correlation (r) as high (0.7-1), moderate (0.5-07), low (0.3-0.5) and negligible for values are equal to or less than (0.3) for the purpose of assessing the correlation and linear regression test was done [14]. p-Values less than 0.05 were considered statistically significant.

4. Results

A total 140 cases examined 30 cases discarded because of exclusion criteria and 10 cases discarded because of missing data, the remaining eligible No. was 100 cases (Table 2), The mean age of the patients in the study was 57.38 ±17.567 years, maximum 90 years, minimum 21 years old (figure 1).

Table 2: Descriptive statistics of collected data.

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	100	21	90	57.38	17.567
SPO2	100	.80	1.00	.9632	.04035
PaO2	100	48	247	100.81	36.640
FiO2	100	.24	1.00	.4459	.17937
P/F	100	48	500	258.77	118.782

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S/F	100	80	417	244.75	78.198
Valid N (listwise)	100				

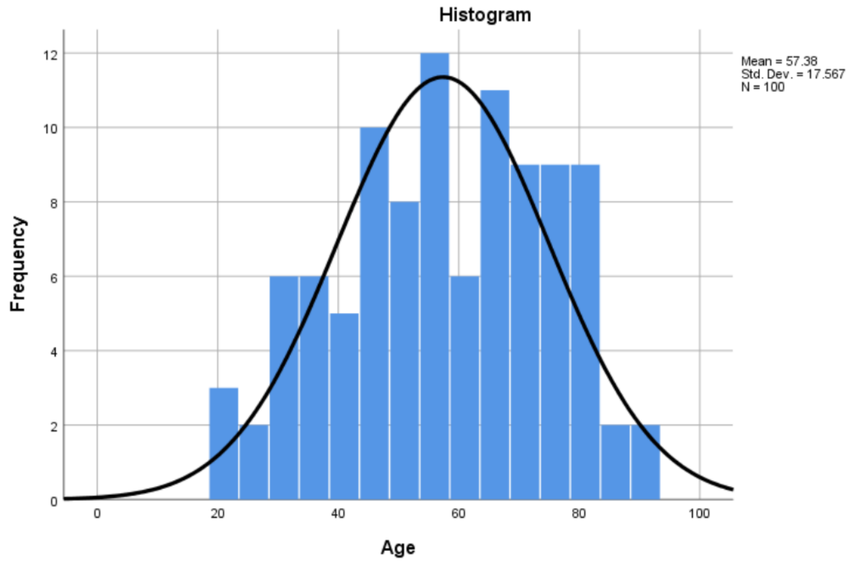

Figure 1: Histogram showing normal distribution of age.

The study included 53 Male and 47 Female (figure 2). The variables analyzed was PaO_2, SPO_2, and FiO_2. The PaO_2 mean was 100.81 ±36.64 SD with maximum was 247 and the minimum was 48 (figure 3), The SPO_2 mean was 96.32% ± 4% SD the maximum was 100% and the minimum was 80%, the P/F ratio calculated and the mean was 258.77 ± 118.782 SD , the maximum 500 , the minimum 48 severe ARDS (P/F ratio < 100) was 12 cases (12%), moderate ARDS (P/F between 100 and 200) was 21 cases (21%), mild ARDS (P/F ratio < 300) was 33 cases (33%) and the normal (P/F > 300) was 34 cases 34% (figure 4), the S/F ratio also calculated the mean was 244.75 ± 78.198 SD maximum 417 , minimum 80 (Figure 5).

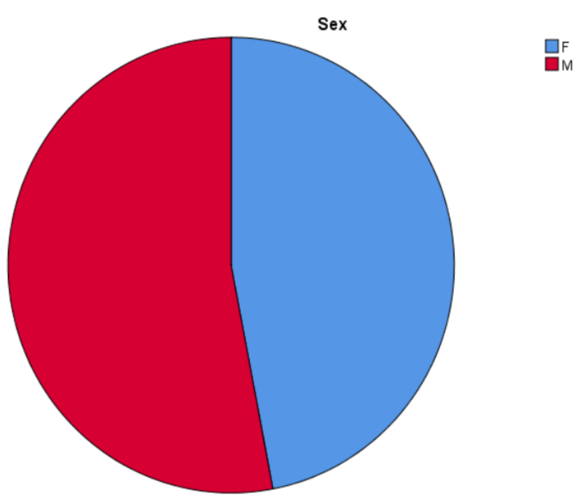

Figure 2: gender distribution of study samples.

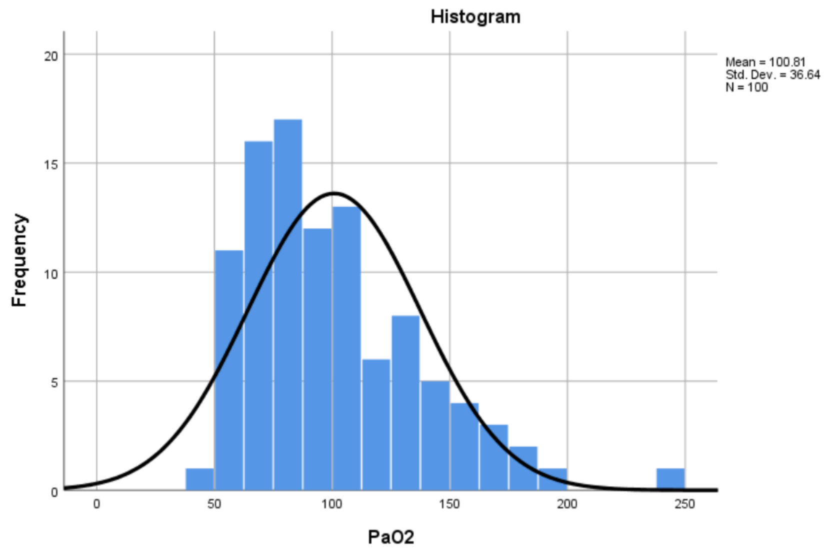

Figure 3: Histogram showing the normal distribution of PaO2.

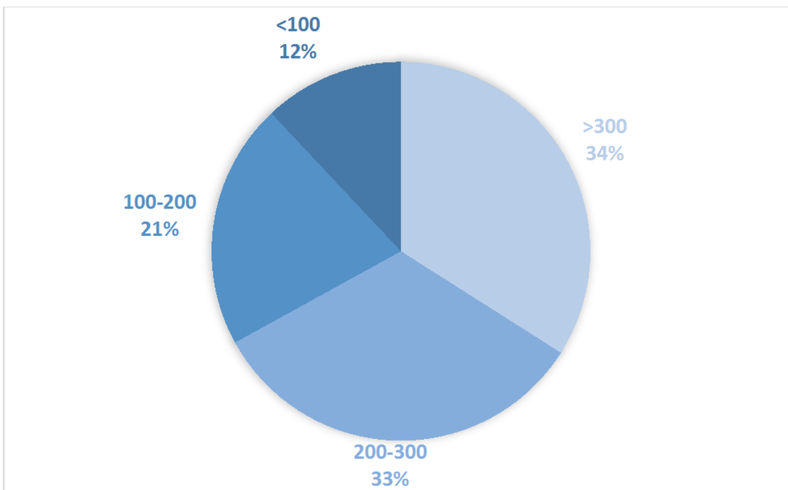

Figure 4: The distribution of cases according to P/F ratio.

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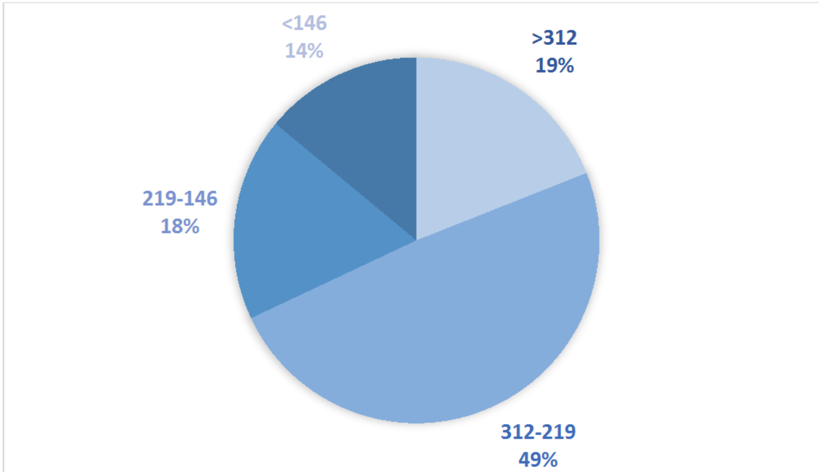

Figure 5: The distribution of cases according to S/F ratio.

Next step was that we plotted a scattered diagram with fit line of P/F (x axis) the independent variable against S/F ratio (y axis) the dependent variable from the figure we saw there is linear correlation between P/F and S/F (Figure6).

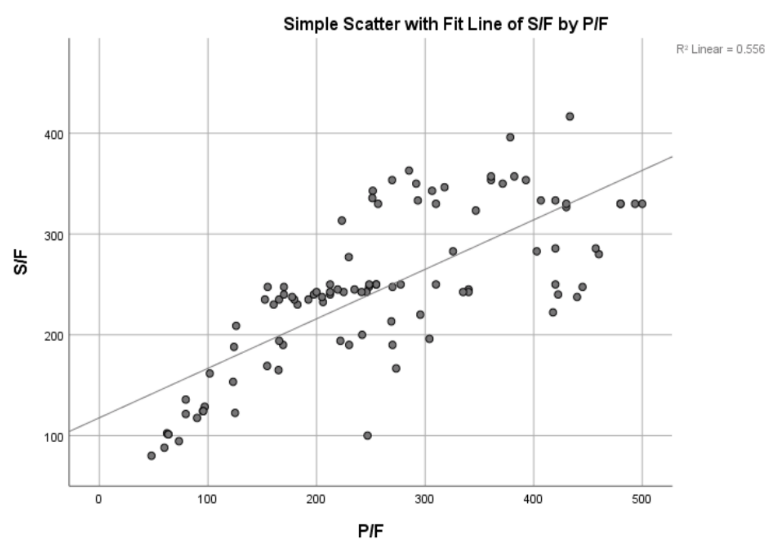

Figure 6: simple scatter plot with fit line.

Next, we proved this correlation mathematically by measuring the strength of this correlation and finding the Pearson correlation coefficient (r), before that we should see the observations are normally distributed (Figures 7,8).

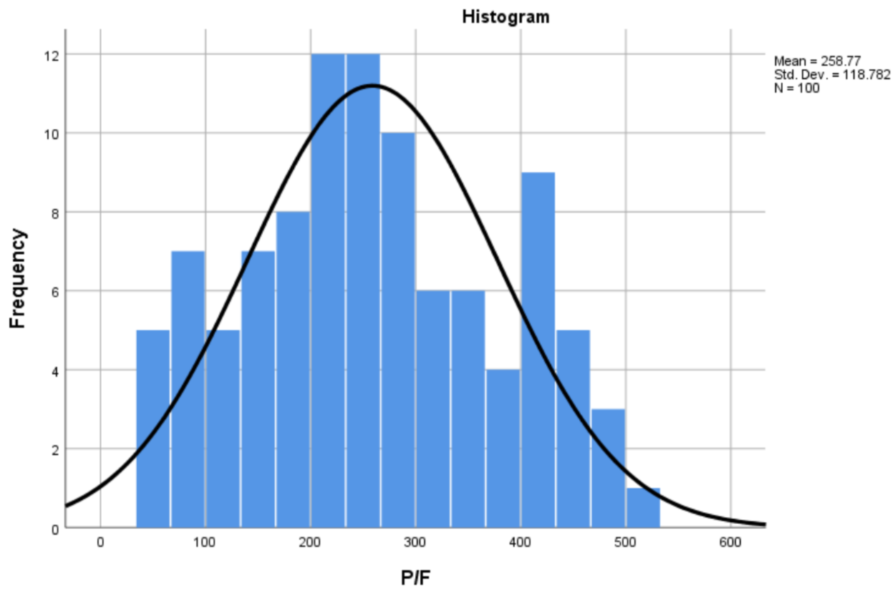

Figure 7: Normal distribution of P/F ratios.

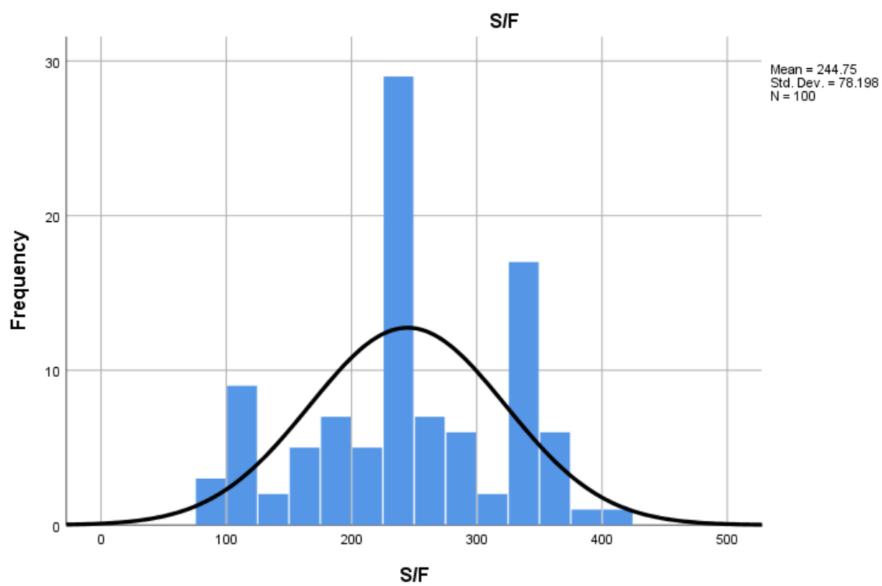

Figure 8: Normal distribution of S/F ratio.

Then we calculate the Pearson correlation coefficient (r) which is between -1 to +1, r calculated was 0.746 which means there is strong correlation between the dependent and independent variables with standard error 52.365 and r^2 0.556 which is the coefficient of determination.

The 2nd object of the study was to find the cutoff value for S/F to P/F ratio, it is done by simple regression model best line fit, by which the S/F can be predicted by $y = a + b x$.

Where y being the predicted outcome (dependent variable), a is the intercept of the line with y and b is the regression coefficient and x is the independent variable or called predicts.

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For P/F ratio 300, the predicted S/F is 64 + 0.829 * 300 = 312.7 Sensitivity 92%, Specificity 85%.
For P/F ratio 200, the predicted S/F is 64 + 0.829* 200 = 229.8 Sensitivity 71%, Specificity 98%.
For P/F ratio 100, the predicted S/F is 64 + 0.829*100 = 146.9 Sensitivity 92% Specificity 97%.

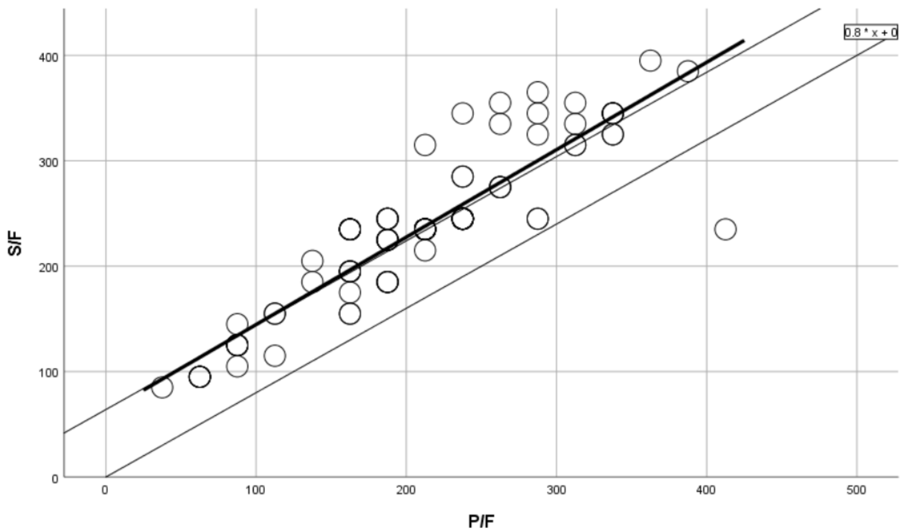

Figure 9: Scatter plot with linear regression relationship between S/F and P/F.

After categorizing the S/F results according to their cutoff and in correspondence to that of P/F ratio as one of Berlin criteria for the diagnosis of ARDS and assessing the degree of oxygenation status, we found those patients with S/F ratio below 146 which correspond those with P/F < 100 was 14% while those with S/F 146-229 corresponds P/F 100-200 was 18%, while those with S/F ratio between 229-312 which corresponds to P/F 200-300 was 49% while those with S/F ratio above 312 which corresponds to P/F above 300 was 19%.

5. Discussion

One of the major causes of acute hypoxemic respiratory failure is acute respiratory distress syndrome which are syndrome with high mortality and morbidity, PaO_2/FiO_2 ratio is one of the Berlin criteria that used to diagnose ARDS and to categorize them into mild ARDS if < 300, moderate if < 200 and severe if < 100. But ABG analyzer is not available in some limited resources or sometime not practical and sometime this assessment is required for plan for early oxygenation or invasive or non-invasive ventilation as discussed by [15] study for that reason we try to search non-invasive measures to replace this ratio.

In this study we found a strong positive correlation between P/F and S/F ratios. By this study also we determined the S/F cutoff values for the diagnosis of mild, moderate and severe ARDS as 312, 229 and 146 in reference to P/F ratios of 300, 200, 100 respectively, it means if S/F ratio is 312 or higher, no immediate respiratory injury and if it is between 312 and 229 it means mild ARDS, and between 229 and 146 it means moderate ARDS and below 146 mean severe ARDS, also it shows that the P/F and S/F ratio can be used in both invasive and non-invasive ventilation and with any mode of oxygen supplementation, for that reason we can conclude that S/F ratio can be used in place of P/F ratio in diagnosis, assessment and starting treatment.

These findings ($r > 0.6$, $p < 0.05$) of strong positive correlation between S/F and P/F ratios concluded in many studies across the world, in general, in various studies across the world the S/F ratio cutoff for P/F ratio of 300 and 200 range from (263-450) and (201-370) respectively.

Our findings go along with another study by [16] in patients under GA when he included the S/F in SOFA score the correlation coefficient (r was 0.87) and the S/F ratio threshold correlate with P/F ratio of 200, 300 was 214 and 357 respectively. A study by Rice et al in 2007 conducted for adult patients also show linear correlation with S/F ratio of 235 corresponding P/F of 200 and S/F ratio of 315 corresponding with P/F of 300(20). A similar study was done by [17] on pediatric patients the correlation was moderate (r =0.47) and the S/F ratio cut off was 263 and 201corresponding to P/F ratio of 300 and 200 respectively. [17] while the study conducted by Laila et al, the result was not agreed with other studies in pediatric populations the correlation was weak (r =0.215). While another study by [7] show also strong correlation while the cutoff S/F values was 285 and 323 corresponding to the P/F ratio of 200 and 300 respectively. The difference in the correlation values between studies may be due to difference in sample size (table 3).

Table 3: summary of studies comparing S/F and P/F ratios including our study.

Author	Year	S/F for P/F 200	S/F for P/F 300
Rice TW et al(20)	2007	235	315
Sheetal Babu et al(9)	2010	285	323
Khemani et al (27)	2013	201	263
Rakesh Alur et al (28)	2024	252	321
Our study	2024	229	312

In our study the PaO_2 and SpO_2 measurements done simultaneously while the others done within period of 5-8 min because rapid changes happen to the measurement PaO_2 and SpO_2 which affect the result.

The slight difference between our study and the others like Rice et al may be due to in our study, the SpO_2 reading above 97% was not excluded because some patients remain in liberal oxygen therapy with high SpO_2 control this cause the reading of PaO_2 may be overestimated in compares with SpO_2 as explained by the sigmoid pattern of oxyhemoglobin curve, which shows the curve will be flat if SpO_2 more than 97% if we did exclude these cases which have SpO_2 more than 97% it will affect the sample size too much, however [18] reported that S/F ratio in cases that have SpO_2 more than 97% was useful for predicting acute deterioration.

If we compare the results of S/F and P/F ratios Fig and categorize the S/F ratio of the cases in correspondence to the categorization of P/F ratios according to ARDS severity by Berlin criteria, we will find the percentage the same and only the difference is the smaller percentage (19% of total) of supposed to be normal (S/F > 312) which correspond to (P/F > 300) and larger percentage (49%) of those (S/F 219-312) which correspond to mild ARDS (P/F 200-300), for that the S/F ratio may detect more cases with impairment in oxygenation than P/F including cases with early ARDS which need special monitoring and management like early admission to ICU, early intubation and protective lung strategies, etc. The same conclusion got by [17].

For that reason, S/F ratio is rapid and suitable tool for the early diagnosis of acute respiratory distress

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syndrome which lead to rapid intervention e.g. early intubation, in patient admitted to the ICU especially in cases of difficulty in getting arterial blood sample like in pediatric or in environment with limited resources, as demonstrated by study conducted by [17] that by Berlin criteria identified 7% of all child patients under mechanical ventilation with mortality rate of 33% while by using SF ratio in the Berlin definition identify 17% of patient child with mechanical ventilation with 22 % mortality rate.

Also, the easy calculation of S/F ratio minimize the errors related to calibration of the device e.g. ABG analyzer also we can include the S/F ratio in organ failure score in place of P/F ratio like modified SOFA score, another application that it recognizes the ARDS in early stages without doing arterial sampling. Another benefit it lessens the times of phlebotomy, skin bricks, pain and anemia.

One of the suggested application of utilizing S/F ratio in clinical practice is the calculation of P/F ratio from the S/F ratio for the diagnosing and assessing the severity of ARDS thus reducing the percentage of missing P/F ratio which by Stephane et al reduced from 98.6 to 68% [19].

The other application is the suggestion of using S/F ratio as well as the early warning signs as a screening tool to identify patients who at risk for deteriorating and requiring ICU admission [20].

S/F may be useful in many organ failure scores one of most important one is what is called modified SOFA score (mSOFA) which is appear in COVID-19 epidemics, similar to SOFA score in assessing the severity of multiorgan dysfunction with predicting mortality of patients but using mostly clinical variables rather than lab variables (ABG and LFT) it is validated but still need more studies in compare with SOFA score [21].

6. Limitations

There are some limitations in this study, for example the conditions in which there is difficulty in getting SpO_2 like shock, hypothermia, Nail pathology, abnormal Hb like methemoglobinemia, skin color, etc. all might reduce the accuracy of SpO_2 measurement.

The ABG recorded in the studies are those routine clinical ABGs which is done twice daily or as requested by physician which may be associated with non-standardization. So, another limitation is the fixed time of taking oxygen variables (PaO_2, SpO_2) by daily routine investigation for most of the readings which also affect the validity of the study.

The other problem, there is some factors cannot be controlled like Hb, pH, ventilator setup may affect the reading or the respiratory mechanics which also may affect the relationship between PaO_2 and SpO_2.

The other variable involved in these ratios is the FiO_2 which is sometime is predicted not calculated in cases of non-invasive ventilation by for example face mask or nasal prongs and this FiO_2 will be variable according to respiratory rate, inspiratory flow, the non-invasive device for oxygen supply.

The imperfect correlations between P/F and S/F ratios can be explained physiologically by the non-linearity relation between SpO_2 and the PaO_2 , during changing cardiovascular and metabolic status, peripheral blood circulation disturbances, hydration status, P50, Hb concentration and more important the inherent complexity of extra and intrapulmonary factors that affecting gas exchange after injury, these multifactorial circumstances suggest the need for assessing the accuracy versus the feasibility as applicable to the measurement conditions. In the present time, only the multiple inert gas elimination technique can provide accurate alveolar and arterial PaO_2 assessment but it is not practical in real time and only available in few labs in the world [22].

In addition to these physiological factors, logistics of SpO_2 signal accuracy and reliability specially during patient transport, handover and equipment changes should be noticed for that reason still the P/F and S/F correlation need more investigation in more dynamic changes such as inter and intrahospital transport of patient, patient handover, ventilator changes other environmental condition such as high altitude for example transport trauma patients by helicopter in war surgeries [22].

For many reasons we cannot abandon the P/F ratio completely because the S/F ratio may be not applicable in all patient population, or not agree about specific classification for specific intervention as for example the prone position in sever ARDS with P/F < 150 or 100.

Or the ABG samples not only taken for assessing the PaO_2 and P/F ratio but also $PaCO_2$ for assessing ventilation, pH and HCO_3 for assessing the acid base status, electrolyte, blood sugar, lactate, etc. which make the ABG valuable not only for assessing the ARDS but also sepsis, acute kidney injury, etc.

From all these prospects and limitations, there is a proposed approach globally by categorizing patients from oxygenation prospects into

- Intubated ARDS.
- Non intubated ARDS.
- ARDS in limited resources.

And by including other elements in the definition of ARDS like ultrasound of lung and use of HFNC devise in addition to S/F ratio [23].

However, the aim of this study is to use it as a bases for further cross-sectional data collection where these limitations can be controlled or bypassed. This study was done in single center with small sample size, its use over wider health settings with a wider range of patient population be limited and in spite of this strong correlation, the exact ratio between the two cannot be assumed based on single study otherwise we should observe the trend of values.

7. Conclusions

This study shows a positive correlation of P/F and S/F ratio with S/F cutoff values for diagnosis of mild and moderate and severe ARDS was 312, 219 and 146 corresponding to P/F value of 300, 200 and 100 in both invasive and non-invasive ventilation and in all mode of oxygen supplementation, thus we can use S/F ratio as surrogate to the invasive P/F ratio specially in limited resources settings.

8. Recommendations

- We recommend further researches that answer the clinical question of whether the S/F ratio used clinically in guidelines in treatment of AHRF specifically in ARDS whether it is feasible, applicable and reliable specially in association with other advanced technique like lung ultrasound.
- Future researches should be conducted with collaboration between the Iraqi and international researchers for adopting the S/F ratio or advice for further studies on specific population within Iraq.
- We need more researches conducted around the limitations of adopting S/F ratio e.g. how often pulse oximetry is not accurate for assessing hypoxemia because patients' or physiological factors.

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- We need researches conducted in limited resource setting (outside ICU) to determine the incidence of diagnosis ARDS in patient without oxygen supplement (room air) and compared with patients treated with supplemental Oxygen and the associated outcome specially the mortality.

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