Application of standard bicarbonate/carbonic acid ratio in arterial blood gas analysis

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Abstract
Arterial blood gas (ABG) analysis is a challenging but clinically very important diagnostic test in intensive care unit patients but combined acid base disorders either due to compensatory mechanisms or mixed disorders are often difficult and sometimes confusing. The aim of the current research study is to find out the clinical significance of two newer ratios derived using standard bicarbonate, bicarbonate and carbonic acid values. The study included 176 arterial blood gas samples collected from I.C.U patients and ABG analysis were done which classified them into various acid base disorder groups. Bicarbonate/carbonic acid ratio and standard bicarbonate/carbonic acid ratio values were calculated for all the samples. These two values were divided to form a newer ratio 1 (HCO$_3$-H$_2$CO$_3$/[Std HCO$_3$/H$_2$CO$_3$]) and the difference between the two values form an another newer ratio 2 (HCO$_3$-Std HCO$_3$/H$_2$CO$_3$). The relation between pH, pCO$_2$ and the two newer ratios were graphically analysed. Mean ± standard deviation was calculated for both the ratios 1 and 2 in various acid-base disorder groups. One way ANOVA statistical test was applied and the two ratios are found to be statistically significant at p<0.01 for different acid-base disorder groups. The current research study shows that the ratios are altered in various acid-base disorders depending on the changes in pCO$_2$ values. The study concluded that the two newer ratios derived may provide some clues regarding the disturbances affecting the acid-base homeostasis which may be used as a discriminator between various acid-base disorders.

Keywords: Standard bicarbonate, Bicarbonate, Carbonic acid, Acid base disorders.

Introduction
Arterial blood gas analysis is very essential in the management of critically ill patients but the interpretation is sometimes a challenging task especially if the acid-base disturbances are complex. Simple acid base disorders are very easy to diagnose but combined acid base disorders either due to compensatory mechanisms or mixed disorders are often difficult and sometimes confusing. The three main parameters in ABG analysis are the pH, pCO$_2$ and bicarbonate. Bicarbonate is a calculated parameter (derived using modified Henderson equation) while pH and pCO$_2$ are measured parameters in ABG analyzer.

The four acid base disorders are metabolic acidosis, metabolic alkalosis, respiratory acidosis and respiratory alkalosis. Simple acid base disorder is the presence of any of the four disorders with appropriate compensations. Mixed acid base disorder denotes presence of more than one primary disturbances which can be suspected from a lesser or greater than expected compensations. Respiratory disorders are associated with appropriate renal compensatory mechanisms and similarly metabolic disorders are compensated by respiratory mechanisms.

Under normal ventilation, bicarbonate parameter is useful, but in patients with abnormal ventilation (respiration) it may not reflect the true status because bicarbonate is a dependent variable and it changes with the concentration of pCO$_2$. Carbon-dioxide combines with water to form carbonic acid which dissociates into hydrogen and bicarbonate ions. So, the concentration of bicarbonate increases with increase in pCO$_2$ values and it decreases as pCO$_2$ value decreases.

Standard bicarbonate is the concentration of bicarbonate in the plasma from blood which is equilibrated with a normal pCO$_2$ (40 mmHg) and a normal pO$_2$ (over 100 mmHg) at a normal temperature (37°C). The actual bicarbonate and the standard bicarbonate concentrations are approximately equal under normal ventilation but in abnormal respiration (either hypoventilation or hyperventilation) the two values alter and deviate from each other depending on the changes in the concentration of pCO$_2$.

The bicarbonate value is increased in respiratory acidosis and decreased in respiratory alkalosis. So, the difference between bicarbonate and standard bicarbonate value is positive for respiratory acidosis and negative for respiratory alkalosis. If the acid-base disorder is purely metabolic without respiratory compensation then the bicarbonate and standard bicarbonate values are more or less closer. If the metabolic disorder is compensated by respiratory mechanisms, then the two values alter and deviate from each other.

In the current research study, standard bicarbonate/carbonic acid ratio and bicarbonate/carbonic acid ratio was calculated in various acid base disorders which is divided into groups and sub-groups. The present research study uses the standard bicarbonate, bicarbonate and carbonic acid value to derive two newer ratios. The aim of the current study is to find out whether...
the two ratios derived has any clinical significance under certain circumstances.

Materials and Methods

176 Arterial blood gas analysis samples were analyzed. Strict precautions were taken to avoid pre-analytical errors. The samples were analyzed using ABG Analyzer GEM PREMIER 3000. The parameters like measured pH, pCO₂, HCO₃⁻, standard base excess were noted. Carbonic acid concentration was calculated from pCO₂.

Calculation of Carbonic acid Concentration:
The carbonic acid concentration (mmol/L) was calculated by the given formula.
H₂CO₃=0.03 X pCO₂
Then the bicarbonate/carbonic acid and standard bicarbonate/carbonic acid ratios were calculated.

Results

Table 1: Ratio 1 and Ratio 2 values for the acid base disorders (divided into groups and sub-groups)

| S. No | Acid-base disturbances | (HCO₃⁻/H₂CO₃)/ (Std HCO₃/H₂CO₃) | Values Range | Mean ± std dev |
|-------|------------------------|----------------------------------|--------------|---------------|
| 1     | Normal (23 cases)      | 0.949 to 1.049                   | 0.986 ± 0.0303 | -1.14 to 0.909 | -0.34 ± 0.65 |
| 2     | Mixed Disorder (35 cases) | 0.692 to 0.928 | 0.856 ± 0.066 | -9.629 to -1.505 | -3.69 ± 2.23 |
|       | Respiratory Alkalosis  |                                  |              |               |
|       | + Metabolic Alkalosis  |                                  |              |               |
|       | (20 cases)             |                                  |              |               |
|       | Respiratory Acidosis   |                                  |              |               |
|       | + Metabolic Alkalosis  |                                  |              |               |
|       | (12 cases)             |                                  |              |               |
|       | Respiratory Acidosis   |                                  |              |               |
|       | + Metabolic Alkosis    |                                  |              |               |
|       | (3 cases)              |                                  |              |               |
| 3     | Respiratory Acidosis   |                                  | 1.06 to 1.27 | 1.174 ± 0.080 | 0.849 to 2.95 | 2.16 ± 0.792 |
| 4     | Respiratory Alkalosis  |                                  |              |               |
|       | (49 cases)             |                                  |              |               |
|       | A. Decreased pCO₂      |                                  |              |               |
|       | With HCO₃⁻ (<18 mEq/L) |                                  |              |               |
|       | (8 cases)              |                                  |              |               |
|       | B. Decreased pCO₂      |                                  |              |               |
|       | With HCO₃⁻ (≥18 <22 mEq/L): (16 cases) |      |              |               |
|       | C. Decreased pCO₂      |                                  |              |               |
|       | With Normal HCO₃⁻ (22-26 mEq/L): (25 cases) |      |              |               |
| 5     | Metabolic Acidosis     |                                  |              |               |
|       | (34 cases)             |                                  |              |               |
|       | A. Decreased HCO₃⁻     |                                  |              |               |
|       | With pCO₂ (<30 mm Hg) : (15 cases) |      |              |               |
|       | B. Decreased HCO₃⁻     |                                  |              |               |
|       | With pCO₂ (30-34 mm Hg) : (6 cases) |      |              |               |
|       | C. Decreased HCO₃⁻     |                                  |              |               |
|       | With Normal pCO₂       |                                  |              |               |

Calculation of Ratio 1: (HCO₃⁻/H₂CO₃) / (Std HCO₃/H₂CO₃)
Ratio 1 is calculated by dividing the bicarbonate/carbonic acid and standard bicarbonate/carbonic acid ratios
Ratio 1 = (HCO₃⁻/H₂CO₃) / (Std HCO₃/H₂CO₃)

Calculation of Ratio 2: (HCO₃⁻ - Std HCO₃)/ H₂CO₃
Ratio 2 is the differences between bicarbonate/carbonic acid and standard bicarbonate/carbonic acid ratio. Obviously, the ratio 1 denotes the ratio between bicarbonate and standard bicarbonate value.
Ratio 2 = (HCO₃⁻ - Std HCO₃)/ H₂CO₃

Arterial blood gas analysis was done for all the 176 samples which revealed 23 normal cases, 35 mixed disorder cases, 8 respiratory acidosis, 49 respiratory alkalosis, 34 metabolic acidosis and 27 metabolic alkalosis cases.
Table 2: One way ANOVA Statistical Analysis between Normal, Respiratory Acidosis and Mixed Disorder cases

| Parameter | Normal | Resp acid | Mixed (Resp alk + Met acid) | Mixed (Resp acid + Met alk) | Mixed (Resp acid + Met acid) | Total |
|-----------|--------|-----------|-----------------------------|-----------------------------|-----------------------------|-------|
| N         | 23     | 8         | 20                          | 12                          | 3                           | 66    |
| ΣX        | 22.68  | 17.303    | 17.1121                     | 13.6111                     | 3.6463                      | 74.3524 |
| Mean      | 0.9861 | 2.1629    | 0.8556                      | 1.1343                      | 1.2154                      | 1.1266 |
| ΣX²       | 22.3846 | 41.8181   | 14.7244                     | 15.45                       | 4.4355                      | 98.8126 |
| Std.Dev.  | 0.0303 | 0.7923    | 0.0662                      | 0.0325                      | 0.0434                      | 0.4812 |

Result: The f-ratio value is 35.61306. The p-value is < .00001. The result is significant at p < .01.

Source
SS   df   MS
Between cases   10.5382  4   2.6346
Within same cases   4.5126 61   0.074
Total                  15.0508 65

Ratio 2

| Parameter | Normal | Resp acid | Mixed (Resp alk + Met acid) | Mixed (Resp acid + Met alk) | Mixed (Resp acid + Met alk) | Total |
|-----------|--------|-----------|-----------------------------|-----------------------------|-----------------------------|-------|
| N         | 23     | 8         | 20                          | 12                          | 3                           | 66    |
| ΣX        | -7.8347 | 17.303    | -73.8289                    | 28.9787                     | 4.7999                      | -30.5821 |
| Mean      | -0.3406 | 2.1629    | -3.6914                     | 2.4149                      | 1.6                         | -0.4634 |
| ΣX²       | 12.0372 | 41.8181   | 366.8743                    | 72.3676                     | 7.7423                      | 500.8394 |
| Std.Dev.  | 0.6526 | 0.7923    | 2.2283                      | 0.4659                      | 0.1769                      | 2.7363 |

Result: The f-ratio value is 51.88379. The p-value is < .00001. The result is significant at p < .01.

Source
SS   df   MS
Between cases   376.1179  4   94.0295
Within same cases   110.5509 61   1.8123
Total                   486.6688 65

Table 3: One way ANOVA Statistical Analysis between Metabolic acidosis (3 subgroups) and Metabolic alkalosis (2 subgroups) cases

| Parameter | Metabolic acidosis | Metabolic alkalosis |
|-----------|---------------------|----------------------|
| Decreased HCO₃ With pCO₂ (<30 mm Hg) | Decreased HCO₃ With pCO₂ (30-34 mmHg) | Decreased HCO₃ With Normal pCO₂ (35-45 mm Hg) | Increased HCO₃ With Normal pCO₂ | Increased HCO₃ With Increased pCO₂ | Total |
| N         | 15      | 6       | 13     | 16     | 11     | 61    |
| ΣX        | 11.9945 | 5.4493  | 12.8395 | 16.1348 | 12.3847 | 58.8028 |
| Mean      | 0.7996  | 0.9082  | 0.9877  | 1.0084  | 1.1259  | 0.964 |
| ΣX²       | 9.6831  | 4.951   | 12.703  | 16.2732 | 13.9465 | 57.5568 |
| Std.Dev.  | 0.0811  | 0.0195  | 0.0428  | 0.0124  | 0.0166  | 0.1206 |

Result: The f-ratio value is 86.97267. The p-value is < .00001. The result is significant at p < .01.

Source
SS   df   MS
Between cases   0.751   4   0.1878
Within cases   0.1209   56   0.0022
Total                0.8719 60

Ratio 2
### Table 4: One way ANOVA Statistical Analysis between Respiratory acidosis (no sub-group) and Respiratory alkalosis (3 sub-groups) cases

#### Ratio 1

| Parameter | Respiratory acidosis | Respiratory alkalosis | Total |
|-----------|----------------------|-----------------------|-------|
|           | Decreased pCO₂ with HCO₃⁻ (≤18 mEq/L) | Decreased pCO₂ with HCO₃⁻ (≥18 ≤22 mEq/L) | Decreased pCO₂ with Normal HCO₃⁻ (22-26 mEq/L) |
| N         | 8                    | 8                     | 16        | 25       | 57       |
| ΣX        | 9.3956               | 6.2666                | 14.1825   | 23.2159  | 53.0606  |
| Mean      | 1.1745               | 0.7833                | 0.8864    | 0.9286   | 0.9309   |
| ΣX²       | 11.0798              | 4.9219                | 12.5759   | 21.5698  | 50.1473  |
| Std.Dev.  | 0.0803               | 0.0432                | 0.0172    | 0.0211   | 0.116    |

Result: The f-ratio value is 164.10096. The p-value is < .00001. The result is significant at p < .01.

| Source | SS   | df | MS  |
|--------|------|----|-----|
| Between- cases | 0.6806 | 3  | 0.2269 | F = 164.10096 |
| Within- cases    | 0.0733 | 53 | 0.0014 |
| Total            | 0.7538 | 56 |       |

#### Ratio 2

| Parameter | Respiratory acidosis | Respiratory alkalosis | Total |
|-----------|----------------------|-----------------------|-------|
|           | Decreased pCO₂ with HCO₃⁻ (≤18 mEq/L) | Decreased pCO₂ with HCO₃⁻ (≥18 ≤22 mEq/L) | Decreased pCO₂ with Normal HCO₃⁻ (22-26 mEq/L) |
| N         | 8                    | 8                     | 16        | 25       | 57       |
| ΣX        | 17.303               | -59.4815              | -51.3827  | -52.3992 | -145.9603 |
| Mean      | 2.1629               | -7.4352               | -3.2114   | -2.096   | -2.5607  |
| ΣX²       | 41.8181              | 482.6724              | 171.8984  | 130.1103 | 826.4993 |
| Std.Dev.  | 0.7923               | 2.4029                | 0.6776    | 0.9193   | 2.8433   |

Result: The f-ratio value is 93.45073. The p-value is < .00001. The result is significant at p < .01.

| Source | SS   | df | MS  |
|--------|------|----|-----|
| Between- cases | 380.7564 | 3  | 126.9188 | F = 93.45073 |
| Within- cases    | 71.9812 | 53 | 1.3581 |
| Total            | 452.7377 | 56 |       |

### Table 5: One way ANOVA Statistical Analysis between Normal, Respiratory alkalosis with normal HCO₃⁻, Metabolic acidosis and Metabolic alkalosis with normal pCO₂ cases

#### Ratio 1

| Parameter | Normal | Decreased pCO₂ with Normal HCO₃⁻ | Decreased HCO₃⁻ with Normal pCO₂ (35-45 mm Hg) | Increased HCO₃⁻ with Normal pCO₂ | Total |
|-----------|--------|---------------------------------|-----------------------------------------------|---------------------------------|-------|
| N         | 23     | 25                              | 13                                            | 16                              | 77    |
| ΣX        | 22.68  | 23.2159                         | 12.8395                                       | 16.1348                         | 74.8703 |
| Mean      | 0.9861 | 0.9286                          | 0.9877                                        | 1.0084                          | 0.9723 |
| ΣX²       | 22.3846| 21.5698                         | 12.703                                        | 16.2732                         | 72.9306 |

International Journal of Clinical Biochemistry and Research, April-June, 2018;5(2):314-320
T. Rajini Samuel  
Application of standard bicarbonate/carbonic acid ratio in arterial blood gas analysis

| Std.Dev. | 0.0303 | 0.0211 | 0.0428 | 0.0124 | 0.0415 |
|----------|--------|--------|--------|--------|--------|

**Result:** The $f$-ratio value is 33.53558. The $p$-value is < .00001. The result is significant at $p < .01$.

| Source | SS   | df | MS    | $F = 33.53558$ |
|--------|------|----|-------|----------------|
| Between- cases | 0.076 | 3  | 0.0253 |                |
| Within- cases   | 0.0551 | 73 | 0.0008 |                |
| Total            | 0.1311 | 76 |        |                |

**Ratio 2**

| Parameter | Normal | Decreased pCO$_2$ With Normal HCO$_3$ | Decreased HCO$_3$ With Normal pCO$_2$ (35-45 mm Hg) | Increased HCO$_3$ With Normal pCO$_2$ | Total |
|-----------|--------|--------------------------------------|------------------------------------------------|--------------------------------------|-------|
| N         | 23     | 25                                   | 13                                           | 16                                   | 77    |
| $\Sigma X$ | -7.8347 | -52.3992                      | -3.7013                                      | 3.5108                               | -60.4245 |
| Mean      | -0.3406 | -2.096                             | -0.2847                                      | 0.2194                               | -0.7847 |
| $\Sigma X^2$ | 12.0372 | 130.1103                        | 5.7636                                       | 2.4652                               | 150.3764 |
| Std.Dev.  | 0.6526 | 0.9193                            | 0.6265                                       | 0.3361                               | 1.1639 |

**Result:** The $f$-ratio value is 45.15061. The $p$-value is < .00001. The result is significant at $p < .01$.

| Source | SS   | df | MS    | $F = 45.15061$ |
|--------|------|----|-------|----------------|
| Between- cases | 66.9029 | 3  | 22.301 |                |
| Within- cases   | 36.0564 | 73 | 0.4939 |                |
| Total            | 102.9593 | 76 |        |                |

**Graph 1:** pH vs (HCO$_3$/H$_2$CO$_3$)

**Graph 2:** pH vs (Std HCO$_3$/H$_2$CO$_3$)

**Graph 3:** (Std HCO$_3$/H$_2$CO$_3$) vs (HCO$_3$/H$_2$CO$_3$)

**Graph 4:** (HCO$_3$ / (Std HCO$_3$/H$_2$CO$_3$)) vs (HCO$_3$ - Std HCO$_3$) / H$_2$CO$_3$
Graph 5: pCO2 vs (HCO3/H2CO3) / (Std HCO3/H2CO3)

Graph 6: pCO2 vs (HCO3 - Std HCO3) / H2CO3

Discussion

The arterial blood gas analysis is very essential in critically ill patients but interpretation is sometimes challenging for combined or mixed acid base disorders which are not uncommon in I.C.U patients. For arterial blood gas analysis, usually bicarbonate and standard base excess values are used and not the standard bicarbonate values. The ratio between bicarbonate and carbonic acid is 20 at pH 7.4 under normal conditions. The changes in pH value depends only on the ratio and not on the absolute value of bicarbonate and carbonic acid (derived from pCO2) which is clearly shown in graph 1.5,6 Standard bicarbonate calculation and it’s clinical application is clearly shown in the previous research studies. But Standard bicarbonate/carbonic acid ratio calculation is not clearly documented in any of the previous research studies.

In this current research study, 176 arterial blood samples collected from I.C.U patients were analyzed and the ABG parameters like pH, pCO2, bicarbonate, standard bicarbonate and Standard base excess values were noted. ABG interpretation was done and all the samples were classified into various acid base disorders. The various groups included in this study are normal cases, mixed disorder, respiratory acidosis, respiratory alkalosis, metabolic acidosis and metabolic alkalosis cases.

Mixed acid base disorder includes cases with more than one primary acid-base disorder. Renal compensations (either increased or decreased bicarbonate levels) are seen in respiratory acid-base disorders. Similarly metabolic acid-base disorders are compensated by respiratory mechanisms (either decreased pCO2 or increased pCO2). Based on this, some groups were divided into sub-groups. Respiratory alkalosis cases were further divided into three subgroups namely decreased pCO2 with HCO3 (<18 mEq/L), decreased pCO2 with HCO3 (≥18 <22 mEq/L) and decreased pCO2 with normal HCO3 (22-26 mEq/L). Metabolic acidosis were further divided into three subgroups namely decreased HCO3 with pCO2 (<30 mm Hg), decreased HCO3 with pCO2 (30-34 mmHg) and decreased HCO3 with normal pCO2 (35-45 mm Hg). Similarly two subgroups included in metabolic alkalosis are increased HCO3 with normal pCO2 and increased HCO3 with increased pCO2 cases.

The present research study uses the standard bicarbonate, bicarbonate and carbonic acid values to derive two newer ratios. The aim of the current study is to find out whether the two ratios derived has any clinical significance under certain circumstances. The Bicarbonate/carbonic acid ratio and standard bicarbonate/carbonic acid ratio values were calculated for all the cases. The two newer ratios derived from them namely ratio 1 (HCO3/H2CO3)/(Std HCO3/H2CO3) and the ratio 2 (HCO3 - Std HCO3) / H2CO3 were calculated for each acid-base disorder groups. Mean ± standard deviation was calculated and range of values for both the ratios were noted for each group of the acid-base disorders which is shown in the table 1.

The relation between pH, standard bicarbonate/carbonic acid ratio and bicarbonate/carbonic acid ratio is shown in the graphs 2 and 3. The correlation between the two newer ratios ratio 1 and the ratio 2 clearly depicted in the graph 4 shows that ratio 2 values are positive for greater ratio 1 values and negative for lesser ratio 1 values. Obviously, the value of ratio 2 is zero if the ratio 1 value is one.

The relation between pCO2 and the ratio 1 (HCO3/H2CO3) / (Std HCO3/H2CO3) depicted in the graph 5 clearly shows that as the pCO2 increases, the ratio 1 also increases and afterwards the curve flattens. The relation between pCO2 and the ratio 2 (HCO3 - Std HCO3) / H2CO3 is shown in the graph 6. As the pCO2 increases, the ratio 2 also increases and afterwards the curve flattens. At pCO2 40 mmHg, both the bicarbonate and standard bicarbonate values are equal and so the difference is zero. Ratio 2 values are negative for pCO2 lesser than 40 mmHg and the values are positive if the pCO2 is more than 40 mmHg.

Statistical Analysis

Statistical analysis was done using one way ANOVA statistical chart. F-ratio value and p value was calculated for different groups of the acid-base disorders. Statistical analysis between normal cases, respiratory acidosis and mixed disorder cases are shown in the table.
2. Metabolic acid-base disorders (metabolic acidosis and metabolic alkalosis) and respiratory acid-base disorders (respiratory acidosis and respiratory alkalosis) were independently statistically analysed and shown in the table 3 and 4 respectively. Normal cases and the subgroups like respiratory alkalosis with normal bicarbonate, metabolic acidosis with normal pCO₂ and metabolic alkalosis with normal pCO₂ cases were statistically analyzed and shown in table 5.

Statistical analysis shows that the two newer ratio values are statistically significant at p <0.01 for all the groups. The ratio 1 value is greater for increased pCO₂ values and lesser for decreased pCO₂ values when compared to the normal cases values. Similarly, the ratio 2 is greater positive for increased pCO₂ values (hypoventilation or respiratory acidosis) and greater negative for decreased pCO₂ values (hyperventilation or respiratory alkalosis). The alteration of ratio values are minimal in purely metabolic acid-base disturbances without respiratory compensation but they are statistically significant at p<0.01. The ratio values are greatly altered in metabolic acid-base disturbances with appropriate respiratory compensatory mechanisms.

The major advantage of these ratios is that they can be easily calculated and applied at bedside if the bicarbonate, standard bicarbonate and pCO₂ values are known. Standard bicarbonate values sometimes may not be available because it is not calculated in all the ABG analyzer which could be a major restriction in the application of these ratios. Otherwise, if available the two newer ratios derived namely ratio 1 and ratio 2 values give some clues regarding the disturbances affecting the acid-base homeostasis which may help in discriminating various acid base disorders.

Conclusion

The study concludes that the application of standard bicarbonate ratio in arterial blood gas interpretation provide a better understanding of the acid-base homeostasis. The two newer ratios derived using bicarbonate, standard bicarbonate and carbonic acid concentrations may be used as a discriminator between various acid-base disorders especially in combined or mixed acid base disturbances which are not uncommon in critically ill patients.

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Conflict OF Interest: None

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