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_2CO_3)/(Std HCO_3 /H_2CO_3)** and the difference between the two values form an another newer ratio 2 **(HCO_3 - Std HCO_3)/H_2CO_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.[1-3] 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.[4,5]

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.[6-8] Respiratory disorders are associated with appropriate renal compensatory mechanisms and similarly metabolic disorders are compensated by respiratory mechanisms.[9]

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.[9,10]

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.[10]

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.[9,10]

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.[4,5] The samples were analyzed using ABG Analyzer GEM PREMIER 3000.

The parameters like measured pH, pCO_2, HCO_3, standard base excess and Standard HCO_3 values were noted. Carbonic acid concentration was calculated from pCO_2.

Calculation of Carbonic acid Concentration:
The carbonic acid concentration (**mmol/L**) was calculated by the given formula.
H_2CO_3=0.03 X pCO_2
Then the bicarbonate/carbonic acid and standard bicarbonate/carbonic acid ratios were calculated

Calculation of Ratio 1: (HCO_3/H_2CO_3) / (Std HCO_3/H_2CO_3)
Ratio 1 is calculated by dividing the bicarbonate/carbonic acid and standard bicarbonate/carbonic acid ratios
Ratio 1= **(HCO_3/H_2CO_3) / (Std HCO_3/H_2CO_3)**
Calculation of Ratio 2: (HCO_3 - Std HCO_3) / H_2CO_3
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 = (HCO_3/H_2CO_3)- (Std HCO_3/H_2CO_3)
= **(HCO_3 - Std HCO_3) / H_2CO_3**

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.

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	(HCO_3/H_2CO_3)/ (Std HCO_3/H_2CO_3)		(HCO_3 - Std HCO_3) / H_2CO_3	
		Values Range	**Mean ± std dev**	**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)**				
	Respiratory Alkalosis + Metabolic Acidosis **(20 cases)**	0.692 to 0.928	0.856 ±0.066	-9.629 to -1.505	-3.69 ± 2.23
	Respiratory Acidosis + Metabolic Alkalosis **(12 cases)**	1.07 to 1.19	1.134 ± 0.033	1.503 to 3.088	2.41 ± 0.465
	Respiratory Acidosis + Metabolic Acidosis **(3 cases)**	1.18 to 1.26	1.215 ± 0.043	1.48 to 1.80	1.59 ± 0.176
3	**Respiratory Acidosis (8 cases)**	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 pCO_2 With HCO_3 (<18 mEq/L) : **(8 cases)**	0.726 to 0.843	0.783 ± 0.043	-10.98 to -4.4	-7.43 ± 2.40
	B. Decreased pCO_2 With HCO_3 (≥18 <22 mEq/L): **(16 cases)**	0.857 to 0.907	0.886 ± 0.017	-4.53 to -2.36	-3.21 ± 0.677
	C. Decreased pCO_2 With Normal HCO_3 (22-26 mEq/L) : **(25 cases)**	0.885 to 0.960	0.929 ± 0.021	-4.848 to -0.980	-2.096 ± 0.919
5	**Metabolic Acidosis (34 cases)**				
	A. Decreased HCO_3 With pCO_2 (<30 mm Hg) : **(15 cases)**	0.674 to 0.884	0.799 ± 0.081	-7.22 to -2.29	-3.949 ± 1.704
	B. Decreased HCO_3 With pCO_2 (30-34 mm Hg) : **(6 cases)**	0.886 to 0.937	0.908 ± 0.019	-2.15 to -0.937	-1.635 ± 0.3958
	C. Decreased HCO_3 With Normal pCO_2	0.944to 1.055	0.988 ± 0.043	-1.018 to 0.569	-0.285 ± 0.626

	(35-45 mm Hg) :**(13 cases)**				
6	**Metabolic Alkalosis (27 cases)**				
	A. Increased HCO_3 With Increased pCO_2: **(11 cases)**	1.101 to 1.148	1.126 ± 0.016	2.22 to 3.950	2.900 ± 0.525
	B. Increased HCO_3 With Normal pCO_2: **(16 cases)**	0.983 to 1.027	1.008 ± 0.012	-0.463 to 0.9009	0.219 ± 0.336

Table 2: One way ANOVA Statistical Analysis between Normal, Respiratory Acidosis and Mixed Disorder cases

Ratio 1						
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
∑X	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
$\sum X^2$	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	F = 35.61306
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 acid)**	**Total**
N	23	8	20	12	3	66
∑X	-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
$\sum X^2$	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	*F* = 51.88379
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

Ratio 1						
Parameter	**Metabolic acidosis**			**Metabolic alkalosis**		**Total**
	Decreased HCO_3 With pCO_2 (<30 mm Hg)	**Decreased HCO_3 With pCO_2 (30-34 mmHg)**	**Decreased HCO_3 With Normal pCO_2 (35-45 mm Hg)**	**Increased HCO_3 With Normal pCO_2**	**Increased HCO_3 With Increased pCO_2**	
N	15	6	13	16	11	61
∑X	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
$\sum X^2$	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	*F* = 86.97267
Within- cases		0.1209		56	0.0022	
Total		0.8719		60		
Ratio 2						

Parameter	Decreased HCO_3 With pCO_2 (<30 mm Hg)	Decreased HCO_3 With pCO_2 (30-34 mm Hg)	Decreased HCO_3 With Normal pCO_2 (35-45 mm Hg)	Increased HCO_3 With Normal pCO_2	Increased HCO_3 With Increased pCO_2	Total
N	15	6	13	16	11	61
∑X	-59.236	-9.8146	-3.7013	3.5108	31.9051	-37.336
Mean	-3.9491	-1.6358	-0.2847	0.2194	2.9005	-0.6121
∑X²	274.5836	16.8378	5.7636	2.4652	95.3044	394.9547
Std.Dev.	1.7041	0.3958	0.6265	0.3361	0.5258	2.4903
Result: The ***f*-ratio value is 88.93281. The *p*-value is < .00001**. The result is significant at $p < .01$.						
Source		**SS**		**df**	**MS**	
Between- cases		321.4925		4	80.3731	*F* = 88.93281
Within- cases		50.6101		56	0.9038	
Total		372.1026		60		

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

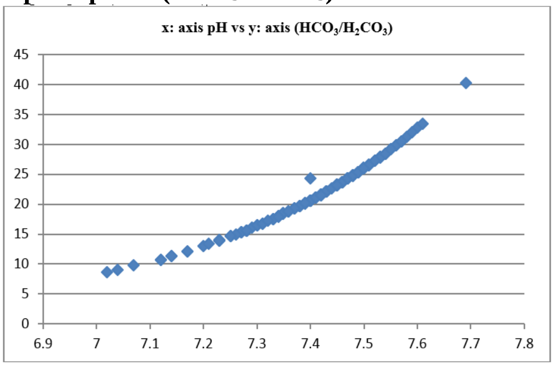
Ratio 1					
Parameter	**Respiratory acidosis**	**Respiratory alkalosis**			**Total**
		Decreased pCO_2 With HCO_3 (<18 mEq/L)	**Decreased pCO_2 With HCO_3 (≥18 <22 mEq/L)**	**Decreased pCO_2 With Normal HCO_3 (22-26 mEq/L)**	
N	8	8	16	25	57
∑X	9.3956	6.2666	14.1825	23.2159	53.0606
Mean	1.1745	0.7833	0.8864	0.9286	0.9309
∑X²	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**	**Decreased pCO_2 With HCO_3 (<18 mEq/L)**	**Decreased pCO_2 With HCO_3 (≥18 <22 mEq/L):**	**Decreased pCO_2 With Normal HCO_3 (22-26 mEq/L)**	**Total**
N	8	8	16	25	57
∑X	17.303	-59.4815	-51.3827	-52.3992	-145.9603
Mean	2.1629	-7.4352	-3.2114	-2.096	-2.5607
∑X²	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 HCO_3, Metabolic acidosis and Metabolic alkalosis with normal pCO_2 cases

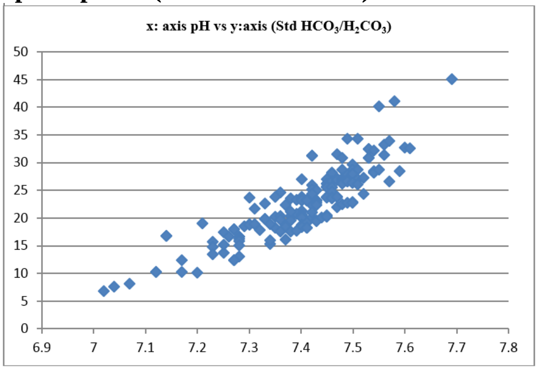
Ratio 1					
Parameter	**Normal**	**Decreased pCO_2 With Normal HCO_3**	**Decreased HCO_3 With Normal pCO_2 (35-45 mm Hg)**	**Increased HCO_3 With Normal pCO_2**	**Total**
N	23	25	13	16	77
∑X	22.68	23.2159	12.8395	16.1348	74.8703
Mean	0.9861	0.9286	0.9877	1.0084	0.9723
∑X²	22.3846	21.5698	12.703	16.2732	72.9306

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**	
Between- cases		0.076	3	0.0253	*F* = 33.53558
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
∑X	-7.8347	-52.3992	-3.7013	3.5108	-60.4245
Mean	-0.3406	-2.096	-0.2847	0.2194	-0.7847
$\sum X^2$	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**	
Between- cases		66.9029	3	22.301	*F* = 45.15061
Within- cases		36.0564	73	0.4939	
Total		102.9593	76		

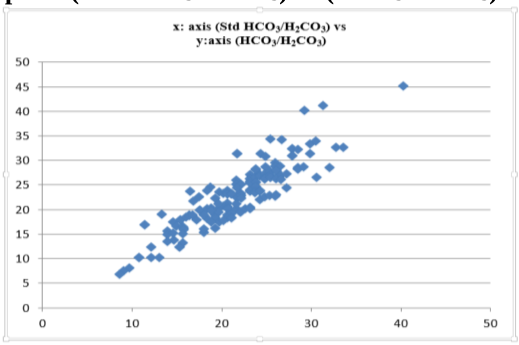
Graph 1: pH vs (HCO_3/H_2CO_3)



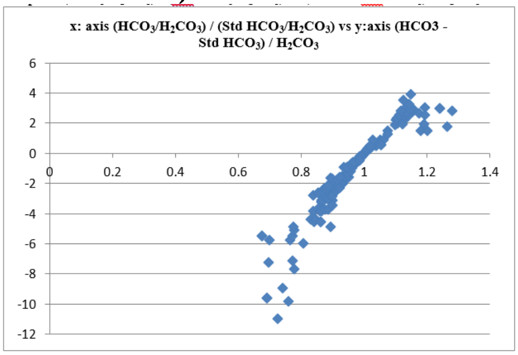
Graph 2: pH vs (Std HCO_3/H_2CO_3)



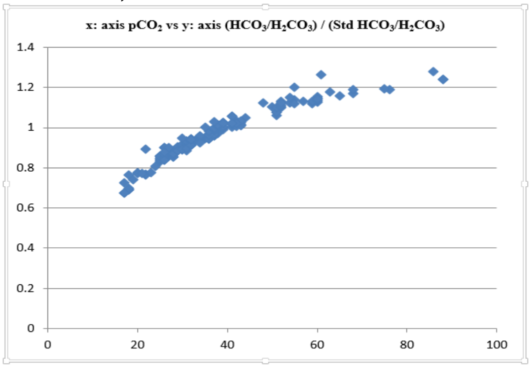
Graph 3: (Std HCO_3/H_2CO_3) vs (HCO_3/H_2CO_3)



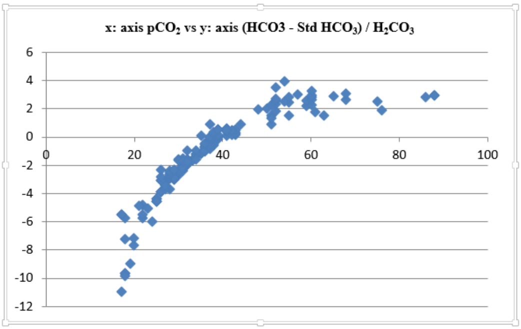
Graph 4: (HCO_3/H_2CO_3) / (Std HCO_3/H_2CO_3) vs (HCO_3 - Std HCO_3) / H_2CO_3



Graph 5: pCO_2 vs (HCO_3/H_2CO_3) / (Std HCO_3/H_2CO_3)



Graph 6: pCO_2 vs (HCO3 - Std HCO_3) / H_2CO_3



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.[1-3] 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 pCO_2) which is clearly shown in graph1.[4,5] Standard bicarbonate calculation and it's clinical application is clearly shown in the previous research studies.[9,10] 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, pCO_2, 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.[6-8] 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 pCO_2 or increased pCO_2).[9] Based on this, some groups were divided into sub-groups. **Respiratory alkalosis** cases were further divided into **three subgroups** namely decreased pCO_2 with HCO_3 (<18mEq/L), decreased pCO_2 with HCO_3 (≥18 <22 mEq/L) and decreased pCO_2 with normal HCO_3 (22-26 mEq/L). **Metabolic acidosis** were further divided into **three subgroups** namely decreased HCO_3 with pCO_2 (<30 mm Hg), decreased HCO_3 with pCO_2 (30-34 mmHg) and decreased HCO_3 with normal pCO_2 (35-45 mm Hg). Similarly **two subgroups** included in **metabolic alkalosis** are increased HCO_3 with normal pCO_2 and increased HCO_3 with increased pCO_2 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** (HCO_3/H_2CO_3)/(Std HCO_3/H_2CO_3) and the **ratio 2** (HCO_3 - Std HCO_3) / H_2CO_3 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 pCO_2 and the ratio 1 (HCO_3/H_2CO_3) / (Std HCO_3/H_2CO_3) depicted in the **graph 5** clearly shows that as the **pCO_2 increases**, the **ratio 1** also **increases** and afterwards the **curve flattens**. The relation between pCO_2 and the ratio 2 (HCO_3 - Std HCO_3) / H_2CO_3 is shown in the **graph 6**. As the pCO_2 increases, the ratio 2 also increases and afterwards the curve flattens. At **pCO_2 40 mmHg**, both the bicarbonate and standard bicarbonate **values** are **equal** and so the **difference** is **zero**. Ratio 2 values are negative for pCO_2 lesser than 40 mmHg and the values are positive if the pCO_2 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 sub-groups like respiratory alkalosis with normal bicarbonate, metabolic acidosis with normal pCO_2 and metabolic alkalosis with normal pCO_2 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 pCO_2 values and lesser for decreased pCO_2 values when compared to the normal cases values. Similarly, the ratio 2 is greater positive for increased pCO_2 values (hypoventilation or respiratory acidosis) and greater negative for decreased pCO_2 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 pCO_2 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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