Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

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Abstract: The concept of Non-Respiratory Hydrogen Ion Concentration (NRH⁺) is an older and tenable concept but often not discussed in detail during Arterial blood gas (ABG) interpretation. Simple method to calculate the same and its inter-relationship with other ABG parameters is not clearly documented in the previous studies. In the current research study 188 Arterial blood gas sample data’s were utilized. Measured parameters like pH, pCO₂ and derived parameters like HCO₃⁻, Standard HCO₃⁻ and Standard base excess values were noted. NRH⁺ calculated by Modified Henderson Equation using standard bicarbonate is related to the Non-Respiratory pH (NRpH). Then, ΔRpH (pH - NRpH) denoting the changes in pH due to respiratory influence is derived. The inter-relationship between the parameters like NRH⁺, NRH⁺/H⁺, ΔRpH, bicarbonate, standard bicarbonate, base excess and carbonic acid were graphically analyzed. The calculations were tabulated for all the 188 samples divided into different acid base disorder groups. The current research study enumerates the postulates of the acid base balance theory and concludes that understanding of the inter-relationship of NRH⁺ in acid base balance theory may play a vital role in ABG interpretation which has immense clinical value.

Keywords: Non-Respiratory Hydrogen Ion concentration, Acid-Base Balance Theory

1. INTRODUCTION

It was suggested even before a century by Hasselbalch that measuring the reduced pH after equilibrating the blood with a pCO₂ of 40 mm of Hg would be an index of the acid-base situation which is relatively independent of arterial pCO₂.[I,II] Even after many decades, there had been attempts to introduce the same and Non-respiratory hydrogen ion concentration parameter had been suggested as one of the measure of metabolic acid-base disorders but at that time it was not readily accepted partly because the derivation is not simple and carbon dioxide tension had to be estimated by Astrup method.[I] The inter-relationship and the orientation between the Non-respiratory hydrogen ion concentration and the traditional acid-base parameters had not been available.[I]

Numerous studies had been done with the commonly used parameters like bicarbonate and base excess. Standard base excess has been well validated both for accuracy and for clinical correlation through many decades. The physicochemical approach by Fencl-Stewart has gained popularity in recent times in the intensive care unit setting because it is useful towards the understanding of complex acid-base disorders and to define the causation and severity of acid base disorders.[III,IV]

The current research study re-introduces the clinical significance of non-respiratory hydrogen ion concentration and other parameters derived from it by simple formulae and graphical methods. The inter-relationship between these and the other commonly used parameters in ABG were graphically analyzed and applied in the acid-base balance theory.

2. MATERIALS AND METHODS

188 arterial blood gas analysis sample data’s were collected. The measured parameters like pH, pCO₂ and the derived parameters like HCO₃⁻, Std HCO₃⁻ and Std Base Excess values are noted. The following derivations and calculations are applied to these obtained data’s.
Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

Calculation of $H^+$:

$H^+$ - Hydrogen ion concentration at actual pH

(calculated using Modified Henderson Equation)

$$H^+(\text{Hydrogen ion concentration}) = \frac{24 \times \text{pCO}_2}{\text{HCO}_3}$$

$$\text{pH} = \log[H^+ \text{ nanomoles/L}]$$

$$= \log \left( \frac{H^+ \times 10^{-9} \text{ moles/L}}{10^{-9} \text{ moles/L}} \right)$$

$$\text{pH} = 9 - \log [H^+]$$

Calculation of NRH$^+$ (Non-Respiratory hydrogen ion concentration)

NRH$^+$ - Hydrogen ion concentration at non-respiratory pH

(at $\text{pCO}_2$ 40 mm of Hg)

This calculated hydrogen ion concentration equivalent of standard bicarbonate has thus been called the 'non-respiratory' hydrogen ion concentration or NRH$^+$.[I]

$$\text{NRH}^+ = \frac{24 \times \text{pCO}_2}{\text{Std HCO}_3}$$

$$= \frac{24 \times 40}{\text{Std HCO}_3(p\text{CO}_2\text{is 40 mm of Hg})}$$

$$\text{NRH}^+ = 960 / \text{Std HCO}_3$$

$$\text{NRpH} = 9 - \log [\text{NRH}^+]$$

Calculation of $\Delta RH^+$

The changes in pH is expressed in nano-equivalents of hydrogen ion per litre and dividing the change into two components namely respiratory and non-respiratory.[V]

The changes in total hydrogen ion concentration is due to changes in respiratory component and non-respiratory(metabolic)component affecting the hydrogen ion concentration.

$$\Delta H^+ = \Delta RH^+ + \Delta \text{NRH}^+$$

$$\Delta H^+ = [H^+ - 40]$$ (changes in total hydrogen ion concentration)

40 is the hydrogen ion concentration at pH 7.4 which denotes the homeostatic set point of acid base balance.[VI]

$$\Delta \text{NRH}^+ = [\text{NRH}^+ - 40]$$ (changes due to Non-respiratory component)

Hydrogen ion concentration changes due to Respiratory component is given by $\Delta RH^+$.

$$\Delta RH^+ = \Delta H^+ - \Delta \text{NRH}^+$$

$$= [H^+ - 40] - [\text{NRH}^+ - 40]$$

$$= [H^+ - 40 - \text{NRH}^+ + 40]$$

$$= [H^+ - \text{NRH}^+] = RH^+$$

$\Delta RH^+$ and $RH^+$ both are numerically same value.

$$\Delta RH^+ = \left[ H^+ \right] - \left[ \text{NRH}^+ \right]$$

The difference between the actual hydrogen ion concentration present and hydrogen ion concentration at non-respiratory pH (non respiratory hydrogen ion concentration) denotes the changes in hydrogen ion concentration due to the respiratory component (pCO$_2$).

Calculation of Hydrogen Ion Excess or Deficit [NRH$^+ - 40$]:

The hydrogen ion excess or deficit is determined by titrating to a pH of 7.4 at a pCO$_2$ of 40 mm of Hg at a temperature of 37 °C. It is the preferred indicator of a non-respiratory acid base disturbance being independent of acute changes in pCO$_2$ in vivo.[II,VI]
Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

In the present study using the above concept, the difference between the hydrogen ion concentration at non-respiratory pH and pH at 7.4 is related to hydrogen ion excess or deficit. So, the parameter [\text{NRH}^+ - 40] denotes the hydrogen ion excess which is directly proportional to the base deficit. This quantity with opposite sign (40 - \text{NRH}^+) is directly proportional to the base excess.

Calculation of \( \Delta \text{RpH} \):

\[
\text{pH} = \text{pka} + \log\frac{\text{HCO}_3^-}{\text{H}_2\text{CO}_3}
\]

\[
\text{H}_2\text{CO}_3 = 0.03 \times \text{pCO}_2
\]

\[
\text{pH} = \text{pka} + \log\frac{\text{HCO}_3^-}{0.03 \times \text{pCO}_2}
\]

\[
\text{NRpH} = \text{pka} + \log\frac{\text{Std} \text{HCO}_3^-}{\text{H}_2\text{CO}_3}
\]

\[
\text{NRpH} = \text{pka} + \log\frac{\text{Std} \text{HCO}_3^-}{0.03 \times \text{pCO}_2}
\]

\( \text{pCO}_2 \) is 40 mm of Hg at non-respiratory pH

\[
\text{NRpH} = \text{pka} + \log\frac{\text{Std} \text{HCO}_3^-}{(0.03 \times 40)}
\]

\[
\Delta \text{RpH} (\text{pH} - \text{NRpH})
\]

\[
= \{ \text{pka} + \log\frac{\text{HCO}_3^-}{(0.03 \times \text{pCO}_2)} \} - \{ \text{pka} + \log[\text{StdHCO}_3^-/(0.03 \times 40)] \}
\]

\[
= \log\frac{\text{HCO}_3^-}{0.03 \times \text{pCO}_2} - \log[\text{StdHCO}_3^-/(0.03 \times 40)]
\]

\[
= \log \frac{\text{HCO}_3^-}{(0.03 \times \text{pCO}_2)}/\text{pCO}_2 + \log 40
\]

\[
(\text{the value of log 40 is 1.6})
\]

\[
\text{pH} - \text{NRpH} = 1.6 + \log\frac{\text{HCO}_3^-/\text{Std} \text{HCO}_3^-}{\text{pCO}_2}
\]

or

\[
= 1.6 + \log (\text{HCO}_3^-/\text{Std} \text{HCO}_3^-) - \log(\text{pCO}_2)
\]

Another method:

\[
\text{pH} = 9 - \log [\text{H}^+]
\]

\[
\text{NRpH} = 9 - \log [\text{NRH}^+]
\]

\[
\text{pH} - \text{NRpH} = 9 - \log [\text{H}^+] - 9 + \log [\text{NRH}^+]
\]

\[
= \log [\text{NRH}^+/\text{H}^+] - \log [\text{H}^+/\text{NRH}^+]
\]

\[
\text{H}^+(\text{Hydrogen ion concentration}) = \{24 \times \text{pCO}_2\}/\text{HCO}_3
\]

\[
\text{NRH}^+(\text{non respiratory hydrogen ion concentration}) = \{24 \times 40\}/\text{Std} \text{HCO}_3
\]

\[
\frac{\text{NRH}^+}{[\text{H}^+]} = \{24 \times 40\}/\text{Std} \text{HCO}_3/[24 \times \text{pCO}_2]/\text{HCO}_3
\]

\[
= 40 \times \{\text{HCO}_3^-/\text{Std} \text{HCO}_3^-\}/\text{pCO}_2
\]

Or in terms of carbonic acid\(\text{pCO}_2 = \text{H}_2\text{CO}_3/0.03\) this can be written as,

\[
= 1.2 \times \{\text{HCO}_3^-/\text{Std} \text{HCO}_3^-\}/\text{H}_2\text{CO}_3
\]

\[
\text{pH} - \text{NRpH} = \log \frac{\text{NRH}^+}{\text{H}^+}
\]

\[
\text{pH} - \text{NRpH} = \log 40 + \log (\text{HCO}_3^-/\text{Std} \text{HCO}_3^-) - \log(\text{pCO}_2)
\]

\[
[\text{pH} - \text{NRpH}] = 1.6 + \log(\text{HCO}_3^-/\text{Std} \text{HCO}_3^-)/\text{pCO}_2
\]

At \text{pCO}_2 40 mm of Hg, \text{pH} - \text{NRpH} is zero. (Because bicarbonate and standard bicarbonate values are equal.; log 1 is zero and log 40 is 1.6). At higher \text{pCO}_2 levels (> 40 mm of Hg), the value of [\text{pH} - \text{NRpH}] is negative which denotes the acidic influence of increased \text{pCO}_2. At lower \text{pCO}_2 levels (<40 mm of Hg), the value of [\text{pH} - \text{NRpH}] is positive which denotes the alkaline influence of decreased \text{pCO}_2.

The net changes in total \(\text{pH}\) (Actual \(\text{pH}\)) includes both the changes in respiratory and non-respiratory (metabolic) component affecting the \(\text{pH}\).\[V,VII\]

\[
\Delta \text{pH} = \Delta \text{RpH} + \Delta \text{NRpH}
\]
Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

\[ \Delta \mathrm{pH} = [\mathrm{pH} - 7.4] \] (net changes in total pH (Actual pH))
\[ \Delta \mathrm{NRpH} = [\mathrm{NRpH} - 7.4] \] (changes due to Non-respiratory component)
\[ \Delta \mathrm{RPH} = [\mathrm{pH} - 7.4] - [\mathrm{NRpH} - 7.4] \]
\[ \Delta \mathrm{RPH} = [\mathrm{pH} - \Delta \mathrm{RPH}] \]

NRpH = [pH - \Delta RPH]

Calculation of TCO\textsubscript{2}/H\textsubscript{2}CO\textsubscript{3}:
The concentration of total carbon-dioxide in blood is equal to sum of the concentrations of bicarbonate and carbonic acid in blood.
\[ \text{TCO}\textsubscript{2} = \text{HCO}\textsubscript{3}^- + \text{H}_2\text{CO}_3 \] (where H\textsubscript{2}CO\textsubscript{3} = 0.03 X pCO\textsubscript{2})
\[ \text{TCO}\textsubscript{2}/\text{H}_2\text{CO}_3 = (\text{HCO}\textsubscript{3}^- + \text{H}_2\text{CO}_3)/\text{H}_2\text{CO}_3 \]
\[ = \text{HCO}\textsubscript{3}^-/\text{H}_2\text{CO}_3 + \text{H}_2\text{CO}_3/\text{H}_2\text{CO}_3 \]
\[ = \text{HCO}\textsubscript{3}^-/\text{H}_2\text{CO}_3 + 1 \]
At pH of 7.4, HCO\textsubscript{3}^-/H\textsubscript{2}CO\textsubscript{3} ratio is 20. So, TCO\textsubscript{2}/H\textsubscript{2}CO\textsubscript{3} ratio is 21.

Calculation of TCO\textsubscript{2}(at 40 mm Hg)/H\textsubscript{2}CO\textsubscript{3}:
Standard bicarbonate is the concentration of bicarbonate at pCO\textsubscript{2} 40 mm of Hg.[I,II]
\[ \text{TCO}\textsubscript{2}(at 40 \text{ mm Hg}) = \text{Std HCO}_3^- + \text{H}_2\text{CO}_3 \]
\[ = \text{Std HCO}_3^- + 40 \times 0.03 \]
\[ \text{TCO}\textsubscript{2}(at 40 \text{ mm Hg}) = \text{Std HCO}_3^- + 1.2 \]
\[ \text{TCO}\textsubscript{2}(at 40 \text{ mm Hg})/\text{H}_2\text{CO}_3 = (\text{Std HCO}_3^- + 1.2)/\text{H}_2\text{CO}_3 \]
\[ = \text{Std HCO}_3^-/\text{H}_2\text{CO}_3 + 1.2/\text{H}_2\text{CO}_3 \]

Differences between TCO\textsubscript{2}/H\textsubscript{2}CO\textsubscript{3} and TCO\textsubscript{2}(at 40 mm Hg)/H\textsubscript{2}CO\textsubscript{3}:
\[ \text{TCO}\textsubscript{2}/\text{H}_2\text{CO}_3 - \text{TCO}\textsubscript{2}(at 40 \text{ mm Hg})/\text{H}_2\text{CO}_3 = \]
\[ \{\text{HCO}\textsubscript{3}^-/\text{H}_2\text{CO}_3 + 1\} - \{\text{Std HCO}_3^-/\text{H}_2\text{CO}_3 + 1.2/\text{H}_2\text{CO}_3\} \]
\[ (\text{TCO}_2 - \text{TCO}_2(at 40 \text{ mm Hg})/\text{H}_2\text{CO}_3) = \]
\[ \{\text{HCO}_3^- - \text{Std HCO}_3^-)/\text{H}_2\text{CO}_3\} + \{\text{H}_2\text{CO}_3 - 1.2)/\text{H}_2\text{CO}_3\} \]

(HCO\textsubscript{3}^- - Std HCO\textsubscript{3}^-)/H\textsubscript{2}CO\textsubscript{3} ratio is greater positive for respiratory acidosis and greater negative for respiratory alkalosis.[VIII] At pCO\textsubscript{2} 40 mm of Hg, both the ratios (TCO\textsubscript{2} - TCO\textsubscript{2}(at 40 mm Hg))/H\textsubscript{2}CO\textsubscript{3} and (HCO\textsubscript{3}^- - Std HCO\textsubscript{3}^-)/H\textsubscript{2}CO\textsubscript{3} are zero because standard bicarbonate and bicarbonate values are equal and H\textsubscript{2}CO\textsubscript{3} value is 1.2 at pCO\textsubscript{2} 40 mm of Hg.

Derivation of another newer parameter denoting Respiratory influence of pCO\textsubscript{2}:
It is already derived to calculate the parameter pH - NRpH.
\[ \Delta \mathrm{RPH} = (\mathrm{pH} - \mathrm{NRpH}) = 1.6 + \log(\{\text{HCO}_3^-/\text{Std HCO}_3^-\}/\text{pCO}_2) \]

From the above equation it is very clear that the value depends on the ratio HCO\textsubscript{3}^-/Std HCO\textsubscript{3} and the pCO\textsubscript{2} values. pCO\textsubscript{2} influences by changing both the bicarbonate (represented by the ratio HCO\textsubscript{3}^-/Std HCO\textsubscript{3}) and carbonic acid (represented by the parameter (H\textsubscript{2}CO\textsubscript{3} - 1.2)/H\textsubscript{2}CO\textsubscript{3}).
The increase in the ratio HCO\textsubscript{3}^-/Std HCO\textsubscript{3} has alkaline effect and the decrease has acidic effect. The increase in the parameter (H\textsubscript{2}CO\textsubscript{3} - 1.2)/H\textsubscript{2}CO\textsubscript{3} has acidic effect and decrease has alkaline effect which is opposite to the effect of ratio HCO\textsubscript{3}^-/Std HCO\textsubscript{3}.

So, the net Respiratory influence of pCO\textsubscript{2} in causing acidic or alkaline effect in pH is given by the difference between them i.e

\[ \text{Net Respiratory influence of } \text{pCO}_2 = (\text{HCO}_3^-/\text{Std HCO}_3^-) - \{(\text{H}_2\text{CO}_3 - 1.2)/\text{H}_2\text{CO}_3\} \]
or (HCO\textsubscript{3}^-/Std HCO\textsubscript{3}) - \{1 - (1.2/\text{H}_2\text{CO}_3)\} 

3. RESULTS
The results are tabulated in the tables 1 to 4. In the table 1, verification of the relation \[ \Delta \text{H}^+ = \Delta \text{RH}^+ + \Delta \text{NRH}^+ \] is shown for the groups Normal, Metabolic Acidosis and Metabolic Alkalosis Cases. Total
International Journal of Clinical Chemistry and Laboratory Medicine (IJCCLM) | Page 18

Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

Cases, mean ± Std deviation of the parameters like NRH⁺, NRH⁺/H⁺, ΔH⁺ (H⁺ - 40), ΔRH⁺ (H⁺ - NRH⁺), ANRH⁺ (NRH⁺ - 40) and Standard Base Excess (SBE) are tabulated.

Table 1. Verification of the relation Δ H⁺ = ΔRH⁺ + Δ NRH⁺ in Normal, Metabolic Acidosis and Metabolic Alkalosis Cases (Total cases, mean ± Std deviation of the parameters: NRH⁺, NRH⁺/H⁺, ΔH⁺ (H⁺ - 40), ΔRH⁺ (H⁺ - NRH⁺), Δ NRH⁺ (NRH⁺ - 40) & SBE are tabulated)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal (22 cases)</th>
<th>Metabolic acidosis (43 cases)</th>
<th>Metabolic Alkalosis (26 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRH⁺ Mean &amp; Std Dev</td>
<td>38.61 ± 1.35</td>
<td>↓ HCO₃⁻ (pCO₂&lt;30 mm Hg) 18 cases</td>
<td>↓ HCO₃⁻ (pCO₂&lt;30-34 mm Hg) 11 cases</td>
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<td></td>
<td></td>
<td>↓ HCO₃⁻ (pCO₂&lt;30-34 mm Hg) 11 cases</td>
<td>↓ HCO₃⁻ (pCO₂&lt;30-34 mm Hg) 11 cases</td>
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<tr>
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<td></td>
<td>↓ HCO₃⁻ (Normal pCO₂&lt;45 mm Hg) 14 cases</td>
<td>↓ HCO₃⁻ (Normal pCO₂&lt;45 mm Hg) 14 cases</td>
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<td></td>
<td>↑ HCO₃⁻ (Normal pCO₂&lt;45 mm Hg) 16 cases</td>
<td>↑ HCO₃⁻ (Normal pCO₂&lt;45 mm Hg) 16 cases</td>
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<td>↑ HCO₃⁻ (Normal pCO₂&lt;45 mm Hg) 16 cases</td>
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</tr>
<tr>
<td>NRH⁺/H⁺ Mean &amp; Std Dev</td>
<td>1.03 ± 0.05</td>
<td>1.47 ± 0.04</td>
<td>1.015 ± 0.045</td>
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<tr>
<td>Δ H⁺ Mean &amp; Std Dev</td>
<td>-2.48 ± 2.06</td>
<td>16.31 ± 9.07</td>
<td>11.84 ± 7.77</td>
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<tr>
<td>Δ RH⁺ Mean &amp; Std Dev</td>
<td>-1.09 ± 1.83</td>
<td>-29.31 ± -7.37</td>
<td>-0.58 ± 2.39</td>
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<tr>
<td>Δ NRH⁺ Mean &amp; Std Dev</td>
<td>-1.39 ± 1.35</td>
<td>45.62 ± 16.44</td>
<td>12.42 ± 4.29</td>
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<tr>
<td>SBE Mean &amp; Std Dev</td>
<td>-0.112 ± 1.27</td>
<td>-17.26 ± -10.64</td>
<td>-8.54 ± 2.84</td>
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</tbody>
</table>

NRH⁺ is increased in Metabolic acidosis and decreased in Metabolic alkalosis. Δ NRH⁺ is related to Base deficit (opposite sign of Base Excess).

In the table 2, verification of the relation ΔpH = ΔRpH + ΔNRpH is shown for the groups Normal, Metabolic Acidosis and Metabolic Alkalosis Cases. Total cases, mean ± Std deviation of the parameters like NRpH, ΔpH (PH-7.4), ANRpH (NRpH-7.4), ΔRpH (pH-NRpH), HCO₃⁻/ Normal pCO₂ and Net Respiratory Influence of pCO₂ are tabulated.

Table 2. Verification of the relation ΔpH = ΔRpH + Δ NRpH in Normal, Metabolic Acidosis and Metabolic Alkalosis Cases: (Total cases, mean ± Std deviation of the parameters: NRpH, ΔpH (PH-7.4), ANRpH (NRpH-7.4), ΔRpH (pH-NRpH), HCO₃⁻/ Normal pCO₂, and Net Respiratory Influence of pCO₂ are tabulated)

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<th>Metabolic Alkalosis (26 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRpH Mean &amp; Std Dev</td>
<td>7.4037 ± 0.015</td>
<td>7.088 ± 0.15</td>
<td>0.06 ± 0.05</td>
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<td></td>
<td></td>
<td>7.243 ± -0.122</td>
<td>-0.126 ± 0.04</td>
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<td>7.274 ± 0.05</td>
<td>0.04 ± 0.02</td>
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<td>7.579 ± 0.045</td>
<td>7.4598 ± 0.079</td>
</tr>
<tr>
<td>ApH (pH-7.4) Mean &amp; Std Dev</td>
<td>0.0145 ± 0.024</td>
<td>0.15 ± 0.08</td>
<td>0.06 ± 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-0.155 ± -0.1</td>
<td>-0.126 ± -0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-0.157 ± -0.126</td>
<td>0.04 ± 0.03</td>
</tr>
<tr>
<td>ANRpH(NRpH-7.4) Mean &amp; Std Dev</td>
<td>0.0037 ± 0.015</td>
<td>0.15 ± 0.06</td>
<td>0.05 ± 0.04</td>
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<td></td>
<td>-0.312 ± -0.157</td>
<td>-0.126 ± 0.04</td>
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<td>0.179 ± 0.059</td>
<td>0.0598 ± 0.079</td>
</tr>
<tr>
<td>ARpH(pH-NRpH) Mean &amp; Std Dev</td>
<td>0.0108 ± 0.021</td>
<td>0.157 ± 0.057</td>
<td>0.004 ± -0.0828</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.057 ± 0.02</td>
<td>-0.0828 ± 0.0192</td>
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<tr>
<td></td>
<td></td>
<td>0.004 ± 0.02</td>
<td>0.026 ± 0.02</td>
</tr>
<tr>
<td>HCO₃⁻/ Normal pCO₂ Mean &amp; Std Dev</td>
<td>0.983 ± 0.025</td>
<td>0.787 ± 0.098</td>
<td>0.985 ± 0.03</td>
</tr>
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<td></td>
<td></td>
<td>0.015 ± 0.02</td>
<td>0.03 ± 0.02</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.132 ± 0.093</td>
<td>0.993 ± 0.02</td>
</tr>
<tr>
<td>Net Respiratory Influence of pCO₂ Mean &amp; Std Dev</td>
<td>1.034 ± 0.05</td>
<td>1.694 ± 1.172</td>
<td>1.019 ± 0.868</td>
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<tr>
<td></td>
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<td>1.053 ± 0.04</td>
<td>1.053 ± 0.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.04 ± 0.06</td>
<td>0.06 ± 0.06</td>
</tr>
</tbody>
</table>

NRpH is decreased in Metabolic acidosis and increased in Metabolic alkalosis.
In the table 3, Verification of the relation $\Delta H^+ = \Delta RH^+ + \Delta NRH^+$ is shown for the groups Respiratory acidosis, respiratory alkalosis and Miscellaneous cases. Total cases, mean ± Std deviation of the parameters like $NRH^+$, $NRH^+/H^+$, $\Delta H^+(H^+ - 40), \Delta RH^+(H^+ - NRH^+), \Delta NRH^+(NRH^+ - 40)$ and SBE are tabulated.

Table 3. Verification of the relation $\Delta H^+ = \Delta RH^+ + \Delta NRH^+$ in Respiratory acidosis, respiratory alkalosis and Miscellaneous cases. (Total cases, mean ± Std deviation of the parameters: $NRH^+$, $NRH^+/H^+$, $\Delta H^+(H^+ - 40), \Delta RH^+(H^+ - NRH^+), \Delta NRH^+(NRH^+ - 40)$ & SBE are tabulated)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Respiratory Acidosis (18 cases)</th>
<th>Respiratory alkalosis (44 cases)</th>
<th>Miscellaneous cases (35 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$NRH^+$   Mean &amp; Std Dev</td>
<td>36.98 ± 48.17</td>
<td>41.85 ± 37.35</td>
<td>47.51 ± 30.77</td>
</tr>
<tr>
<td>$NRH^+/H^+$ Mean &amp; Std Dev</td>
<td>0.729 ± 1.55</td>
<td>1.28 ± 1.20</td>
<td>1.24 ± 0.97</td>
</tr>
<tr>
<td>$\Delta H^+$ Mean &amp; Std Dev</td>
<td>11.43 ± 8.53</td>
<td>-7.12 ± 8.78</td>
<td>-1.78 ± 1.24</td>
</tr>
<tr>
<td>$\Delta NRH^+$ Mean &amp; Std Dev</td>
<td>-3.02 ± 8.17</td>
<td>1.85 ± 1.57</td>
<td>3.76 ± 2.59</td>
</tr>
<tr>
<td>SBE       Mean &amp; Std Dev</td>
<td>5.98 ± 2.80</td>
<td>1.63 ± 1.23</td>
<td>2.50 ± 4.69</td>
</tr>
</tbody>
</table>

$NRH^+/H^+$ is decreased (<1) in Respiratory acidosis and increased (>1) in Respiratory alkalosis.

In the table 4, verification of the relation $\Delta pH = \Delta RpH + \Delta NRpH$ is shown for the groups Respiratory acidosis, respiratory alkalosis and Miscellaneous cases. Total cases, mean ± Std deviation of the parameters like $NRpH$, $\Delta pH (pH - 7.4)$, $\Delta NRpH (pH - 7.4)$, $\Delta RpH (pH - NRpH)$, $HCO_3$/Std $HCO_3$ and Net Respiratory Influence of $pCO_2$ are tabulated.

Table 4. Verification of the relation $\Delta pH = \Delta RpH + \Delta NRpH$ in Respiratory acidosis, respiratory alkalosis, and Miscellaneous cases: (Total cases, mean ± Std deviation of the parameters: $NRpH$, $\Delta pH (pH - 7.4)$, $\Delta NRpH (pH - 7.4)$, $\Delta RpH (pH - NRpH)$, $HCO_3$/Std $HCO_3$ & Net Respiratory Influence of pCO2 are tabulated)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Respiratory Acidosis 18 cases</th>
<th>Respiratory alkalosis (44 cases)</th>
<th>Miscellaneous cases (35 cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$NRpH$    Mean &amp; Std Dev</td>
<td>7.426 ± 7.309</td>
<td>7.369 ± 7.418</td>
<td>7.315 ± 7.5037</td>
</tr>
<tr>
<td>$\Delta pH (pH - 7.4)$ Mean &amp; Std Dev</td>
<td>-0.118 ± 0.092</td>
<td>0.094 ± 0.094</td>
<td>0.006 ± 0</td>
</tr>
<tr>
<td>$\Delta NRpH (pH - 7.4)$ Mean &amp; Std Dev</td>
<td>0.026 ± 0.045</td>
<td>-0.031 ± 0.018</td>
<td>-0.085 ± 0.1037</td>
</tr>
<tr>
<td>$\Delta pH (pH - NRpH)$ Mean &amp; Std Dev</td>
<td>-0.144 ± 0.183</td>
<td>0.076 ± 0.091</td>
<td>0.091 ± 0.1037</td>
</tr>
<tr>
<td>$HCO_3$/Std $HCO_3$ Mean &amp; Std Dev</td>
<td>1.626 ± 0.759</td>
<td>0.879 ± 0.926</td>
<td>0.871 ± 1.128</td>
</tr>
<tr>
<td>Net Respiratory Influence of $pCO_2$ Mean &amp; Std Dev</td>
<td>0.797 ± 1.860</td>
<td>1.332 ± 1.224</td>
<td>1.310 ± 0.835</td>
</tr>
</tbody>
</table>

$\Delta pH (pH - NRpH)$ is decreased (negative) in Respiratory acidosis and increased (positive) in Respiratory alkalosis.
The inter-relationship between these various parameters were graphically analyzed and shown in the figures (figures or graphs 1 to 11).

**Figure 1 (Graph 1). Relation between NRH+ vs Std HCO3**

**Figure 2 (Graph 2). Relation between NRH+ vs Std Base Excess**

**Figure 3 (Graph 3). Relation between [40- NRH+] vs Std Base Excess**
Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

Figure 4 (Graph 4). Relation between pH-NRpH vs Log\left[\frac{HCO_3/Std HCO_3}{pCO_2}\right]

Figure 5 (Graph 5). Relation between pCO_2 vs \left(TCO_2 - TCO_2(\text{at 40 mm Hg})\right) / H_2CO_3

Figure 6 (Graph 6). Relation between pCO_2 vs (HCO_3 - Standard HCO_3) / H_2CO_3
Figure 7 (Graph 7). Relation between $pCO_2$ vs $(H_2CO_3 - 1.2)/H_2CO_3$

Figure 8 (Graph 8). Relation between $pCO_2$ vs $HCO_3/\text{Std } HCO_3$

Figure 9 (Graph 9). Relation between $pH - NRpH$ vs $[HCO_3/\text{Std } HCO_3] - (H_2CO_3 - 1.2)/H_2CO_3$
Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory

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4. DISCUSSION

A total of 188 arterial blood gas sample data’s were used and classified into various acid-base disorder groups like Normal acid-base status, Metabolic acidosis ( further divided into three subgroups namely a. decreased HCO₃⁻ with pCO₂ (<30 mm Hg), b. decreased HCO₃⁻ with pCO₂ (30-34 mmHg) and c. decreased HCO₃⁻ with normal pCO₂ (35-45 mm Hg)). Metabolic alkalosis (further divided into two subgroups namely a. increased HCO₃⁻ with normal pCO₂ and b. increased HCO₃⁻ with increased pCO₂). Respiratory acidosis, Respiratory alkalosis (further divided into three subgroups namely a. decreased pCO₂ with HCO₃⁻ (<18mEq/L) , b. decreased pCO₂ with HCO₃⁻ (≥18 <22 mEq/L) and c. decreased pCO₂ with normal HCO₃⁻ (22-26mEq/L) and Miscellaneous cases (further divided into three subgroups namely a. pH : 7.38-7.42 with decreasedpCO₂ and decreasedHCO₃⁻, b.pH : 7.38-7.42 with increasedpCO₂ and increasedHCO₃⁻, c. pH around: 7.04 with increasedpCO₂ and decreasedHCO₃⁻).

It is very clear from the table1 that non-respiratory hydrogen ion concentration (NRH⁺) is increased in Metabolic acidosis and decreased in Metabolic alkalosis. A NRH⁺(NRH⁺ - 40) is related to Base deficit (opposite sign of Base Excess) or [40- NRH⁺] is related to base excess. Similarly, non-respiratory pH(NRpH)is decreased in Metabolic acidosis and increased in Metabolic alkalosis which is shown in table 2.

The ratio NRH⁺/H⁺ decreased (<1) in Respiratory acidosis and increased(>1) in Respiratory alkalosis is shown in table 3. The parameter ΔRpH (pH-NRpH) that denotes the changes in pH due to respiratory influence is decreased(negative) in Respiratory acidosis and increased(positive) in Respiratory alkalosis is clearly shown in table 4.

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Figure 10(Graph 10). Relation between NRH⁺/H⁺ vs [HCO₃⁻ / Std HCO₃⁻ -(H₂CO₃ -1.2)/H₂CO₃]

Figure 11(Graph 11). Relation between pH-NRpH vs NRH⁺/H⁺
The inter-relationship and orientation between these various parameters were graphically analyzed. The relation between NRH° and standard Bicarbonate shown in the graph 1 clearly depicts that as NRH° increases the std Bicarbonate decreases and vice versa. The relation between NRH° and standard Base Excess shown in the graph 2 is very clear that as NRH° increases the standard base excess decreases and vice versa.

The parameter [NRH -40] denotes the concentration of hydrogen ion excess which is directly proportional to the base deficit. This quantity with negative sign [40 –NRH] is directly proportional to the base excess. Standard base excess or extracellular base excess is the base excess at Haemoglobin concentration of 5 g/dl. The relation between [40 –NRH] and the standard base excess is shown in the graph 3. The relation between the parameter [pH-NRpH] and log{(HCO₃⁻/ Std HCO₃)/ pCO₂} is a straight line, at pH-NRpH equal to zero, the value is -1.6 in the y: axis which is shown in the graph 4.

The relation between pCO₂ and the ratios namely (TCO₂ - TCO₂/at 40 mm Hg) / H₂CO₃ and (HCO₃⁻ - Std HCO₃)/ H₂CO₃ is similar which is shown in the graphs 5 & 6 respectively. As pCO₂ value increases, the two ratio values also increase and afterwards the curve flattens. As pCO₂ decreases, the ratio values also decreases. The two ratios are greater positive for respiratory acidosis and greater negative for respiratory alkalosis.[VIII]

The relation between pCO₂ and the parameter (H₂CO₃ – 1.2)/ H₂CO₃ is clearly shown in the graph 7. It denotes that the respiratory influence of pCO₂ in changing the pH through bicarbonate is a constant.

The relation between pCO₂ and the ratio HCO₃⁻/ Std HCO₃ is shown in graph 8. As pCO₂ increases, the rational so increases and afterwards it slightly flattens. It denotes that the respiratory influence of pCO₂ in changing pH through bicarbonate is a variable one depending on acute or chronic conditions or compensations. The ratio HCO₃⁻/ Std HCO₃ values shown in the tables 2 and 4 clearly depicts that the values are greater (>1) for increased pCO₂ and lesser (<1) for decreased pCO₂.

A Newer parameter respiratory influence of pCO₂ is given by the relation

[HCO₃⁻/ Std HCO₃] - (H₂CO₃ -1.2)/H₂CO₃

At pCO₂ 40 mm of Hg, Net Respiratory influence of pCO₂ in causing acidic or alkaline effect in pH is one and pH - NRpH is zero. (standard bicarbonate and bicarbonate values are equal and H₂CO₃ value is 1.2 at pCO₂ 40 mm of Hg.). If the value is more than one or pH - NRpH is positive it denotes alkaline effect and if the value is lesser than one or pH - NRpH is negative then it denotes an acidic effect. These values are clearly shown in the tables 2 and 4.

The relation between pH-NRpH and a newer parameter respiratory influence of pCO₂ shown in the graph 9 clearly depicts that the curve increases steadily and finally it flattens which is similar for the relation between NRH°/H° and the respiratory influence parameter shown in the graph 10.

It is a well known fact that the pH and the hydrogen ion concentration are inversely related. So, NRpH is inversely related to NRH° and [pH-NRpH] is inversely related to [ H°/ NRH°]. The relation between the parameters[PH-NRpH] and the [NRH°/H°] is directly proportional which is shown in the graph 11. It is very clear from the graphs 9, 10 and 11 that the three parameters ΔRpH (pH-NRpH), [NRH°/H°] and net respiratory influence of pCO₂ given by the relation [HCO₃⁻/ Std HCO₃] -(H₂CO₃ -1.2)/H₂CO₃ are very closely related to each other.

The non-respiratory hydrogen ion concentration is inter-related in various acid-base balance theory. The assessment of acid base disturbances is most commonly done by the physiological approach based on CO₂/ carbonic acid/bicarbonate equilibrium and another similar approach using base excess developed by astrup and siggaard Anderson.[IX] Siggaard Andersen implemented a method based on the Van Slyke equation which emphasizes the use of base excess (BE) or deficit. Base excess was criticized because it represented measurements done on whole blood and did not accurately represent the whole body behaviour. Standard base excess or extracellular base excess was introduced which is the base excess at haemoglobin concentration of 5g/dl. Standard base excess as a parameter for metabolic acid base disorder is well validated for accuracy and clinical correlation but have been criticized for merely quantifying rather than truly explaining acid-base disturbances. [II,III]
Stewart had proposed a newer concept of acid-base balance, based on reworking of the buffer base concept of Singer and Hasting in a different way.[II,III] According to Stewarts theory, hydrogen ion and bicarbonate concentration are dependent variables whose concentrations are determined by three independent variables namely, strong ion difference(SID), pCO₂ and [ATOT] which reflects the plasma concentration of weak non-volatile acids namely albumin and phosphate.[III,IX,X]

According to Stewarts theory, the respiratory acid base disorders are due to the alterations pCO₂ in which is similar to the traditional approach, but the metabolic disorders are due to primary alterations in SID or ATOT and not bicarbonate. The changes in the concentration of plasma Bicarbonate is a marker of metabolic acid base disorder and not its causative mechanism. The principal element of the plasma SID is the sodium chloride difference (Na-Cl) and the principal weak acid in plasma is albumin.[III,IX] This approach had complex equations and so it was not quite popular until it was later simplified and modified by Fencel and others. In the Fencel-Stewart approach, the four basic mechanisms of major metabolic alterations in pH is by water effects, chloride effects, protein effects and changes in other factors which are not measured.[IX,X] The advantage of this approach is that it gives a better understanding of the mechanisms behind acid-base abnormalities that help in taking immediate clinical decision which can prevent or correct the abnormalities.[IX] The traditional approach helps in the diagnostic description easily while the physicochemical approach is important to define the causation and severity of acid base disorders.[IV]

The interdependence of the traditional and Stewart variables are documented in the previous studies and are important in clinical application.[III] The base excess (BE) is a measure of the net effect of changes in SID and weak acids. The Changes in base excess are associated with changes in sodium, chloride, lactate, other strong ions and weak acids. So, the changes in Base Excess is determined by the changes in strong ion difference (SID) and the changes in the concentration of weak non-volatile acids namely albumin and phosphate.[IX,X] In the current research study, low non-respiratory hydrogen ion concentration (NRH⁺) or a high non-respiratory pH is seen in metabolic alkalosis which is related to a higher value (more positive) of base excess. Base deficit(lower or more negative value of base excess ) is related to a higher non-respiratory hydrogen ion concentration(NRH⁺) or a low non respiratory pH which is seen in metabolic acidosis cases.[I, VII]

The current research study integrates all these concepts and enumerates the postulates of the acid-base balance theory.

The Postulates of the Acid-Base Balance Theory are:

1. The net changes in pH of the blood reflects the sum total changes in the hydrogen ion concentration in the blood. The net changes in total or actual pH [Δ pH (pH - 7.4)] is due to both the changes in respiratory [Δ RpH(pH – NRpH)] and non-respiratory(metabolic ) component [Δ NRpH (NRpH - 7.4)] affecting the pH.
2. The sum total changes in the hydrogen ion concentration (Δ H⁺=[H⁺]- [40]) in the blood includes both the changes due to respiratory (ΔRH⁺ = [H⁺] – [NRH⁺]) and non-respiratory(metabolic) component(Δ NRH⁺ = [NRH⁺]- [40]).
3. The non-respiratory hydrogen ion concentration [NRH⁺] has a unique value for a given standard bicarbonate concentration represented by the relation NRH⁺ = 960/Std Bicarbonate.
4. The concentration of Hydrogen ion excess given by [NRH⁺ - 40] is directly proportional to the base deficit. This quantity with opposite sign [40- NRH⁺] is directly proportional to the base excess. Standard base excess is the base excess at haemoglobin concentration of 5 g/dl.
5. The changes in the dependent variable non-respiratory hydrogen ion concentration [NRH⁺] representing the non-respiratory (metabolic component) is due to the changes by the independent variables namely strong ion difference (SID) and the total concentration of weak non-volatile acids namely albumin and phosphate [ATOT].
6. The changes in the dependent variable [HCO₃⁻] is a marker of metabolic acid-base disturbances and not its causative mechanism.
7. The magnitude and direction (positive or negative) of the changes in the parameter ΔNRpH(NRpH-7.4) is due to the accumulation of acids other than carbonic acid or bases. The value is negative for acidic effect and positive for alkaline effect.
8. The **magnitude** and **direction** (positive or negative) of the changes in the parameter \( \Delta R_{pH} (pH - NR_{pH}) \) denotes the respiratory influence in causing changes in \( pH \) represented by the relation \( pH - NR_{pH} = 1.6 + \log{(HCO_3^-/Std\ HCO_3^-)/pCO_2} \). The value is **negative** for acidic effect and **positive** for alkaline effect.

9. The ratio \([NRH^+/H^+] \) is directly proportional to the parameter \( \Delta R_{pH} (pH - NR_{pH}) \) which denotes the respiratory influence of \( pCO_2 \).

10. The respiratory influence of \( pCO_2 \) in changing \( pH \) through bicarbonate is a **variable one** (ratio \( HCO_3^-/Std\ HCO_3^- \)) depending on the acute or chronic conditions or compensations and through carbonic acid is a **constant one** given by \( (H_2CO_3 - 1.2)/H_2CO_3 \).

5. **CONCLUSION**

Arterial blood gas analysis is sometimes confusing, often challenging and also an arduous task. However, understanding the concept of non-respiratory hydrogen ion concentration and its inter-relationship with other ABG parameters in various acid base balance theory may play a crucial role in interpretation of the ABG reports to overcome this arduous task.

**REFERENCES**


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