International Journal of Clinical Chemistry and Laboratory Medicine (IJCCLM)
Volume 4, Issue 3, 2018, PP 14-26
ISSN No. (Online) 2455-7153
DOI: http://dx.doi.org/10.20431/2455-7153.0403003
www.arcjournals.org

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, pCO_2 and derived parameters like HCO_3, Standard HCO_3 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 pCO_2 of 40 mm of Hg would be an index of the acid-base situation which is relatively independent of arterial pCO_2.[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, pCO_2 and the **derived parameters** like HCO_3, Std HCO_3 and Std Base Excess values are noted. The following derivations and calculations are applied to these obtained data's.

Calculation of H^+:

H^+ - Hydrogen ion concentration at actual pH

(calculated using **Modified Henderson Equation**)

H^+(Hydrogen ion concentration) = {24 X pCO_2}/ HCO_3

pH = - log[H^+ nanomoles/L]

= - log [H^+ x 10^{-9} moles/L]

= -log [H^+] –log[10^{-9}] {nanomoles/L =10^{-9} moles/L }

pH = 9 – log [H^+]

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

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

(at 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]

NRH^+ = {24 X pCO_2}/ Std HCO_3

= {24 X 40}/ Std HCO_3(**pCO_2**is **40 mm of Hg**)

NRH^+=960 / Std HCO_3

NRpH= 9 – log [NRH^+]

Calculation of ΔRH^+

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.

$\Delta H^+ = \Delta RH^+ + \Delta NRH^+$

ΔH^+ = [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]

ΔNRH^+ = [NRH^+ - 40] (changes due to Non-respiratory component)

Hydrogen ion concentration changes due to Respiratory component is given by **ΔRH^+.**

$\Delta RH^+ = \Delta H^+ - \Delta NRH^+$

= [H^+ - 40] -[NRH^+ - 40]

= [H^+ - 40 - NRH^+ + 40]

= [H^+- NRH^+] = RH^+

ΔRH^+ and RH^+ both are numerically same value.

ΔRH^+ = [H^+] - [NRH^+]

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]

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**[NRH $^{+}$ - 40]** denotes the **hydrogen ion excess** which is directly proportional to the **base deficit**. This quantity with opposite sign **(40- NRH $^{+}$)** is directly proportional to the **base excess**.

Calculation of ΔRpH:

pH= pka + log[HCO_3/ H_2CO_3]

[H_2CO_3 = 0.03 X pCO_2]

pH = pka + log[HCO_3/ (0.03 X pCO_2)]

NRpH= pka + log[Std HCO_3/ H_2CO_3]

NRpH = pka + log[StdHCO_3/ (0.03 X pCO_2)]

(pCO_2 is 40 mm of Hg at non-respiratory pH)

NRpH = pka + log[StdHCO_3/ (0.03 X 40)]

ΔRpH (pH - NRpH)

={pka + log[HCO_3/ (0.03 X pCO_2)]} - {pka + log[StdHCO_3/ (0.03 X 40)]}

= log[HCO_3/ (0.03 X pCO_2)] - log [StdHCO_3/ (0.03 X 40)]}

= log {(HCO_3/ StdHCO_3)/ pCO_2} + log 40

(the value of log 40 is 1.6)

pH - NRpH = 1.6 + log{(HCO_3/Std HCO_3)/ pCO_2}

or = 1.6 + log (HCO_3/Std HCO_3)-log(pCO_2)

Another method:

pH= 9 – log [H^+]

NRpH= 9 – log [NRH^+]

pH – NRpH = 9 – log [H^+] - 9 + log [NRH^+]

= log [NRH^+/ H^+]or **- log [H^+/ NRH^+]**

H^+(Hydrogen ion concentration) = {24 X pCO_2}/ HCO_3

NRH^+(non respiratory hydrogen ion concentration) = {24 X 40}/ Std HCO_3

[NRH^+]/ [H^+] = {24 X 40}/ Std HCO_3 /{24 X pCO_2}/ HCO_3

= **40 X {(HCO_3/ Std HCO_3)/ pCO_2}**

Or in terms of carbonic acid[**pCO_2 = H_2CO_3/0.03**] this can be written as,

= 1.2 X {(HCO_3/ Std HCO_3)/ H_2CO_3**}**

pH – NRpH = log [NRH^+/ H^+]

pH – NRpH = Log 40 + log (HCO_3/ Std HCO_3) – log(pCO_2)

[pH – NRpH]= 1.6 + log{(HCO_3/ Std HCO_3)/ pCO_2}

At pCO_2 **40 mm of Hg**, **pH - NRpH** is **zero**.(Because bicarbonate and standard bicarbonate values are equal.; log 1 is zero and log 40 is 1.6).At higher pCO_2 levels (> **40 mm of Hg**), the value of [**pH – NRpH]** is **negative** which denotes the **acidic influence** of increased pCO_2.At lower pCO_2 levels (<**40 mm of Hg**), the value of [**pH – NRpH]** is **positive** which denotes the **alkaline influence** of decreased pCO_2.

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

Δ pH = ΔRpH + ΔNRpH

Δ pH = [pH - 7.4] (net changes in **total pH (Actual pH)**)

Δ NRpH =[NRpH - 7.4] **(**changes due to Non-respiratory component)

Δ RpH = [pH - 7.4] - [NRpH - 7.4]

Δ RpH = [pH – NRpH]

NRpH=[pH - ΔRpH]

Calculation of TCO_2/ H_2CO_3:

The concentration of total carbon-dioxide in blood is equal to sum of the concentrations of bicarbonate and carbonic acid in blood.

$TCO_2 = HCO_3 + H_2CO_3$(where $H_2CO_3 = 0.03$ X pCO_2)

TCO_2/ H_2CO_3 = ($HCO_3 + H_2CO_3$)/ H_2CO_3

= HCO_3/ H_2CO_3 +H_2CO_3/ H_2CO_3

= **HCO_3/ H_2CO_3 + 1**

At **pH of 7.4**, **HCO_3/ H_2CO_3** ratio is **20**. So, **TCO_2/ H_2CO_3** ratio is **21**.

Calculation of $TCO_{2(at\ 40\ mm\ Hg)}$/ H_2CO_3

Standard bicarbonate is the concentration of bicarbonate at pCO_2 40 mm of Hg.[I,II]

$TCO_{2(at\ 40\ mm\ Hg)}$ = Std HCO_3 + H_2CO_3

= Std HCO_3+ 40 X 0.03

$TCO_{2(at\ 40\ mm\ Hg)}$ = Std HCO_3 + 1.2

$TCO_{2(at\ 40\ mm\ Hg)}$/ H_2CO_3 = (Std HCO_3 + 1.2)/ H_2CO_3

= Std HCO_3 / H_2CO_3 + 1.2/ H_2CO_3

= **Std HCO_3 / H_2CO_3 + 1.2/ H_2CO_3**

Differences between TCO_2/ $H_2CO_3$and $TCO_{2(at\ 40\ mm\ Hg)}$/ H_2CO_3:

TCO_2/ H_2CO_3 - $TCO_{2(at\ 40\ mm\ Hg)}$/ H_2CO_3 =

{HCO_3/ H_2CO_3 + 1} - {Std HCO_3 / H_2CO_3 + 1.2/ H_2CO_3}

(TCO_2 - $TCO_{2(at\ 40\ mm\ Hg)}$) / H_2CO_3 =

{(HCO_3 - Std HCO_3)/ H_2CO_3} + {(H_2CO_3 – 1.2)/ H_2CO_3}

(HCO_3 - Std HCO_3)/ H_2CO_3 ratio is greater positive for respiratory acidosis and greater negative for respiratory alkalosis.[VIII] At **pCO_2 40 mm of Hg**, both the **ratios((TCO_2- $TCO_{2(at\ 40\ mm\ Hg)}$) / H_2CO_3** and **(HCO_3 - Std HCO_3) / H_2CO_3)** are **zero** because standard bicarbonate and bicarbonate values are equal and H_2CO_3 value is 1.2 at pCO_2 40 mm of Hg.

Derivation of another newer parameter denoting Respiratory influence of pCO_2:

It is already derived to calculate the parameter pH – NRpH.

Δ RpH (pH – NRpH) = 1.6 + log{(HCO_3/ Std HCO_3) / pCO_2}

From the above equation it is very clear that the value depends on the ratio **HCO_3/ Std HCO_3** and the **pCO_2**values. pCO_2**influences** by changing both the **bicarbonate**(represented by the ratio HCO_3/ Std HCO_3) and **carbonic acid** values. (represented by the parameter (H_2CO_3 – 1.2)/ H_2CO_3).

The increase in the ratio **HCO_3/ Std HCO_3**has alkaline effect and the decrease has acidic effect. The increase in the parameter **(H_2CO_3 – 1.2)/ H_2CO_3)** has acidic effect and decrease has alkaline effect which **is opposite** to the effect of ratio **HCO_3/ Std HCO_3**.

So, the net Respiratory influence of pCO_2 in causing acidic or alkaline effect in pH is given by the difference between them i.e

Net Respiratory influence of pCO_2 =(HCO_3/ Std HCO_3) -{(H_2CO_3 – 1.2)/ H_2CO_3}

or (HCO_3/ Std HCO_3) - {1 – (1.2/ H_2CO_3)}

3. RESULTS

The results are tabulated in the tables 1 to 4.In the **table 1**, verification of the relation **$\Delta H^+ = \Delta RH^+ + \Delta NRH^+$** is shown for the groups Normal, Metabolic Acidosis and Metabolic Alkalosis Cases. Total cases, mean ± Std deviation of the parameters like **NRH^+, NRH^+/H^+, ΔH^+ (H^+ - 40), ΔRH^+ (H^+ - NRH^+), ΔNRH^+ (NRH^+ - 40) and Standard Base Excess (SBE)** are tabulated.

Table1. *Verification of the relation $\Delta H^+ = \Delta RH^+ + \Delta NRH^+$ 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^+), ΔNRH^+ (NRH^+ - 40) & SBE** are tabulated)*

Parameter	**Normal**	**Metabolic acidosis (43 cases)**			**Metabolic Alkalosis (26 cases)**	
	(22cases)	↓ HCO_3 pCO_2(<30 mm Hg) **18 cases**	↓ HCO_3, pCO_2(30-34 mm Hg) **11 cases**	↓ HCO_3& Normal pCO_2 (35-45 mm Hg) **14 cases**	↑ HCO_3& pCO_2(>45 mm Hg) **16 cases**	↑ HCO_3& Normal pCO_2 (35-45 mm Hg) **10 cases**
NRH^+Mean:	38.61	85.62	56.44	52.42	25.89	33.97
Std Dev:	1.35	41.64	8.50	6.45	2.48	1.74
NRH^+/H^+Mean&Std	1.03	1.47	1.15	1.015	0.83	1.05
Dev:	0.05	0.31	0.04	0.045	0.05	0.056
ΔH^+ Mean & Std	-2.48	16.31	9.07	11.84	-8.81	-7.609
Dev:	2.06	11.79	6.03	7.77	3.002	2.37
ΔRH^+Mean:	-1.09	-29.31	-7.37	-0.58	5.30	-1.579
&Std Dev:	1.83	30.54	2.65	2.39	1.76	1.767
ΔNRH^+Mean:	-1.39	45.62	16.44	12.42	-14.11	-6.03
Std Dev:	1.35	41.64	8.50	6.45	2.48	1.74
SBE Mean:	-0.112	-17.26	-10.64	-8.54	19.14	4.62
Std Dev:	1.27	4.45	3.32	2.84	5.2	2.09

***NRH^+** is increased in Metabolic acidosis and decreased in Metabolic alkalosis. **ΔNRH^+** 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),ΔNRpH (NRpH-7.4),ΔRpH (pH-NRpH), HCO_3/ Std HCO_3**and **Net Respiratory Influence of pCO2** are tabulated.

Table2.*Verification of the relation **Δ pH = Δ RpH + Δ NRpH** in Normal, Metabolic Acidosis and Metabolic Alkalosis Cases: (Total cases, mean ± Std deviation of the parameters: **NRpH, ΔpH (PH-7.4), ΔNRpH (NRpH-7.4), ΔRpH (pH-NRpH), HCO_3/ Std HCO_3&Net Respiratory Influence of pCO2** are tabulated)*

Parameter	**Normal**	**Metabolic acidosis (43 cases)**			**Metabolic Alkalosis (26 cases)**	
	(22 cases)	↓ HCO_3 pCO_2(<30 mm Hg) **18 cases**	↓HCO_3, pCO_2(30-34 mm Hg) **11 cases**	↓ HCO_3, Normal pCO_2(35-45 mm Hg)**14 cases**	↑ HCO_3 , pCO_2(>45 mm Hg) **16 cases**	↑ HCO_3, Normal pCO_2(35-45 mm Hg) **10 cases**
NRpH Mean	7.4037	7.088	7.243	7.274	7.579	7.4598
Std Dev:	0.015	0.15	0.06	0.05	0.04	0.02
ΔpH (pH-7.4)	0.0145	-0.155	-0.1	-0.122	0.0962	0.079
Mean & Std Dev:	0.024	0.08	0.05	0.06	0.04	0.03
ΔNRpH(NRpH-7.4) Mean & Std	0.0037	-0.312	-0.157	-0.126	0.179	0.0598
Dev:	0.015	0.15	0.06	0.05	0.04	0.02
ΔRpH(pH-NRpH)	0.0108	0.157	0.057	0.004	-0.0828	0.0192
Mean & Std Dev:	0.021	0.08	0.015	0.02	0.026	0.02
HCO_3/ Std HCO_3	0.983	0.787	0.908	0.985	1.132	0.993
Mean & Std Dev:	0.025	0.09	0.02	0.04	0.03	0.02
Net Respiratory	1.034	1.694	1.172	1.019	0.868	1.053
Influence of pCO2 Mean & Std Dev:	0.05	0.46	0.05	0.05	0.04	0.06

***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 Missellaneous cases. Total cases, mean ± Std deviation of the parameters like **NRH^+, NRH^+/H^+, ΔH^+(H^+ - 40),ΔRH^+ (H^+ - NRH^+), ΔNRH^+(NRH^+ - 40)** and **SBE** are tabulated.

Table3. *Verification of the relation $\Delta H^+ = \Delta RH^+ + \Delta NRH^+$ in Respiratory acidosis, respiratory alkalosis and Missellaneous cases. (Total cases, mean ± Std deviation of the parameters: **NRH^+, NRH^+/H^+, ΔH^+ (H^+ - 40), ΔRH^+ (H^+ - NRH^+), ΔNRH^+(NRH^+ - 40) & SBE** are tabulated)*

Parameter	**Respira-tory Acidosis (18cases)**	**Respiratory alkalosis (44 cases)**			**Missellaneous cases (35 cases)**		
		↓pCO_2, HCO_3 (< 18 mmol/L) **13 cases**	↓ pCO_2, HCO_3 (≥18 <22 mmol/L) **12 cases**	↓ pCO_2 , Normal HCO_3 (22-26mmol/L) **19 cases**	pH : 7.38-7.42 ↓ pCO_2, ↓ HCO_3 **22cases**	pH : 7.38-7.42↑ pCO_2, ↑ HCO_3 **10cases**	pH around: 7.04 ↑ pCO_2, ↓ HCO_3 **3 cases**
NRH^+Mean	36.98	48.17	41.85	37.35	47.51	30.77	72.05
Std Dev:	5.45	5.35	2.25	1.40	4.22	2.75	8.77
NRH^+/H^+	0.729	1.55	1.28	1.20	1.24	0.793	0.817
Mean: Std Dev	0.114	0.22	0.070	0.065	0.098	0.067	0.063
ΔH^+	11.43	-8.53	-7.12	-8.78	-1.78	-1.24	47.96
Mean: Std Dev	8.38	3.68	2.34	2.14	1.29	1.19	5.047
ΔRH^+	14.45	-16.70	-8.97	-6.13	-9.29	7.99	15.91
Mean :Std Dev	7.302	5.50	1.85	1.57	3.76	2.59	4.76
ΔNRH^+Mean	-3.02	8.17	1.85	-2.65	7.51	-9.23	32.05
Std Dev:	5.45	5.35	2.26	1.40	4.22	2.75	8.77
SBE	4.185	-7.924	-3.39	0.578	-6.89	10.77	-14.24
Mean :Std Dev	5.98	2.80	1.63	1.23	2.50	4.69	2.097

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 Missellaneous cases. Total cases, mean ± Std deviation of the parameters like **NRpH, ΔpH (pH-7.4), ΔNRpH (NRpH-7.4), ΔRpH (pH-NRpH), HCO_3/ Std HCO_3**and **Net Respiratory Influence of pCO2**are tabulated.

Table 4. *Verification of the relation **Δ pH = Δ RpH +Δ NRpH** in Respiratory acidosis, respiratory alkalosis, and Missellaneous cases: (Total cases, mean ± Std deviation of the parameters: **NRpH, ΔpH (pH-7.4), ΔNRpH (NRpH-7.4), ΔRpH (pH-NRpH), HCO_3/ Std HCO_3&Net Respiratory Influence of pCO2** are tabulated)*

Parameter	**Respira-tory Acidosis 18 cases**	**Respiratory alkalosis (44 cases)**			**Missellaneous cases (35 cases)**		
		↓pCO_2, HCO_3 (< 18 mmol/) **13cases**	↓ pCO_2, HCO_3 (≥18 <22 mmol/) **12cases**	↓ pCO_2, Normal HCO_3 (22-26 mmol/L) **19 cases**	pH: 7.38-7.42 ↓ pCO_2, ↓ HCO_3 **22cases**	pH: 7.38-7.42 ↑ pCO_2 ↑ HCO_3 **10cases**	pH around: 7.04 ↑ pCO_2↓ HCO_3 **3 cases**
NRpH Mean	7.426	7.309	7.369	7.418	7.315	7.5037	7.134
Std Dev:	0.063	0.044	0.023	0.017	0.038	0.039	0.055
ΔpH(pH-7.4) Mean	-0.118	0.092	0.072	0.094	0.006	0	-0.356
Std Dev:	0.069	0.054	0.032	0.031	0.014	0.013	0.025
ΔNRpH(NRpH-7.4)	0.026	-0.091	-0.031	0.018	-0.085	0.1037	-0.266
Mean & Std Dev	0.063	0.044	0.023	0.017	0.038	0.039	0.055
ΔRpH (pH-NRpH)	-0.144	0.183	0.103	0.076	0.091	-0.1037	-0.09
Mean & Std Dev:	0.068	0.059	0.023	0.0232	0.0332	0.037	0.034
HCO_3/ Std HCO_3	1.162	0.759	0.879	0.926	0.871	1.128	1.215
Mean & Std Dev:	0.08	0.09	0.02	0.02	0.05	0.05	0.04
Net Respiratory Influence of pCO2	0.797	1.860	1.332	1.224	1.310	0.835	0.888
Mean & Std Dev	0.07	0.51	0.086	0.08	0.17	0.045	0.06

ΔRpH (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**).

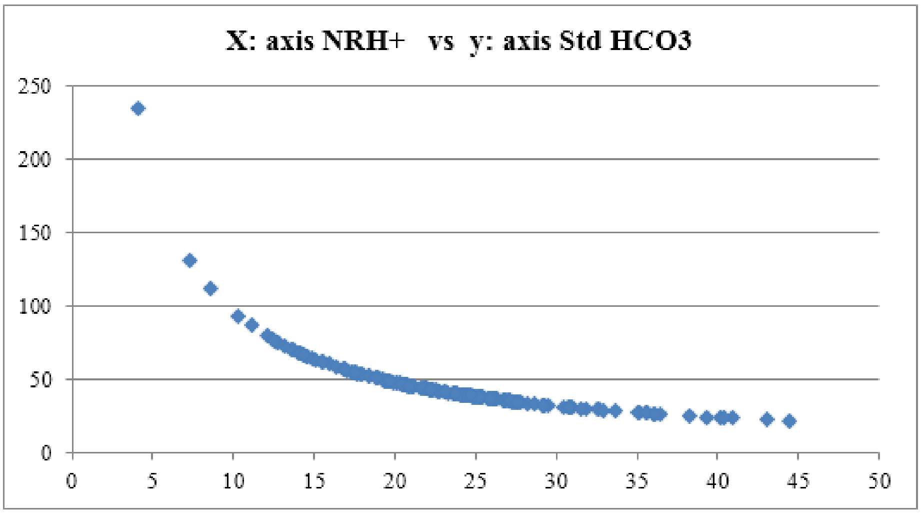

Figure1(Graph 1).*Relation between* ***NRH***$^{+}$*vs****Std HCO***$_{3}$

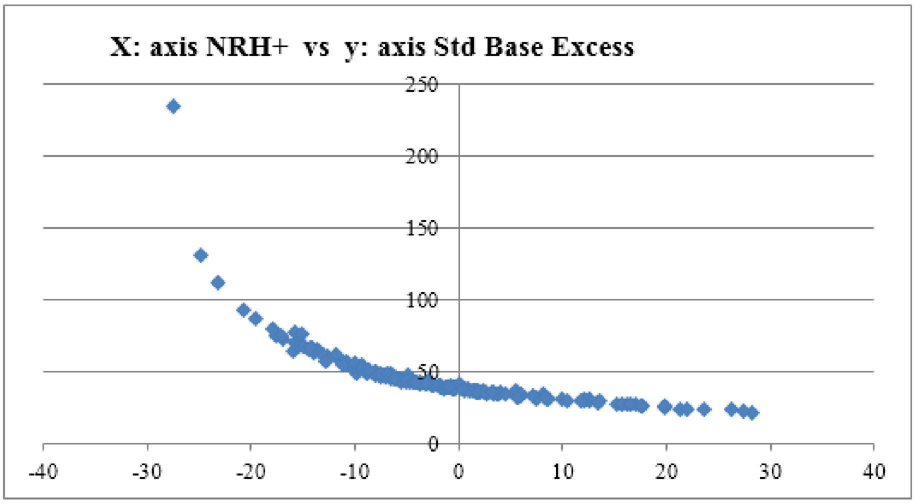

Figure2(Graph 2).*Relation between* ***NRH***$^{+}$*vs****Std Base Excess***

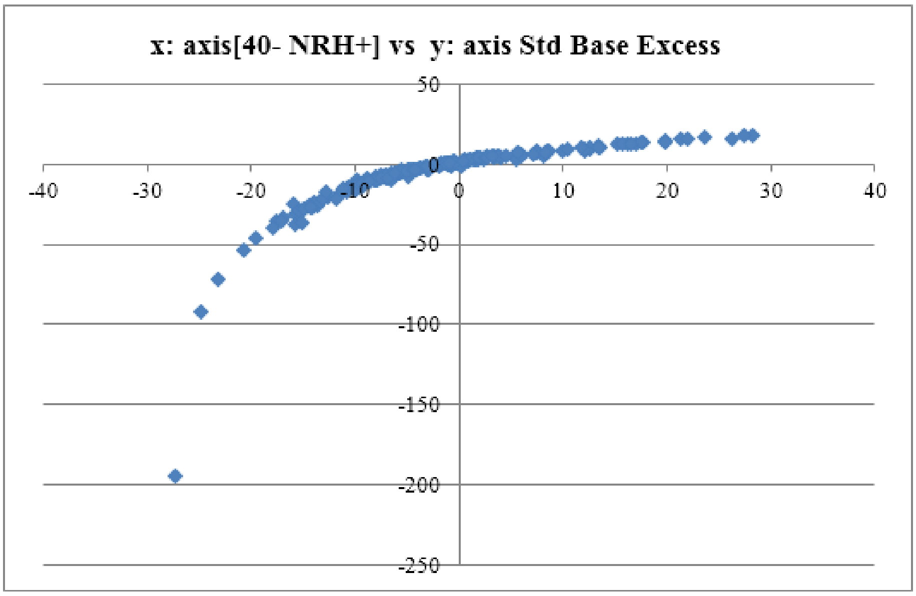

Figure3(Graph 3).*Relation between* ***[40- NRH***$^{+}$***]*** *vs****Std Base Excess***

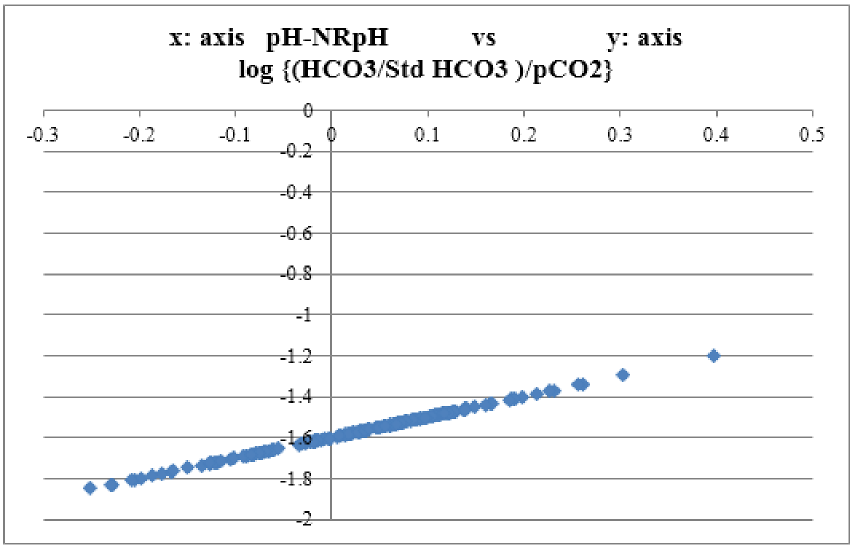

Figure4(Graph 4).*Relation between* ***pH-NRpH vs Log{(HCO$_3$/Std HCO$_3$)/pCO$_2$ }***

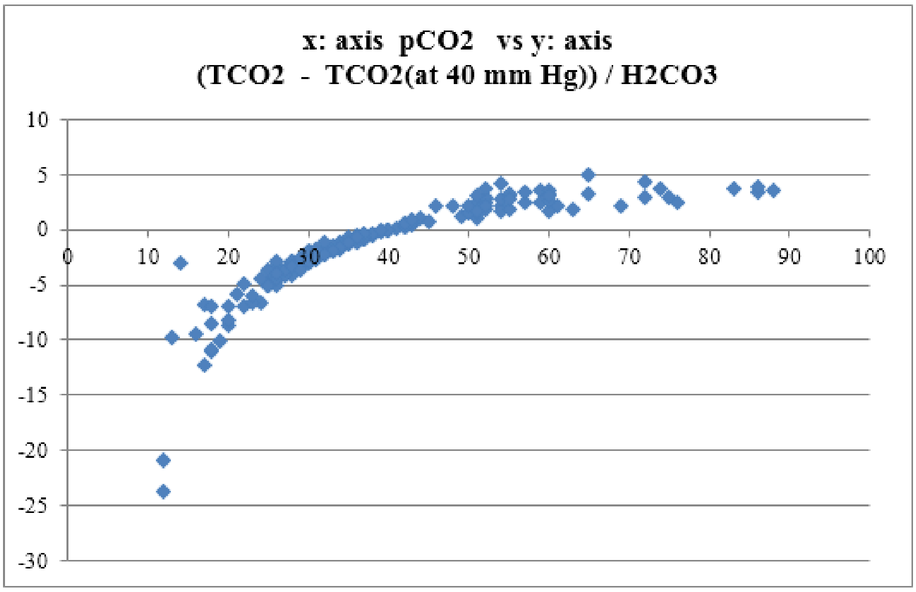

Figure5(Graph 5).*Relation between* **pCO$_2$** *vs* ***(TCO$_2$ -TCO$_{2(at\ 40\ mm\ Hg)}$) / H$_2$CO$_3$***

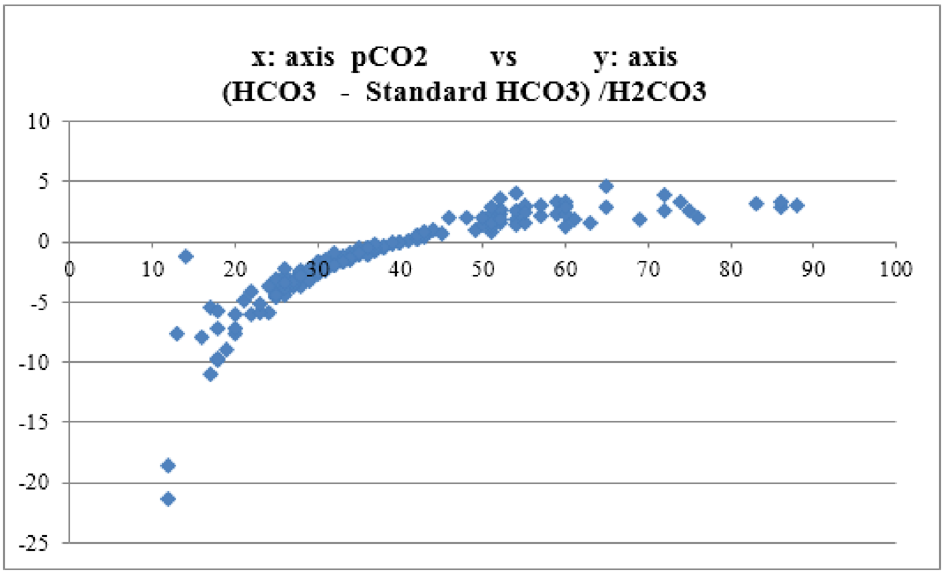

Figure6(Graph 6).*Relation between* **pCO$_2$** *vs* ***(HCO$_3$- Standard HCO$_3$) /H$_2$CO$_3$***

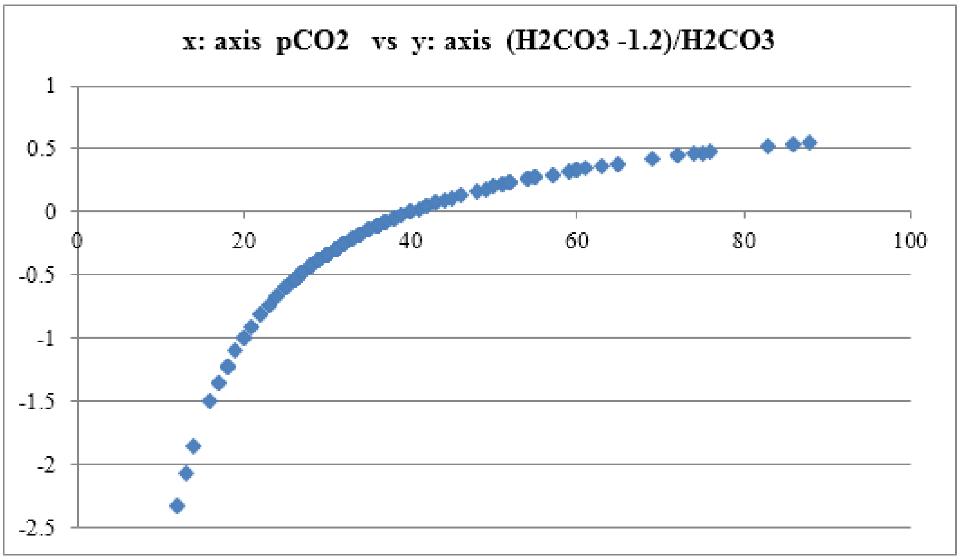

Figure7(Graph 7).*Relation between* pCO_2 *vs* $(H_2CO_3 - 1.2)/H_2CO_3$

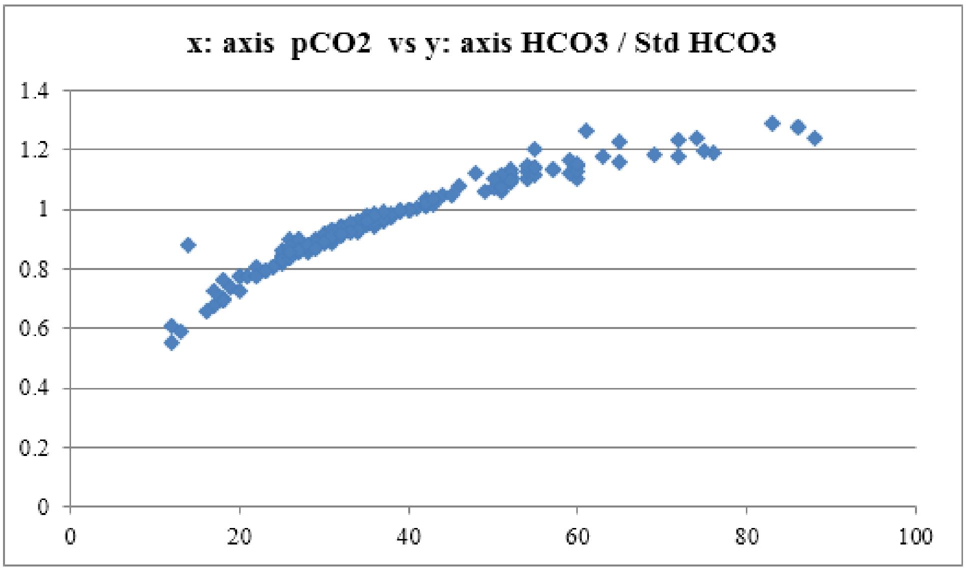

Figure8(Graph 8).*Relation between* pCO_2 *vs* HCO_3 / Std HCO_3

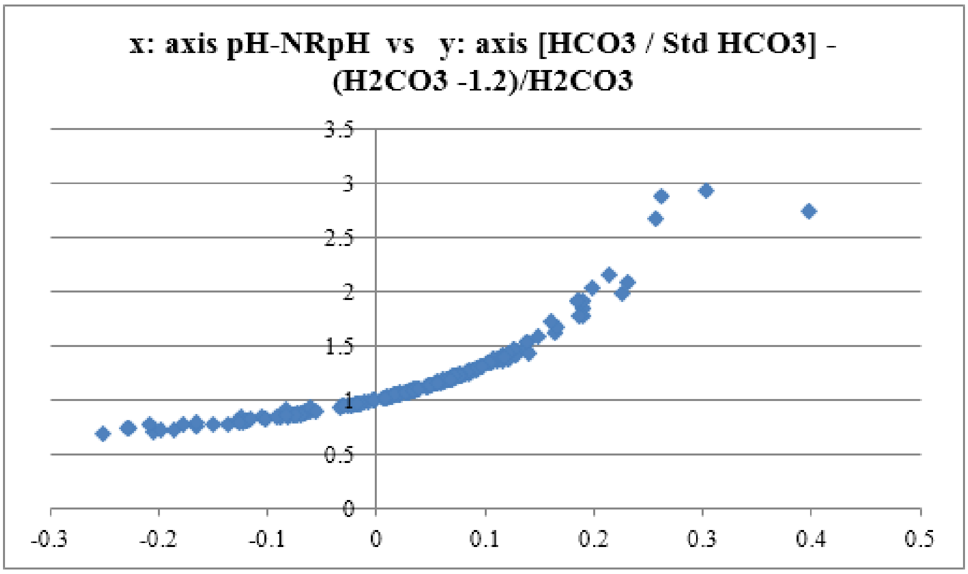

Figure9(Graph 9).*Relation between* **pH-NRpH** *vs* [HCO_3 / Std HCO_3] - $(H_2CO_3 - 1.2)/H_2CO_3$

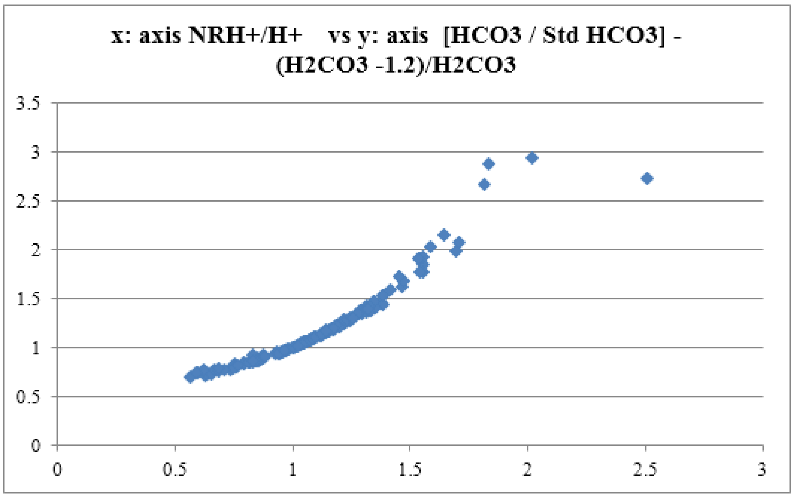

Figure10(Graph 10).*Relation between* ***NRH^+/H^+*** *vs* ***$[HCO_3 / Std\ HCO_3]$ $-(H_2CO_3 -1.2)/H_2CO_3$***

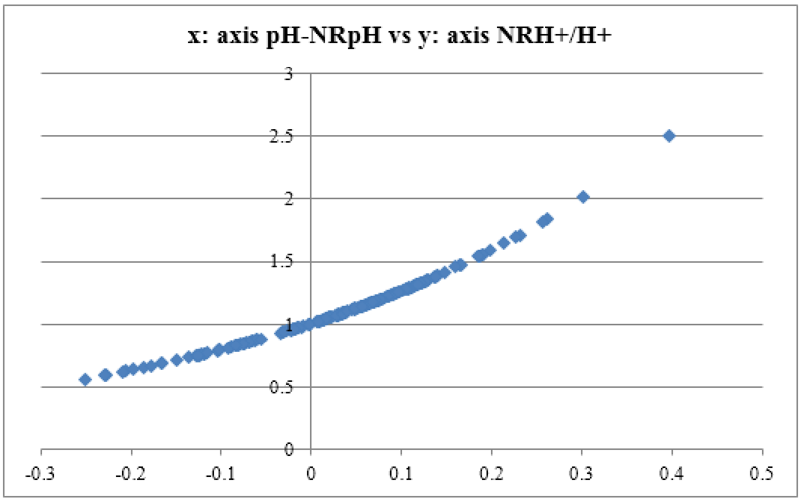

Figure11(Graph 11).*Relation between* ***pH-NRpH*** *vs* ***NRH^+/H***

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 HCO_3 with pCO_2 (<30 mm Hg), **b**. decreased HCO_3 with pCO_2 (30-34 mmHg) and **c**. decreased HCO_3 with normal pCO_2 (35-45 mm Hg),**Metabolic alkalosis** (further divided into **two subgroups** namely **a**. increased HCO_3 with normal pCO_2 and **b.** increased HCO_3 with increased pCO_2), **Respiratory acidosis**, **Respiratory alkalosis**(further divided into **three subgroups** namely **a.** decreased pCO_2 with HCO_3 (<18mEq/L) , **b.** decreased pCO_2 with HCO_3 (≥18 <22 mEq/L) and **c.** decreased pCO_2 with normal HCO_3 (22-26mEq/L) and **Missellaneous cases** (further divided into **three subgroups** namely **a**. pH : 7.38-7.42 with decreasedpCO_2 and decreasedHCO_3, **b.**pH : 7.38-7.42 with increasedpCO_2 and increasedHCO_3,**c.** pH around: 7.04 with increasedpCO_2 and decreasedHCO_3).

It is very clear from the **table1** that non-respiratory hydrogen ion concentration (**NRH^+)** is **increased** in Metabolic acidosis and **decreased** in Metabolic alkalosis. **Δ 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**.

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{(HCO_3/ Std HCO_3)/ pCO_2}** 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 pCO_2 and the ratios namely **(TCO_2 - $TCO_{2(at\ 40\ mm\ Hg)}$) / H_2CO_3** and **(HCO_3 - Std HCO_3)/ H_2CO_3** is similar which is shown in the **graphs 5 &6** respectively. As pCO_2value increases, the two ratio values also increase and afterwards the curve flattens. As pCO_2 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 pCO_2 and the parameter **(H_2CO_3 – 1.2)/ H_2CO_3**is clearly shown in the **graph 7.** It denotes that the respiratory influence of pCO_2 in changing the pH through carbonic acid is a **constant**.

The relation between pCO_2 and the ratio HCO_3/ Std HCO_3 is shown in **graph 8**. As pCO_2 increases, the rational so increases and afterwards it slightly flattens. It denotes that the respiratory influence of pCO_2 in changing pH through bicarbonate is a **variable one** depending on acute or chronic conditions or compensations. The ratio **HCO_3 / Std HCO_3**values shown in the **tables 2** and **4** clearly depicts that the values are **greater(>1)** for increased pCO_2 and **lesser(<1)** for decreased pCO_2.

A Newer parameter respiratory influence of pCO_2 is given by the relation

[HCO_3 / Std HCO_3] - (H_2CO_3 -1.2)/H_2CO_3

At pCO_2 40 mm of Hg, **Net Respiratory influence of pCO_2** in causing acidic or alkaline effect in pH is **one** and **pH - NRpH** is **zero.** (standard bicarbonate and bicarbonate values are equal and H_2CO_3 value is 1.2 at pCO_2 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 pCO_2** 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 pCO_2 given by the relation **[HCO_3 / Std HCO_3] -(H_2CO_3 -1.2)/H_2CO_3**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 onpCO_2/ carbonic acid/bicarbonate equilibrium and an another similar approach using **base excess** developed by astrup and siggard 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 **critized** 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),**pCO_2** 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 pCO_2 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 **Fencl** and others. In the **Fencl–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 **traditiona**l 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 **($\Delta H^+=[H^+]-[40]$)** in the blood includes both the changes due to respiratory **($\Delta RH^+ = [H^+] - [NRH^+]$)** and non-respiratory(metabolic) component**($\Delta NRH^+ = [NRH^+] - [40]$).**

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 [HCO_3]** 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 **ΔRpH (pH-NRpH)** denotes the respiratory influence in causing changes in pH represented by the relation **pH –NRpH =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 **ΔRpH (pH - NRpH)** which denotes the respiratory influence of pCO_2.
10. The respiratory influence of pCO_2in 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.

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Citation: *T. Samuel, "Application and Inter-Relationship of Non-Respiratory Hydrogen Ion Concentration in Acid-Base Balance Theory", International Journal of Clinical Chemistry and Laboratory Medicine (IJCCLM), vol. 4, no. 3, pp. 14-26, 2018. http://dx.doi.org/10.20431/2455-7153.0403003*