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ORIGINAL ARTICLE

ESTABLISHING CORRELATION OF pH WITH VARIOUS PHYSIOCHEMICAL AND TRADITIONAL PARAMETERS OF ACID BASE BALANCE: A CROSS-SECTIONAL STUDY

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ABSTRACT

OBJECTIVE: To evaluate the effectiveness of Physiochemical versus traditional approach in diagnosing acid-base disorders (ABD).

METHODS: This cross-sectional observational study was conducted on 212 patients, admitted during January to June 2020, in intensive care unit of Rehman Medical Institute, Peshawar, Pakistan. Samples were obtained from these patients for pH, PCO_2, HCO_3, Lactate, Na, K and Cl processed on Cobas ABG analyzer b 221. Ca, Mg, albumin and phosphate were analyzed on Cobas-601. Data was analyzed to assess the association among different parameters in traditional and physiochemical approach.

RESULTS: Males were predominant in total cohort group (n=125/212; 59%) as well as in metabolic subgroup (n=109/184; 59%). Mean age of males and females was 55.01±11.80 years and 54.99±14.76 years respectively. pH showed a strong negative correlation with PO_4 (p-value=0.001) (r_s 0.238) in the total cohort of subjects and no significant correlation (p=0.005) (r_s -.206) in the metabolic subgroup in physiochemical approach. In traditional approach acid base parameters, Standard Base Excess (SBE) showed strong positive correlation (p=0.001) (r_s 0.413 and r_s 0.567) and pCO_2 showed the strongest negative correlation (p value 0.001) (r_s value -0.721 and r_s -0.673) with pH in both total cohort and metabolic subgroup. HCO_3 (p=0.003) (rs value 0.221) and AG (p=0.024) (rs value -0.167) both showed a significant strong positive and strong negative correlation with pH respectively.

CONCLUSION: No significant association between physiochemical parameters and blood pH was found in adults. Traditional approach is the simplest, most rigorous, and useful for diagnosing ABD.

KEYWORDS: Acid-Base Equilibrium (MeSH); Anion Gap (MeSH); Acid-Base Imbalance (MeSH); Acidosis (MeSH); Alkalosis (MeSH); Hydrogen Ion Concentration (MeSH); Blood (MeSH); Body Fluids (MeSH); Fluid Shifts (MeSH).

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INTRODUCTION

Correct and prompt diagnosis of acid-base disorders (ABD) is of vital importance in avoiding morbidity and mortality in critically ill patients. Three approaches for diagnosing ABD have been in practice. First is the traditional approach also called as conventional or physiological approach. It is based on the Henderson-Hassel Balch equation that relies on bicarbonate (HCO_3) and carbon dioxide (pCO_2) buffer system. In this approach, pCO_2 is used to diagnose respiratory disorders, while HCO_3 is used to diagnose metabolic disorders.[1]

Second approach is based on Base Excess (BE) suggested by Anderson. It differs slightly from the traditional approach in the diagnosis of metabolic acid base disorders by using base excess instead of HCO_3.[2] Third approach known as Stewart approach or strong ion difference approach or physiochemical approach is based on the theory proposed by Stewart. According to this theory, there are three independent variables which determine the solution's pH. These include:

(a) pCO_2,

(b) The difference between the completely dissociated cations (Na^+, K^+, Ca^{++}, and Mg^{++}) and anions (Cl^- and lactate$^-$) (Strong Ionic Difference or SID) and

(c) The concentration of nonvolatile weak acids (Atot) that includes other non-bicarbonate body buffers such as albumin and phosphate.[3]

According to Stewart, pH and HCO_3 are dependent variables. Different studies show that physiochemical approach is better than traditional one in diagnosing acid base disorders due to metabolic derangements.[4,5] However, because ABD caused by respiratory conditions are dependent on critical changes in pCO_2, both approaches are equivalent in this regard.

To get a clear understanding of the Physiochemical approach, certain terminologies need to be understood.

Strong ions are defined as ions dissociating completely in a solution at a pH of 7

Strong cations are: Na^+, K^+, Ca^{++}, Mg^{++}
Strong anions are: Cl^- and lactate$^-$

Apparent Strong ion difference (SIDa)= $[Na^+ + K^+ + Ca^{++} + Mg^{++}]-[Cl^- + lactate^-]$ [3,6,7]

The SIDa for normal human plasma is 42 mEq/L

Alkalosis results in increased SIDa (increase in unmeasured anions) and decreased SIDa leads to acidosis.

Effective Strong ion difference (SIDe):[8] It consists of bicarbonate as well as other weak acids including albumin and phosphate.

SID e= HCO_3+Albumin+Phosphate[9]

SIDe (0.0301 * pCO2 * 10pH-6.1)+ {([albumin *pH * 0.123 – 0.631)}+ {([phosphate]*pH *0.309 - 0.469))}[9]

SIDa and SIDe must be equal to each other in body under normal circumstances. If not so, then according to the law of electro neutrality it leads to a difference between the two referred to as the strong ion gap (SIG).[10]

SIG= SIDa-SIDe.[11-13]

Nonvolatile weak acids (Atot): This includes all the non-bicarbonate buffers including albumin and phosphate.[14]

We intend to select a cohort of patients and to establish the correlation of pH with various acid base parameters of physiochemical approach in order to illustrate its importance in acid base disorders determination in critically ill patients of intensive care unit (ICU).

The present study was conducted to evaluate if traditional and physiochemical approach can be used interchangeably for diagnosing acid base disorders.

METHODS

This cross-sectional descriptive study was conducted from January 2020 to June 2020. Samples were collected through non-probability convenient sampling technique, from patients admitted in general ICU of Rehman Medical Institute, Peshawar, Pakistan. All adult patients admitted to ICU for more than 24 hours and undergoing Arterial Blood Gas Analysis (ABGs) were included. All patients who were admitted in wards were excluded. A total of 212 critically ill patients from both genders admitted in general ICU of Rehman Medical Institute, Peshawar, Pakistan were included in the study. Patients were divided into two groups;

1. **Total cohort group** comprising of 212 individuals

2..**Metabolic subgroup** comprising of 184 individuals.

The metabolic subgroup was created by removing the patients with acidic pH (<7.4) and high HCO_3 (>24 mmol/L) and the basic pH (>7.4) with low HCO_3 (<24 mmol/L).[9] These two groups were made due to the fact that physiochemical and traditional approaches have shown differences in diagnosing metabolic component of acid base disorders.[11,15] This difference is due to the fact that beside bicarbonate albumin and phosphate also plays a major role in diagnosing metabolic acid base disorders according to Stewart approach.[11,16]

Study was approved by ethical review committee of Rehman Medical Institute, Peshawar, Pakistan. Data collection was performed using standard clinical practice. Paired samples were obtained from these patients and two sets of analytes were analyzed. Set A comprised of pH, pCO_2, HCO_3, lactate, Na^+, K^+ and Cl^- processed on ABG analyzer Cobas® b 221 using direct ISE. Set B comprised of Ca^{++}, Mg^{++}, albumin and phosphate analyzed on Cobas® 601 using indirect ISE. Demographic details (gender, age) of all the patients were obtained.

Data was analyzed using SPSS 23. Mean and standard deviations of demographic data were derived. Median and IQR of different traditional and physiochemical approach variables were calculated. Spearman correlation was applied to evaluate association of pH with different parameters of traditional and physiochemical approach in total cohort of subjects and the metabolic subgroup.

TABLE I: MEDIAN AND INTERQUARTILE RANGES OF VARIOUS PARAMETERS OF TRADITIONAL AND PHYSIOCHEMICAL APPROACH

Variables	Total Cohort		Metabolic Subgroup	
	N	IQR	N	IQR
pH	7.39	7.33 - 7.42	7.40	7.33 - 7.42
PCO_2	38.15	33.1 - 44.9	37.4	33.1 - 42.90
HCO_3	22.70	20.7 - 24.5	22.3	20.6 - 24.6
Lactate	3.10	2.02 - 4.70	3.10	2.00 - 4.67
Albumin	2.6	2.10 - 3.00	2.6	2.10 - 3.00
PO_4	4.85	3.12 - 9.27	4.70	3.10 - 9.22
SIDa	53	48.87 - 57.57	52.2	48.4 - 56.47
SIDe	31.38	27.03 - 37.34	30.55	27.00 - 36.22
SIG	21.57	15.8 - 25.94	21.89	15.83 - 25.94
AG	16.72	14.5 - 19.3	16.38	14.43 - 19.34
SBE	-3.83	5.5 - 1.66	-4.17	5.54 - 2.42

PCO_2: partial pressure of CO_2; pH: concentration of hydrogen ion; HCO_3: bicarbonate; PO_4: phosphate; SIDa: apparent strong ion difference; SIDe: Effective strong ion difference; SIG: strong ion gap; AG: Anion gap; SBE: standard base excess.

RESULTS

Out of 212 patients, 125 (59%) were males and 87 (41%) were females. The mean age of male and female patients in total cohort was 55.01±11.80 and 54.99±14.76 years respectively (p=0.992). The metabolic subgroup consisted of 184 patients, of which 109 (59%) were males and 75 (40%) were females. The mean age of males and females was 55±12.28 years and 55.01±14.39 years (p=0.995).

Median and Interquartile ranges (IQR) of various parameters were established (Table I).

pH showed a strong negative correlation with PO4 (p-value=0.001) (rs 0.238) (Figure 1) in the total cohort of subjects and no significant correlation (p value 0.005) (rs -0.206) in the metabolic subgroup in physiochemical approach.

No significant correlation of pH was found with the SIDa and SIDe in both

TABLE II: CORRELATION OF PH WITH PHYSIOCHEMICAL AND TRADITIONAL APPROACH PARAMETERS

Characteristics		Total Cohort		Metabolic Subgroup	
		r_s	P Value	r_s	P Value
Traditional Approach Parameters	PCO_2	-0.721	<0.001	-0.673	<0.001
	HCO_3	0.36	0.598	0.221	0.003
	SBE	0.413	<0.001	0.567	<0.001
	AG	-0.124	0.71	-0.167	0.024
	Lactate	-0.82	0.236	-0.102	0.167
Physiochemical Approach Parameters	Albumin	-0.35	-0.609	0.037	0.618
	PO_4	-0.238	<0.001	-0.206	0.005
	SIDa	-0.076	0.272	-0.023	0.753
	SIDe	-0.133	0.053	-0.025	0.739
	SIG	0.032	0.646	-0.205	0.737

PCO_2: partial pressure of CO_2; pH: concentration of hydrogen ion; HCO_3: bicarbonate; PO_4: phosphate; SIDa: apparent strong ion difference; SIDe: Effective strong ion difference; SIG: strong ion gap; AG: Anion gap; SBE: standard base excess.

total cohort as well as metabolic subgroup.

In traditional approach acid base parameters, Standard Base Excess (SBE) showed strong positive correlation (p value 0.001 rs 0.413) and (p value 0.001 rs 0.567) (Figure 2A and 2B) and pCO2 showed the strongest negative correlation (p value 0.001 rs value -0.721) and p value 0.001 rs -0.673) with pH in both total cohort and metabolic subgroup (figure 3A and 3B). HCO3 (p value 0.003 rs value .221) and AG (p value 0.024) (rs value -0.167) both showed a significant strong positive and strong negative correlation with pH in metabolic subgroup respectively (Figure 4 and 5) (Table II).

DISCUSSION

After the introduction of Peter Stewart's physiochemical approach in 1981, the theory was subjected to numerous studies and updates.[15,17-19] Very few studies have been conducted to assess the impact of the independent components of physiochemical approach, pCO_2, SIDa, and SIDe on pH except the work done by Chaiyakulsil C et al.[9] Present study was also conducted in the same manner and assessed the correlation of pH with parameters of physiochemical as well as traditional approach. Subjects were divided into a total cohort and a metabolic subgroup to assess the effectiveness of both the approaches in diagnosing metabolic component of acid base disorders.

In present study, the number of males was more as compared to females in total cohort as well as metabolic subgroup which is consistent with studies conducted by Chaiyakulsil C et al and Juan José Diaztagle-Fernández IJM-L et al.[9,20] On descriptive analysis of both the total cohort and metabolic subgroup traditional acid base parameter pCO_2 and SBE were significantly correlated with pH. Besides that, in Metabolic subgroup pH also had significant correlation with AG and HCO_3 which was in accordance with

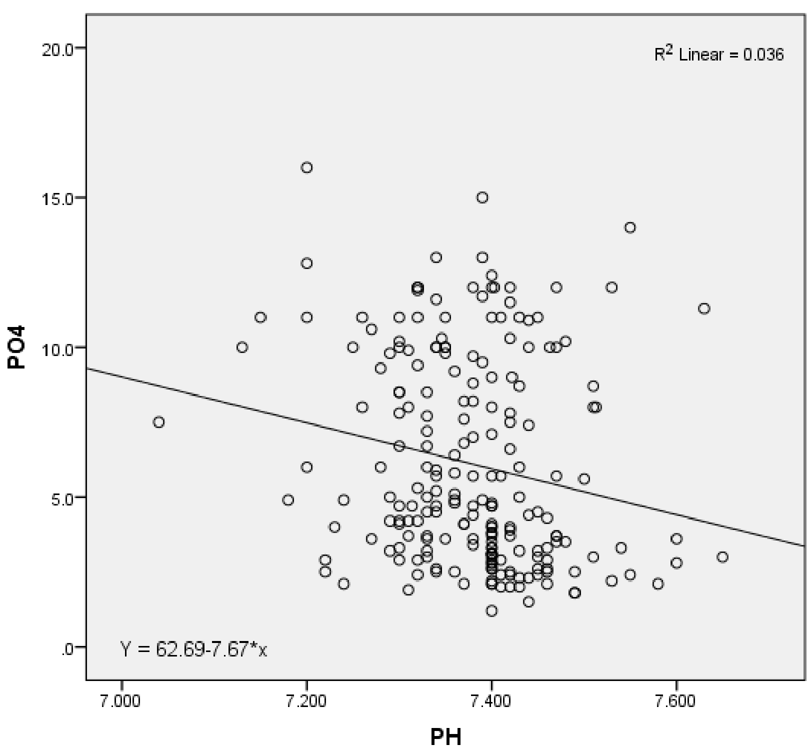

Figure 1: Correlation of pH with Phosphate (PO_4) in total cohort

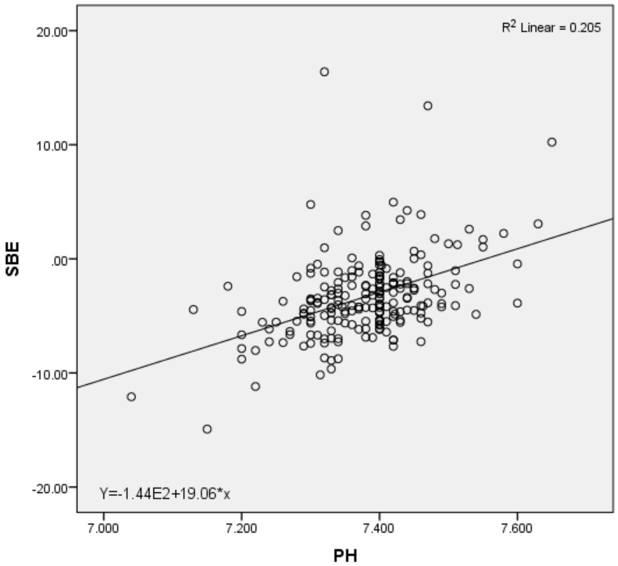

Figure 2 A: Positive correlation between pH and standard base excess (SBE) in total cohort

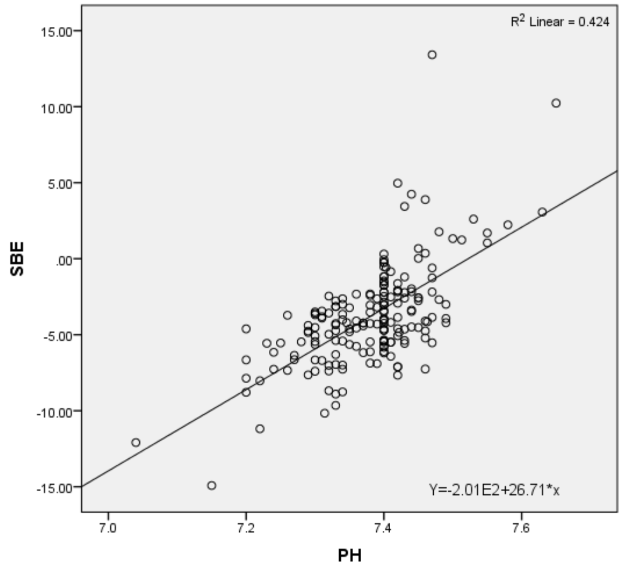

Figure 2 B: Positive correlation between pH and standard base excess (SBE) in metabolic subgroup

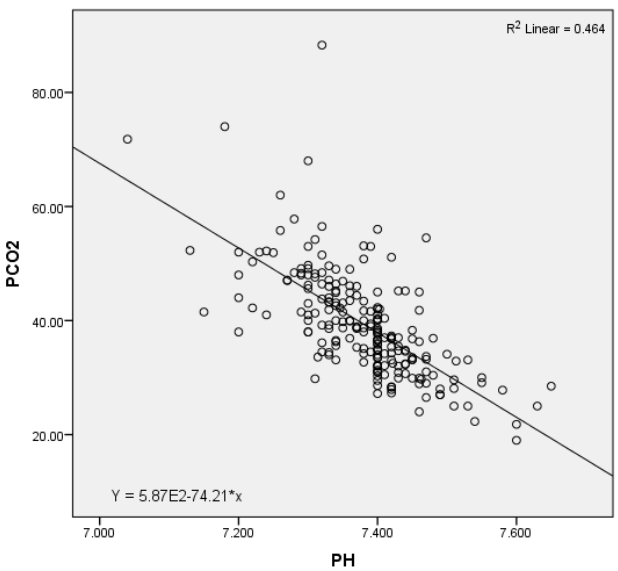

Figure 3 A: Correlation of pH with partial pressure of CO_2 (PCO_2) in total cohort

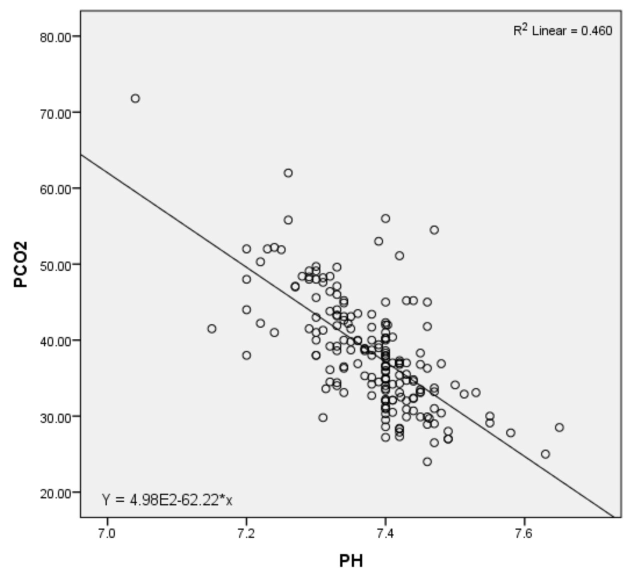

Figure 3 B: Correlation of pH with partial pressure of CO_2 (PCO_2) in metabolic subgroup

the study of Chaiyakulsil C et al and Cusack RJ RA et al.[9,21]

The only parameter of physiochemical approach which was significantly correlated with pH in both groups was PO_4. But it was negatively correlated with pH. The physiochemical approach's independent variables, SIDa and SIDe showed no correlation with pH. This reflects that a single parameter might not be adequate in diagnosing complex metabolic acid base disorders.

Our results showed a difference between the traditional approach and Stewart's approach for the interpretation of metabolic component of acid base disorders, the traditional approach being more reliable than Stewart approach in critically ill patients. Doberer D et al[22] concluded the same. Moreover, we found that traditional approach is relatively simple and practical to use.[23]

CONCLUSION

Despite the fact that physiochemical approach which is complementary to traditional approach offers the same knowledge regarding acid base disorders, our research concludes no significant association between physiochemical approach parameters and blood pH in adults. Thus, we conclude that the traditional approach is the simplest, most rigorous, and most useful in diagnosing acid base disorders.

LIMITATIONS OF THE STUDY

Our study had some limitations. First, our study did not observe any clinical correlation of acid base determination

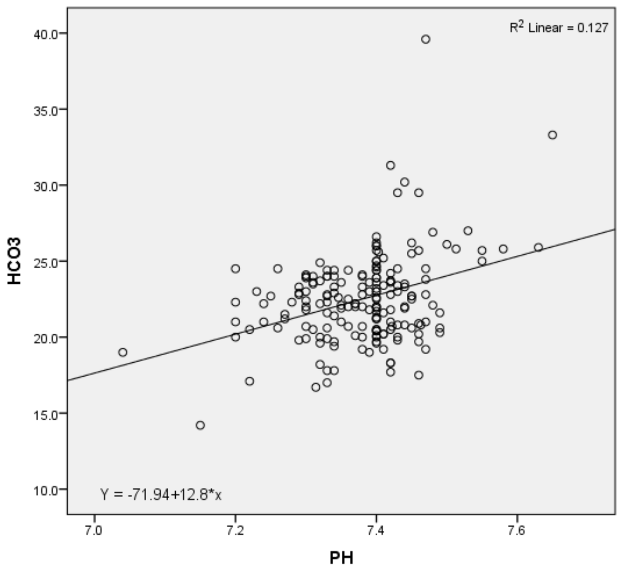

Figure 4: Correlation of pH with bicarbonate (HCO_3) in metabolic subgroup

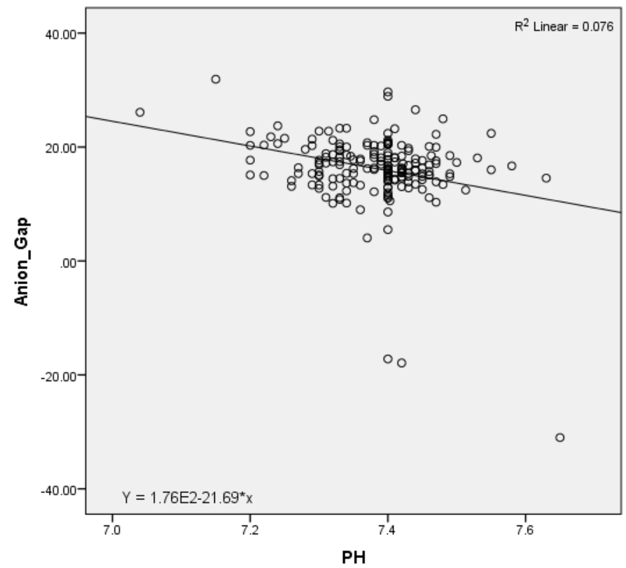

Figure 5: Correlation of pH with Anion gap (AG) in metabolic subgroup

using physiochemical approach with factors like length of the hospital stay, morbidity and mortality. Secondly more work on establishing the correlation of traditional as well as physiochemical approach is encouraged using a larger sample size.

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AUTHORS' CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

SS: Acquisition of data, drafting the manuscript, approval of the final version to be published

AI: Conception & study design, critical review, approval of the final version to be published

MH: Analysis and interpretation of data, drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

Authors declared no conflict of interest

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DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request