Review Article

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Acid-Base Disturbance Analysis: Comparison of the Traditional and Stewart Approaches

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Abstract

***Introduction*: The new approach to acid-base balance which initially proposed by Stewart in 1978 was success to provide a new insight which more easy to understand what is the cause, the mechanism and the degree of acid-base disturbance. The purpose of the present study was to compare two different methods of analysis acid-base disturbance in patients admitted to Pediatric Intensive Care Unit (PICU).**

***Methods*: The study was performed in 43 patients admitted to the pediatric intensive care unit of Cipto Mangunkusumo Hospital, Jakarta. Sodium, potassium, chloride, albumin, lactate and arterial blood gases were measured. All samples were taken from artery in every patient. The anion gap (AG) was calculated using the Narins method (1977), the corrected anion gap (AG_{corr}) using the Moviat method (2003), the strong ion gap (SIG) using Kellum method (1995) and the base excess unmeasured anions (BE_{UA}) using the Fencl-Stewart method simplified by Story (2003).**

***Results*: The presence of unmeasured ions identified by significantly abnormal BE_{UA} was poorly identified by SBE. Of the 43 patients included in the study, 18 (41.9%) had a different interpretation of acid-base balance when the Fencl-Stewart method was used compared to using SBE. There was good correlation between SIG and AG (r =0.831), and there was excellent correlation between SIG and AG_{corr} (r =0.991).**

***Conclusions*: In the condition of electrolyte unbalance and hypoalbuminemia the Stewart approach is better than the traditional approach. Nevertheless, the calculation of SIG is more time-consuming, therefore the corrected anion gap (AG_{corr}) was suggested to use in clinical practice as a combination with SBE.**

Key words: Acid-base, acidosis, Stewart, Henderson-Hasselbalch, anion gap corrected, strong ion gap.

Introduction

Disturbance of acid-base balance is common in patients with critical illness. The presence of this disturbance often as a signal of severe underlying pathophysiology and it is significant marker of outcome [1,2]. Unfortunately, traditional approach to acid-base balance is often inadequate to explain the mechanisms and to quantify the degree of acid-base disturbance [3].

The new approach to acid-base balance which initially proposed by Stewart in 1978 was success to provide a new insight which more easy to understand what is the cause, the mechanism and the degree of acid-base disturbance [3]. This Stewart's theory based on the principles of electroneutrality, conservation of mass and the dissociation equilibria of all incompletely dissociated substances [3,4]. According to him, body fluid is a very complex dynamic system which contains of water, electrolytes (strong and weak electrolytes)

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and non electrolytes which interact one to another [3]. Water is a virtually inexhaustible source of H^+ [1,3,5]. In these solution, $[H^+]$ is determined by the dissociation of water into H^+ and OH^- [3].

Stewart divided these substances of a physiological solution into two variables, dependent and independent. There are three important independent variables controlling the acid-base status ($[H^+]$). These variables are the strong ion difference (SID), the total concentration of non volatile weak acid (A_{tot}) and the partial pressure of carbon dioxide (pCO_2). The role of carbon dioxide controlled by the lungs is similar to the Henderson-Hasselbalch approach. These independent variables will control dependent variables including bicarbonate (HCO_3), hydroxyl ions (OH^-) and hydrogen ions (H^+) [1,3,4].

The purpose of the present study was to compare two different methods of analysis acid-base disturbance in patients who were admitted to the PICU.

Methods

We performed a comparative cross-sectional study in a single PICU in a university teaching hospital from February 2005 until April 2005. We asked consent to the parent of each patient, although the intervention in this study was not different from usual one. Approval for the study was obtained from the local medical ethical committee.

The patient population consisted of medical, surgical and trauma patients requiring critical care. The only criterion for inclusion was agreement from the parent of each patient to follow the study by signing informed consent. To be excluded from the study if the blood sample was damage before or during inspection in laboratory and if the laboratory data was not complete to analyze.

Routine arterial blood gas, sodium, potassium, chloride, albumin and lactate measurements were made in patients who were admitted to the PICU. All measurements were taken from a single arterial blood vessel by nursing staff and handled according to standardized hospital-approved procedures. Arterial blood samples were collected using a vacuum lithium heparin tubes. Blood gas analysis and lactate measurement were performed using the i-STAT portable clinical analyzer 200 series (i-STAT Corporation, East Windsor, USA) on bed side, which underwent daily calibration and quality control checks. The samples for sodium, potassium, chloride and albumin measurements were sent to the hospital core laboratory in the Department of Clinical Pathology. Serum electrolytes measurement were performed using the Ciba Corning 644 (Ciba Corning Diagnostics, Beverly, MA, USA) and serum albumin measurement was performed using the Miraplus (ABX Diagnostics, Montpellier, France).

The normal acid-base status was defined as a standard base excess (SBE) between >-2 mmol/L and <2 mmol/L [6]. The base excess unmeasured anion was calculated with the formula BE_{UA}=SBE–{$[Na^+]$–$[Cl^-]$ –38}–{0.25x(42–[albumin] g/L)} [7], and the value between >-2 mmol/L and <2 mmol/L was defined as normal. The anion gap was calculated with the formula AG=$[Na^+]+[K^+]–[Cl^-]–[HCO_3^-]$ [8], where by potassium was considered as a "measured" rather than "unmeasured" cation. The normal AG calculated by this formula was defined as 16 mEq/L, with variation of 2 to 4 mEq/L [8,9]. The anion gap corrected for albumin and lactate was calculated with the formula AG_{corr}=AG+0.25 (42-[albumin] g/L)–lactate [10]. The apparent strong ion difference was calculated using the formula $SID_{app}=[Na^+]+[K^+]–[Cl^-]–[lactate^-]$ [11]. Because plasma concentration of calcium and magnesium are low, therefore quantitatively unimportant in determining plasma pH, and they were not included in the calculation [3]. The effective strong ion difference was calculated using the formula $SID_{eff}=[HCO_3^-]+$[albumin] g/Lx(0.123xpH–0.631) [11], where $[HCO_3^-]$ was obtained from arterial blood gas measurements [12,13]. Phosphate concentration was not included in the calculation because normally contribute only about 5% of the weak acid component [3]. The SIG was calculated by subtracting the effective strong ion difference from the apparent strong ion difference ($SIG=SID_{app}–SID_{eff}$) [11].

Data were stored on a computer spread-sheet (Excel, Microsoft, Seattle, WA, USA). Fisher's Exact test was used to compare SBE and BE_{UA}. Correlation

of SIG with AG and AG_{corr} were measured using Pearson's correlation coefficient. All analysis was performed using SPSS version 11.0.

Results

Forty three patients were enrolled in the study. Patient characteristics are presented in **Table 1**. The mean age of the patients was 28 months (range 1 day to 14 years). The range of values and means for the variables included in the study are given in **Table 2**.

The range of Na-Cl effect and albumin effect to SBE were -14 to 8 and -1.8 to 6.2 mmol/L and equal to zero in 2 (4.7%) and 0 (0%) of samples, respectively. The range of serum albumin concentration was very wide (17.2 to 49.2 g/L) (**Table 2**). In 26 (60.5%) patients of the study, albumin concentrations were <34 g/L; and in 2 (4.7%) patients, they were <20 g/L.

The traditional method of identifying patients with unmeasured ions (SBE) led to a different clinical interpretation of acid-base status than the Fencl-Stewart method (BE_{UA}) in 18 of 43 (41.9%) patients, presented in **Table 3**.

Plasma lactate concentrations were measured in all patients, and they were increased (>2 mEq/L) in 24 (55.8%) patients. Plasma lactate concentration was stronger correlated to BE_{UA} ($r = -0.742$, $p < 0.01$) than to SBE ($r = -0.516$, $p < 0.01$), presented in **Figure 1**.

The correlation of SIG with AG and AG_{corr} are shown in **Figure 2**. There was a good correlation between AG and SIG ($r = 0.831$, $p < 0.01$). However, the correlation between SIG and AG_{corr} was stronger ($r = 0.991$, $p < 0.01$).

Figure 3 shows the correlation between acid-base status (pH) and the three independent variables. There was a moderate and significant correlation between acid-base status (pH) and pCO_2. However, the correlation of acid-base status (pH) with SID and non volatile weak acid (albumin) were not significant.

Figure 4 shows that there were weak significant correlations of SID with lactate, sodium and chloride, which the correlation between SID and lactate was the strongest one. However, there was no significant correlation between SID and potassium.

Figure 5 shows the correlation of SID with sodium, chlorides and potassium when used a formula $SID=[Na^+]+[K^+]-[Cl^-]$. There was significant correlation between SID and chloride. However, there were no significant correlation of SID with sodium and potassium.

Discussion

The patients in this study demonstrated a variety of pathologies, from relative stabile after surgery to serious illness due to septic shock. Twenty-four patients (55.8%) had elevated lactate levels between 2.01 and 18.98 mEq/L. As we know, the elevated lactate levels can cause the disturbance of acid-base balance.

SBE and AG are commonly used to assess acid-base disturbances [14]. However, this methods frequently fail to identify unmeasured ion that can be found using the BE_{UA} method [12,15]. The AG is influenced by the abnormalities of plasma albumin [9,16], while the SBE is influenced by the abnormalities of plasma sodium, chloride, and albumin [13,16], as it is often seen in critically ill patients. The greater the deviations in plasma sodium, chloride, and albumin from normal, the greater are the differences between the SBE and BE_{UA} methods. The BE_{UA} represents the corrected base excess for changes in sodium, chloride, and albumin. Therefore, theoretically the BE_{UA} method is better than the SBE method in identifying patients with unmeasured ion. Although the comparison between SBE and BE_{UA} in this study was not significant, we found that the BE_{UA} method is superior to the SBE method in identifying patients with increased plasma lactate concentrations. Results of this study support the findings of others [15,17] that BE_{UA} identifies a greater number of patients with an acid-base derangement than SBE. Possibly, by adding the number of sample in this study, we will get a significant result.

Abnormalities in fluid status, electrolytes, and albumin caused significant changes in base excess or deficit in these patients. SBE would be equal to BE_{UA} if there were no abnormalities in sodium, chloride, and

albumin. However, SBE and BE_{UA} were never the same in critically ill patients. SBE caused by the effects of (Na-Cl), and albumin equaled to zero in 2 (5%) and 0 (0%) of samples respectively, showing the important contribution to SBE.

Sodium-chloride is the principal component of the plasma strong ion difference, and albumin is the principal component of the plasma total weak acid concentration. By using the simplified sodium-chloride equation, we can estimate the base excess effects of electrolyte changes from intravenous fluid therapies. For example, Kellum and colleagues [18,19] studied acid base changes during resuscitation. Patients received 0.9% saline, hextend, or lactated Ringer's solution. The saline group had a greater metabolic acidosis, as shown by a more negative base excess. One cause of this acidosis was a decreased SID. In addition to the acidifying effects of saline, Hatherill *et al* [20] and Durward *et al* [21] found that hypoalbuminemia is associated with a low observed anion gap that may fail to detect clinically significant amounts of lactate and other occult tissue anions. Decreased plasma albumin leads to a decreased total weak acid concentration that produces a metabolic alkalosis. Our work supports this finding since the physiology is the same: changes in plasma sodium, chloride, and albumin will alter the SBE.

Unmeasured anion as suggested by increased base deficit and increased anion gap may be due to organic (e.g. lactate, ketoacids, albumin), inorganic (e.g. sulfate, phosphate), exogenous (e.g. salicylate, formate, nitrate, penicillin, carbenicillin), and other acids (e.g. paraldehyde, acetate, ethylene glycol, methanol, salicylates, urea, glucose) [22]. Proteolysis associated with sepsis may release organic and inorganic acids, some of which are poorly defined [23]. High concentrations of some of these acids are not present during health, and thus, the presence of unmeasured anion may serve as a marker for organ dysfunction.

As discussed by Stewart [3], acute acid-base disturbances result from change in pCO_2 or SID. The compensatory responses to primary disturbance that interfere the independent variables are purposed to minimize the changes in pH ($[H^+]$). Although $[A_{tot}]$ (mainly albumin) does not change acutely, it does have a direct influence on the final concentration of $[H^+]$ for a given pCO_2 and SID. SID is the charge difference between the sum of strong cations and strong anions ($[Na^+]+[K^+]+[Ca^{2+}]+[Mg^{2+}]-[Cl^-]-$[unmeasured strong anions]). We did not include calcium and magnesium in the calculation of SID because in normal condition the concentrations in plasma are low, so quantitatively unimportant in determining plasma pH. SID influences the concentration of weak electrolytes in that, as a net positive charge, it must be balanced by the sum of all weak anions to maintain electrical neutrality. The magnitude of the dissociation constants for bicarbonate and weak acids compared with other dissociation constants is such that SID is closely approximated by the sum of $[HCO_3^-]$ and $[A^-]$ [1,3,5]. Our data support the findings of Wilkes [24] that pH ($[H^+]$) was significantly correlated to pCO_2, but has a lack of correlation with SID and albumin ($[A_{tot}]$). Wilkes also found that SID was inverse significantly correlated to $[Cl^-]$, but not to $[Na^+]$. Results of our study demonstrated that SID was significantly correlated to $[La^-]$, $[Cl^-]$, and $[Na^+]$, but not to $[K^+]$. The different result may be caused by using the formula of SID=$[Na^+]+[K^+]-[Cl^-]-[La^-]$. When we use the formula SID=$[Na^+]+[K^+]-[Cl^-]$, its result is equal to Wilkes's. From these results, it could be said that $[Cl^-]$ and unmeasured anions are very important to determine the value of SID. It is proved that $[Cl^-]$ have very important role in controlling of acid-base balance through its influence to SID, whereas $[Na^+]$ is responsible to control intravascular volume and osmolality, and $[K^+]$ is responsible to cardiac and neuromuscular function. It become clear here that kidney controls the acid-base balance through the arrangement of $[Cl^-]$ balance. According to this fact, $[Cl^-]$ is the important acid-base regulator in the body.

Results of Wilkes [24] also demonstrated that $[HCO_3^-]$ and $[A^-]$ were significantly correlated to SID. pCO_2 was significantly correlated to $[HCO_3^-]$, but not to $[A^-]$. $[A_{tot}]$ was not significantly correlated to $[HCO3^-]$, but significantly correlated to $[A^-]$ directly. $[Cl^-]$ was inversely correlated significantly to $[A_{tot}]$, and had a stronger correlation to SID. Therefore, the relation between independent and dependent variable can be described as shown in **Figure 6**.

It shows that only pCO_2 has direct relation and significant to $[H^+]$. It is proved that lungs, which have the function of ventilation, have very important role in controlling of acid-base balance. $[HCO_3^-]$ also has direct relation and significant to pCO_2 and SID, and it is proved that $[HCO_3^-]$ cannot be used as a metabolic parameter in analysis of acid-base disturbance. The change of $[HCO_3^-]$ is a direct effect of the changes of pCO_2 and SID, or as a mediator of respiratory component and metabolic component in controlling pH ($[H^+]$). From the relationship of those independent variables, we may say that pCO_2 will be the first to compensate the disturbances of acid-base balance, followed by SID and A_{tot} respectively.

Similar to the SBE, AG is commonly used to assist in the diagnosis and management of cases with disturbance of acid-base balance but the accuracy is often questioned. To avoid this inaccuracy, use the physical chemical technique that calculates the Strong Ion Gap (SIG). The primary importance of this technique is in the evaluation of anions and cations in low concentration (<10 mEq/L) and for use in exploring ion fluxes across organs and between cellular and extracellular compartments [11]. Unfortunately the use of SIG is more time consuming and less convenient in daily practice [25]. In the study of Moviat and colleagues [10], it was found that anion gap which was corrected by the abnormality of albumin and lactate could be used to replace strong ion gap in daily practice. It is supported by our finding that the correlation between SIG and AG_{corr} was stronger than between SIG and AG. So, the using of SBE that is combined with AG_{corr} will become an easy method, modestly and accurate in the assisting of diagnosis and management of cases with derangement of acid-base balance.

In conclusion, the present study demonstrated that in the condition of electrolyte unbalance and hypoalbuminemia, the Stewart approach is better than the traditional approach. Nevertheless, the calculation of SIG is more time-consuming, therefore AG_{corr} is suggested to use in clinical practice as a combination with SBE.

Table 1. SUMMARY OF PATIENT CHARACTERISTICS

Patient characteristics			Number of patients (%)
Age:	After birth	– <30 days	14 (32.6%)
	1	– <12 months	11 (25.6%)
	1	– <5 years	9 (20.9%)
	5	– <10 years	7 (16.3%)
	10	– 14 years	2 (4.7%)
Sex:	Male		23 (53.5%)
	Female		20 (46.5%)
Mechanical ventilation			21 (48.8%)
Organ dysfunction:			
	Nervous system		10 (23.3%)
	Cardiovascular system		8 (18.6%)
	Respiratory system		11 (25.6%)
	Gastrointestinal system		15 (34.9%)
	Genitourinary system		3 (6.9%)
	Systemic (sepsis)		13 (30.2%)
	Surgical		21 (48.8%)
	Others		4 (9.3%)
Death:			14 (32.6%)

Table 2. MINIMUM, MAXIMUM AND MEAN±SD VALUES FOR VARIABLES

Variable	Minimum	Maximum	Mean±SD
Measured quantities			
pH	6.717	7.630	7.36 ± 0.167
pCO_2 (mmHg)	18.10	110.20	45.05 ± 20.94
HCO_3 (mmol/L)	8.40	55.10	24.86 ± 8.86
SBE (mmol/L)	-28.00	30.00	-0.71 ± 9.74
Na (mEq/L)	122.00	144.00	134.35 ± 5.24
K (mEq/L)	2.39	7.19	3.90 ± 0.81
Cl (mEq/L)	87.00	112.00	102.14 ± 6.02
Albumin (g/L)	17.20	49.20	32.04 ± 7.21
Lactate (mEq/L)	0.73	18.98	3.43 ± 3.61
Derived quantities			
AG (mEq/L)	-8.06	29.79	11.25 ± 6.69
AG_{corr} (mEq/L)	-6.18	18.47	10.31 ± 4.84
SIG (mEq/L)	-18.05	7.39	-0.97 ± 5.01
SID_{app} (mEq/L)	19.21	49.27	32.68 ± 5.71
SID_{eff} (mEq/L)	14.00	63.77	33.64 ± 9.31
BE_{UA} (mmol/L)	-24.30	21.80	2.59 ± 7.61
Effect Na-Cl (mmol/L) (=$[Na^+]$-$[Cl^-]$-38)	-14.00	8.00	-5.79 ± 4.84
Effect alb (mmol/L) (=0.25x(42-[alb]g/L))	-1.80	6.20	2.49 ± 1.80

Table 3. IDENTIFICATION OF UNMEASURED IONS BY TRADITIONAL METHOD (SBE) AND COMPARISON TO THE FENCL-STEWART METHOD (BE_{UA}).
(FISHER'S EXACT TEST: p >0.01)

Methods		Fencl - Stewart method (BE_{UA})		Total
		Normal (-2 to + 2)	Abormal (<-2 to >+ 2)	
Traditional method (SBE)	Normal (-2 to +2)	3	14	17
	Abnormal (<-2 and >+2)	4	22	26
Total		7	36	43

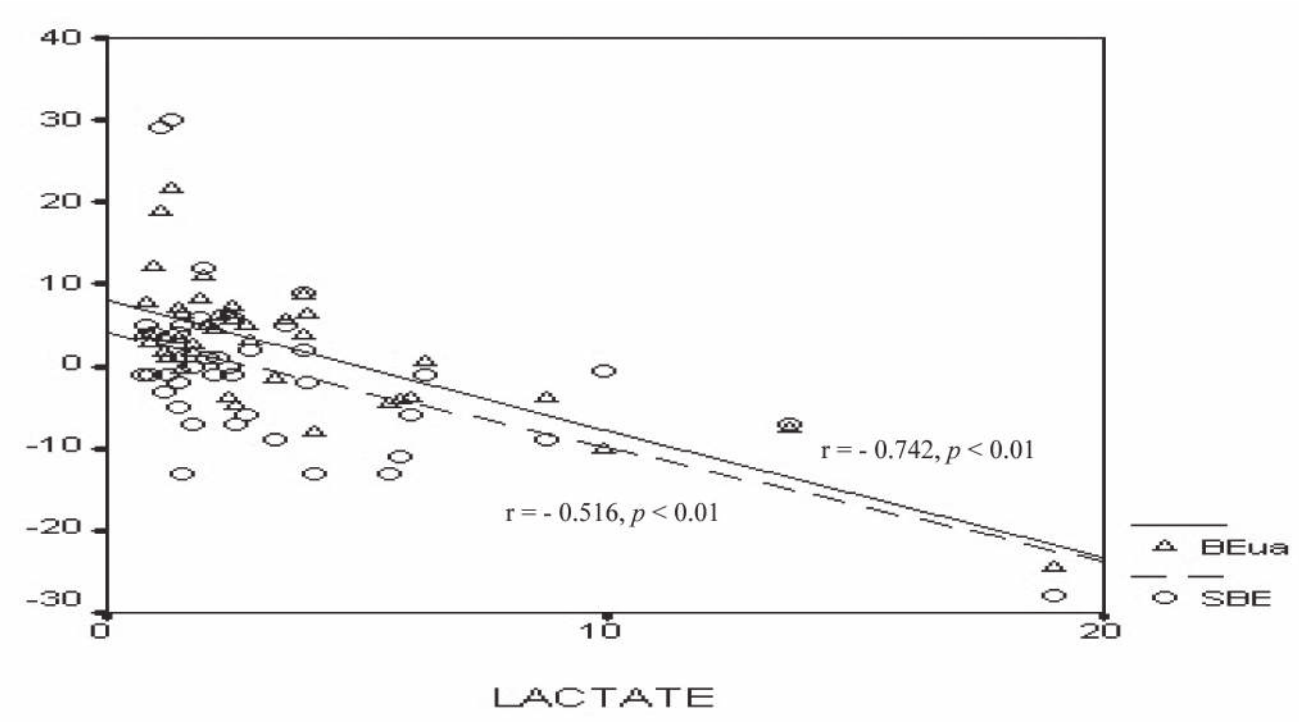

Figure 1. CORRELATION OF PLASMA LACTATE CONCENTRATION WITH SBE AND BE_{UA}

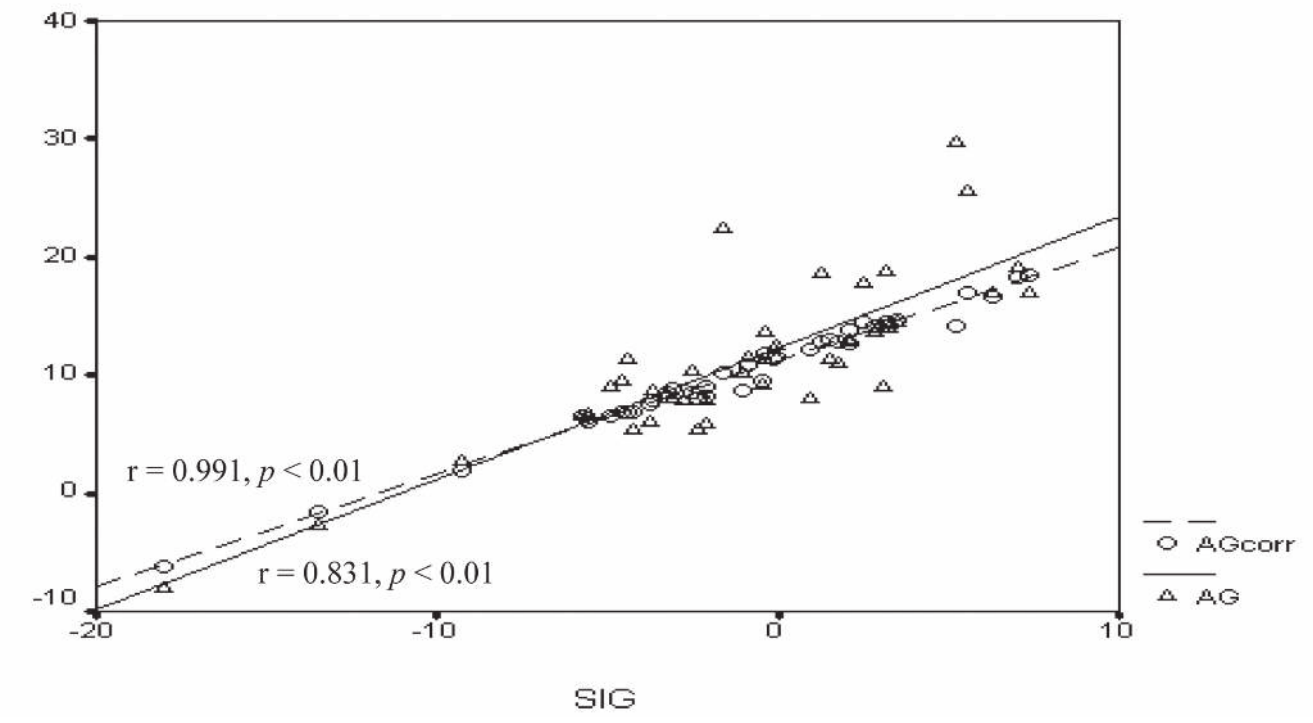

Figure 2. CORRELATION OF SIG WITH AG AND AG_{CORR}

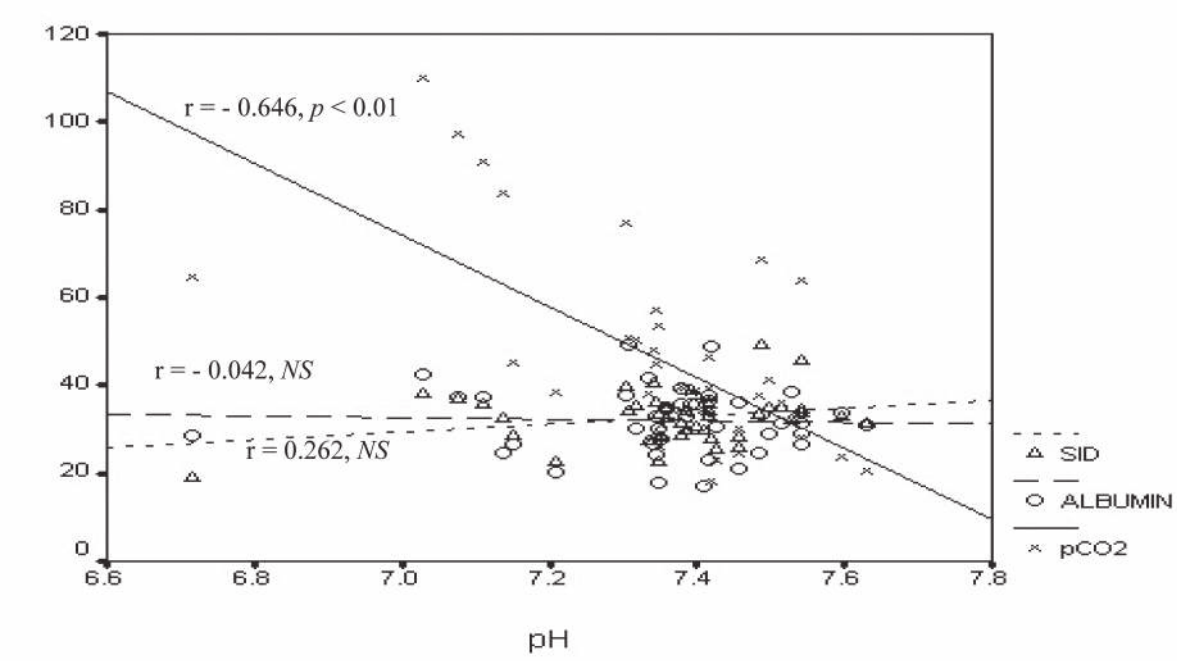

Figure 3. CORRELATION OF ACID-BASE STATUS (pH) WITH pCO_2, SID, AND ALBUMIN. (SID=$[NA^+]+[K^+]-[CL^-]-[LACTATE^-]$)

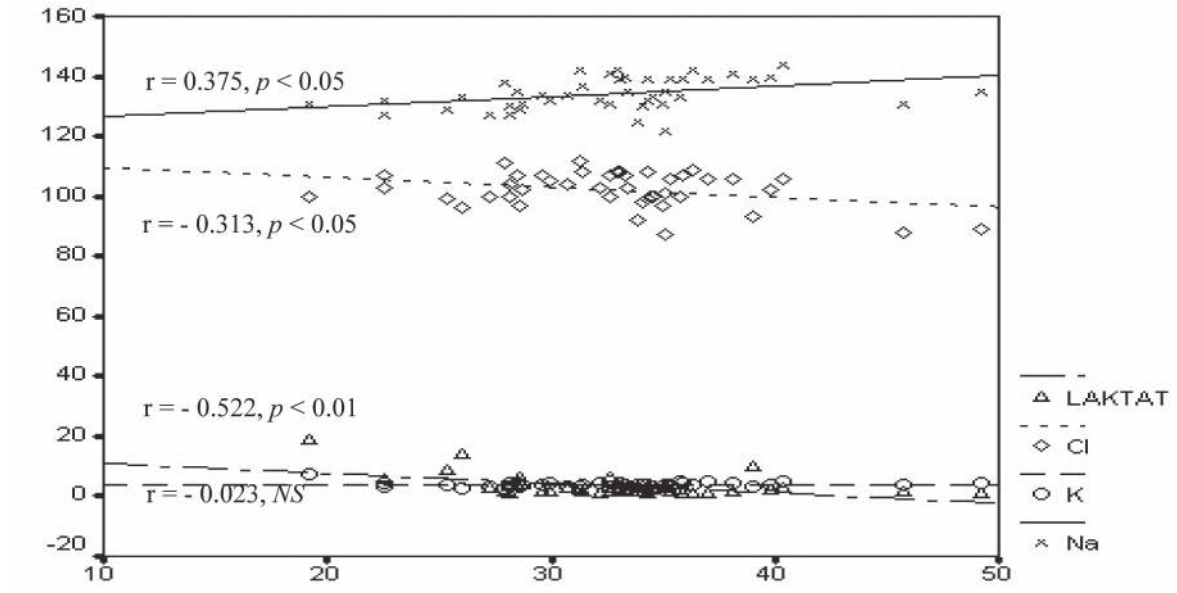

Figure 4. CORRELATION OF SID WITH SODIUM, POTASSIUM, CHLORIDE, AND LACTATE. (SID=$[NA^+]+[K^+]-[CL^-]-[LACTATE^-]$)

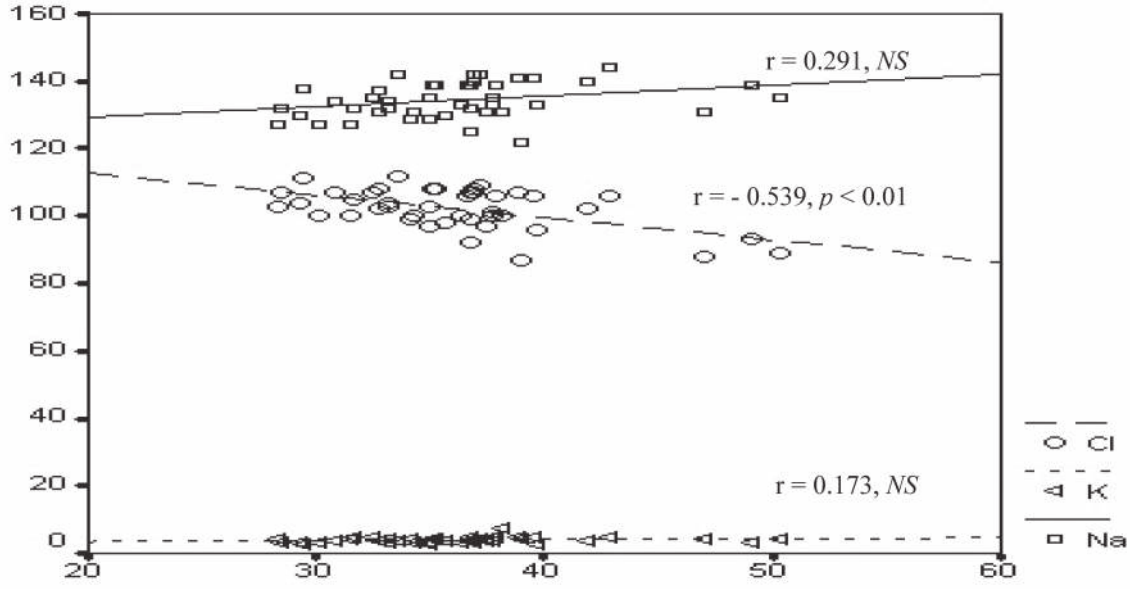

Figure 5. CORRELATION OF SID WITH SODIUM, POTASSIUM, AND CHLORIDE. (SID=$[NA^+]+[K^+]-[CL^-]$)

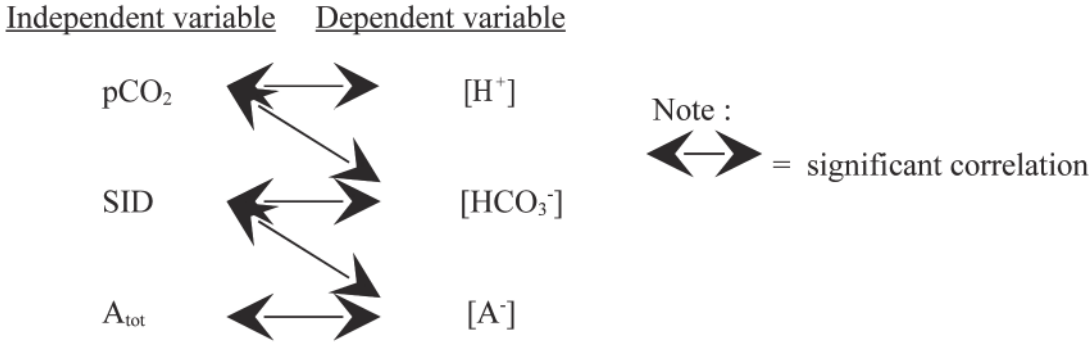

Figure 6. THE RELATION BETWEEN INDEPENDENT AND DEPENDENT VARIABLE

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