Research Article / Araştırma Makalesi

Comparison Between Manually and Automatically Calculated Analyses: Blood Gases in Pediatric Intensive Care

Manuel ve Otomatik Hesaplanan Analizlerin Karşılaştırması: Pediatrik Yoğun Bakımda Kan Gazları

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Abstract

Background: One of the most significant situations in patients with critical illness is an acid-base imbalance. Blood gas analysis is a fundamental laboratory investigation employed to assess a patient's acid-base equilibrium and oxygenation status. The accurate interpretation of the blood gas is essential for the management and treatment of disease. The aim of this study is to compare analyzes of manually and automatically calculated blood gas parameters in the pediatric intensive care unit (PICU).
Materials and Methods: This retrospective study evaluated the serum ions and blood gas parameters values at the time of admission of patients aged between 0 and 18 years who were admitted to the PICU between April and October 2023. Furthermore, the relationship between automatically (with ABL800 FLEX autoanalyzer) and manually calculated standard base excess (SBE), anion gap, and the type of blood gas samples was investigated.
Results: The study included 184 patients admitted to the PICU, of whom 105 (57.1%) were male and 79 (42.9%) female. The most common diseases were 47(25.5%) physical traumas and 43(23.4%) lower respiratory tract infections. A positive correlation was detected between the results obtained from the blood gas automatically and manually calculated values for SBE. (correlation coefficient(Cc): 0.970; p<0.001). However, a significant difference was found between the SBE automatically and manually calculation when capillary (p=0.007) or venous (p<0.001) blood gas was taken, but this difference was not found for arterial samples (p=0.089).
Conclusions: The automatic measurements of the blood gas analyser are reliable, based on this study, and we should to be say between two methods no differences automatically and manually values. Nevertheless, in cases where there is an elevated risk of base deficit in critically ill patients, it is recommended that an arterial blood gas sample be obtained.

Keywords: Acidosis, Blood gas, Pediatrics, Ion difference, Intensive care

Öz

Amaç: Kritik hastalığı olan hastalarda karşılaşılan en önemli durumlardan biri asit-baz dengesizliğidir. Kan gazı analizi, bir hastanın asit-baz dengesini ve oksijenasyon durumunu değerlendirmek için kullanılan temel bir laboratuvar incelemesidir. Kan gazının doğru yorumlanması hastalığın yönetimi ve tedavisi için önemlidir. Bu çalışmanın amacı, pediatrik yoğun bakım ünitesindeki (PYBÜ) hastalardan alınan kan gazı örneklerinde manuel ve otomatik olarak hesaplanan sonuçların karşılaştırılmasıdır.
Materyal ve Metod: Bu retrospektif çalışmada, Nisan-Ekim 2023 tarihleri arasında PYBÜ'ne yatırılan 0-18 yaş arasındaki hastaların yatış anındaki serum iyon ve kan gazı parametre değerleri incelenmiştir. Kan gazı cihazında otomatik (ABL800 FLEX otoanalizörü ile) ve manuel olarak hesaplanan standart baz açığı (SBA), anyon gap ve kan gazı örneği alım tipleri arasındaki ilişki araştırılmıştır.
Bulgular: PYBÜ'ye kabul edilen 184 hastanın 105'i (%57.1) erkek, 79'u (%42.9) kızdı. Yatış nedenleri en sık 47 (%25.5) fiziksel travmalar ve 43 (%23.4) alt solunum yolu enfeksiyonuydu. Kan gazı cihazından otomatik elde edilen sonuçlar ile SBA değeri için manuel olarak hesaplanan değerler arasında pozitif korelasyon tespit edildi (korelasyon katsayısı (Kk): 0.970; p<0.001). SBA otomatik ile manuel hesaplama arasında kapiller (p=0.007) veya venöz (p<0.001) alınan kan gazı türleri arasında istatistiksel anlamlı fark bulundu, ancak arteriyel örneklerde anlamlı fark bulunmamıştır (p=0.089).
Sonuç: Kan gazı analizörünün otomatik ölçümleri güvenilirdir. Bu çalışmaya dayanarak, iki yöntem arasında otomatik ve manuel değerler arasında anlamlı fark olmadığını söyleyebiliriz. Bununla birlikte, kritik hastalarda baz açığı riskinin yüksek olduğu durumlarda, hastadan arteriyel kan gazı örneği alınması önerilir.

Anahtar kelimeler: Asidoz, Kan gazı, Pediatri, İyon farkı, Yoğun bakım

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Introduction

One of the most serious problems affecting almost all critically patients is acid-base imbalance, and especially metabolic acidosis. This imbalance has an impact on morbidity and mortality (1). Blood gas analysis is one of the most crucial laboratory tests employed to evaluate a patient's acid-base equilibrium and oxygenation status. In addition to facilitating a diagnosis, this analysis is also employed to evaluate the patient's subsequent course of treatment and response to it (2,3). In blood gas measurement systems, some parameters such as pH, partial oxygen pressure (pO_2), partial carbon dioxide pressure (pCO_2), electrolytes [sodium (Na), potassium (K), calcium (Ca), etc.], metabolites (glucose, urea, etc.) are measured directly, while for some parameters (anion gap (AG), bicarbonate (HCO_3^-), etc.) calculation results are reported using different formulae. While some parameters, such as AG, HCO_3^-, etc. are measured directly, for some parameters the calculation results are reported using different formulae, which causes differences in the reported results between devices (4).

Bicarbonate, the second most important anion of extracellular fluid and the main component of buffering systems in blood, is one of the most important parameters used to determine the acid-base balance of blood. Standard bicarbonate concentration ($cHCO_3^-$(std)) is the bicarbonate value that should be present in the blood under 40 mmHg pCO_2 at 37°C, while actual bicarbonate concentration ($cHCO_3^-$(act)) is the instantaneous bicarbonate value of the sample calculated by the Hendersen-Hasselbalch equation using pH, pCO_2. Under normal conditions, these two values are equal to each other (4,5). In addition to bicarbonate, the formation of pH value in blood gas is influenced by other factors, including lactate derived from anaerobic metabolism and the anion gap, which is calculated based on the balance between cations and anions from intracellular and extracellular buffering systems (3). Anion gap refers to the difference between measured serum cations (positively charged particles) and anions (negatively charged particles). In routine clinical practice, the cation that is measured is sodium, while the anions are chlorine and bicarbonate. It is employed to ascertain whether metabolic acidosis is attributable to the accumulation of non-volatile acids (ketoacids, lactic acid etc.) (increased AG, normochloremic metabolic acidosis) or loss of bicarbonate (hyperchloremic metabolic acidosis, normal AG). The normal range for AG is 12 ± 4 mEq/L. In patients with low albumin, the AG should be corrected in accordance with the albumin level (6). Blood gas is important in the clinical management of patients, particularly in intensive care units, in the diagnosis, treatment, follow-up and determination of procedures to be applied (e.g. respiratory support treatments, hemodialysis) for both respiratory and metabolic disorders. It is often used in intensive care units because it is a quick, inexpensive and easy-to-use test (5,6).

The aim of this study is to compare manually and automatically calculated analyses in blood gas measurements in PICU. We also aimed to examine the relationship and correlation of pH, and bicarbonate the type of blood gas. At the same time, blood gas parameters, demographic data, diseases that caused hospitalization, and mortality status were also evaluated.

Materials and Methods

Study design

In this retrospective study, clinical data and laboratory results were collected from the electronic medical records of pediatric patients aged 1 month to 18 years who were admitted to the Aydin Adnan Menderes University Hospital PICU in April and October 2023. The characteristics of the patients, including age, gender, the primary disease of admission to the PICU, as well as the laboratory results, were reviewed. The study included patients admitted to the PICU whose blood gases, hemogram, serum ions and serum albumin values were recorded in the electronic file at the time of admission. The study excluded those who did not undergo the examinations at the same time, as well as individuals outside the 0-18 age range.

The laboratory data of a simultaneous collection of blood gas analysis (e.g., pH, pCO_2, pO_2, HCO_3) were analyzed with ABL800 FLEX autoanalyzer and blood serum chemistry (i.e., [Na^+], [K^+], [Cl^-], [Ca_2^+], [Mg_2^+], [PO_4^-], and albumin) data were saved. Additionally, descriptives analysis (comorbid diseases that may affect the data, previous treatments, the hospitalization periods), the type of blood gas samples were recorded. Depending on the clinical condition of the patients at the time of admission, Glasgow Coma Score (GCS), Pediatric Risk of Mortality Score III (PRISM III), primary diagnosis, congenital metabolic disease and/or renal failure, initiation of respiratory invasive/noninvasive mechanical ventilation, intravenous bicarbonate using was saved. The base excess resulting from the patient's blood gas on the blood gas analyzer was calculated and the base excess calculated manually according to their biochemical examinations was compared.

Calculation formulas of anion gap and base excess

In general, the cation measured is sodium and the anions are chlorine and bicarbonate [AG (anion gap) = Na - (HCO_3 + Cl)]. It is used to show whether metabolic acidosis is due to accumulation of non-volatile acids (lactic acid, ketoacids, etc.) (increased AG, normochloremic metabolic acidosis) or loss of bicarbonate (normal AG, hyperchloremic metabolic acidosis) [Normal AG: 12±4 mEq/L].

In patients with low albumin level, AG should be corrected according to albumin level. In patients with hypoalbuminemia (< 3.5 g/dL), the normal anion gap is less than 12 meq/L; In patients with hypoalbuminemia, the normal anion gap is 2.5 meq/L lower for every 1 g/dL decrease in plasma albumin concentration (6).

Standard base excess (SBE), arterial lactate, serum bicarbonate and serum chloride were included to serve as a traditional approach for evaluation of acid–base disturbances. SBE was calculated from the measured pH and HCO_3^- as following;

SBE = 0.9287 x HCO_3 − 24.4 + 14.83 x (pH-7.4)

Statistical Analysis

Statistical calculations of the obtained were made with the SPSS (ver. 25.0; SPSS, USA). The suitability of the groups for normal distribution was tested with the Shapiro-Wilk. Oneway analysis of variance (Oneway ANOVA) was performed to compare the three groups with each other in parameters that comply with normal distribution. Kruskal Wallis Analysis and Mann Whitney U test were performed for parameters that did not show normal distribution. The Spearman correlation test for variables with non-normal distribution and the Pearson correlation test for normal distribution determined the relationship between the parameters. Correlation analysis was performed between SBE value, manually and automatically values, and pH and AG. $p<0.05$ was considered significant.

Results

Among 184 pediatric patients admitted to the PICU between April 2023 and October 2023, 105 (57.1%) were male and 79 (42.9%) were female. When examined at the disease groups, there were most commonly 47 (25.5%) physical trauma patients and 43 (23.4%) lower respiratory tract infections. The distribution of the primary diseases that caused PICU admission is shown in Table.1.

Table 1. The distribution of the patients' primary diseases

Primary diseases	n (%)
Traumas	47 (25.5)
Lower respiratory tract infection	43 (23.4)
Postoperative care	22 (12)
Diabetic ketoacidosis	17 (9.2)
Sepsis	16 (8.7)
Status epilepticus	10 (5.4)
Postressussitative care	6 (3.3)
Oncological diseases	5 (2.7)
Intoxication	4 (2.2)
Renal diseases	3 (1.6)
Acute gastroenteritis	3 (1.6)
Ensefalitis	2 (1.1)
Congenital metabolic diseases	2 (1.1)
Cardiavasculary failure	2 (1.1)
Arrhythmias	2 (1.1)
Total	184 (100)

A total of 122 patients (66.3%) had no previously known comorbid disease. Of the subjects with a known history of chronic disease, 11 (6%) had a diagnosis of congenital metabolic disease and 5 (2.7%) had chronic renal failure.

Upon admission to the PICU, 39 patients (21.2%) required invasive mechanical ventilation, while 35 (19%) required non-invasive. The mortality rate was 9.2%. Intravenous bicarbonate was administered to 17 patients (9.2%) prior to admission and 21 patients (11.4%) during their stay in the hospital. This was due to the presence of metabolic acidosis in their blood gas analysis. Descriptive analysis of the patients included in the study and clinical and laboratory data at the PICU admission are presented in Table.2.

Table 2. Descriptive analysis, and clinical and laboratory data at the PICU admission

	Median (min-max) IQR
Age (months)	61 (1-216) 119
Glosgow coma scale	15 (3-33) 3
PRISM III	12 (1-99) 26.5
Length of stay (days)	3 (1-152) 5
pH	7.35 (6.81-7.52) 0.12
pCO_2 (mmHg)	43 (4-94.1) 12.5
HCO_3 (mmol/L)	22.9 (5.2-45.3) 6.2
Lactate (mmol/L)	1.7 (0.5-12.3) 1.4
Standard base excess	-1.2 (-26.9-21.5) 7.03
Hemoglobin (gr/dL)	10.5 (3.9-17.8) 2.8
White blood cells (10^3/mkrL)	10940 (10-58790) 8355
Platelets (10^3/μL)	287000 (24700-763000) 193000
Albumin (g/L)	36.8 (19.5-54.14) 10.6
Na (mEq/L)	139 (130-190) 5.0
K (mEq/L)	4.10 (2.1-5.9) 0.95
Cl (mEq/L)	109 (95-150) 7.0
Mg (mEq/L)	1.93 (1.07-4.04) 0.37
Ca (mEq/L)	8.30 (3-11.2) 1.15
Anion gap	7.05 (-8.3-24.5) 5.95

**PRISM III: Pediatric Risk of Mortality Score III.*

In accordance with the purpose of our study, the correlation between pH, AG (automatically and manually) and SBE (automatically and manually) values was examined. Upon examination of the blood gases, a positive correlation was identified between the results obtained from the automated and manually calculated values for the SBE (correlation coefficient (Cc): 0.970; p< 0.001). Upon examination of the entire pH range, an AG negative correlation was identified (Cc: 0.970; p < 0.001); but along with a positive correlation between the automatically analysed SBE (Cc: 0.794; p < 0.001) and the calculated SBE (Cc: 0.878; p < 0.001). Upon examination of all AG levels, it was found that the SBE value of the automatically analysed data set (Cc: 0.724; p < 0.001) and the calculated SBE (Cc: 0.743; p < 0.001) exhibited a negative and statistically significant correlation (Table.3).

Table 3. The general correlation between pH, AG (automatically and manually) and SBE (automatically and manually) values

Variables	Statistics Term	AG	SBE Automatically	SBE Manually
pH	**r**	-0.625	0.794	0.878
	p	<0.001	<0.001	<0.001
AG	**r**		-0.724	-0.743
	p		<0.001	<0.001
SBE Automatically	**r**	-0.724		0.970
	p	<0.001		<0.001

**AG: Anion gap, SBE: Standard base excess, r: Spearman's rho correlation coefficient, p is significant <0.05.*

Of the blood gas samples analysed, 19 (10.33%) were capillary, 140 (76.09%) were venous and 25 (13.58%) were arterial. When the automatically SBE value (p=0.493), the manually SBE (p=0.181), and AG (p=0.067) values, were examined according to whether the blood gas sample was artery, vein, or capillary, no statistically significant difference was detected (Table 4). On the contrary, if the blood gas was capillary (p=0.007) or venous (p<0.001), a significant difference was detected between the automatically SBE and manually SBE calculation, but this difference was not found in arterial blood samples (p=0.089). Depending on the type of blood gas sample, Independent-Samples Kruskal-Wallis test results of automatically SBE, manually SBE, and AG analyses are shown schematically in Figure 1.

Table 4. Comparison of BE automatically, manually and anion gap measurements among blood gas groups

Variables	Capillary (n=18)	Venous (n=140) Median (min-max) IQR	Arterial (n=25)	p value
BE Calculation Automatically	-0.1 (-14.2 - 15.8) 7.2	-1.2 (-26.9-21.5) 7.3	-0.2 (-12.8-13.0) 6.4	0.458
BE Calculation Automatically	-1.8 (-13.6-14.9) 6.5	-2.5 (-27.9-21.8) 7.4	-0.9 (-12.6-10.9) 4.9	0.197
Anion Gap	6.1 (-1.7-11.3) 5.4	7.4 (-8.3-24.5) 6.6	6.3 (-3.0-14.7) 5.4	0.067

**Kruskal-Wallis analysis used and p<0.05 considered significant.*

Discussion

The findings of our study indicate that the automated readings from the blood gas analyser are reliable source of data, as evidenced by the strong correlation between the automatically and manually values with key parameters such as pH, AG and SBE, which are appropriate to the blood gas samples obtained from pediatric patients under optimal conditions. Nevertheless, in cases where there is an elevated risk of base deficit in critically ill patients, it is recommended that an arterial blood gas sample be obtained.

In critically ill children, an investigation of acid-base imbalances is required for the majority of those admitted to the PICU (7). Disorders in oxygenation and glucose distribution throughout the body can occur in critically ill patients, depending on the underlying cause of their illness. Consequently, metabolic deteriorations, particularly metabolic acidosis with an increased anion gap, may arise as a result of the patient's elevated metabolic rate.

In pediatric patients, venous and capillary samples are also taken in addition to arterial samples due to the low number of collaterals, the risk of developing peripheral circulatory disorders, and the difficulties in obtaining them. In addition, it is important to analyze the blood gas samples taken before clotting occurs in the heparin syringes and to quickly deliver them to the location of the blood gas device under cold chain conditions to reach the correct result (2). In this study, a critical analysis was conducted on blood samples from patients in the PICU who were treated by the same PICU team. This approach ensured that the level of each sample, the injection apparatus, the method of transport to the laboratory for analysis, and the investigative process were all conducted by the same team, thereby facilitating standardisation.

The physicochemical approach to acid-base status, as developed by Peter Stewart, has been the subject of extensive study to establish the most appropriate analytical techniques for use in studies, updates and refinements in adults. Nevertheless, the majority of these studies demonstrate the potential of a physicochemical approach in pediatrics. However, they are primarily focused on the correlation between physicochemical parameters and the efficacy of the treatment, rather than pH (8-12). The present study is distinguished by its investigation of pH, AG, and automatically and manually calculated SBE levels, which have been relatively understudied in the pediatric age group.

In a study conducted by Chaiyakulsil and colleagues, the correlation between the pH levels measured in blood gas analysis and various physicochemical parameters in the PICU was

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evaluated. It was reported that SBE exhibited the most significant correlation with the measured pH, whereas the single parameters, such as serum chloride and arterial lactate, demonstrated the least association. This finding indicated that a single parameter may not be sufficient for accurately assessing complex acid-base disturbances in the PICU (13). It is an established fact that unmeasurable anions and cations also have an impact on the evaluation of the clinical condition in pediatric patients. Accordingly, the present study was designed to investigate the correlation between pH, AG and SBE (both automatically and manually calculated). While AG and pH showed a negative correlation, both SBE values (automatically and manually) were found to be positively correlated with AG. Additionally, the anion gap was examined and both SBE values were found to be negatively correlated. AG increases and severe metabolic acidosis occurs due to reasons such as severe sepsis, multiple organ failure, severe metabolic imbalances in patients with severe postoperative surgery, and an increase in intracellular-extracellular ion transfer. In this case, pH decreases in case of increased AG due to physiology, and our detection of a negative correlation in the data in our study supports this situation. In the same study, Chaiyakulsil et al., found a positive correlation between blood gases and pH and physicochemical approach in the PICU (13). Similarly, in our study, a positive correlation was found between the automatically SBE value in the blood gas analyzer and the manually calculated SBE value of critically ill patients in PICU. This confirms our data in blood gas analysis.

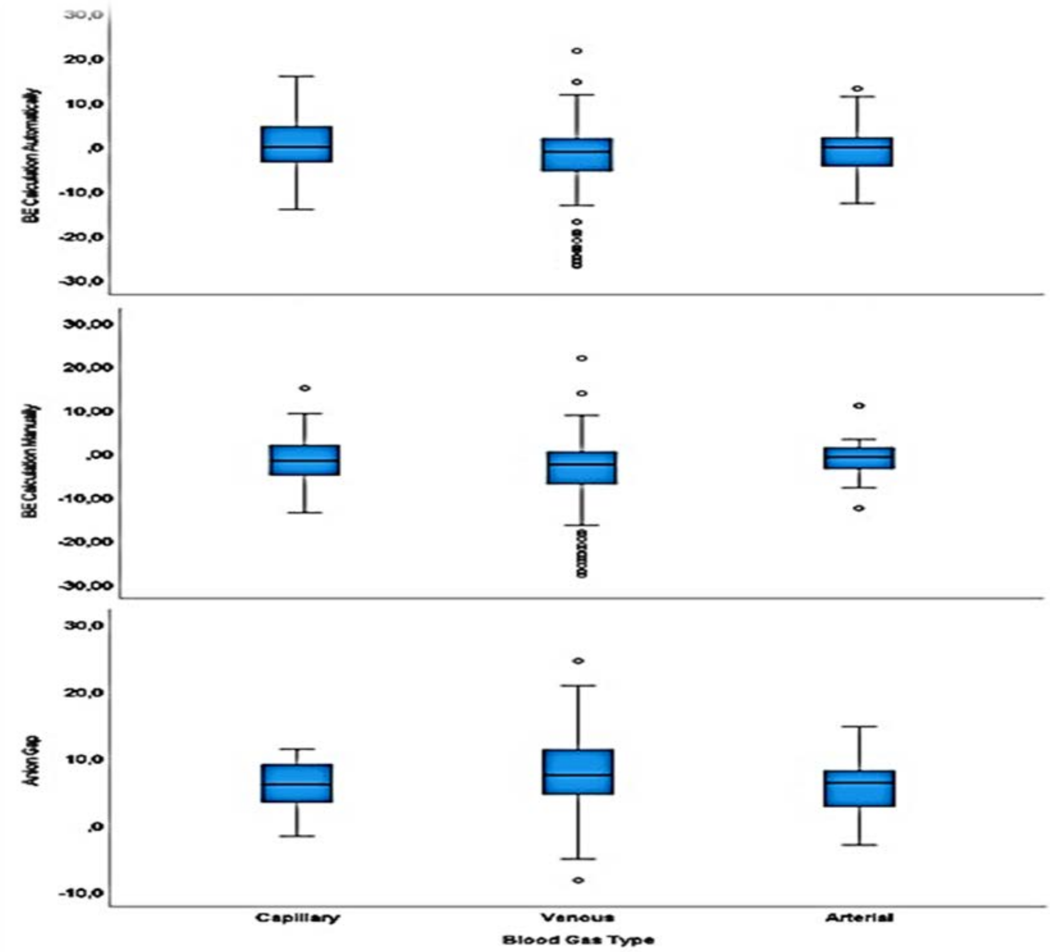

Figure 1. Comparison of BE automatically, manually and anion gap measurements between blood gas groups

The sample taken in standard blood gas analysis is arterial. However, due to the risk of arterial spasm, thrombosis, and bleeding in children, less invasive venous or capillary blood gas samples are also analyzed (7). Many studies are comparing arterial or venous blood samples. According to a study in India, there was a correlation between pH while their CO_2 concentrations were less correlative (14). With mechanical ventilation support for acute respiratory failure patients in treating from Taiwan study showed that venous samples analysis could accurately correlate values of pH, PCO_2, and HCO_3 from arterial (15). In a study conducted in Australia study with the same objective, a correlation was identified between the pH of venous and arterial blood samples at a rate of 90% (16). Similarly, in the study conducted in Turkey study demonstrated that there was a high correlation between pH, PCO_2

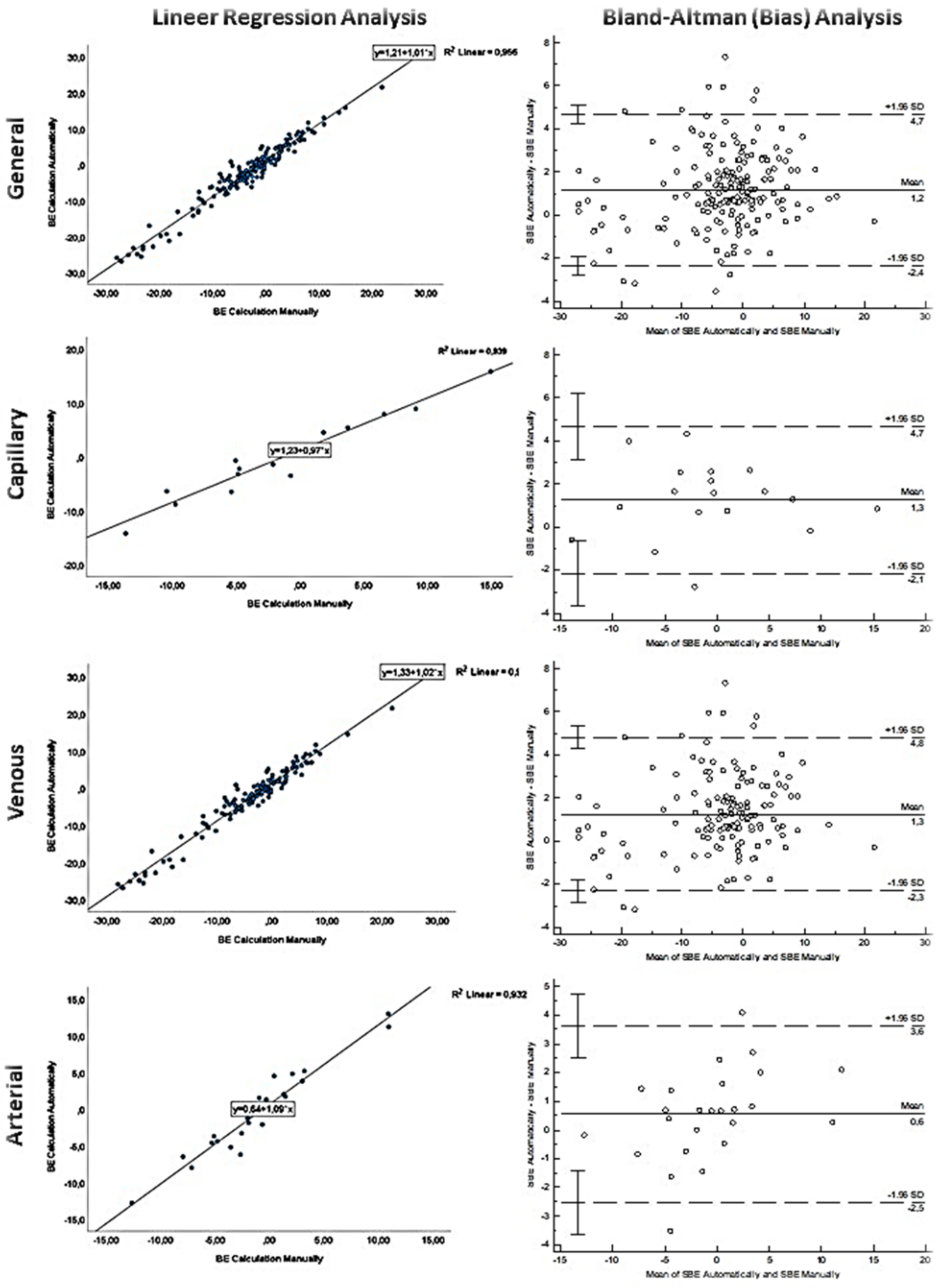

Figure 2. Correlation, regression and Bland-Altman (bias) analysis results for automatic and manual calculation of BE in general and blood gas types

and HCO_3 in both arterial and venous blood samples, including in patients with a variety of different diseases (17). On the contrary to all these studies, in Iran, acute exacerbation of chronic obstructive pulmonary disease adult patients study showed a relative correlation between arterial and venous analysis values of pH and pCO_2. Therefore, they suggested be use of arterial blood gase analysis still though sampling difficulties (18). Additionally, another study about the tricyclic antidepressants poisoning in Iran patients reported that venous pH was the only value that correlated value with arterial samples (19). In our study, we detected no statistically significant difference in the blood gas sample was artery, vein, or capillary for SBE (both automatically and manually calculation) and AG results. On the contrary, if the blood gas taken was capillary or venous, a significant difference was detected between the SBE automatically and manually calculation, but this difference was not found in arterial samples. This may be evidence that taking arterial samples in critically ill patients with high SBE values would be more beneficial in terms of clinical analysis and management, especially in pediatric patients. Although our study did not find a significant difference in SBE according to the method of the three types of blood gas sampling, when comparing manual and automated sampling, the most compatible result is arterial, followed by capillary and then venous sampling (according to lineer regression and Bland-Altman (bias) analysis). This supports the use of capillary samples in patients where arterial sampling is difficult and risky, such as neonates and infants.

This study has limitations as it is single-center and retrospective, but since the dataset covers critically ill patients of the same age group under the care of the same PICU team, we believe that it is a reliable source of information that will contribute to the existing literature on the subject. Multicenter studies covering a larger population and including specific patient groups on blood gas analysis and calculations are needed.

In conclusion, the automatic measurements of the blood gas analyser are reliable, as evidenced by the correlation between automatically and manually values with parameters such as pH, AG and SBE, which are inherent to the blood gas samples obtained from pediatric patients under optimal conditions. Nevertheless, in cases where there is an elevated risk of base deficit in critically ill patients, it is advisable to obtain an arterial blood gas sample.

Ethical Approval: *Prior to the commencement of the study, approval was granted by the Aydin Adnan Menderes University Faculty of Medicine Ethics Committee (decision dated 23/10/2023; protocol ID: 2023/182) in accordance with the ethical standards set out in the committee's guidelines*

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