

EVALUATION OF ELECTROLYTE ESTIMATION IN WHOLE BLOOD VERSUS SERUM – A COMPARATIVE STUDY

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Abstract

Background: Obtaining and interpreting blood gases and electrolytes is fundamental to the management of many critically ill patients. In such conditions, the speed and accuracy of tests, particularly ABG and electrolytes, to detect and monitor metabolic derangements is very important. Even though most ABG equipment can measure electrolyte concentrations, 2 separate samples –one whole blood and the other –serum are drawn and sent for analysis. Also there is a lack of consensus on the interchangeability of the values of electrolytes obtained from the two machines, which prevents the use of just one sample for the estimation of both these analytes. This study is being undertaken to assess the concordance between whole blood electrolytes measured by a point-of-care device and serum electrolytes measured in an auto-analyzer. **Materials and Methods:** This is a cross-sectional, data of samples from patients hospitalized, in a tertiary care between January 2017 to March 2018. Patients of all age groups tested for electrolytes i.e. Sodium, Potassium and Chloride were both by the ABL800 FLEX from RADIOMETER COPENHAGEN (Direct ISE technology) and Dimension Clinical Chemistry System from SIEMENS (Indirect ISE technology). **Results & Conclusion:** There were a total of 255 samples were used for the study in whom electrolytes was done by both ABG analyser and Chemistry Analyser. The values of sodium potassium and chloride done on ABG analyser and the Chemistry analyser the p value was statistically significant it was found to have a strong positive correlation ($r = 0.8325$ for K^+ ; $r = 0.8763$ for Na^+ ; and $r = 0.8695$ for Cl^-). Furthermore, the Bland Altman plot showed that the values were lying between the 95% CI of the mean difference which shows there is a good agreement between the two instruments.

Keywords: ABG, Chloride, Electrolytes, POCT, Potassium, Sodium.

Introduction

Maintenance of water homeostasis is paramount to life for all organisms. In humans, the maintenance of water homeostasis in various body fluid compartments is primarily a function of the four major electrolytes, Na^+ , K^+ , Cl^- , and HCO_3^-

Electrolytes are charged elements that are important for various functioning of the body. They play an important role in physiological, biochemical, and metabolic functions such as

cell membrane potential generation, neurohormonal pathways coordination, energy generation, and acid–base balance in the body.²

Almost all metabolic processes are directly coordinated by the electrolytes.

The most imperative aspect of patients in emergency and critical care settings is their dynamic physiological status with rapid deterioration that may require early diagnosis and clinical decisions to be made for better patient outcome.

This requires prompt lab results, most of which are done serially, ideally a point of care test (POCT), to meet the urgency of clinical decision and avoid subsequent damage to vital organs and systems.^{3,4} POCT improves patient's outcome through real-time treatment of the physiological deterioration.³

Electrolyte values are measured both by arterial–blood gas (ABG) analysers and Chemistry analysers. In Intensive Care Unit (ICU) setups, intensivist mainly uses the point-of-care measurement of electrolytes by ABG analyser to combat the time gap and prompt treatment. Typically, a turnaround time of about 2 h for obtaining the laboratory report is noted on average in acute care laboratories of most tertiary care hospitals in the developing countries.

The technology for detecting the electrolyte assay both ABG analyser and the chemistry analyser is ion-sensing electrode method.

The indirect assay is preanalytical dilution of the sample, sending them to laboratory, and sensing the electrode by flame photometry (the recognized reference method), subsequently finding out the result.⁵

In the point-of-care technology, the electrode surface meets a complete undiluted blood sample and senses the movement of the electrolytes by the ISE technology. Sodium and potassium levels measured in the whole blood and plasma have been shown to be essentially identical.⁵ Hence, we assume that the blood and the plasma used for electrolyte measurement in ABG and chemistry analyser, respectively, should be equal.⁶

Despite the advantage of a rapid turnaround time with point-of-care testing(POCT), that may translate to prompt decision making, concerns have been raised regarding the accuracy and reliability.^{1,2} Whilst some studies concluded that results differed significantly for plasma sodium and chloride concentrations, others also found significant differences in potassium values. There is no consensus on inter exchangeability of results of these analyzers as studies using different devices have shown different results. It is, therefore, important to determine the concordance of electrolyte values obtained by ABG and serum sample for each hospital as analyser type and calibration methods may differ among different laboratories.²

This study was thus undertaken to assess the correlation between whole blood electrolytes measured by a point-of-care device (ABG analyser) and serum electrolytes measured at a chemistry analyser, of patients in whom samples were collected simultaneously for both the tests. Whole blood electrolyte estimation in ABG analyser and serum electrolyte estimation at the chemistry analyser were chosen as the comparators since these reflect practice in most hospitals (whole blood is used at ABG analyser and serum sample at the chemistry analyser).

Materials And Methods

The source of data was, samples from patients hospitalized, in a tertiary care between January 2017 to March 2018, as per the inclusion and exclusion criteria. The study was approved by the Ethics Committee.

A total of 255 Patient samples of all age group in whom test for electrolytes i.e. Sodium, Potassium and Chloride was done both by the ABL800 FLEX from RADIOMETER COPENHAGEN (Arterial blood gas analyser) and Dimension Clinical Chemistry System from SIEMENS (Chemistry analyser)

The Data from Arterial blood samples collected in heparinized blood–gas syringes with aseptic precautions and analyzed using arterial blood–gas analyzer which employs direct ISE technology. And data from the sample taken simultaneously by venipuncture with aseptic precautions in pneumatically sealed vacuum tubes were analyzed via Integrated Multisensor Technology (IMT) on chemistry analyser.

Inclusion criteria: Data of patients samples from January 2017 to March 2018 in whom blood gas analysis was requested (electrolyte estimation is a part of the ABG analysis) and simultaneously a serum sample sent for an independent analysis as apart of treatment protocol.

Exclusion criteria: Unlabeled, wrongly labeled, contaminated specimens; sample containing air bubbles Serum, plasma exceeding HIL interference limits.

Specific performance characteristics:

a. Assay Range/ Analytical Measurement Range:

- Serum Na⁺: 50-200 mEq/L
- Serum K⁺: 1-10 mEq/L
- Serum Cl⁻: 50-200 mEq/L

b. Analytical Sensitivity:

- Serum Na⁺: < 50 mEq/L
- Serum K⁺: < 1 mEq/L

Serum Cl⁻: <50 mEq/L

c) Interfering substances / analytical specificity: Hemoglobin up to 500 mg/dL, Bilirubin up to 40 mg/dL and Triglycerides up to 2000 mg/dL do not cause significant interference.

Reference Range

Serum Na⁺: 136 – 145 mEq/L

Serum K⁺: 3.5 – 5.1 mEq/L

Serum Cl⁻: 98-107 mEq/L

Study design

This is a cross- sectional study, wherein data of samples from patients hospitalized, in tertiary care between January 2017 to March 2018, as per the inclusion and exclusion criteria was taken.

A comparative study was carried out between the ABG analyser (Direct ISE) and the Chemistry analyser (Indirect ISE) with respect to the electrolytes.

Statistical software: The Statistical software namely SPSS 16.0 was used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Statistical methods: Comparative statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD. Significance is assessed at 5 % level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two analysers. Pearson’s correlation is used to find the correlation between the two analysers. A bland Altman plot was plotted between the mean on the X-axis and difference on the Y-axis of the two analysers

Results

There were a total of 255 samples for which electrolytes was done by both ABG analyser and Chemistry analyser

The mean value of serum sodium by chemistry analyser is 136.84 ± 5.7 and in ABG analyser is 134.678 ± 6.56 . The mean value of serum potassium by Chemistry analyser is 4.18 ± 0.7 and in ABG analyser is 3.89 ± 0.66 . The mean value of serum chloride by chemistry analyser is 102 ± 5.7 and in ABG analyser is 107.756 ± 6.4 .

Table -1 shows the Mean and standard deviation of serum electrolytes by the two instruments.

Independent student T test was used to analyse the dataset for electrolytes between the ABG and chemistry analysers. The p value obtained using independent student T test is <0.001 , which being lesser than 0.05 is statistically significant

Table 1: Mean and standard deviation of serum electrolytes by the two instruments

Electrolytes	Chemistry analyser	ABG analyser	Significance P value
Sodium	136.84 ± 5.7	134.678 ± 6.56	$<.000042$
Potassium	4.18 ± 0.7	3.89 ± 0.66	$<.00001$
Chloride	102 ± 5.7	107.756 ± 6.4	$<.00001$

Figures- 1 shows the graphical representation of difference in serum electrolytes between the chemistry analyser and the ABG analyser.

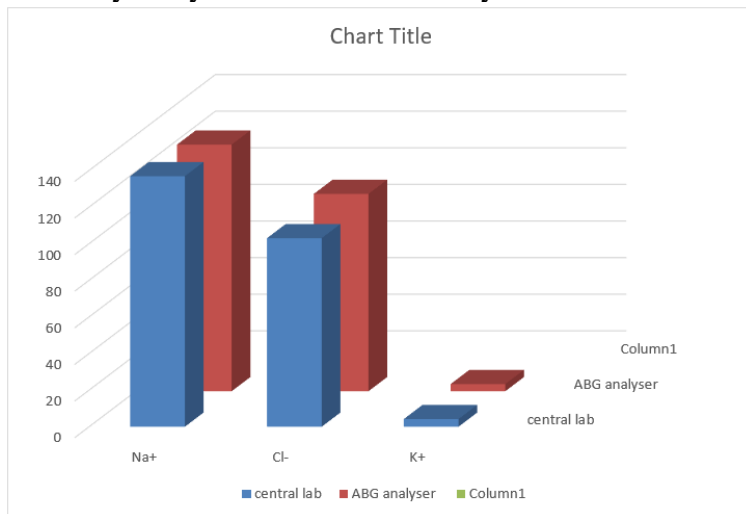


Figure 1: This is a clustered column showing the difference values of the electrolytes Sodium Potassium and Chloride done in the Chemistry analyser and the ABG analyser

Correlation of whole blood ABG analyser Vs Chemistry analyser in sodium estimation

The Pearson's correlation (ρ) between serum Sodium done in Chemistry analyser and whole blood done in ABG analyser is 0.8325 0.8763 0.8695 is found to have a positive correlation, which is shown using a scatter plot in figure 3. The p value for comparison of the variables serum Sodium done in central laboratory analyser and whole blood done in ABG analyser was $<.000042$, which being lesser than 0.05 is statistically significant.

Table 2: Correlation of whole blood ABG analyzer Vs Chemistry analyser in sodium estimation

Electrolytes	Pearson correlation (r value)	Significance (P value)
Sodium	0.8325	<.000042

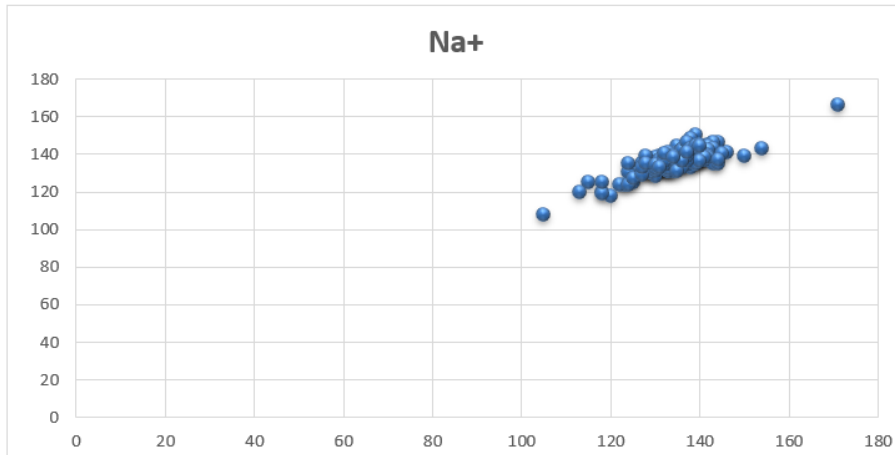


Figure 2: Scatter plot showing pearsons correlation for sodium

Correlation of whole blood ABG analyzer Vs Chemistry analyser in Potassium estimation

The pearson’s correlation (ρ) between serum Potassium done in chemistry analyser and whole blood done in ABG analyser is 0.8763 0.8695 is found to have a positive correlation, which is shown using a scatter plot in figure 4. The p value for comparison of the variables serum Sodium done in central laboratory analyser and whole blood done in ABG analyser was <.00001, which being lesser than 0.05 is statistically significant.

Table 3: Correlation of whole blood ABG analyzer Vs Chemistry analyser in Potassium estimation

Electrolytes	Pearson correlation (r value)	Significance (P value)
Potassium	0.8763	<.00001

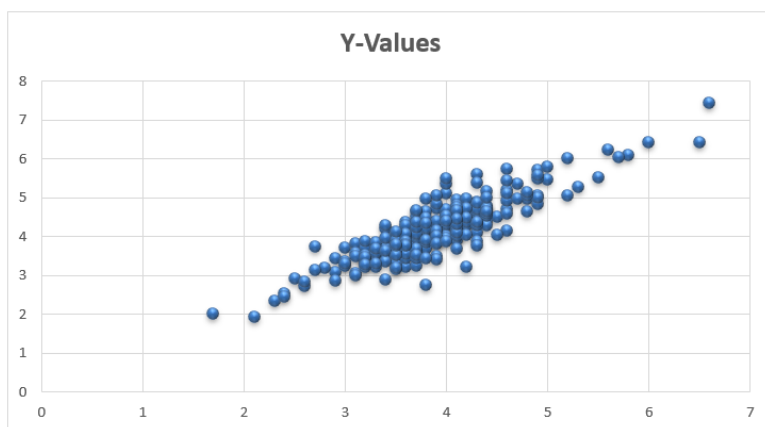


Figure 3: Scatter plot showing pearsons correlation for sodium

Correlation of whole blood ABG analyzer Vs Chemistry analyser in Chloride estimation

The pearson’s correlation (ρ) between serum Chloride done in Chemistry analyser and whole blood done in ABG analyser is 0.8695 is found to have a positive correlation, which is shown

using a scatter plot in figure 5. The p value for comparison of the variables serum Sodium done in Chemistry analyser and whole blood done in ABG analyser was $<.00001$, which being lesser than 0.05 is statistically significant.

Table 4: Correlation of whole blood ABG analyzer Vs Chemistry analyser in Chloride estimation

Electrolytes	Pearson correlation (r value)	Significance (P value)
Chloride	0.8695	$<.0000$

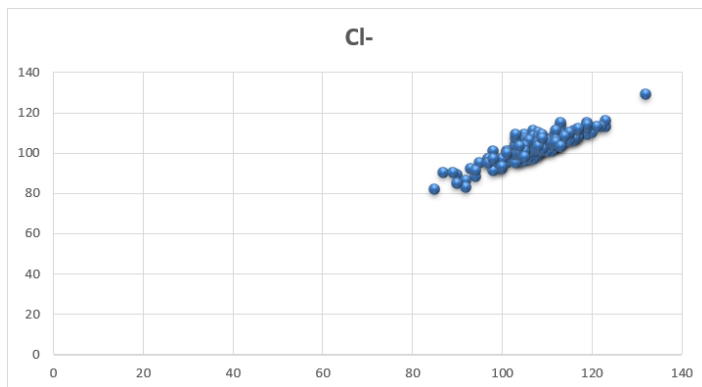


Figure 4: Scatter plot showing Pearson's correlation for chloride

A Bland Altman plot was constructed to show the limits of agreement between the two analysers. The mean difference (d) and standard deviation (s) of difference of most values lie between $d \pm 1.96*s$ (-0.455- 1.0268). It was seen that 95% of the data points was lying within the 2SD of mean difference. Bias for potassium was found to be 0.285.

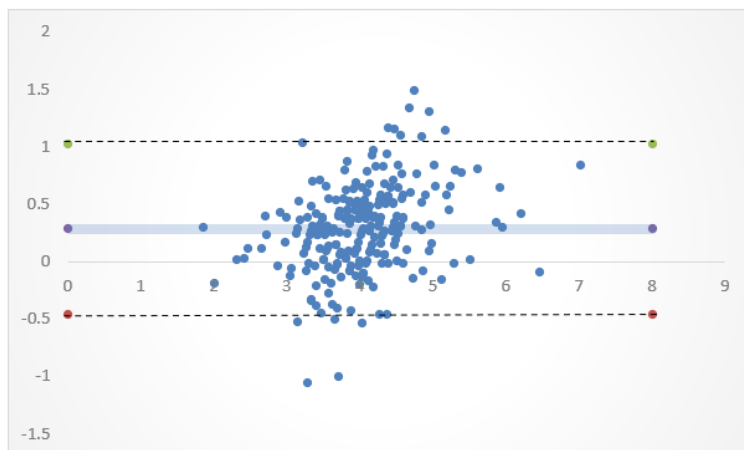


Figure 5: Bland Altman plot for potassium. the dotted line represents the $\pm 2s$ and the faint blue line represents the Bias

A bland altman plot was constructed to show the limits of agreement between the two analysers. The mean difference (d) and standard deviation (s) of difference of most values lie between $d \pm 1.96*s$ (-5.023 - 9.234). It was seen that 95% of the data points was lying within the 2SD of mean difference. Bias for Sodium was found to be 2.105.

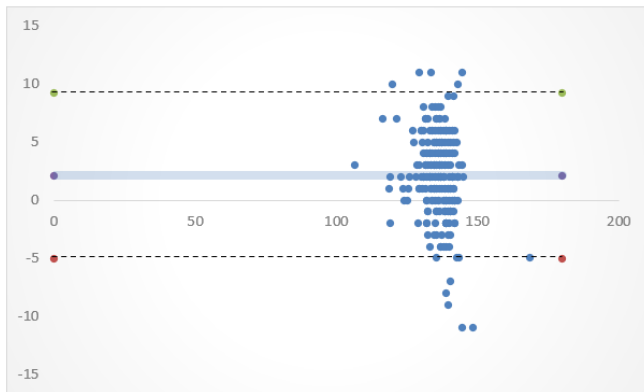


Figure 6: Bland Altman plot for Sodium. The dotted line represents the $\pm 2s$ and the faint blue line represents the Bias

A bland altman plot was constructed to show the limits of agreement between the two analysers. The mean difference (d) and standard deviation (s) of difference of most values lie between $d \pm 1.96*s$ (-11.130- 1.240). It was seen that 95% of the data points was lying within the 2SD of mean difference. Bias for chloride was found to be -4.945.

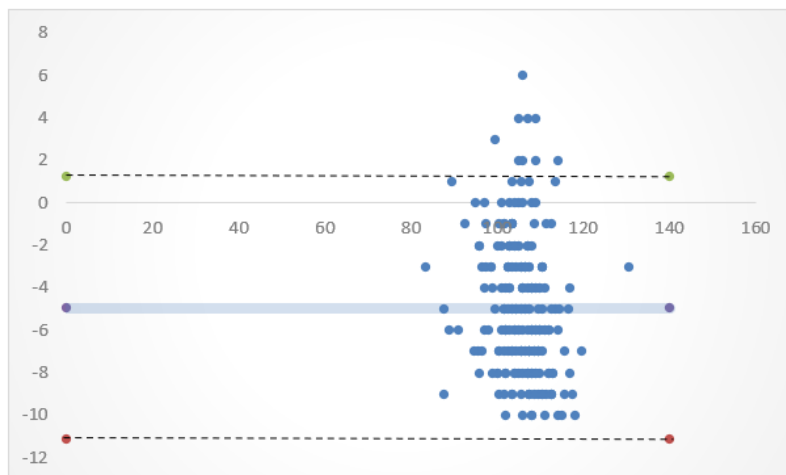


Figure 7: Bland Altman plot for Chloride. The dotted line represents the $\pm 2s$ and the faint blue line represents the Bias

In conclusion, the results obtained after statistical analysis was as follows-

The p value obtained using independent student T test is <0.001 , which being lesser than 0.05 is statistically significant. even though there was a statistical difference the pearsons correlation observed between the ABG analyser and the central laboratory analyser values was strongly positive, but this does not conclude that they agree with each other.

Therefore a Bland Altman plot was constructed and it was found that most of the values were within the 95% CI of mean difference.

Discussion

The critically ill patients require more frequent monitoring of metabolic parameter. Hence, TAT plays a crucial role for emergency and ICU services. However, a greater number of hospitals still do not have such high-end facilities. Point-of-care approach of monitoring is done to have rapid bedside result that can help in quick decision and making prompt treatment.¹ The labor costs, reagent cost, and analysis cost are also reduced when compared with the Chemistry analyzing costs.⁷

In the present study we tried to find out if the two analysers namely ABG analyser and the Chemistry analyser could give us similar values when the electrolytes Na⁺ K⁺ and Cl⁻ were measured. and if similar results were obtained an ABG analyser could be used in place of a chemistry analyser, thereby saving a lot of time.

From the results obtained in this study it was found that the p value was statistically significant and the Pearsons correlation between the ABG analyser and the Chemistry analyser ($r = 0.8325$ for K⁺; $r = 0.8763$ for Na⁺; and $r = 0.8695$ for Cl⁻) was strongly positive. A Bland Altman plot was constructed it showed that most of the values lie between the 95% CI of the mean difference values, which shows that there is a good agreement between the two methods. Hence theoretically POCT can be a reliable choice for estimation of electrolytes as it uses the Direct ISE method, and the TAT is far less compared to the Chemistry analyser. But this cannot be conclusive until clinical correlation studies are done.

Similar results were obtained in studies conducted by Yasemin Ustundag-Budak et.al; were in they found that the sigma levels were better on the ABG analyser compared to the automated analyser of the central lab. Furthermore, the study states that the sigma values obtained from all analysers suggest that running more controls and increasing the calibration frequency for electrolytes is necessary for quality assurance.

Currently, electrolyte measurements are done on more than one analyser, but this can increase the variability.^{5,8,9} During instrument selection, it is critical to select methods with acceptable sigma metrics level versus standard reference methods.

There have been trials conducted for head-to-head comparison between ABG analyser and Chemistry analysers for analytic performance with analytes (blood gas parameters, electrolytes, and lactate) and practicability (ease of operation and user interface, quality control, and maintenance, etc.) Beneteau-Burnat and Pernet *et al.*,¹⁰ showed that GEM Premier 4000 device had CV lower than the imprecision goals and high coefficient of correlation ($r = 0.92$) when compared to central laboratory equipments-ABL 725 (Radiometer) and OMNI S (Roche Diagnostics, Basel, Switzerland). Also, the instrument was accepted with ease by both technical and non-technical staff. Indeed, training of non-technical staff required only 30 minutes of formal training.

It is known that patients in ICUs are critically ill and tend to have low blood protein levels. The ABG results are not affected by serum protein levels, which make the ABG electrolyte results more accurate for critically ill patients.⁵ Moreover, patients can have pseudohyponatremia if protein or cholesterol level is on the rise in ICU patients. Considering using ABG only for evaluating electrolytes can have a high operational cost, but when we consider in total, the amount of information, we get from an ABG, in a critically ill patient such as the oxygen requirement, lactate level, and acidosis per se, the use of ABG machines at critical areas of hospitals such as emergency department, operation theaters, and ICUs are well justified. Furthermore, the direct cost of the machine to the hospital has been on decreasing trend as the supply of such analyzers increases with time.¹¹

In the study conducted by Morimatsu *et al.*, it was revealed that results with Chemistry analyser and ABG analyser differed significantly for the plasma sodium and chloride levels. The mean plasma sodium concentration was 140.4 ± 5.6 mmol/L with central laboratory testing versus 138.3 ± 5.9 mmol/L with point-of-care testing ($P \leq 0.0001$). The mean plasma chloride concentration was 102.4 ± 6.5 mmol/L versus 103.4 ± 6.0 mmol/L ($P \leq 0.0001$).¹²

Furthermore, Chacko *et al.* also concluded that the differences in the measured sodium levels between the two methods were significant. There was a significant difference in the mean \pm SD of sodium value between whole blood and serum samples, 135.8 ± 5.7 mmol/L versus 139.9 ± 5.4 mmol/L ($P \leq 0.001$). Although the agreement between whole blood and

serum potassium was good, and the average difference was small, still the individual differences were clinically significant, particularly at lower potassium values.¹¹

On the other hand results observed from some of the earlier studies showed a significant difference between the mean values of sodium and potassium obtained by ABG analyser and Chemistry analyser.^{2,13} This could be probably attributed to the characteristics of different devices, variations in the calibrator used in device, type of sample used (whole blood vs. serum), dilution agent used, and the effect of transportation on samples.² Chako *et al.*, compare whole blood electrolyte estimation with ABG analyser versus serum electrolyte estimation with Chemistry analyser. They observed that the difference in values were large, particularly of potassium with values below 3 mmol/L. However, the difference for potassium values >3 mmol/L and sodium values were observed to be uniform and in good concordance.¹⁴ They quantified the magnitude of difference between two aforesaid methods of estimations and suggested the "correction factor" that could be applied to the POCT values to attain accurate results.² The characteristics of electrodes used for analysis may also influence the difference between the two methods of estimations.² Most of the ABG analyser has direct ion-selective electrodes, which measure the activity of ions in plasma. In contrast, the Chemistry analyser has indirect ion-selective electrodes and measures the activity of ions in pre-diluted sample and is affected by dissolved solids such as proteins, hence influencing the values obtained by various electrodes.² Chhapola *et al.*, compared the reliability of POC sodium and potassium estimation in pediatric ICU population. They found that ABG analyser underestimates the sodium and potassium values.¹³ They infer that it may be due to the addition of liquid sodium heparin added to the sample which increases the volume of the sample and dilutes its plasma portion, resulting in lower values of measured electrolytes. Further, the high volume of heparin binds with electrolytes and underestimates the values of electrolytes.¹⁵ They advocated the formulation of standardize sampling protocol, formal training of the manpower, and formation of correction equation, before introducing POCT devices in any institute to offset the sampling errors.¹² They stressed for use of dried balanced heparin syringes instead of conventional syringes with liquid heparin, to attenuate the errors further due to dilution effects.¹² Clinicians frequently calculate anion gap (AG) and the strong ion difference (SID; quantitative measure of unmeasured anions) from electrolytes value, which assist them in outlining the acid-base status and guide them for clinical decision making. A study by Morimatsu *et al.*,¹² observed that the differences between the electrolyte values (sodium and chloride) obtained by ABG analyser and Chemistry analyser significantly affects the conventional AG and SID values with marked variations. These variations may lead to significant misinterpretations and misdiagnosis and could confound the clinical management strategies. Currently, there are limited studies to evaluate the efficacy of ABG analyser and certainly needs more prospective controlled trials for its evaluation in critically ill patients.¹⁶

Conclusion

The p values of sodium potassium and chloride done on ABG analyser and the Chemistry analyser was statistically significant and it was found to have a strong positive correlation ($r = 0.8325$ for K^+ ; $r = 0.8763$ for Na^+ ; and $r = 0.8695$ for Cl^-). Furthermore, the Bland Altman plot showed that the values were lying between the 95% CI of the mean difference which shows there is a good agreement between the two instruments. But studies should be conducted in view with the clinical correlation so that we can conclude on which instrument is better. Furthermore, the ABG analyser which uses the direct ISE method gives the results in a very short TAT and excludes the electrolyte exclusion effect, helps the Physicians to come to a conclusion and give prompt treatment. ABG analyser for maintaining the accuracy

care should be taken that proper sampling procedures are followed use of dry heparin or electrolyte balanced heparin; regular Quality Control check should be maintained. Moreover, each institution should set up their own pilot study as they use different equipment's, calibrators and QC to establish their own correction factor so that the ABG analyser and the chemistry analyser could be used interchangeably.

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