**Original Article**

# Comparison between measurement of sodium and potassium by Blood Gas Analyzer versus Laboratory based Auto-analyzer among critically ill patients in a tertiary care hospital

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**Abstract:**

***Background:*** *Electrolytes imbalances can lead to critical life threatening events so immediate and accurate assessment is needed. There is always a time delay in receiving results from the central laboratory auto analyzer (AA). To overcome this drawback, arterial blood gas (ABG) analyzer can be used as an alternative to measure electrolytes where results can be obtained within two minutes, allowing for prompt management.*

***Methods:*** *This cross-sectional study was carried out on 384 intensive care unit (ICU) patients of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic disorders (BIRDEM) General Hospital. The average values of sodium and potassium in ABG analyzer and laboratory AA were calculated and then the mean difference or bias was obtained of sodium and potassium measurements analyzed by the two methods. Bland-Altman plot and Lin's concordance correlation coefficient ($\rho_c$) was used to measure the agreement between the two methods. Test results were considered reliable, if the bias was non-significant and within the United States Clinical Laboratory Improvement Amendment (US CLIA) criteria (±4 mmol/l for sodium and ±0.5 mmol/l for potassium), 95% limits of agreement (LOA) were narrow and $\rho_c$ showed good concordance.*

***Results:*** *The mean difference or bias, 95% LOA and $\rho_c$ for sodium was -1.2 mmol/l, -11 mmol/l to 8.6 mmol/l and 0.85 respectively whereas for potassium this was 0.8 mmol/l, -0.39 to 1.98 mmol/l and 0.63 respectively. The bias for sodium was within the US CLIA criteria but not so for potassium. However, the 95% LOA was wide and there was poor concordance for both the measurement. On account of these differences, correction factor was calculated for sodium and potassium values. Serum sodium (in mmol/l) was 2.48 + 0.97 x ABG sodium (in mmol/l) and serum potassium (in mmol/l) was 1.18 + 0.89 x ABG potassium (in mmol/l).*

***Conclusion:*** *The sodium and potassium measurements obtained from the ABG analyzer was found to be unreliable. However, a correction factor to the ABG analyzer results could be applied to initiate treatment and then changing the management, if required, once laboratory AA reports become available.*

***Keywords:*** *Comparison; sodium; potassium; Blood Gas Analyzer; Laboratory Auto-analyzer.*

## Introduction

Conventionally electrolytes are measured from serum by central laboratory auto-analyzers (AA) available in a hospital. This use of laboratory AA often results in a long delay between the time at which the test is ordered and the time at which the results are obtained, thus compromising the treatment of critically ill patients.[1] An Indian study showed a turnaround time of 4.5-5 h for measuring electrolytes in ward setting and 1-1.5 h for measuring electrolytes in emergency basis.[2] The delay in service may be attributed to interruption in transport of samples to central laboratory either due to lack of sufficient human couriers or absence of quick transport systems.[3, 4]

To overcome this limitation, arterial blood gas (ABG) analyzer, particularly used in ICU, can be used to measure electrolytes in arterial blood where results can be obtained in two minutes thus reducing the turnaround time. The results from ABG analyzer, sometimes referred to as point of care testing (POCT), not only reduces the therapeutic turnaround time but also helps in quick clinical decision making, providing rapid availability of data and reducing pre-analytic and post-analytic testing errors.[5] Moreover, user-friendly instrument, small blood volume and frequent whole blood testing are other advantages of POCT or ABG analyzer.[6-8]

However, the reliability of use of ABG analyzer to measure

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electrolytes is debatable.[3] Studies showed that the result obtained from the two different measurement technologies showed reliable result for potassium values only but not for sodium values[9, 10] while other studies found unreliable results for both sodium and potassium measurements.[11-13] Some authors revealed that electrolytes measured in point of care analyzers showed acceptable accuracy.[3, 14-18]

A study demonstrates that 85% of physicians relied on results obtained from laboratory AA while only 34% trusted and 38% did not trust the bedside blood tests including that of electrolyte measurement of ABG analyzer.[19]

Hence the present study aims to investigate the comparison between intensive care unit based ABG analyzer and hospital laboratory based AA for measurement of sodium and potassium to see whether the results obtained from the two machines are interchangeable or not. If the ABG analyzer electrolyte results are reliable then prompt management could be initiated for critically ill patients.

## Methods

### Study design and procedure

This cross sectional study was carried out in the Department of Critical Care Medicine, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic disorders(BIRDEM) General Hospital aiming to compare intensive care unit (ICU) based ABG analyzer and hospital laboratory based AA for measurement of sodium and potassium. Three hundred and eighty four adult patients, from 1st February 2018 to 31st January 2019, admitted to BIRDEM ICU was consecutively selected for the purpose of the study, excluding those that denied to take part in the study. Informed written consent was taken from all patients and ethical clearance of the study was taken from the institutional review board.

Blood was drawn routinely from patients by experienced nurses in the ICU using sterile gloves. Arterial blood samples (1 ml) were collected in heparinized 1ml plastic syringes and analyzed in ABG analyzer, GEM Premier 3000 (Instrumentation Laboratory, Lexington, MA, USA), within 3 minutes of blood being taken. Simultaneously, venous blood samples (5 ml) were taken and was sent, pneumatically sealed, to the hospital laboratory. The venous blood sample for electrolyte measurement was analyzed in laboratory AA, Abbott Architect Plus c8000 (Abbott Laboratories, Abbott Park, IL, USA).

All instruments used in this study was maintained according to the manufacturer's manual. In the present study, the normal value of sodium was considered within 135 mmol/l to 145 mmol/l and that of potassium was within 3.5 mmol/l to 5.5 mmol/l. The results of sodium and potassium obtained from both analyzers were entered into a data collection form.

### Statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) software (version 23), MedCalc statistical software version 14.8.1 and Microsoft Excel 2016. The mean, standard deviation, minimum and maximum values were calculated for continuous variables. Paired t-test was used to compare parametric values. A value of $p < 0.05$ was considered statistically significant. Mean difference or bias was calculated of sodium and potassium values analyzed in ABG analyzer and laboratory AA and checked to see whether they were non-significant and in accordance to the The United States Clinical Laboratory Improvement Amendment (US CLIA) 2006 guidelines. US CLIA 2006 accepts a bias or difference of ±0.5 mmol/l for potassium measurement and ±4 mmol/l for sodium measurement, from the target values.[10, 15, 16,18] Bland-Altman plot was used to construct the limits of agreement (LOA) and to compare the sodium and potassium measurements. Narrow LOA was suggestive of good agreement between the measured values of ABG analyzer and laboratory AA.[20] Lin's concordance correlation coefficient ($\rho_c$) was calculated. A $\rho_c$ value of <0.9 indicated poor, 0.9-0.95 showed moderate, 0.95-0.99 signified substantial and >0.99 denoted almost perfect agreement between the measurements of the two methods.[21] Deming regression analysis was used to calculate the correction factor for both sodium and potassium measurements.

## Results

Table I showed the mean sodium level measured by laboratory AA was 136.61 ±9.28 mmol/l, ranging from 105 mmol/l to 175 mmol/l, and the mean sodium level measured by ABG analyzer was 137.82 ±9.51 mmol/l, ranging from 108 mmol/l to 169 mmol/l. The mean difference of sodium measured by the two different methods was -1.2 mmol/l ($p<0.05$). The mean potassium measured by laboratory AA and ABG analyzer was 4.23 ±0.98 mmol/l and 3.43 ±1.04 mmol/l respectively ($p<0.05$). The mean difference between the two measurements was 0.8 mmol/l. The laboratory AA potassium value ranged from 2.1 mmol/l to 7.6 mmol/l and that of ABG analyzer value ranged from 1.3 mmol/l to 6.4 mmol/l.

The Bland-Altman plot showed the 95% LOA of the sodium values measured by laboratory AA and ABG analyzer was -11 mmol/l to 8.6 mmol/l. Sixteen values (4.2%) were outside the LOA. The mean difference or bias was -1.2 mmol/l and 127 measurements (33.1%) were outside the US CLIA limits. (Figure 1) The lin's concordance correlation coefficient ($\rho_c$) was 0.85. The 95% confidence interval (CI) for $\rho_c$ was 0.82 to 0.88. There was poor concordance between the two measurement values. (Figure 2)

Figure 3 showed the 95% LOA of the potassium values analyzed by the methods were -0.39 to 1.98 mmol/l. Forty six (12%) of the potassium values were not within the 95% LOA. The mean bias was 0.8 mmol/l (95% CI, 0.74-0.86 mmol/l) and 263 values (68.5%) were outside the US CLIA limits. There was poor concordance between the ABG analyzer and laboratory AA potassium measurements ($\rho_c$=0.63, 95% CI 0.58 to 0.67). (Figure 4)

The Deming regression equation showed the following correction factors:

Serum sodium (in mmol/l) = 2.48 + 0.97 x ABG sodium (in mmol/l)

Serum potassium (in mmol/l) = 1.18 + 0.89 x ABG potassium (in mmol/l)

The coefficient of variation was assumed 1% for both the methods as was the standard when no second group of measurements or quality control data were available.[22]

**Table I: Distribution of sodium and potassium measurement in the study population (n=384)**

| | Minimum (mmol/l) | Maximum (mmol/l) | Mean (mmol/l) | Mean difference** (mmol/l) | Standard deviation (mmol/l) | Standard error mean (mmol/l) | p value* |
|---|---|---|---|---|---|---|---|
| Sodium measurement | | | | | | | |
| Laboratory AA | 105 | 175 | 136.61 | -1.20 | 5.01 | 0.26 | <0.0001 |
| ABG analyzer | 108 | 169 | 137.82 | | | | |
| Potassium measurement | | | | | | | |
| Laboratory AA | 2.1 | 7.6 | 4.23 | 0.8 | 0.60 | 0.03 | <0.0001 |
| ABG analyzer | 1.3 | 6.4 | 3.43 | | | | |

* p value calculated by paired t-test
**Mean difference = Laboratory AA mean – ABG analyzer mean
p value <0.05 is considered significant

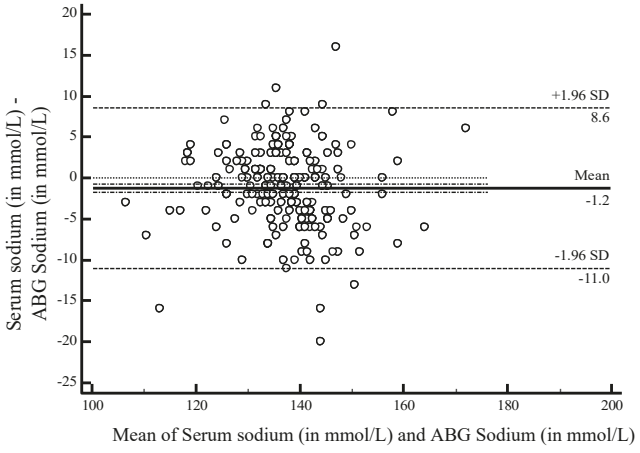


**Figure 1: Bland-Altman plot showing the agreement of sodium measurements between the two methods.** The solid blue line indicates the mean difference or bias (-1.2 mmol/l). The green dotted lines designate the 95% confidence interval of the mean bias (-1.71 to -0.70 mmol/l). The brown dotted lines signify the 95% LOA of the bias (-11 to 8.6 mmol/l). The orange dotted line shows the line of equality (difference=0).

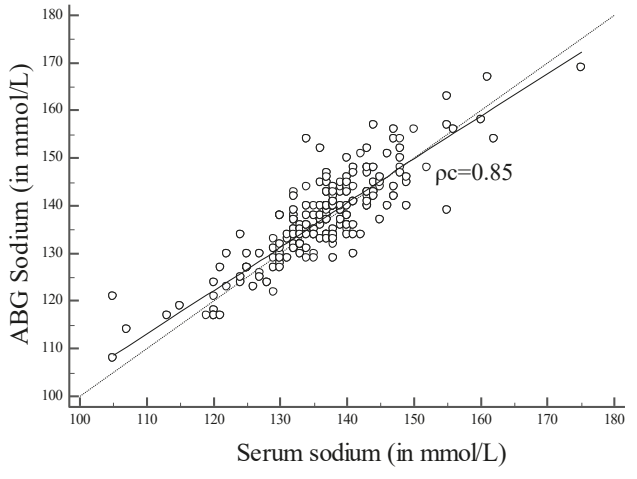


**Figure 2: Concordance plot showing the agreement of sodium measurements between the two methods.** The brown dotted line indicates the line of perfect concordance and the solid blue line show the best fitted line for the data.

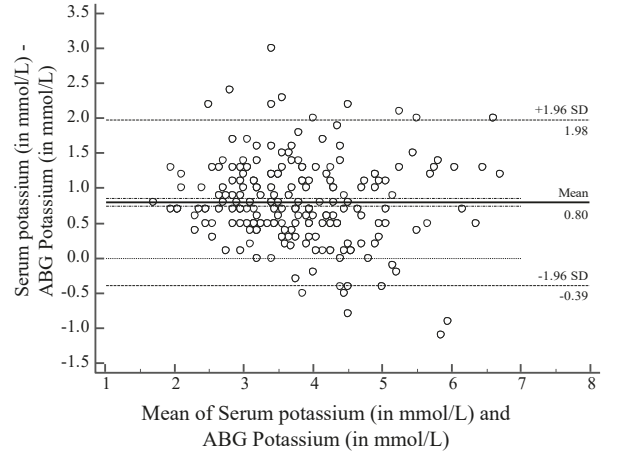


**Figure 3: Bland-Altman plot showing the agreement of potassium measurements between the two methods.** The solid blue line indicates the mean difference or bias (0.8 mmol/l). The green dotted lines designate the 95% confidence interval of the mean bias (0.74 to 0.86 mmol/l). The brown dotted lines signify the 95% LOA of the bias (-0.39 to 1.98 mmol/l). The orange dotted line shows the line of equality (difference=0).

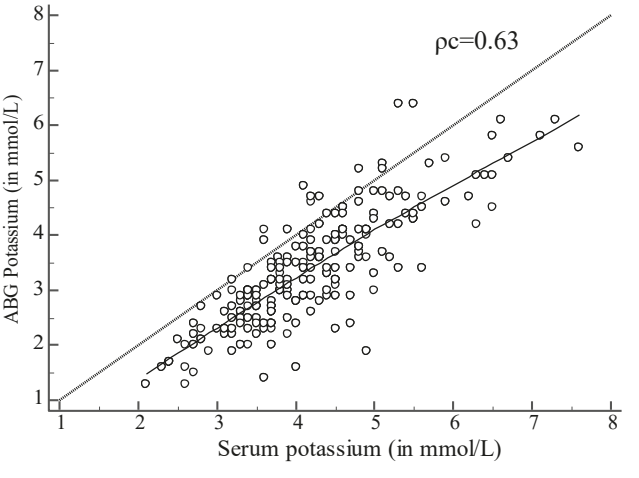


**Figure 4: Concordance plot showing the agreement of potassium measurements between the two methods.** The brown dotted line indicates the line of perfect concordance and the solid blue line show the best fitted line for the data.

## Discussion

Even though the mean difference or bias (-1.2 mmol/l) was within the US CLIA criteria of 4 mmol/l for sodium, the result was statistically significant ($p<0.05$). Bland-Altman plot showed wide 95% LOA (-11 mmol/l to 8.6 mmol/l), which cannot be accepted clinically. The Lin's concordance correlation coefficient (0.85, 95% CI 0.82-0.88) also showed poor concordance between the two methods of analysis. Therefore, it can be concluded that sodium measurement by the ABG analyzer was unreliable when compared to the laboratory AA. The same conclusion was drawn in several other studies as well.[4, 9-12, 23, 24]

Similarly, the mean difference of potassium (0.8 mmol/l) was also statistically significant and beyond the acceptable US CLIA criteria of 0.5 mmol/l for potassium. Potassium measurement between the methods showed wide range of 95% LOA (-0.39 to 1.98 mmol/l) and there was poor concordance ($\rho_c$=0.63). Thus it can be inferred that the potassium measurements by the ABG analyzer was also not reliable. There are many studies supporting this fact.[4, 11, 12, 23, 24]

On the other hand, there are other contradictory studies. There are studies that found the results of electrolytes, sodium and potassium, measured on laboratory AA and ABG analyzer were interchangeable.[3, 16, 17, 25, 26] However, these studies used mean difference or bias and correlation coefficient (r) for statistical analysis to show agreement between the data of the two analyzers. Care must be taken while interpreting mean difference between the ranges of results of two tests as the test may under or overestimate values over extremes of range.[20] Another thing of note is that correlation coefficient has no practical use when comparing data from two tests.[27, 28] Most commonly used is the Pearson's correlation coefficient, where a value of +1 indicates perfect positive linear relationship, a value of -1 indicates a perfect negative linear relationship and 0 values indicates no relationship between variables.[29] So it would seem Pearson's correlation coefficient would be a good method to use. However, it would be highly unlikely when two methods measuring the same variable does not show significant correlation. The Pearson's correlation coefficient is sensitive to the range of values studied (the wider the range, the higher the correlation coefficient) and does not take into account systematic difference.[20] There would be no difference in correlation coefficient, even if all the variables in a study are added by 5. Pearson's correlation coefficient is better used to see associations between variables rather than agreement.[28] A better method to see agreement between variables is the Bland-Altman plot.[20, 30, 31] From this plot it is much easier to see systematic difference, scatter of values from the mean, random errors and relationship between values and measured errors. Furthermore, small LOA, derived from the plot, is indicative of interchangeability of results between two methods.[20] Bland-Altman plot was used to show agreement between variables in several studies.[4, 9, 11, 12, 15, 18] Alternative method that can be used is Lin's concordance correlation coefficient, which is a modified version of Pearson's correlation test. While Pearson's correlation only measures the scatter of data from the best fit line (degree of precision), the Lin's concordance correlation measures both the precision and how far the best fit line is from a 45$^o$ line drawn through the origin (degree of accuracy), which is considered to be the line of perfect agreement.[31]

In contrast to the previous studies, Allerdat-Servant et al. using good statistical analysis, concluded that the results of sodium and potassium were interchangeable with that of laboratory AA.[18] The difference of result of this study compared to the current study may be attributed to the use of different ABG analyzer machines.

There are several theories regarding the difference in sodium and potassium measurements in laboratory AA and ABG analyzer. The different samples, serum for laboratory AA and whole blood for ABG analyzer, used can result in the dissimilar results of the two methods. ABG analyzer uses direct ion sensing electrodes and laboratory AA uses indirect ion sensing electrodes for analysis. These two different techniques may also be a contributing factor.[4, 11] The use of different calibrators can also be responsible for variable results.[4, 16] One reason could be due to the fact that heparin flushed syringes were used to draw arterial blood for ABG analyzer. This dilutes the blood, underestimating the sodium and potassium results.[4, 10] The heparin in the syringe can also react with the electrolytes in the sample, producing erroneous outcomes.[12] However, this was tried to be minimized by using experienced nurses to draw the blood and ensuring all the heparin was flushed out of the syringe before drawing blood. Delay in transport of the venous blood for laboratory AA can be a major factor to incorrect results.[4, 11] The delay causes the blood to clot, releasing potassium from platelets.[32] The current study found positive mean difference (+0.8 mmol/l) for potassium values between the two methods which indicate that potassium levels were higher in laboratory AA measurement than in ABG analyzer measurement. The laboratory AA results are sensitive to protein levels in blood.[33] Since the present study was performed in an ICU setting, all of the patients were critically ill so about 70% of the patients had hypoalbuminaemia, which may result in altered values provided by the laboratory AA.

Considering the differences in values of ABG analyzer and laboratory AA, Deming regression (DR) analysis was used to establish a correction factor. DR was chosen over ordinary linear regression (OLR) as it takes into account the measurement error of both methods in the x and y axis while OLR ignores the measurement error of x-axis and considers the error in y-axis only, resulting in a downward slope.[34] Other studies had also used the DR equation.[12, 15, 18] Chacko et al. advocated the use of correction factor in clinical practice while Budak et al. was hesitant on its use as there are subtle biological variations that are not taken into account during statistical analysis and hence can provide a wrong result.[4, 12] However, the objective of a correction factor is not to provide an accurate result but rather to provide a result that minimizes the difference of values between the two methods. It may sometimes be more and sometimes be less than the actual value.[35] Keeping that concept in mind, this study recommends the use of correction factor on the ABG analyzer sodium and

potassium measurements by the clinician during initial analysis to start treatment and then change the management as required when the laboratory AA reports are available. A similar proposal was also given by Zhang et al. as well.[15] The correction factor calculated in the present study is specific for this hospital and consequently if correction factors are to be used then each institution must generate their own.[4]

Therefore, it can be concluded that the sodium and potassium results measured by the two analyzers are not interchangeable. However, a correction factor can be used to adjust the ABG analyzer electrolyte result to use for clinical purpose.

There are some limitations to the study. The study was carried out in critically ill patients, who may have low protein. Whether the result will be same in normal patient remains to be seen. However, this ICU has patients with a wide range of diagnosis so this study finding maybe similar when compared to other medical ICU. Only one ABG analyzer machine and one laboratory AA machine were used to carry out the analysis. Dry heparin syringe instead of heparin washed out syringe probably would have provided a better result.

## Conclusion

The sodium and potassium measurements obtained from ABG analyzer are not similar to that of laboratory AA. Hence, the ABG analyzer results are unreliable to be used directly for clinical practice. However, a correction factor can be applied to the ABG analyzer measurements for starting treatment immediately and then changing the management, if required, once laboratory AA results are available.

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