

## THE ENIGMA OF USING SERUM ELECTROLYTES AND ARTERIAL BLOOD GAS ELECTROLYTES INTERCHANGEABALY

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### ABSTRACT:

**BACKGROUND and AIM:** The determination of the electrolytes sodium and potassium are quite essential in critical care. Electrolyte values are measured both by arterial blood gas (ABG) analysers and central laboratory auto-analysers (AA), however a significant time gap exists between the availability of both these results, with the ABG giving faster results than the AA. In this study we compare the measurement of electrolytes by these two methodologies and analyse the reliability of using the results interchangeably.

The aim of the present study was to investigate whether electrolyte levels assessed using an ABG and an AA were equivalent and whether the results can be used interchangeably.

**METHODS:** A retrospective observational study was conducted in Intensive Care Unit (ICU) of tertiary care hospital of Kashmir ,India . 223 arterial samples were studied and were analysed for electrolytes on the ABG machine and the AutoAnalyser machine .

**RESULTS:** Mean sodium difference was found to be  $3.525 \pm 2.84$  mmol/L which is acceptable as per United States Clinical Laboratory Improvement Amendments (CLIA) Mean difference in potassium was found to be  $0.292 \pm 0.240$  mmol/L acceptable as per CLIA. Both electrolytes (sodium and potassium) showed positive correlation between two methods of measurement. ( $R^2: 0.758, 0.882$  respectively)

**CONCLUSION:** Na<sup>+</sup> and K<sup>+</sup> test results obtained using an ABG analyser and an automated analyser differ, however, the observed difference is within acceptable range and therefore , the results can be used interchangeably in emergency situations .

**KEYWORDS:** Electrolytes, sodium, potassium

## **INTRODUCTION:**

Fluid and electrolyte disorders are usually encountered in most of the clinical scenarios and if not treated appropriately can have fatal consequences. Various critical disorders such as severe burns, sepsis, trauma, sepsis and heart failure lead to electrolyte disturbances. More caution needs to be exercised in critically ill patients as its often difficult to adequately asses symptoms and signs of electrolyte imbalances in them [1].

Two types of devices are used in hospital for electrolyte measurements. One is blood gas analyser(BGA) ,that uses direct ISE (ion selective electrode) and second is central laboratory autoanalyser(AA) that uses indirect ISE technology. BGA measures electrolytes in undiluted sample types. The principle of the method is based on the determination of the electromotive power (potential) changes occurring between the measuring electrode and the reference electrode, whereas the ion to be measured interacts with the ISE membrane [2]. Before measuring electrolyte concentrations with the indirect ISE method, the same diluent volume is used by estimating the amount of dilution by the expected solid fraction (7%). However, if the solid fraction is increased, as, during hyperproteinemia, the measured ion concentration is underestimated because of the higher dilution [2] .

However, current data regarding the comparability and validity between the two processes are ambiguous. Some recent studies revealed considerable differences between the( Arterial Blood Gas) ABG and AA measurements[3, 4] .S Rajavi et al., observed higher levels of sodium and potassium in serum when compared to sodium and potassium in arterial blood [5]. Flegar Mestic Z et al., observed that electrolytes measured in whole blood by point of care analyzer were comparable to electrolytes measured in plasma or venous serum samples [6]. Anunya Jain et al., observed that there was no significant difference between potassium measured in ABG analyzer and potassium measured by

routine chemistry auto analyzer but they observed significant difference between sodium measured by ABG analyzer and sodium measured by chemistry auto analyzer [7].

Despite ABG results being readily available bedside and help in making critical decisions in intensive care unit , many still rely on electrolytes as measured using auto analyser which usually takes lot of time. With the observation of differences between the two results (BGA versus AA), even if samples are taken at the same time, physicians are often faced with the question of which test result to use in patient treatment, especially when therapy is to be initiated or frequent measurements are made to guide treatment. We aimed to find whether the electrolyte test results using  $\text{Na}^+$  and  $\text{K}^+$  test results obtained with BGA and AA could be used interchangeably.

#### **MATERIALS AND METHODS:**

Paired blood samples from 223 adult patients admitted to the surgical ICU of a tertiary health care hospital were included in the study. The study was a retrospective analysis of medical records of patients from November 2021 to January 2022.Blood samples were collected simultaneously for electrolyte analysis using ABG machine and AA machine. As per the ICU protocol it was ensured that the blood samples were collected by trained staff of a single ICU unit in the hospital and analyzed in the two analyzers located in the central laboratory under similar environmental conditions. Analysis was done on the GEM Primum blood gas analyser and the Siemen Dimension RxL Auto analyser, both located in the central laboratory, unlike in the previous studies where the analysers were in different environments. Ethics approval and consent to participate:Our study was a retrospective analysis of medical records with the study posing lowest risk to the research subject . The blood samples studied were drawn routinely every morning as a part of ICU protocol and no additonal blood samples were taken out for the study. Statistical Analysis: The data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 28.0 (SPSS Inc., Chicago, Illinois, USA). Kolmogorov or Shapiro-Wilk test was applied for the normality test. Continuous variables were expressed as Mean  $\pm$  Standard deviation and categorical variables were summarized as frequencies and percentages. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever is appropriate, was applied to compare categorical variables. The P-value of less than 0.05 was considered statistically significant.

**RESULTS:**

Mean sodium as measured from ABG analyser was  $140.96 \pm 8.64$  mmol/L while as mean sodium as measured from Auto analyser was  $142.23 \pm 8.28$  mmol/L . (p value 0.114). The maximum difference was found to be 16 where as minimum difference was zero between the two groups. Mean sodium difference was found to be  $3.525 \pm 2.84$  mmol/L.[Table 1].

TABLE 1: serum sodium levels as determined by ABG analyser and Auto analyser

SODIUM LEVELS	GROUP	N	Mean (mmol/L)	Std. Deviation (mmol/L)	Mean difference (mmol/L)	95% Confidence interval (CI) (mmol/L)	P VALUE
	ABG ANALYZER	223	140.96	8.647	$3.525 \pm 2.84$	139.83- 142.10	0.114
	AUTO ANALYZER	223	142.24	8.280		141.12- 143.37	

As per Clinical Laboratories Improvement Amendment (CLIA) guidelines , acceptable limit for sodium variation is 4 mmol/L , therefore , the mean difference as found in our study is acceptable. Sodium analysis was stratified based upon the standard laboratory values, and 135–145 mmol/L was considered as normal serum sodium. Anything above 145 mmol/L was considered hypernatremia. Patients with serum sodium less than 135 mmol/L were diagnosed as having hyponatremia . Out of 223 patients, 42 patients had low sodium levels. Analysis of sodium measurements in group of patients with low sodium (hyponatremia,  $Na^+$  less than 135 mmol/L ) showed statistically significant difference in sodium measurement from autoanalyzer and ABG analyser . Mean sodium levels as measured by ABG analyzer in this group was  $128.40 \pm 5.319$  mmol/L and that measured by Auto analyzer was  $132.16 \pm 5.512$  mmol/L . Mean difference was found to be  $4.476 \pm 2.83$  . p value 0.002. [Table 2]

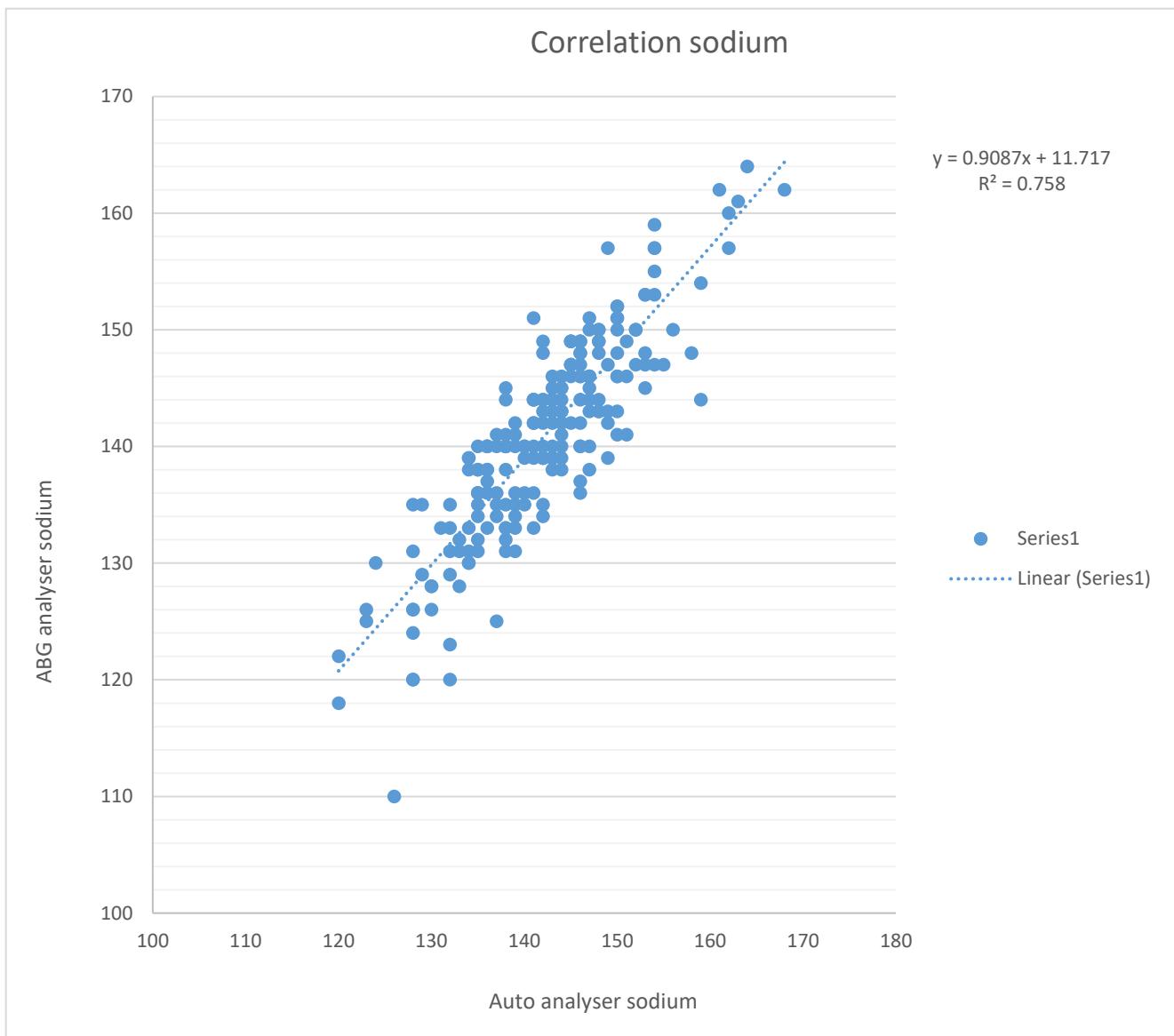
TABLE 2: Serum sodium and potassium as analysed by ABG analyser and auto analyser

GROUP	N	ABG ANALYSER	AUTOANALYSER	MEAN DIFFERENCE	P VALUE
HYPONATREMIA	42	128.40+/- 5.319	132.16+/- 5.512	4.476 +/- 2.83	0.002*
HYPERNATREMIA	76	149.14+/- 5.33	150.01+/- 5.51	3.93+/-2.83	0.296
HYPOKALEMIA	95	3.15+/- 0.42	2.955+/- 0.391	0.312+/-0.224	0.00094*
HYPERKALEMIA	3	5.53+/- 0.378	5.53+/-0.404	0.533+/-0.378	0.99

Patients with sodium levels more than 145 mmol/L ,were diagnosed as having hypernatremia. Mean difference was found to be 3.93+/-2.83 . Around 76 patients belonged to this group with mean sodium levels measured by ABG Analyzer as 149.14+/- 5.33 vs 150.01+/- 5.51 mmol/L as measured by Autoanalyser.( p value 0.296)

The correlation analysis showed a slope of 0.9087 suggesting that as sodium levels increase, the ABG analyser may slightly underestimate the values compared to the reference method. The coefficient of determination ( $R^2=0.758$ ) shows a strong positive correlation, however not a perfect one , as there is some amount of scatter indicating that the two devices wont give the same value for same patient . however , as per our analysis the variability is within the acceptable range as per Clinical Laboratories Improvement Amendment (CLIA) guidelines .[Figure 1]

**Fig 1:** Correlation analysis of serum sodium between ABG analyser and auto analyser .



\* $R^2$ = coefficient of determination

Mean potassium as measured from auto analyzer was  $3.63+/-0.664$  mmol/L and that measured by ABG analyzer was  $3.49+/-0.681$ . pvalue 0.03 [Table 3].

TABLE 3: serum potassium levels as determined by ABG analyser and Auto analyser

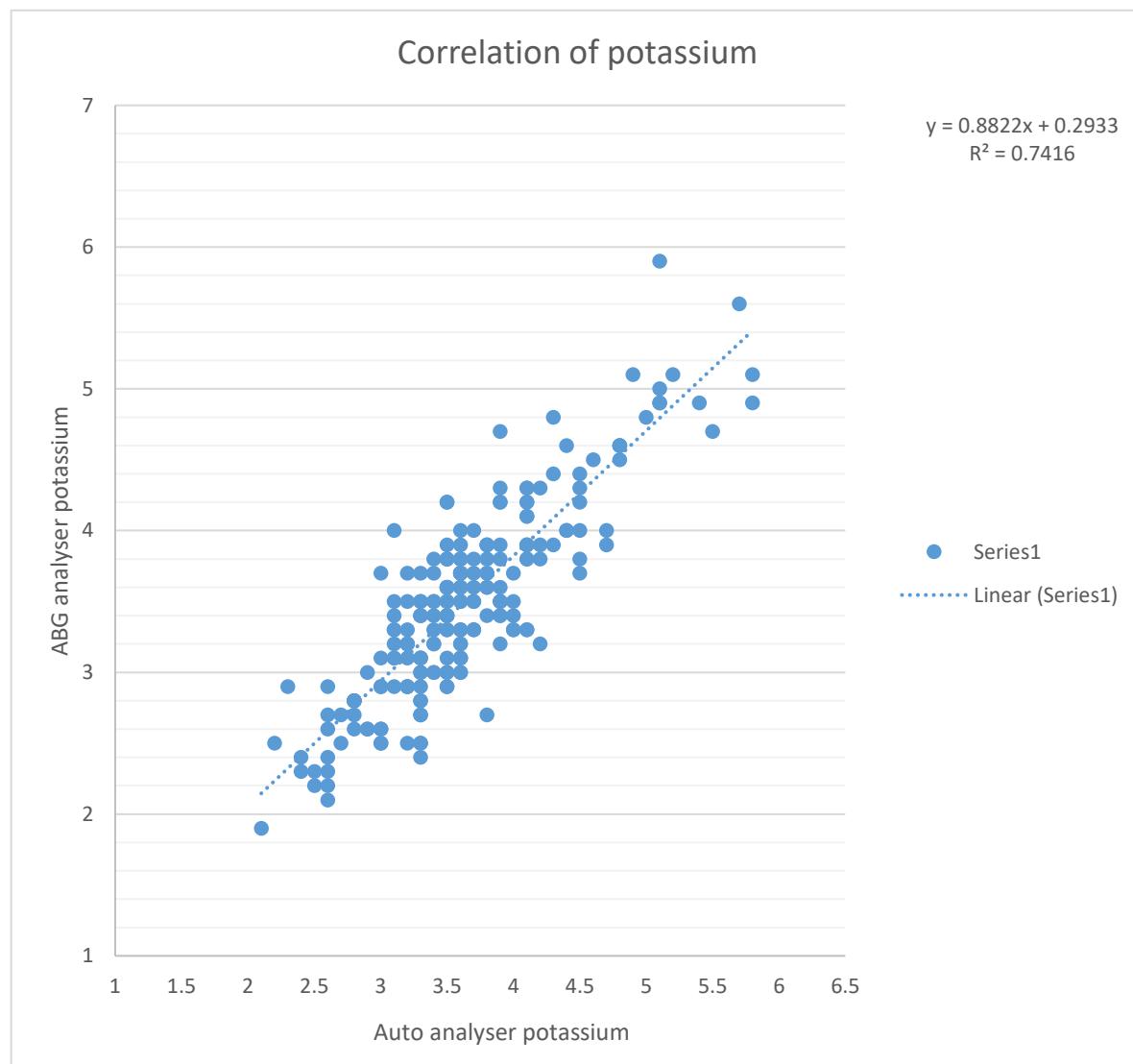
POTASSIUM LEVELS	GROUP	N	Mean (mmol/L)	Std. Deviation (mmol/L)	Mean difference (mmol/L)	95% CI (mmol/L)	P VALUE
	AUTOANALYSER	223	3.63	0.664	0.292+/- 0.240	3.543- 3.717	0.03*
	ABG ANALYSER	223	3.49	0.681		3.401- 3.579	

Mean difference was found to be  $0.292+/-0.240$  mmol/L. Maximum difference was found to be 0.9 where as minimum difference was zero. As per clinical Laboratories Improvement Amendment guidelines , acceptable limit for potassium variation is 0.5 mmol/L , therefore , the mean difference as found in our study is acceptable. Potassium analysis was stratified based upon the standard laboratory values, and 3.5-5.5 mmol/l was considered as normal serum potassium. Anything above was considered hyperkalemia. Patients with serum potassium less than 3.5 mmol/l were diagnosed as hypokalemic . Out of 223 patients, 95 patients had low potassium levels. Analysis of potassium measurements in group of patients with low potassium (hypopkalemia,  $K^+$  less than 3.5 mmol/L ) showed statistically significant difference in potassium measurement from autoanalyzer and ABG analyzer . Mean potassium levels as measured by autoanalyser in this group was  $3.15+/-0.42$  mmol/L and that measured by ABG analyser was  $2.955+/-0.391$  mmol/L . Mean difference was found to be  $0.312+/-0.224$  . pvalue 0.00094. In group of patients , with potassium levels more than 5.5 mmol/L , mean difference was found to be  $0.533+/-0.378$  mmol/L ( Table 2). Around 3 patients belonged to this group with mean potassium levels measured by auto analyzer was  $5.53+/-0.378$  mmol/L vs  $5.53+/-0.404$  mmol/L as measure by ABG analyzer.( p value 0.99) . Since the sample number was very small, we were underpowered to detect a difference. Correlation regression analysis of serum

potassium between ABG analyser and auto analyser shows that there is positive correlation which is consistent between the two measurements. The regression equation shows a slope of 0.8822 which indicates that the two measurements are closely correlated. Coefficient of determination value of 0.7416 indicates 74% variability which is generally considered a strong positive correlation. ( Figure 2).

**Fig 2:** Correlation analysis of serum potassium between ABG analyser and auto analyser .

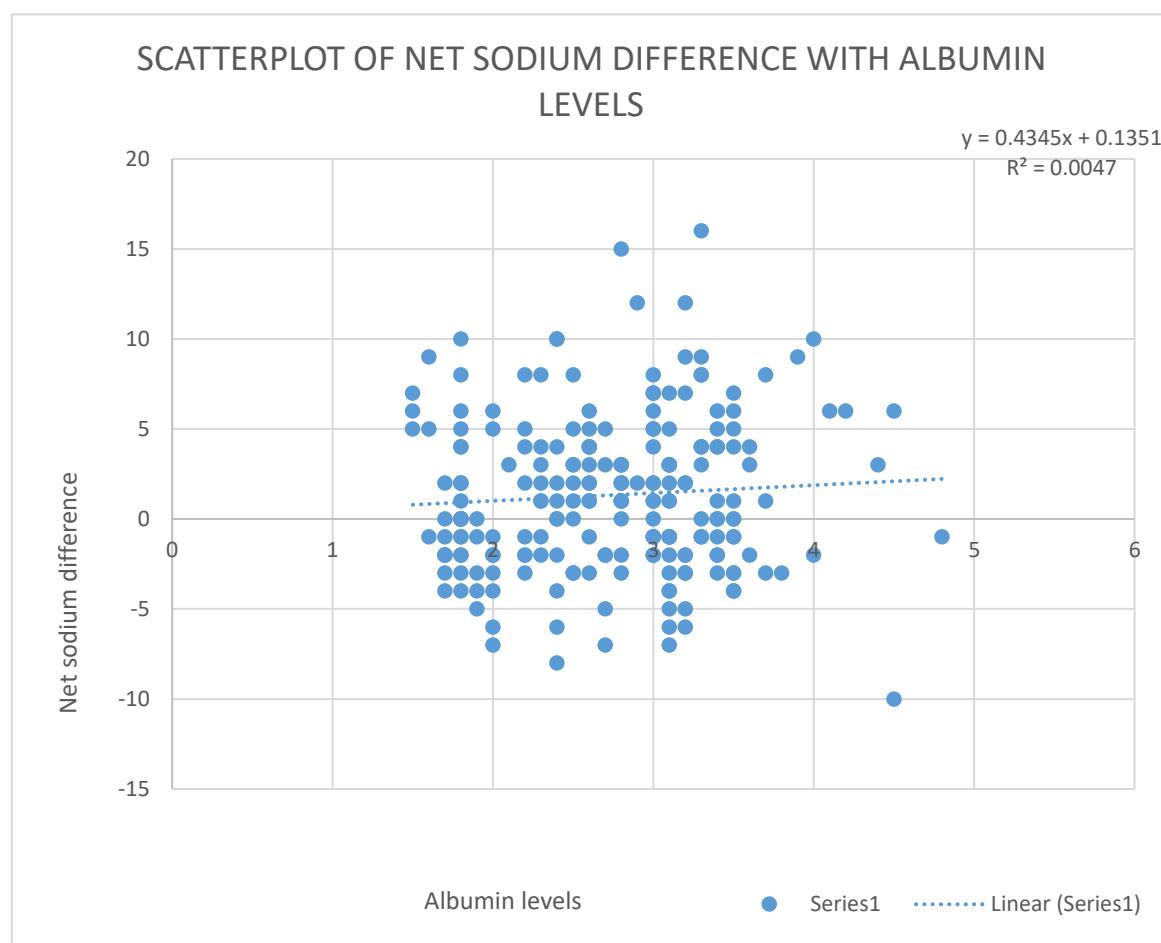
$R^2$ = coefficient of determination



The mean albumin level was found to be  $2.73 \pm 0.63$  g/dl . Out of 223 patients, 24 patients had normal albumin levels . 89.4% of patients admitted in icu had

hypoalbuminemia . Mean protein level was found to be  $5.54 +/0.91$  g/dl . Around 62.34% of patients had hypoproteinemia. Comparing the albumin levels in critically ill patients with the net sodium difference in measurement by ABG analyser and auto analyser ,we found that there was statistically no significant correlation between the two . The regression coefficient of 0.0047 clearly indicates that only 0.47% of variation in sodium difference by ABG analyser and auto analyser can be explained by albumin levels. (Figure 3)

**Fig 3:**Regression analysis of albumin levels with net sodium difference as measured by ABG analyser and autoanalyser



## DISCUSSION:

Electrolyte measurements hold a very pivotal role in ICU and above that correct measurements hold even more important position as very critical decisions need to be taken with respect to it . If not diagnosed properly, electrolyte imbalances can prove lethal .While results from ABG analysers are quick and can help in taking important

clinical decisions at the time of emergency ,serum electrolyte measurement lag behind, as good amount of precious time is lost in the process of transportation of sample to the hospital laboratory then centrifuging the sample and waiting for the auto analyser results . The acceptability criteria of interchangeability of results were derived from The United States Clinical Laboratory Improvement Amendments (US CLIA) guidelines, which state that 95% of results should fall within 0.5 mmol/L for potassium levels and 4 mmol/L for measured sodium levels to assess the intralaboratory quality of clinical chemistry tests [8].

Our study showed that there was no statistically significant difference with regards to sodium as measured from ABG analyser vs Auto analyser . Sodium as measured by ABG analyser was less than that measured by Auto analyser and the mean difference found, is acceptable as per CLIA guidelines. However , there was statistically significant difference among hyponatremic patients and the mean sodium difference was found to be 4.47 mmol/L , slightly higher than the recommended guidelines .Thus, one needs to be careful while considering  $\text{Na}^+$  levels to make clinically important decisions. Sahu S et al found a positive correlation with regards to sodium measurement as done using auto analyser and blood gas analyser [9].Indirect ISE methods are susceptible to the electrolyte exclusion effect, whereby electrolytes are excluded from the fraction of total plasma that is occupied by solids-proteins and lipid),( 7% of total plasma),owing to this dilution [10] . If a patient has a condition that alters this percentage, it will lead to a discrepancy in  $\text{Na}^+$  measurement. Story et al.evaluated electrolytes with albumin levels and demonstrated that if the plasma albumin level was above 40 g/L, the bias was 0, and the indirect ISE Na value was found to be higher in hypoalbuminemia patients which is line to our study , which shows sodium levels to be higher when measured by autoanalyser [11] .

With regards to potassium , we found that a statistically significant difference was present when comparing the two methods of measurement. Potassium levels measured by ABG analyser were less than auto analyser , with mean difference acceptable as per CLIA guidelines . Yip *et al.* suggested that the heparin in the syringes may be affecting point of care results because it raises the total volume of the sample and dilutes the plasma portion of the sample [12]. According to Budak YU et al., one of the causes for high serum potassium levels when compared to arterial potassium levels was the release of potassium from platelets during the clotting process [13]. According to Chow et al , direct ISE

sodium and potassium figures were lower than those obtained using indirect ISE. This was associated with the low blood protein levels characteristic of critically ill patients. In such patients, direct ISE offers more accurate and consistent electrolyte results than does indirect ISE [14]. Gohel M et al , found that their was significant difference is sodium levels as measured by direct and indirect method and therefore, it is recommended that preanalytical variables like serum protein levels should be considered before reporting  $\text{Na}^+$  result via indirect method [15]. This points towards the added advantage of using blood gas analysers as point of care electrolyte measuring mode in critically ill patients.

The observed differences between electrolyte levels measured using an ABG and an AA may be explained by a combination of factors, including delay during sample transport, method of testing which includes dilution of serum samples prior to testing, and variations in instrument calibration. Although the differences in electrolyte levels obtained using the two methods are sufficiently small and within the acceptable range as per CLIA guidelines , It does not raise a risk of inappropriate therapy in most instances . In addition, the ABG samples were collected using conventional syringes containing liquid heparin. The use of dried heparin syringes could have improved the accuracy of the results by decreasing the dilution of the sample [16]. Another limitation was that the ABG analyser was located in the central laboratory in an environment similar to the AA, and in doing so we did undermine the true meaning of point-of-care testing, which is often equated to bedside testing.

#### **CONCLUSION:**

$\text{Na}^+$  and  $\text{K}^+$  test results obtained using an ABG and an AA differ, however, the observed difference is within acceptable range and therefore , the results can be used interchangeably in emergency situations . However , as soon as the laboratory results become available, the treatment should be checked and adjusted if necessary. Physicians need to be aware of between-assay differences to avoid potential misdiagnosis and initiation of unnecessary treatment or investigation. Further caution is required when interpreting indirect (central laboratory) sodium values when albumin concentrations are reduced.

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