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Original Article

Biochemistry Section

Comparison of Sodium and Potassium Levels among COVID-19 Patients on Arterial Blood Gas Analysers and Clinical Chemistry Autoanalysers

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ABSTRACT

Introduction: The electrolytes and Arterial Blood Gas (ABG) analysis are the crucial part of the evaluation in Coronavirus Disease 2019 (COVID-19) patients. Hyponatraemia and hypokalaemia are the electrolyte imbalance, commonly seen in COVID-19 and hence, patients require serial monitoring of electrolytes. Variations of sodium and potassium levels between arterial and venous blood are known, however as per existing literature, there are no previous studies on the comparison of electrolytes in COVID-19 patients, when analysed in arterial and venous blood, by different methods and its significance in clinical practice.

Aim: To determine whether the sodium and potassium levels of COVID-19 patients are comparable when simultaneously analysed in arterial whole blood and venous serum sample, by ABG analyser and chemistry Autoanalyser (AA) respectively.

Materials and Methods: This prospective observational study was conducted among COVID-19 positive patients admitted in Medical Intensive Care Unit at a Tertiary Care Super-specialty Hospital, Pune, Maharashtra, India, from February 2021 to June 2021. A total of 100 arterial and 100 venous blood samples of COVID-19 patients were analysed for sodium and potassium levels on Gem Premier 3000 Blood Gas Analyser and Auto-Quant 400i chemistry AA. The statistical analysis was done by the Bland Altman method to assess the agreement between the method of measurement for sodium and potassium levels in arterial and venous samples. Shapiro-Wilk's test was applied to check normal distribution and statistical variables in sodium and potassium values measured by two methods.

Results: The mean values for sodium in arterial blood were 135.91±8.36 mmol/L and in serum was 140.26±8.49 mmol/L. The mean value of potassium in arterial blood was 4.12±0.76 mmol/L and in serum 4.41±0.67 mmol/L. Coefficients of variation for arterial and venous sample sodium level was 4.21 mmol/L and for potassium was 0.28, with bias (95% limits of agreement) of 4.96-3.46 mmol/L and 0.35-0.21 mmol/L, respectively.

Conclusion: The present study found a significant difference in electrolyte levels when compared between arterial whole blood in ABG analyser and venous serum sample in chemistry autoanalyser in COVID-19 patients. So, the clinicians must be aware of these variations and the same has to be kept in mind, while interpreting the results in COVID-19.

Keywords: Coronavirus disease 2019, Electrolytes, Hypokalaemia, Hyponatraemia, Serum, Whole blood

INTRODUCTION

In Intensive Care Unit (ICU) patients, it has been observed that electrolyte abnormalities are one of the most common causes of mortality [1]. The electrolytes and Arterial Blood Gas (ABG) analysis are the crucial part of the evaluation in Coronavirus Disease 2019 (COVID-19) patients admitted in ICU. Hyponatraemia and hypokalaemia are the electrolyte imbalance, commonly seen in COVID-19 and hence, patients require serial monitoring of electrolytes [2]. Electrolytes can be analysed in plasma and as well as in serum samples but, plasma or whole blood sample has the advantage of shortening the turnaround time, because there is no need, to wait for the blood to clot. Further, the haemolysis in the serum sample can cause erroneously high potassium results, which is not a problem with whole blood. For ABG analysis the arterial blood is collected in a heparinised tube. It has been observed that the cause for lower values of electrolytes in arterial blood is because of the binding of heparin to the electrolytes [3].

Electrolytes such as sodium (Na^+) and potassium (K^+) levels and other parameters were measured in all severe COVID-19 patients as per ICU patient investigation protocols, but it was also felt essential to determine, whether Na^+ and K^+ values had variation, when simultaneously analysed in arterial whole blood- Point Of Care Testing (POCT) and venous serum sample, by ABG and chemistry Autoanalyser (AA) respectively in COVID-19 patients admitted in ICU. As per literature, there are no previous studies available on the comparison of electrolytes in COVID-19 patients, when analysed in arterial and venous blood, by different methods and its significance in clinical practice. To the best of the information available in scientific literature, this was the first study, being conducted on comparison of the electrolytes, analysed in ABG and chemistry AA in COVID-19 patients admitted in ICU. This study aimed to determine the Na^+ and K^+ levels of COVID-19 patients in arterial and venous blood samples on an ABG analyser and chemistry AA respectively.

MATERIALS AND METHODS

It was a prospective observational study, conducted among COVID-19 positive patients admitted in Medical Intensive Care Unit at a Tertiary Care Super-specialty Hospital, Pune, India, from February 2021 to June 2021. The ethical clearance was obtained from the Institutional Ethical Committee (IEC no. IEC/2021/377).

Inclusion criteria: The study included the samples of diagnosed cases of COVID-19 (as per positive reverse transcription-polymerase chain reaction report), admitted in medical ICU of the hospital, both males and females of age between 20-70 years.

Exclusion criteria: Blood samples of COVID-19 patients with active therapy on potassium-sparing diuretics, K^+ binders (confounding factor with potassium levels in the blood), Haemolysed samples were not taken for this study (to avoid pseudo-hyperkalemia).

As per the admission rate of COVID-19 patients in the medical ICU during five months, the sample size was estimated as 100. A total of 100 arterial blood samples for ABG analysis and 100 venous serum samples were analysed.

Procedure

The samples were analysed for Na^+ and K^+ levels, on Gem Premier 3000 Blood Gas Analyser (Direct ISE) in ICU as Point-Of-Care Testing (POCT) in ICU and Auto-Quant 400i chemistry AA (Indirect ISE), in a central biochemistry laboratory. Blood samples were received as a part of ICU protocol investigations in COVID-19 patients. All the samples were analysed simultaneously (as and when received and not stored) for sodium and potassium levels on the ABG machine and AA of COVID 19 positive patients, admitted consecutively to the Hospital ICU.

An arterial blood sample was collected in a heparinised 2 mL syringe and venous blood samples were collected in a red top vacuum evacuated tube simultaneously. The arterial blood sample was analysed at the POCT in ABG analyser, placed in ICU and venous blood was transported safely, to the biochemistry laboratory within one hour of collection. Samples were processed with all universal personal protective precautions along with Personal Protective Equipment (PPE) and analysed as and when received consecutively from ICU.

Arterial blood samples were analysed on Gem Premier 3000, ABG Analyser, as a part of evaluation for metabolic disorders in COVID-19 patients [4]. Venous blood samples were received in a red-topped vacuum evacuated tube; the sample was collected simultaneously at the same time as arterial blood was collected in ICU. The venous blood samples were processed every day, without any storage of samples, on Auto-Quant 400i clinical chemistry AA [5].

The Quality Control (QC) samples were run every day, as a part of Internal Quality Control (IQC) checks, before running the patient's serum samples. The ABG machine was auto-programmed for regular IQC checks, before analysing the patient's arterial blood sample. Sodium and potassium levels were measured on both the machines and data was collected and entered in Microsoft excel sheet subsequently.

STATISTICAL ANALYSIS

MedCalc Software windows and Microsoft® Office Excel 2019 (Microsoft, Redmond, Washington, USA) is used for statistical analysis. The statistical analysis was done by the Bland Altman method to assess the agreement between the method of measurement for sodium and potassium levels in arterial and venous samples. Shapiro-Wilk's test was applied to check normal distribution and statistical variables in sodium and potassium values measured by two methods.

RESULTS

This study was conducted in 100 paired blood samples of COVID-19 patients which included 31 females and 69 males. The patients mean age was 50.38 years (mean 48±14.93). On data analysis, it was found that the sodium and potassium levels of COVID-19 positive patients were high in serum samples as compared to arterial blood. Shapiro-Wilk test showed the data for sodium and potassium values measured in both analysers followed a normal distribution. The mean values for sodium in arterial blood were 135.91±8.36 mmol/L and in serum was 140.26±8.49 mmol/L. The mean value of potassium in arterial blood was 4.12±0.76 mmol/L and in serum 4.41±0.67 mmol/L [Table/Fig-1]. Coefficients of variation for arterial and venous sample sodium level was 4.21 mmol/L and for potassium was 0.28, with bias (95% limits of agreement) of 4.96-3.46 mmol/L and 0.35-0.21 mmol/L, respectively [Table/Fig-2].

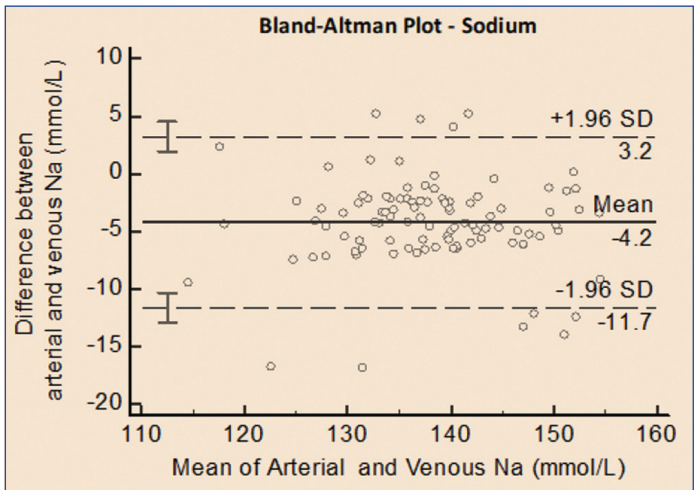
Electrolyte	ABG (mean±SD)	Autoanalyser (mean±SD)
Sodium	135.91±8.36	140.26±8.49
Potassium	4.12±0.76	4.41±0.67

[Table/Fig-1]: Sodium and Potassium levels by ABG and autoanalysers in mmol/L.

Electrolyte	Number of samples	Average (A-V) difference (mmol/L)	95% limits of agreement (mmol/L)
Sodium (Na^+)	100	4.21	4.96 to 3.46
Potassium (K^+)	100	0.28	0.35 to 0.21

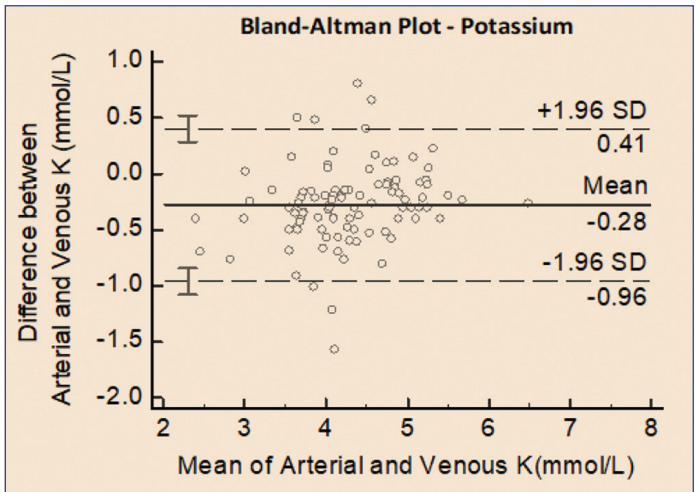
[Table/Fig-2]: Agreement between arterial and venous sodium and potassium levels (Shapiro-Wilk test).

Bland altman plot for sodium showed that values with the difference between arterial and venous sodium on the Y-axis, mean arterial and venous sodium on X-axis, were beyond limits of agreement and found to be significant (p-value <0.001) [Table/Fig-3].



[Table/Fig-3]: Bland-Altman Plot for the agreement of sodium levels in ABG and chemistry autoanalyser.

Bland altman plot for potassium showed that values with the difference between arterial and venous potassium on the Y-axis, mean arterial and venous potassium on X-axis, were beyond limits of agreement and found to be significant (p-value <0.001), see [Table/Fig-4]. The mean values of sodium and potassium at different levels or ranges are shown in [Table/Fig-5,6], respectively. It was observed that there was a significant difference between electrolyte values/levels in arterial and venous blood, 4.21 mmol/L for sodium and 0.28 mmol/L for



[Table/Fig-4]: Bland-Altman Plot for agreement of potassium levels in ABG and chemistry autoanalyser.

Sodium (mmol/L)	ABG	Autoanalyser
110-120	114.65	117.85
>120-130	126	126.8
>130-140	135.39	135.4
>140-150	144.12	143.48
>150-160	151.56	153.29

[Table/Fig-5]: Mean value of sodium (mmol/L) at different levels by ABG and Autoanalyser.

Potassium (mmol/L)	ABG	Autoanalyser
2-3	2.54	2.8
>3-4	3.63	3.71
>4-5	4.48	4.48
>5-6	5.24	5.28
>6-7	6.36	6.62

[Table/Fig-6]: Mean value of potassium (mmol/L) at different levels by ABG and Autoanalyser.

potassium when analysed simultaneously in arterial blood on ABG analyser and chemistry AA respectively in COVID-19 patients.

DISCUSSION

This study found that the mean sodium level in arterial whole blood was 135.91 mmol/L with SD±8.36 and in serum was 140.26 mmol/L with SD±8.49. The mean value of potassium in arterial blood was 4.12±0.76 mmol/L and in serum 4.41±0.67 mmol/L. To the best of the information available in the recent research literature, this is the first study that has been conducted on electrolytes by two different methods in COVID-19 patients admitted to ICU.

The electrolytes are measured by Ion-Selective Electrodes (ISEs) methods that include direct ISE and indirect ISE. In the direct ISE method, the electrode surface is directly in contact with an undiluted blood sample, which is employed, by ABG analysers while, indirect ISE devices use diluted plasma (or serum) samples. The indirect assay features preanalytic dilution and is often employed in high-throughput central hospital laboratories running chemistry AA [6].

Jain A et al., observed that there was not much difference between the potassium values, but a significant difference in sodium, measured by the ABL555 blood gas analyser and the Dade Dimension RxL Max [7]. However, we found a significant difference between sodium (Na^+) as well as potassium (K^+) in COVID-19 patients when analysed by Gem Premier 3000, ABG analyser and Auto-Quant 400i clinical chemistry AA.

Sanakal DB et al., observed that there was not much difference between Na^+ values measured by the ABOTT (ABG) analyser and venous samples were analysed on PROLYTE electrolyte AA [8]. Whereas, according to Budak YU et al., when Na^+ and K^+ levels were measured using a pHOx Stat Profile Plus L blood gas analyser and a Roche Modular P autoanalyser, the mean K^+ level was 3.5±0.9 mmol/L using the ABG and 3.7±1.0 mmol/L using the clinical chemistry AA (p-value <0.001) [9]. However, this study observed the mean K^+ level was 4.12±0.76 mmol/L using the ABG and 4.41±0.67 mmol/L using the clinical chemistry AA, which is found to be different as well as significant in COVID-19 patients admitted in ICU.

Chacko B et al., had found a significant difference in the mean±SD sodium value between whole blood and serum samples (135.8±5.7 mmol/L vs. 139.9±5.4 mmol/L; p-value <0.001) analysed on GEM Premier 3000 (ABG) and Olympus AU2700 discrete chemistry analyser [10]. However, we observed that there was a significant difference in the mean±SD sodium value in arterial blood and serum samples (135.91±8.36 mmol/L vs. 140.26±8.49 mmol/L, p-value <0.001). Alanazi A et al., found a positive and significant correlation between Na^+, K^+ and calcium measured by both in the ABG and serum analyser [11].

Herrington WG et al., had found that the coefficient of variation for arterial and venous K^+ samples were 0.8 and 1.1%, respectively [12]. As per Clinical Laboratory Improvement Amendments (CLIA), proficiency testing regulations related to analytes and acceptable performance, the acceptable performance for sodium and potassium, value ±4 mmol/L and ±0.3 mmol/L, respectively [13].

Sarvazad H et al., observed that blood sodium levels, 55% of patients had normal levels, 38% had hyponatraemia and 7% had hypernatremia and for blood potassium levels, 85% of patients were in the normal range, 1.8% were hypokalaemic, 7.3% were severely hypokalaemic and 5.5% were hyperkalaemic [14].

Lippi G et al., found low levels of Na, K and Ca were related to the severity in COVID-19 patients and hypokalaemia, particularly known to worsen the respiratory distress in patients of COVID-19 [15]. Electrolyte and acid-base disturbances, specifically hypernatremia and acidosis were greatly related to increased hospital mortality and hence these disturbances must be monitored carefully, diagnosed and managed correctly during hospitalisation [16]. It had been found that the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) was associated with SARS-CoV-19 pneumonia and patients had hyponatraemia [17]. As POCT measurements like ABG analysis, which are being applied more, to the care of critically ill patients, clinicians need to be aware of these differences, for the assessment of patients [18]. It is advised that ABG analysers should be used with caution to measure potassium levels and also assessed for, how accurate or reliable, when compared with a venous sample being sent to the laboratory for standard analysis [19].

The electrolyte levels estimated by arterial blood in neonates can be used similarly only for potassium levels, whereas sodium and chloride estimation require further assessment on chemistry AA [20]. Sodium overestimation by indirect ISE due to hypoproteinemia can be seen in a tertiary care hospital laboratory [21]. It was observed that plasma sodium, potassium and chloride measurements were affected by changes in plasma protein concentration when measured by indirect ISE systems [22].

Zhang JB et al., had observed that the variations in Na and K measured in ABG and lab AA did not exceed the criteria given in US CLIA guidelines [12,23]. Hence, it's important to assess patient status, based on serial monitoring of the electrolyte levels in COVID-19 disease and critical decisions should be made by electrolyte values obtained from both the ABG analysis and the serum AA.

Limitation(s)

This study has included critical COVID-19 patients admitted in ICU and only two parameters (Na^+, K^+) levels in arterial and venous blood analysed on ABG and chemistry AA, respectively. However, the study on more parameters on different analysers needs to be conducted on a larger scale in COVID-19 patients.

CONCLUSION(S)

This study found a significant difference in sodium and potassium levels when compared between arterial whole blood in ABG analyser and venous serum sample in chemistry AA in COVID-19 patients. Therefore, the clinicians must be cognizant of these possible variations and the same has to be kept in mind, while interpreting the results in COVID-19 positive patients.

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