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Role of Arterial Blood Gas Analysis in Rapid Assessment of Hypokalaemia in Covid – 19

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Abstract
Background: *Corona Virus Disease–2019 (COVID–19) is the greatest health crisis of the 21st century claiming more than 10 lakh deaths worldwide. Numerous studies on COVID – 19 have demonstrated prevalence of hypokalaemia. The objective of the study is to characterise this hypokalaemia in context of inflammatory state and severity of Acute Respiratory Distress Syndrome (ARDS) in COVID – 19 and therefore find out whether Arterial Blood Gas (ABG) results are comparable to that of the fully Automated Chemistry Analyzer (AA) which may reduce the analysis turnaround time and guide the clinician to expedite intervention.*
Methods: *This hospital based cross-sectional study comprised of 156 active COVID cases admitted between June – August, 2020, at ABVIMS & Dr. R.M.L. Hospital, and their paired arterial and venous samples were processed in the ABG and AA respectively. In addition to serum* Na^+/K^+ *estimation the venous samples were also assessed for serum C reactive protein (CRP) levels. The calculated tests section of ABG reports provided the* $PaO_2:FiO_2$ *ratio. The Spearman rank correlation was performed to assess the strength of association between the parameters. Mean differences of paired samples were calculated by Kruskal – Wallis test and limits of agreement was estimated by Bland – Altman plots. At 95% confidence interval, a p value < 0.05 was considered significant.*
Results: *Forty-four cases (28%) were found to be suffering from varying degrees of ARDS as per the Berlin definition. Hypokalemia was a predominant finding (72.7%) amongst these cases and the measured potassium values showed a significant correlation with* $PaO_2:FiO_2$ *ratio across both platforms (AA: r = 0.660, p < 0.001; ABG: r = 0.639, p < 0.001). Potassium levels from both analyzers also showed a significant negative correlation with serum CRP levels (AA: r = - 0.463, p < 0.001; ABG: r = - 0.429, p < 0.001). The mean potassium level was 3.90 ± 0.84 mmol/L using AA and 3.99 ± 0.86 mmol/L using the ABG. The extent of inter-analyzer agreement was acceptable for* K^+*.*
Conclusions: *There is prevalence of lower plasma concentration of potassium, which has significantly correlated with both the inflammatory state as well as severity of ARDS in COVID–19. A thorough understanding of these abnormalities, may assist in better clinical understanding of the underlying pathophysiological mechanisms of SARS-CoV-2. The electrolyte estimates especially potassium, of both AA and ABG platforms, were comparable and therefore ABG electrolyte values can be used reliably for prompt patient management.*
Keywords: *COVID-19, Hypokalemia, Arterial blood gas analysis, A.R.D.S., C-Reactive Protein*

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I. Introduction

Coronavirus disease 2019 (COVID-19) is caused by a member of the corona virus family called Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2). COVID-19 has quickly risen to become one of the greatest global pandemics of the 21st century. Within public health and hospital systems the persistent and surging threat of this pandemic dictates clinical care. (1)

Some studies in COVID-19 have indicated that at the disease onset, patients may present with electrolyte disorders, especially hypokalaemia, which has shown significant association with overall disease morbidity and poor outcomes. (2,3) The quick assessment of these dyselectrolytemias can not only affect patient management but can also play a major role in identifying pathophysiological mechanisms underlying COVID-19. Though the laboratories of most tertiary care hospitals utilise a fully automated chemistry analyzer (AA) which has a longer turnaround time, electrolyte analysis performed on an ABG analyser can eliminate several processing and achieve prompt results.

The objective of our present study is:
1. To characterise the hypokalaemia in active SARS-CoV-2 patients;
2. To assess the hypokalaemia in the context of severity of ARDS and inflammatory state, quantified by C reactive protein (CRP) levels; and
3. To demonstrate whether the electrolyte values (Sodium & Potassium) obtained from ABG and AA platforms are comparable, so that ABG electrolyte estimates may be used for quick detection of hypokalemia and expedite clinical decision making and improve treatment outcomes.

II. Material and Methods

This hospital based cross sectional study was carried out on patients admitted to the SARI wards/ICUs of Atal Bihari Vajpayee Institute of Medical Sciences & Dr. Ram Manohar Lohia Hospital, New Delhi, from June to August 2020. A total 156 adult subjects (either sex) of age ≥18 years were included in this study after taking their informed consent.

Study Design: Cross-sectional observational study.

Study Location: This was a tertiary care teaching hospital-based study done in Department of Biochemistry, at Atal Bihari Vajpayee Institute of Medical Sciences & Dr. Ram Manohar Lohia Hospital, New Delhi, India.

Study Duration: June 2020 to August 2020.

Sample size: 156 patients.

Patients selection method: Out of 204 cases admitted to the SARI ward/ICU of A.B.V.I.M.S. & Dr. R.M.L. Hospital, New Delhi, India, during the period of June to August, 2020, 156 cases who fit the inclusion criteria were selected for the study.

Inclusion criteria:
1. Patients who were symptomatic and tested positive for COVID 19 by RT-PCR test.
2. Either sex
3. Age ≥18 years

Exclusion criteria:
1. History of diabetes mellitus
2. History of chronic kidney disease or
3. Undergoing diuretic therapy.

III. Procedure methodology

The active cases were first classified as those with and without Acute Respiratory Distress Syndrome (ARDS). ARDS cases were then sub-classified into three groups on the basis of Berlin definition for ARDS [15] by estimation of the PaO_2:FiO_2 ratio. The present study was approved by the Institutional Ethics Committee of the aforesaid institute. All procedures were in accordance with the Second Declaration of Helsinki.

On admission, the patients' arterial and venous blood samples were collected within 5 mins of each other. All samples were collected by the principal and the co-investigator.

For the arterial blood gas analysis, 1.6 ml blood was collected in commercially available plastic arterial blood gas syringes (BD A-LINE arterial blood gas collection syringe, 3.0ml volume with 1.6 ml recommended draw volume, Becton & Dickinson Diagnostics, Plymouth, UK) coated with 80 I.U Sodium-heparin. 2 ml of venous blood samples were collected from the ante-cubital vein of left forearm into yellow-capped vacutainers (BD SST tube with silica clot activator, polymer gel, silicone-coated interior, 3.5 ml with 2.0 ml recommended draw volume, Becton, Dickinson & Company, USA) to be run on the fully automated chemistry analyzer (XL640, TransAsia Biomedicals Pvt Ltd) for both electrolyte and serum C – reactive protein (CRP) estimation. All samples were transported maintaining cold chain, to the COVID (Trauma centre) Laboratory, Department of Biochemistry, Dr. RML Hospital.

The arterial blood gas samples were analysed within 15 mins of collection, using PHOX Ultra ABG Analyzer (NOVA Biomedicals, USA) utilizing the direct ISE method. The blood gas analyzer was calibrated automatically every 4 hourly one point, every 8 hourly 2 points, and an internal quality check was performed routinely every 12 hrs.

Estimation of serum electrolytes (by direct ISE) and serum CRP (by the Quantitative Immunoturbidimetric Assay, using Erba Mannheim Xl System packs) in the venous blood sample was performed within one hour of collection, by the fully automated Erba XL 640 Chemistry Analyzer (TRANSASIA Biomedicals, India). The ISE unit of the auto-analyzer was calibrated routinely every 24 hours by linear calibration, according to the manufacturer's recommendations and internal quality control checks for ISE parameters & serum CRP were performed routinely every 8 hours. External quality check was performed once a month.

Statistical analysis:

The data were evaluated using SPSS version 24.0 (SPSS Inc., Chicago, IL). Normality was tested using Shapiro-Wilk test and data did not follow normal distribution, hence non-parametric tests were used. Mean, standard deviation (SD), median, standard error of mean, and variance were calculated (Table 1). Descriptive statistics were presented as Mean ± SD. Paired sample differences yielded by the AA and ABG devices were estimated using Kruskal – Wallis test. Agreement between the two analyzers was assessed using Bland – Altman plots. Limits of agreement were defined as Mean ± 2SD. The linear relationship between the variables was assessed using the Spearman Rank Correlation analysis method. At 95% confidence interval, a p value of ≤ 0.05 was considered significant.

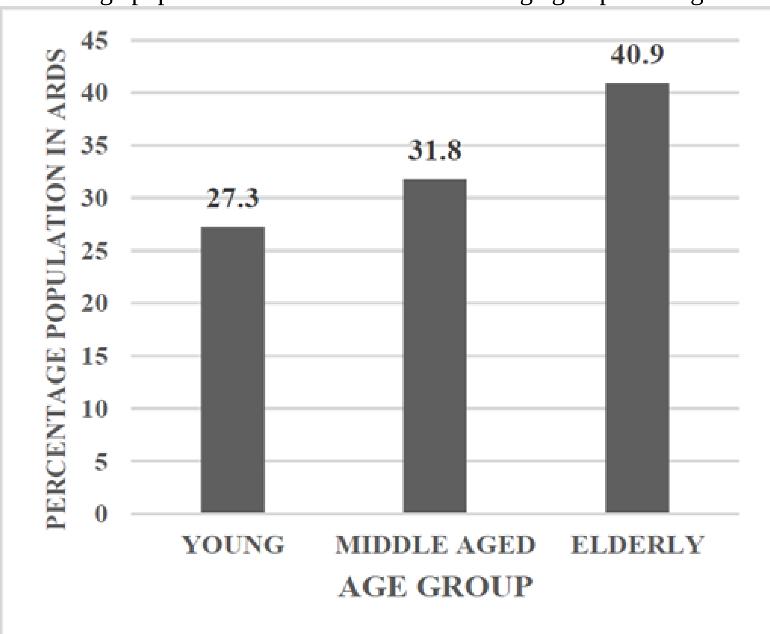
Table 1: Measurements of mean, standard deviation, standard error of mean, median and variance of sodium and potassium in each device.

ELECTROLYTE	PLATFORM	SAMPLE SIZE	MEAN	SD	SE (MEAN)	MEDIAN	VARIANCE	MINIMUM	MAXIMUM
SODIUM	AA	156	138.28	7.97	0.64	137.08	63.45	119.00	164.13
	ABG	156	134.53	8.40	0.67	134.15	70.52	115.20	165.00
POTASSIUM	AA	156	3.90	0.84	0.07	3.73	0.71	2.45	7.28
	ABG	156	3.99	0.86	0.07	3.82	0.73	2.39	7.30

IV. Results

The data obtained from 156 patients of age 18 to 70 years was evaluated. The population was categorized in to three age groups, young: 18 – 35 years, middle-aged: 36 – 49 years and elderly: ≥ 50 years. Among them 57.1% were males and 42.9 % were females. A total 44 cases in the sample population (28.2%) were characterized to be suffering from varying degrees of ARDS and the severity was classified as per the Berlin Classification. [15] 40.9% of the ARDS cases belonged to the elderly population (≥ 50 years) (Fig. 1).

Fig. 1: Percentage population distribution in the three age groups among ARDS cases



This study has shown that 39.1% of the study population were hypokalaemic and among those suffering from ARDS, approximately 70% of cases across both platforms were hypokalaemic. The mean potassium level measured on the AA was 3.90 ± 0.84 mmol/L, and the value obtained in the ABG was 3.99 ± 0.86 mmol/L. On the other hand, the mean sodium level measured on the AA was 138.28 ± 7.97mmol/L while the value obtained on the ABG analyzer was 134.53 ± 8.40 mmol/L. (Table 1). The analysed results of sodium and potassium were grouped according to (i) age (Table 2), (ii) sex (Table 3), (iii) the standard laboratory values (Table 4) and (iv) severity of ARDS (Table 5).

Table 2: Estimation of AA & ABG electrolyte values in each age group.

ELECTROLYTE	AGE (in years)	AA	ABG	*n*	*r*
SODIUM	18 – 35	137.51 ± 8.79	133.52 ± 9.37	90	0.778
	36 – 49	140.71 ± 6.95	136.79 ± 7.24	36	0.554
	≥ 50	137.73 ± 5.86	134.79 ± 6.26	30	0.416
POTASSIUM	18 – 35	3.89 ± 0.85	3.95 ± 0.90	90	0.743
	36 – 49	3.78 ± 0.76	3.85 ± 0.75	36	0.683
	≥ 50	3.95 ± 0.97	4.06 ± 0.95	30	0.766

Table 3: Classification of AA and ABG electrolyte estimates based on sex.

ELECTROLYTE	SEX	AA	ABG	*n*	*r*
SODIUM	M	138.28 ± 8.32	134.64 ± 8.71	98	0.605
	F	137.92 ± 7.72	134.16 ± 8.17	60	0.649
POTASSIUM	M	3.91 ± 0.81	3.90 ± 0.86	98	0.734
	F	3.84 ± 0.91	4.05 ± 0.86	60	0.685

Table 4: Frequency distribution of AA and ABG electrolyte estimates based on standard laboratory ranges.

ELECTROLYTE	CATEGORY	RANGE (in mmol/L)	AA	ABG
SODIUM	SEVERE HYPONATREMIA	<120	1	5
	HYPONATREMIA	120 - 135	57	81
	NORMONATREMIA	135 – 150	98	64
	HYPERNATREMIA	>150	12	6
POTASSIUM	SEVERE HYPOKALAEMIA	<2.5	4	3
	HYPOKALAEMIA	2.5 – 3.5	57	58
	NORMOKALAEMIA	3.5 – 5.0	82	80
	HYPERKALAEMIA	>5.0	13	15

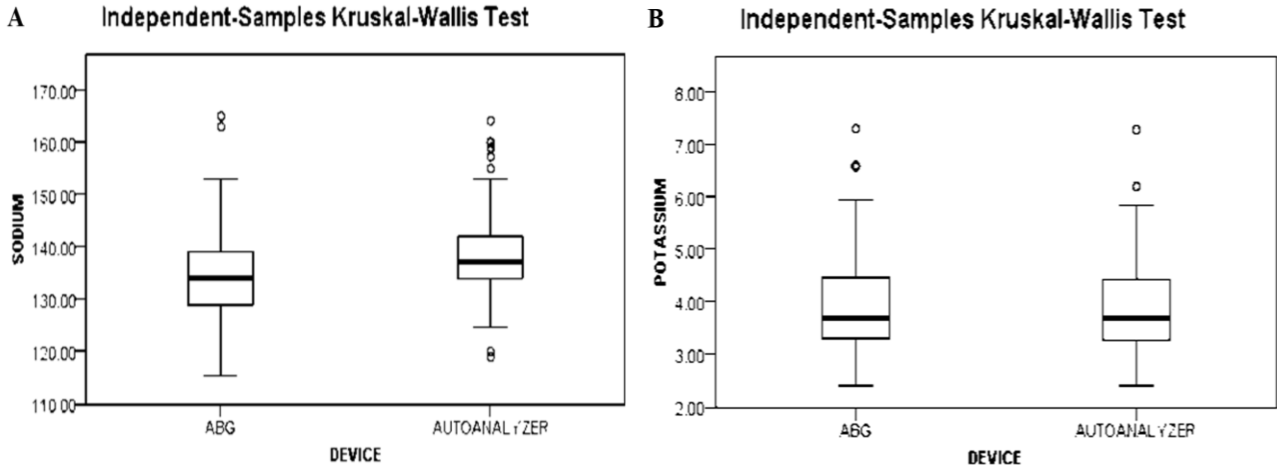
Table 5: Electrolyte estimates in paired samples in varying degrees of ARDS

ELECTROLYTE	ARDS	AA	ABG	*n*	*r*
SODIUM	Mild	138.07 ± 8.12	134.39 ± 8.10	24	0.806
	Moderate	138.30 ± 7.14	133.56 ± 9.03	17	0.672
	Severe	130.00 ± 3.46	126.33 ± 5.33	3	0.866
	Nil	138.07 ± 8.12	134.39 ± 8.10	112	0.609
POTASSIUM	Mild	4.14 ± 0.93	4.19 ± 0.83	24	0.623
	Moderate	3.84+/-0.90	3.88 ± 0.78	17	0.828
	Severe	3.61 ± 1.07	4.03 ± 1.02	3	0.900
	Nil	3.87 ± 0.813	3.95 ± 0.87	112	0.637

The Kruskal – Wallis test showed no significant differences between the mean differences of paired samples for potassium estimates yielded by AA and ABG (p = 0.821). Consequently, the hypothesis suggesting that there was no difference between the two platforms in terms of potassium estimation was accepted.

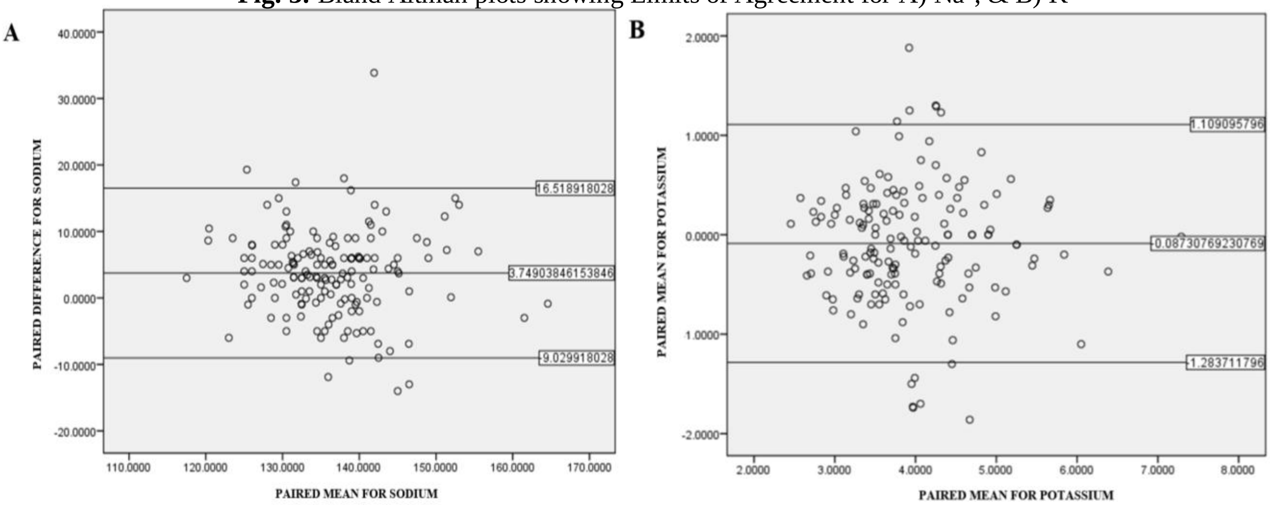
A significant difference was observed when the mean differences of paired samples for sodium levels yielded by AA and ABG were compared using Kruskal – Wallis test (p < 0.001). Therefore, the hypothesis suggesting that there was no difference between the two machine results was rejected (Fig. 2).

Fig. 2: Kruskal-Wallis test between paired samples showed: A) significant difference for sodium ($p < 0.001$), and B) no significant difference for potassium ($p = 0.821$)



A Bland – Altman comparison of AA & ABG potassium measurements yielded the limits of agreement between –1.28 mmol/L (-1.96 SD) to 1.11 mmol/L (+1.96 SD), and for AA & ABG sodium measurements yielded the limits of agreement between –9.03 mmol/L (-1.96 SD) to 16.52 mmol/L (+1.96 SD) (Fig. 3).

Fig. 3: Bland Altman plots showing Limits of Agreement for A) Na^+, & B) K^+



The Spearman's correlation coefficient between paired samples for potassium was $r = 0.742$ ($p < 0.01$) and for sodium was $r = 0.664$ ($p< 0.01$).

In the entire sample population, the AA and ABG potassium estimates show significant negative correlation with the serum CRP levels (AA: $r = -0.463$, $p < 0.001$; ABG: $r = -0.429$, $p < 0.001$). But in ARDS cases, the correlation was significantly stronger (AA: $r = -0.728$, $p < 0.001$; ABG: $r = -0.676$, $p < 0.001$) (Fig. 4 & 5).

Fig. 4: Correlation of AA potassium with Serum CRP A) in ARDS cases & B) in total cases

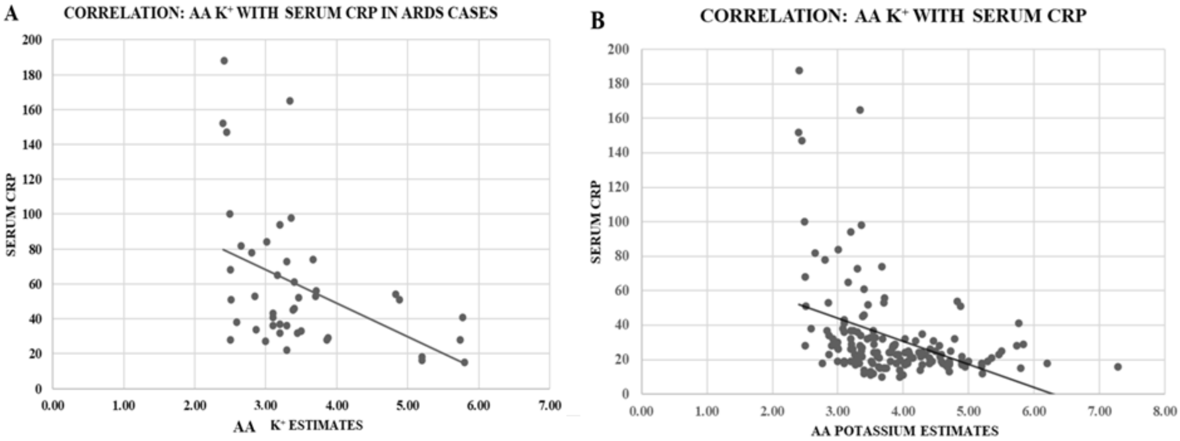
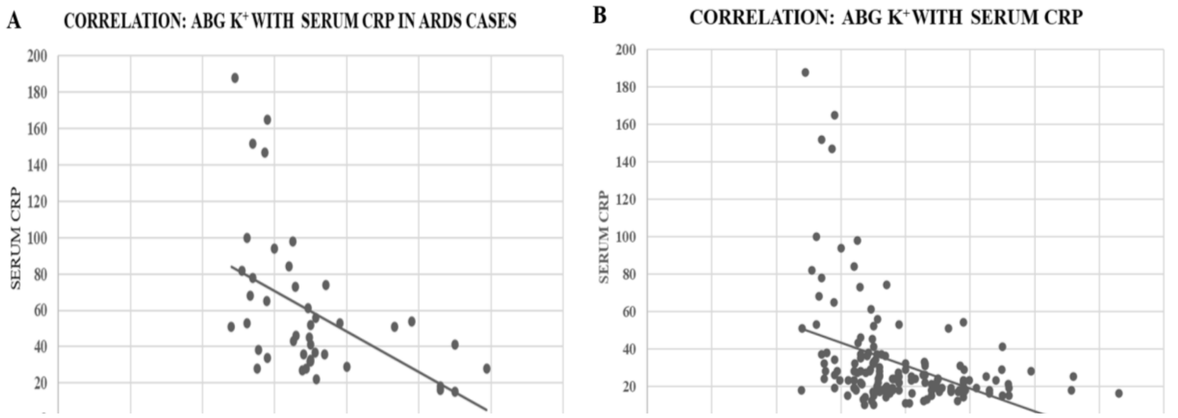
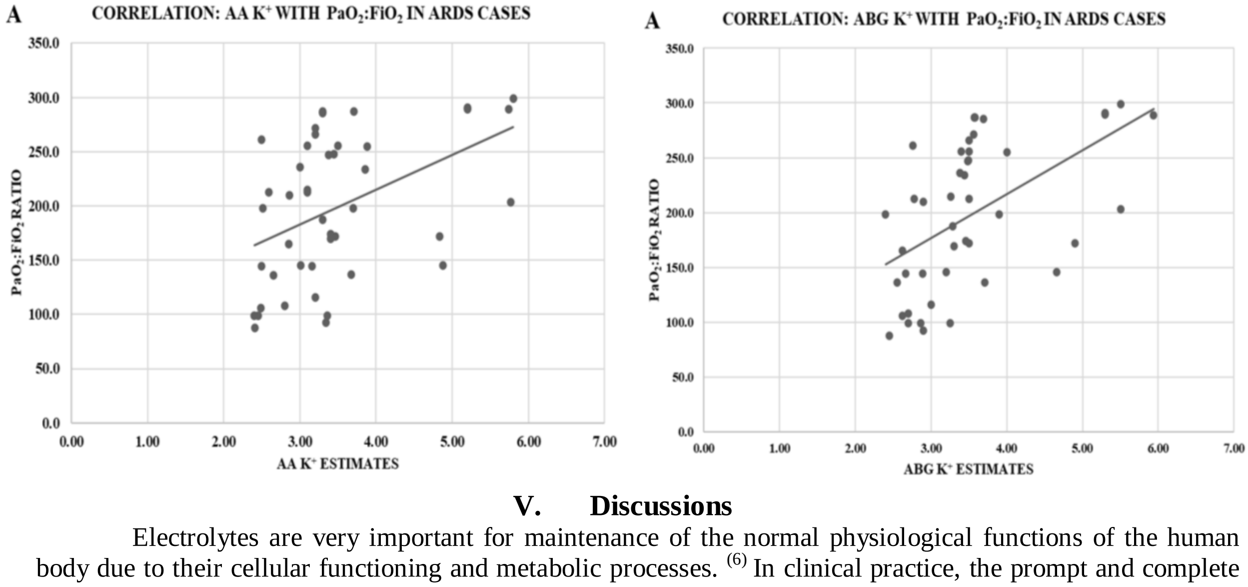


Fig. 5: Correlation of ABG potassium with Serum CRP A) in ARDS cases & B) in total cases.



The AA and ABG potassium values have also shown significant moderate correlation with PaO_2:FiO_2 ratio in ARDS cases (AA: $r = 0.660$, $p < 0.001$; ABG: $r = 0.639$, $p < 0.001$) (Fig. 6).

Fig. 6: Correlation of AA potassium with PaO_2:FiO_2 ratio A) in ARDS cases & B) in total cases.



V. Discussions

Electrolytes are very important for maintenance of the normal physiological functions of the human body due to their cellular functioning and metabolic processes. [6] In clinical practice, the prompt and complete correction of electrolyte imbalance in the patients admitted to Emergency & ICU departments, is not only crucial for management, but also for their accurate quantification at the earliest. [6]

Numerous studies in COVID 19 have demonstrated the presence of hypokalaemia as an atypical presentation at the disease onset. [2-5] Our study has shown that among those suffering from ARDS, as per the AA and ABG potassium estimates, 68.2% and 72.7% of cases respectively, were hypokalaemic. Both the AA and ABG potassium estimates have shown statistically significant negative correlation with the serum CRP levels (AA: $r = -0.463$, $p < 0.001$; ABG: $r = -0.429$, $p < 0.001$) i.e., a rise in CRP levels was associated with a fall in potassium values. However, the correlation was significantly stronger among ARDS cases (AA: $r = -0.728$, $p < 0.001$; ABG: $r = -0.676$, $p < 0.001$). A similar finding has also been observed by the study of Chen et al. [(3)]

The AA and ABG potassium values have also shown significant moderate correlation with PaO_2:FiO_2 ratio in ARDS cases (AA: $r = 0.660$, $p < 0.001$; ABG: $r = 0.639$, $p < 0.001$). Contrary to the findings of Moreno et al. [(4)] our results demonstrate that potassium levels are associated not only with the inflammatory state, but also with the ARDS severity in COVID – 19. The possible cause of these hypokalaemia, is that SARS-CoV-2 binds to angiotensin converting enzyme 2 (ACE 2) receptor and likely reduces ACE 2 expression. ACE 2 metabolizes angiotensin I and II and thus its down-regulation leads to their uninhibited action. This causes increased potassium excretion by the kidneys, ultimately leading to hypokalaemia. [(7, 8)] Another probable cause of hypokalaemia and other electrolyte imbalances in some COVID-19 patients may be due to gastrointestinal losses such as diarrhoea and vomiting presenting in as many as 34.0% of cases. [(9)]

These electrolyte disturbances, if detected at the earliest, have important implications, both from the point of view of patient management as well as for identifying potential pathophysiological mechanisms underlying COVID-19, that could enable clinicians to drive novel therapeutic considerations for emergent conditions such as dyselectrolytemias, thereby benefitting the patient both clinically and economically. [(10)]

Ion-selective electrode (ISE) method is most routinely used for electrolyte estimation in clinical laboratories. There are two types of ISE measurements based on sample preparation. Direct ISE uses an undiluted sample to interact with ISE membrane, while the devices based on indirect ISE use pre-analytical dilution. Direct ISE may use either whole blood as in the case of an arterial blood gas (ABG) analyzer, or serum as in the case of auto-analysers (AAs). [(6)] It is important to determine the concordance of electrolyte values obtained by these two devices. However, electrolytes measured by ABG analysers, are seldom trusted for clinical decision-making due to the dearth of published research regarding the same. [(10)]

In our study, sodium values of AA and ABG analyzer were compared against categories of age and sex, and were found to be moderately correlated ($p < 0.01$). However, while comparing AA to ABG estimates according to pre-defined electrolyte range groups, we found out that the sodium values were not comparable. The B-A's 95% limit of agreement for sodium was wide which was clinically not acceptable. As per AA & ABG estimates, 37.2 % and 55.1 % of total study population were hyponatremic, and 76.9 % and 38.5 % of the sample population was hypernatremic respectively. There was a significant difference between the analysing methods in these two groups ($p < 0.01$). Therefore, considering our study data, clinical decision making for sodium did not seem to be reliable with the ABG analyzer. However United States Clinical Laboratory Improvement Amendments (US CLIA) 1988 rule accepts a difference of 4 mmol/L in sodium levels, in the gold standard measure of the standard calibration solution. [(11)] In our study, the mean difference between the two Na^+ assays was 3.75 mmol/L, which was within the acceptable value of 4 mmol/L. This was contrary to the findings of Budak et al., Yilmaz et al. and Pant et al. [(12-14)]

However, in case of potassium, an AA to ABG results comparison according to pre-defined electrolyte range groups, and in the categories of age and sex distribution revealed that the potassium values were comparable in all categories. The levels were found to be equivalent within accepted limits, in all age categories of 18-35 yrs. ($r = 0.743$, $p < 0.01$), 36 – 49 yrs ($r=0.683$, $p<0.01$) and ≥ 50 yrs. ($r = 0.766$, $p < 0.01$) respectively. The B-A's 95% limit of agreement for potassium was narrow which was clinically acceptable. In our study, difference of means between the two K^+ assays was 0.087 mmol/L, which was within the acceptable value of 0.5 mmol/L as per US CLIA 1988 rule. [(11)] The studies by Budak et al., Yilmaz et al. and Pant et al. have also achieved similar results. [(12-14)] Therefore, considering our study data, clinical decision making for potassium can be reliably made with the ABG analyzer.

As per Berlin definition, [(15)] 28.2 % i.e., 44 patients in the sample population had developed ARDS and were sub divided into 3 categories on the basis of the PaO_2:FiO_2 ratio as Mild, Moderate and Severe ARDS. The Spearman correlation in paired samples showed strong correlation in mild and severe ARDS cases for sodium (r value 0.806 and 0.866 respectively) and for moderate and severe ARDS in case of potassium (r value 0.828 and 0.900 respectively).

VI. Conclusion

The present study has identified the prevalence of hypokalaemia in patients with varying degrees of severity of ARDS in COVID-19 infection. The degree of hypokalaemia has been shown to be significantly associated with both the ARDS severity as well as serum CRP, an indicator of the inflammatory state. An analysis of mean difference between the AA and ABG analyzer values for Na^+ have shown a significant difference in these two groups, which is however, within the US CLIA mandated limits for equivalence and acceptability.

Therefore, though there is a significant difference between the two platforms, ABG sodium estimates may be considered in real life emergencies warranting immediate decision making and rapid electrolyte corrections, though, after weighing the risks of miscalculation of the anion gap. In the case of potassium, the values obtained from the above analysers show no significant difference. Hence the ABG potassium value can be used to expedite management of hypokalaemia in COVID-19.

Conflict of interest

The authors declare no conflict of interest.

References

[1]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb 20;382(8):727-733.

[2]. Lippi G, South AM, Henry BM. Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19). Ann Clin Biochem. 2020 May;57(3):262-265.

[3]. Chen D, Li X, Song Q, Hu C, Su F, Dai J, et al; Assessment of Hypokalemia and Clinical Characteristics in Patients with Coronavirus Disease 2019 in Wenzhou, China. JAMA Netw Open. 2020 Jun 1;3(6): e2011122.

[4]. Moreno-P O, Leon-Ramirez JM, Fuertes-Kenneally L, Perdiguero M, Andres M, Garcia-Navarro M, et al; COVID19-ALC Research Group. Hypokalemia as a sensitive biomarker of disease severity and the requirement for invasive mechanical ventilation requirement in COVID-19 pneumonia: A case series of 306 Mediterranean patients. Int J Infect Dis. 2020 Sep 17; 100:449-454.

[5]. Xiong S, Liu L, Lin F, Shi J, Han L, Liu H, et al; Clinical characteristics of 116 hospitalized patients with COVID-19 in Wuhan, China: a single-centered, retrospective, observational study. BMC Infect Dis. 2020 Oct 22;20(1):787.

[6]. Scott MG, LeGrys VA, Klutts JS: Electrolytes and blood gases. In Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 4th edition. Edited by Burtis DE, Ashwood ER, Bruns DE. St Louis, MO: Elsevier; 2006:983–1018.

[7]. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al; SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020 Apr 16;181(2):271-280.e8.

[8]. Zhang J, Wang M, Ding W, Wan J. The interaction of RAAS inhibitors with COVID-19: Current progress, perspective and future. Life Sci. 2020 Sep 15; 257:118142.

[9]. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al; Clinical Characteristics of COVID-19 Patients with Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. Am J Gastroenterol. 2020 May;115(5):766-773.

[10]. Hoekstra M, Vogelzang M, Drost JT, Janse M, Loef BG, van der Horst IC, et al; Implementation and evaluation of a nurse-centered computerized potassium regulation protocol in the intensive care unit--a before and after analysis. BMC Med Inform Decis Mak. 2010 Jan 25; 10:5.

[11]. Ehrmeyer SS, Laessig RH, Leinweber JE, Oryall JJ (1990) 1990 Medicare/CLIA final rules for proficiency testing: minimum intralaboratory performance characteristics (CV and bias) needed to pass. Clin Chem 36:1736-1740

[12]. Budak YU,Huysal K, Polat M. Use of a blood gas analyzer and a laboratory autoanalyzer in routine practice to measure electrolytes in intensive care unit patients. BMC Anesthesiol. 2012 Aug 3; 12:17.

[13]. Yilmaz S, Uysal HB, Avcil M, Yilmaz M, Dağlı B, Bakış M, et al; Comparison of different methods for measurement of electrolytes in patients admitted to the intensive care unit. Saudi Med J. 2016 Mar;37(3):262-7.

[14]. Pant V, Tumbapo A, Karki B. Inter-instrumental comparison for the measurement of electrolytes in patients admitted to the intensive care unit. Int J Gen Med. 2017 May 16; 10:145-149.

[15]. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al; Acute respiratory distress syndrome: The Berlin Definition. JAMA. 2012 Jun 20;307(23):2526-33.

Dr. Smita Roy, et. al. "Role of Arterial Blood Gas Analysis in Rapid Assessment of Hypokalaemia in Covid – 19." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(01), 2021, pp. 06-13.