Original Article

DOI: 10.7860/NJLM/2020/44436:2411

Biochemistry Section

Reliability of Venous Electrolyte Measurement from the Point-of-Care Blood Gas Analyser- A Comparative Study with the Central Laboratory Autoanalyser in a Tertiary Care Emergency Department

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ABSTRACT

Introduction: Emergency Departments (EDs) utilise Point-Of-Care (POC) equipment based on which the physicians decide on resuscitation and management. Along with many other parameters, POC Blood Gas Analysers (BGA) in the ED provide quick results on blood electrolytes, enabling physicians manage dyselectrolytemia immediately compared to the prolonged turnaround time from Central Laboratory (CL) Auto Analysers (AAs). ED physicians usually wait for AA result for confirmation of dyselectrolytemia.

Aim: To compare sodium and potassium ions measurement in venous sample pairs between BGA and AA, and whether results from BGA could be acceptable as per standard norms, thus avoiding time delay in management of dyselectrolytemia and saving cost.

Materials and Methods: This prospective observational study was done in the ED of a tertiary care centre in North Kerala. After Institutional Ethics Committee approval and obtaining informed consent, the study was conducted in 224 adult patients during July 2018 to July 2019 with clinical indications for Venous Blood Gas (VBG) and serum electrolytes as part of management. Venous samples from the patients were collected successively in heparin rinsed syringes and plain bottles and analysed in the POC BGA (ABL800 Flex Radiometer) in the ED and AA in the hospital central laboratory (Beckman Coulter AU 5800), respectively. Mean, standard deviation and two-tailed p-value were used for statistical analysis. Bland-Altman plots, box plot and scatter diagram were used for inter instrument comparison of results.

Results: Out of 224 (122 males and 102 females) paired venous samples, the mean sodium (Na) were 131.6± 9.0 mmol/L (BGA) and 131.7±8.3 mmol/L (AA) with mean difference of 0.1 mmol/L. The mean patassium (K) was 3.6±0.7 mmol/L (BGA) and 4.0±0.77 mmol/L (AA) with mean difference of 0.4 mmol/L. The 95% limits of agreement for Na and K between equipment were -6.13 to 5.95 mmol/L and -1.28 to 0.6 mmol/L, respectively. Karl Pearson Correlation of Na and K assessment were 0.94 and 0.77 ($p<0.01$), respectively. These values were within the accepted limit of the United States Clinical Laboratory Improvement Amendments (difference of 4 mmol/L in sodium measurements and 0.5 mmol/L in potassium measurement from the gold standard). No Indian Clinical Laboratory Improvement Amendments were found.

Conclusion: The authors found no statistically significant difference between BGA and AA in sodium and potassium measurement. This will enable emergency physician to make critical decisions by trusting sodium and potassium values obtained from the POC BGA.

Keywords: Dyselectrolytemia, Potassium, Sodium

INTRODUCTION

With the popularity of Emergency Medicine subspeciality in developing countries, quality resuscitation and timely decision making and management of critically ill patients are expected by the community. POC equipment are widely used in EDs to aid in resuscitation and early management of seriously ill patients [1,2]. The ED physicians utilise POC equipment as adjuncts for the assessment, resuscitation, management and monitoring of patients. POC BGA provide immediate report on Arterial or Venous Blood Gas (ABG/VBG) parameters including serum electrolytes (sodium, potassium, calcium and chloride) along with other important variables including acid base, respiratory and metabolic parameters such as pH, PO_2, PCO_2, SpO_2, bicarbonate, lactate, creatinine, Haemoglobin (Hb), Haematocrit (Hct), bilirubin and glucose at affordable cost [3]. Both venous and arterial blood can be analysed as indicated.

Electrolytes are charged elements in the body fluids which are important determinants of proper functioning of the body. Two important positively charged electrolytes (cations) in the body are sodium (Na denoted as Na) and potassium (K denoted as K). The seriously ill patients presenting to the ED may have dyselectrolytemia as major presentation or as part of the clinical scenario necessitating resuscitation measures to alleviate mortality and morbidity. Conventionally, the electrolytes are measured in central Laboratory AAs using the serum from venous blood samples for analysis. The AAs, usually placed in the hospital CL, operate on the principle of Indirect Ion Selective Electrodes (ISE), analyse the serum samples with fixed volume diluent, fetch long processing time and their results depend on protein levels in the blood [3-5]. The results of indirect ISE devices are generally comparable to the recognised reference method, flame photometry and can be assumed to be gold standard [6].

Direct potentiometric measurement of Na and K levels in whole blood and plasma were found to be essentially identical [7]. BGAs are based on direct ISE and utilise heparinised whole arterial or venous blood, have short processing time and measurement is not affected by the protein level in the blood which is an advantageous factor in critically ill patients with hypoproteinaemia [4].

The transport of the samples from ED to CL, separation of serum from the blood, the processing of AA, documentation and collection of results can take valuable time averaging to more than one hour in different hospitals in comparison with BGAs placed in the ED which provide results in less than three minutes with less volume of blood. But many a time, the ED physicians are hesitant to manage dyselectrolytemia based on BGA report alone due to the dilemma whether the values are accurate enough to institute corrective measures. It is a trend to confirm the electrolyte results from AA, loosing golden hours of resuscitation leading to possible negative outcome. To manage the patients on electrolyte disturbances based on BGA reports, it is mandatory to study and document the agreement of the same with the AA reports. If the reports on electrolytes are reliable, dyselectrolytemia can be managed timely without additional expense and manpower.

It is ideal to study the concordance of electrolyte values from AA and BGA for each hospital and each POC device even if the devices utilise the same type of ISE. The United States Clinical Laboratory Improvement Amendments (US CLIA) accept a difference of 4 mmol/L in the measurement of Na and 0.5 mmol/L in the measurement of K from the gold standard calibration solutions measurement value [8].

The fact that present day EDs and Intensive Care Units (ICUs) are equipped with number of POC BGAs also necessitate more studies to evaluate these devices for concordance of results with the AAs. The present study was aimed to compare whether the levels of Na and K measured by BGA and AA are in agreement. There was a plan to evaluate the results and find whether the differences were statistically significant and whether the differences were within the accepted range proposed by the US CLIA. Thus the present study was to guide the ED physician about the reliability of Na and K measurement on BGA in comparison to AA on successively collected venous samples so that management practices may be modified to reduce the manpower and cost.

MATERIALS AND METHODS

After the institutional ethics committee approval (No: G1 2747/12/ACME) the prospective observational study was conducted in ED and CL of Government Medical College, Kannur, Pariyaram, a tertiary centre in North Kerala for one year from July 2018 to July 2019.

The sample size was calculated using the below formula:

$\acute{\eta} = 2S_P^2 \{Z_{1-}\alpha_{/2} + Z_{1-}\beta\}/\mu_d^2$

$Sp^2 = S1^2 + S2^{2/2}$

S_1 = Standard deviation in the first group

S_2 = Standard deviation in the second group

µd = Mean difference between the sample (Effect size)

α = Significance level

1-β = Power

Level of significance fixed at 5% (corresponding standard variate value 1.96) of Power fixed at 5% (corresponding standard variate value 0.84)

A sample size of minimum two hundred subjects was required for the present study. A total of 224 patients were enrolled in the study.

Patients above 18 years presenting to the ED in whom VBG measurement and serum electrolyte measurement were considered as part of their management course, were enrolled for the study.

Patients under 18 years, pregnant patients, patients without consent, haemolysed samples and samples in which the blood was not collected simultaneously were not included in the study.

After obtaining informed consent, venous samples were collected consecutively in the same sitting in heparin rinsed plastic syringes (for BGA) and plain bottles (for AA) and sent for processing. VBG samples were collected in 2 ml plastic syringes rinsed with liquid heparin in which 0.1 mL heparin is withdrawn and rinsed and emptied completely and blood sample processed immediately (withih 30 seconds) in the POC BGA in the ED (ABL 800 Flex Radiometer, Copenhagen, Denmark) which works on the principle of direct ISE technology. The manually transported samples to the hospital CL were centrifuged, serum separated and electrolytes were measured on AA (Beckman Coulter AU 5800 Inc., Miami, FL, USA), which works on the principle of indirect ISE technology. The BGA and the AA were well calibrated as per manufacturers' instructions.

The normal reference ranges for Na and K were 135-145 mmol/L and 3.5-5.0 mmol/L, respectively.

STASTICAL ANALYSIS

The reports from BGA and AA were analysed with the statistical tests. Mean, standard deviation and two-tailed p-value were calculated with $p < 0.05$ considered as statistically significant. Bland-Altman plots, box plot and scatter diagram were used for inter instrument comparison of results [9].

RESULTS

A total of 224 {122 males (54%) and 102 females (46%)} paired venous samples were analysed. The age distribution showed majority of the patients were above 40 years of age [Table/Fig-1].

Age*	Number	Percent
≤30	22	9.8
31-40	22	9.8
41-50	31	13.8
51-60	31	13.8
61-70	51	22.8
71-80	39	17.5
81-90	28	12.5
Mean±SD	59±18.7	

[Table/Fig-1]: Percentage distribution of the sample according to age.
*: in years; SD: Standard deviation

The mean difference between the BGA Na value and the AA Na value was 0.1 mmol/L. The mean difference between the BGA K value and the AA K value was 0.4 mmol/L [Table/Fig-2].

Samples (224)	Mean±SD*	Mean Difference*
VBG Na†	131.6±9.0	0.1
AA Na‡	131.7±8.3	
VBG K†	3.6±0.7	0.4
AA K‡	4.0±0.7	

[Table/Fig-2]: Na (Sodium) and K (Potassium) assessed using VBG and AA.
*: in mmol/ L; †VBG Na: Venous blood gas sodium; ‡ AA Na: Auto analyser sodium; †VBG K: Venous blood gas potassium; ‡ AA K: Auto analyser potassium

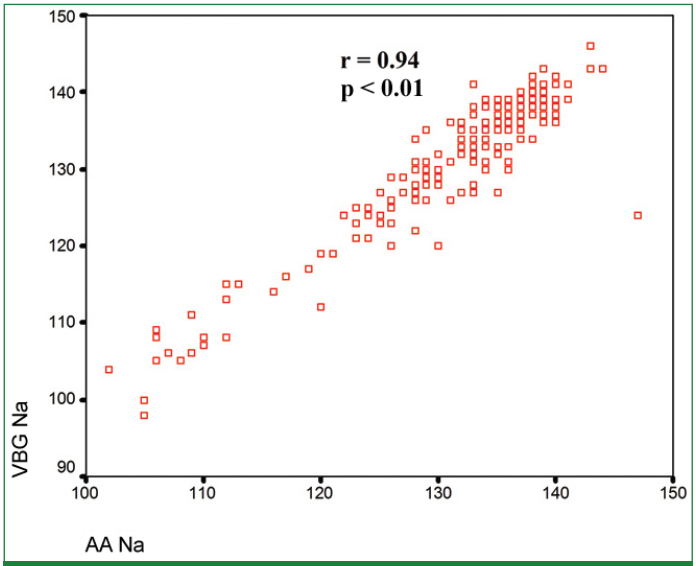
According to the Karl Pearson correlation test, a strong positive correlation was detected between serum Na ($r = 0.94$, $p<0.01$) and moderately strong positive correlation for K ($r=0.77$, $p<0.01$) [Table/Fig-3-5].

Electrolyte	r*	p†
Na (Sodium)	0.94	p<0.01
K (Potassium)	0.77	p<0.01

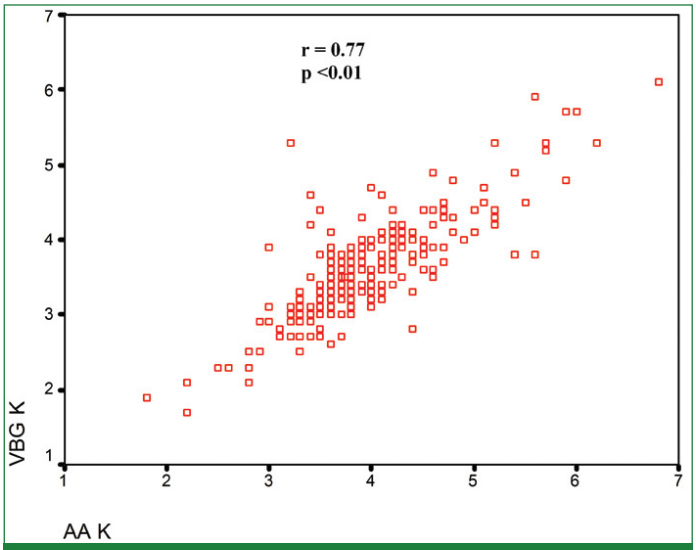
[Table/Fig-3]: Karl Pearson Correlation of Na and K assessed by VBG and AA.
*: r-Karl Pearson Correlation Coefficient; †: p<0.05 is statistically significant

On VBG Na analysis median, maximum value and minimum value were found to be 135 mmol/L, 146 mmol/L and 98 mmol/L, respectively while on AA Na analysis they were found to be 134 mmol/L, 147 mmol/L and 102 mmol/L, respectively [Table/Fig-6]. Similarly, On VBG K analysis median, maximum value and minimum

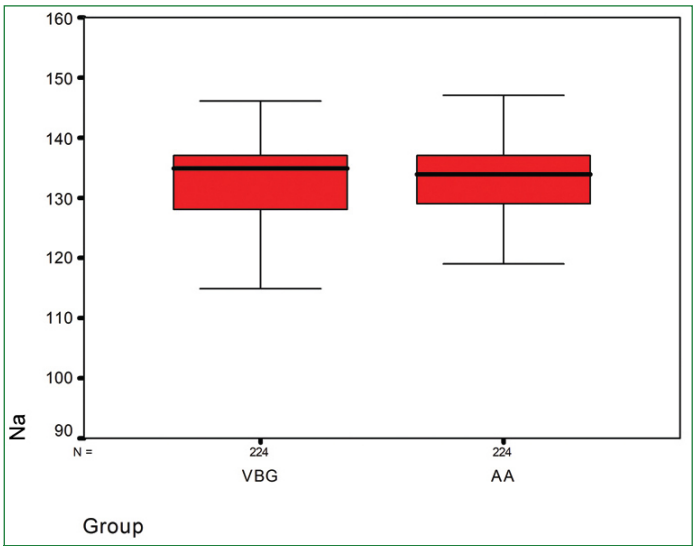
value were found to be 3.6 mmol/L, 6.7 mmol/L and 1.7 mmol/L, respectively while on AA K analysis they were found to be 3.9 mmol/L, 6.8 mmol/L and 1.8 mmol/L, respectively [Table/Fig-7].



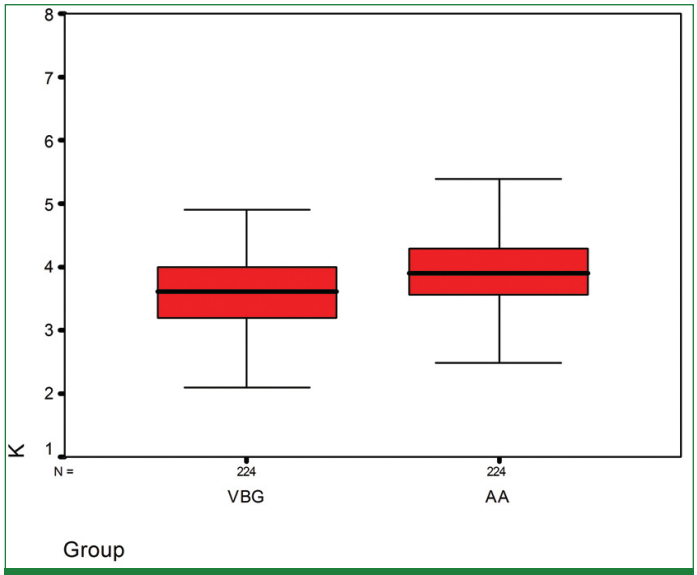
[Table/Fig-4]: Scatter diagram for Na assessed using VBG and AA.
VBG Na: Venous sodium assessed in blood gas analyser; AA Na: Serum sodium assessed in auto analyser



[Table/Fig-5]: Scatter diagram for K assessed using VBG and AA.
VBG K: Venous potassium assessed in blood gas analyser; AA K: Serum potassium assessed in auto analyser

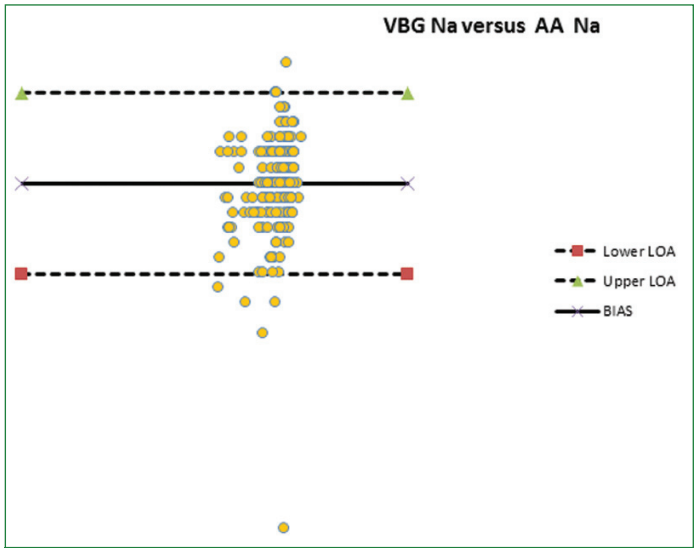


[Table/Fig-6]: Box plot for Na assessed using VBG and AA.
VBG Na analysis Median= 135 mmol/L; Maximum value= 146 mmol/L; Minimum value =98 mmol/L AA Na analysis Median = 134 mmol/L; Maximum value= 147 mmol/L; Minimum value=102 mmol/L

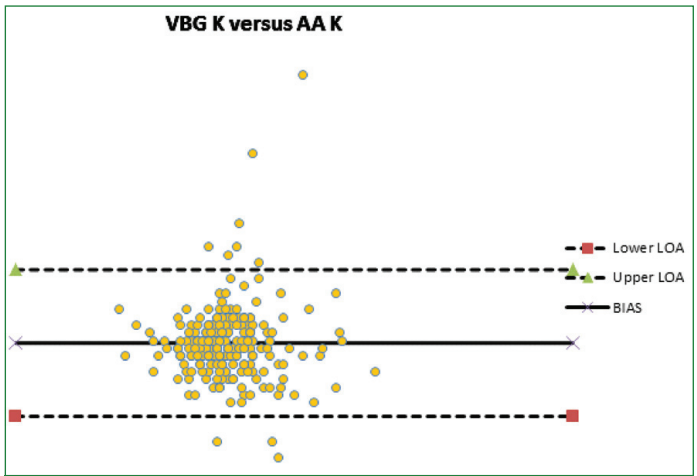


[Table/Fig-7]: Box plot for K assessed using VBG and AA.
VBG K analysis Median= 3.6 mmol/L; Maximum value= 6.7 mmol/L; Minimum value= 1.7 mmol/L AA K analysis Median = 3.9 mmol/L; Maximum value= 6.8 mmol/L; Minimum value= 1.8 mmol/L

The 95% limit of agreement for Na and K were -6.13 to 5.95 mmol/L [Table/Fig-8] and -1.28 to 0.6 mmol/L [Table/Fig-9], respectively.



[Table/Fig-8]: Bland Altman plot for Na assessed using VBG and AA.
The bias in VBG Na measurement was -0.09; The 95% limit of agreement was -6.13 to 5.95 mmol/L; LOA: Limit of agreement; VBG Na: sodium measured in venous blood in blood gas analyser; AA Na: sodium measured in auto analyser



[Table/Fig-9]: Bland Altman plot for K assessed using VBG and AA.
The bias in VBG K measurement was -0.34 mmol/L. The 95% limit of agreement was -1.28 to 0.6 mmol/L; LOA: Limit of agreement; VBG K: potassium measured in venous blood in blood gas analyser; AA K: potassium measured in auto analyser

DISCUSSION

The results of the present study showed a strong correlation and relatively good acceptable agreement for Na and K measurement between BGA and AA.

Different studies compared devices of different manufacturers equipped in the corresponding hospitals so that the investigators must take caution on application or generalisation of inferences from these studies [10]. The most common electrolyte abnormalities presenting in ED which determine morbidity and mortality are hyponatremia (<135 mmol/L) leading to neurological complications and hyperkalemia (>5 mmol/L) leading to defective muscular function and cardiac arrhythmia, both of which need immediate management [11]. Prompt correction is usually warranted only if hyponatremia is <120 mmol/L or hyponatremia with neurological manifestations. Investigators have found some pre analytical bias leading to difference in estimation of ions. Use of different syringes or containers with anticoagulant may be a reason [12].

Underestimation of ions in indirect ISE based AAs in hyperproteinemia due to increased volume of diluents or unexpected increase of solid particles like proteins and albumin in blood and vice-versa can lead to pre analysis bias [13]. Pneumatic transport system can cause haemolysis and estimation of K may be increased [14,15]. In BGA sample, haemolysis may not be detectable [16]. Time elapse between blood withdrawal and estimation can influence K estimation [15]. Dilution of sample with liquid heparin rinsed syringes can result in lower electrolyte estimation [17]. Heparin itself can bind with positively charged ions in blood and lower the value [18].

There are few studies in agreement with the present study results suggesting the venous electrolyte measurement from the POC BGA were reliable. The study by Pouryahya P et al., demonstrated good positive correlation between VBG and laboratory biochemistry measurements of Na, K and creatinine, with the exception of K in acidaemia [19]. Study by Kozacı N et al., demonstrated statistically significant positive correlation between venous blood Na, K, Cl, Hb and Hct values between BGA and standard automated devices in laboratory [20]. Similarly Ahmet K and Ebru C. in 418 adult patients found a strong positive correlation between serum Na, K, glucose and haemoglobin values and blood gas Na, potassium, glucose and haemoglobin values ($r = 0.764$, $p < 0.001$; $r = 0.867$, $p < 0.001$; $r = 0.969$, $p < 0.001$, $r = 0.846$, $p < 0.001$, respectively). They concluded that in critically ill patients in ICU with life-threatening diseases, the rapid blood gas tests might be considered for the treatment planning until the results of the biochemical examination were available [21]. Corbacioglu SK et al., in a retrospective study evaluated the correlations between the results of BGA and AA in 1,374 patients and found that there was strong correlation for K ($r=0.83$, $p<0.001$) while there was poor correlation for Na values. In addition, they found that the different pH stages did not affect these results [22].

In contrast to this study finding, Bozkurt S et al., found a significant difference between laboratory K values and VBG potassium values and they suggested that it was not appropriate to use VBG K value instead of laboratory potassium value [23]. Similarly Ayhan H et al., found statistically significant difference between BGA and AA K results in the normal pH group ($p<0.01$). However, no statistcally significant difference was found between BGA and biochemistry Na results in all pH values or between BGA and biochemistry potassium results in acidic and alkaline blood [24].

Awasthi S et al., studied the extent of correlation between arterial and peripheral venous samples for pH, bicarbonate, base excess, and electrolytes in a group of ICU and critically ill patients. They found that there was a statistically significant, highly positive correlation between K, Na, glucose and haemoglobin values ($r=0.764$, $p <0.001$; $r=0.867$, $p<0.001$; $r=0.969$, $p<0.001$; $r=0.846$, $p<0.001$, respectively) [25]. Johnston HL and Murphy R studied agreement between arterial and venous blood in the measurement of K in patients with cardiac arrest. They found that mean difference between each pair of arterial and venous K measurement was low at 0.106 mmol/L [26].

Complications like local haematoma, dissection and thrombosis are less in venous puncture than in arterial puncture [25]. So, venous blood sampling may be a useful alternative to ABG sampling for electrolyte measurements as evident from the present study. Unlike CL tests where turnaround time varied from one hour to one and half hours, POC BGA could provide results in few minutes.

Limitation(s)

In the present study, plastic syringes were used for collection of VBG samples but the blood was processed within 30 seconds. The bias caused by triglyceride and protein level in indirect ISE based estimation of sodium and K in AA was not taken into consideration. Subcategory analysis of normal, high and low electrolyte levels was not done due to low sample size on subgrouping. Though the AA results were assumed to be the gold standard, due to various confounding factors and bias, the authors were not certain whether the AA/BGA results are really close to the “true” value.

CONCLUSION(S)

In the present study, Na and K measured with the POC BGA device and laboratory AA were comparable and were within the accepted range of US CLIA amendments norms. Venous blood Na and potassium measurement from the POC BGA were reliable. These results can be used for initiating resuscitation and management and monitoring in critically ill patients in ED.

Acknowledgments

The authors are grateful to Dr Suresh G and Dr Sherin Stephen for their guidance and support. The authors are also thankful to Dr Vani Axita for her valuable suggestions and help. The authors thank the physicians, nursing staff, nursing assistants of ED and the laboratory technicians of the Central Clinical Laboratory for their support.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Mar 27, 2020
- Manual Googling: May 09, 2020
- iThenticate Software: Sep 15, 2020 (17%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Mar 26, 2020**
Date of Peer Review: **Apr 23, 2020**
Date of Acceptance: **Jul 02, 2020**
Date of Publishing: **Oct 01, 2020**