Point of care testing of serum electrolytes and lactate in sick children

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ARTICLE

Objective
To evaluate the electrolyte and lactate abnormalities in hospitalized children using a point of care testing (POCT) device and assess the agreement on the electrolyte abnormalities between POCT and central laboratory analyzer with venous blood.

Methods
This observational study recruited hospitalized children aged 1 month to 12 years within two hours of admission. A paired venous sample and heparinized blood sample were drawn and analyzed by the central laboratory and POCT device (Stat Profile Prime Plus-Nova Biomedical, Waltham, MA, USA) for sodium and potassium. Lactate was measured on the POCT device.
only. The clinical and outcome parameters of children with electrolyte abnormalities or elevated lactate (>2mmol/L), and the agreement between POCT values and central laboratory values were assessed.

Results

A total of 158 children with median (IQR) age 11 (6-10) months and PRISM score 5 (2-9) were enrolled. The proportion of children with abnormal sodium and potassium levels, and acidosis on POCT were 87 (55.1%), 47 (29.7%) and 73 (46.2%), respectively. The interclass coefficient between POCT and laboratory values of sodium and potassium values was 0.74 and 0.71 respectively; P<0.001. Children with hyperlactatemia (81, 51.3%) had higher odds of shock (OR 4.58, 95% CI: 1.6-12.9), mechanical ventilation (OR 2.7, 95% CI 1.1-6.6, P=0.02) and death (OR 3.1, 95% CI 1.3-7.5 P=0.01) compared to those with normal lactate.

Conclusion

POCT can be used as an adjunct for rapid assessment of biochemical parameters in sick children. Lactate measured by POCT was a good prognostic indicator.

INTRODUCTION

Point-of-care testing (POCT) is being increasingly used in the emergency department (ED) and the intensive care unit (ICU) to enable the rapid assessment of biochemical, microbiological and radiological evaluations both for single-point assessments and serial monitoring of sick patients. POCT for blood tests circumvents several steps in central laboratory testing including specimen transportation and processing, resulting in faster turn-around time preventing unnecessary delay in clinical decision. These tests require significantly less blood making them a good option for pediatric patients. Early recognition and management of common electrolyte abnormalities are important in the final outcome of the patient. Critical illness may trigger an acute phase response which is associated with several metabolic, electrolyte and acid-base derangements. The presence of these disorders typically reflects the underlying pathology and may be associated with poor outcomes.

Measurement of electrolytes and lactate using a POC blood gas analyzer has shown good agreement with a central laboratory analyzer in several studies, although others have raised concerns regarding their accuracy and reliability. This study was planned in the pediatric department of a tertiary hospital with the aims to assess the proportion of electrolyte and lactate abnormalities in hospitalized children using a POCT device and check the agreement between the electrolyte abnormalities measured by POCT device and venous blood analyzed in the central laboratory.

METHODS

The study was conducted in the pediatric department of a tertiary hospital after permission from the ethics committee of the institute between March-July 2019. Children aged 1 month to 12 years admitted to the pediatric emergency department were assessed for enrollment after parental consent. Criteria for hospitalization were defined based on emergency or priority signs as per Facility based-Integrated Management of Maternal, Neonatal and Child Illnesses (F-IMNCI), which were respiratory distress, cyanosis, shock, coma, seizures, altered sensorium, lethargy, poisoning, bilateral pedal edema, bleeding and anemia requiring transfusion. In addition, as per the unit’s protocol, any patient requiring a surgical intervention, jaundice with decompensation, unexplained fever for seven days, acute flaccid paralysis or poisoning were also admitted. Children with known tubulopathy, severe...
acute malnutrition, diarrhea and chronic malabsorptive states who were predisposed to develop disease related electrolyte abnormalities were excluded from the study.

Clinical history and examination were noted on a predesigned Performa. PRISM III score\textsuperscript{11} was used to assess the severity of illness. The duration of hospitalization and disposition (death/discharge/abscond/left against advice) was recorded. A concurrent two mL venous sample for serum analysis and 0.5 mL heparinized venous blood sample were drawn within two hours of admission after stabilization. The serum sample was analyzed in the central laboratory for case-based management which included measurement of blood urea, creatinine, sodium and potassium. The Stat Profile Prime Plus (Nova Biomedical, Waltham, MA, USA) blood gas analyzer using whole blood co-oximetry technology was used for POCT for blood pH, bicarbonate, blood oxygen, carbon dioxide, lactate, sodium and potassium. The proportion of children who had abnormal electrolytes, blood-gas disturbances or elevated lactate on POCT analysis was recorded. An agreement of POCT values was validated with the concurrently sampled venous blood values. The normal range of sodium and potassium were considered as 135-145 meq/L and 3.5-5.5 meq/L, respectively. The upper limit of normal for BUN was 18mg/dL\textsuperscript{12}, and for lactate 2mmol/L\textsuperscript{13}. A difference of up to 4 mEq/L for sodium and 0.5 mEq/L for potassium between the central laboratory and POCT were considered acceptable as per the United States Clinical Laboratory Improvement Amendment (US CLIA) 2006\textsuperscript{14}.

Sample size: Sample size was calculated using a study by Naseem et al\textsuperscript{15} where electrolyte abnormality was seen in 84% children aged 1 mo-12 yr admitted to the pediatric ICU. The sample size at 5% error and 90% CI was 146 children.

**Statistical analysis**

All analyses were performed using Stata version 15.1 for Windows (Stata Corp., College Station, TX, USA). Quantitative variables were expressed as mean/median and Standard deviation/IQR, and qualitative variables were expressed as proportions (%). A p-value <5% was considered to be statistically significant. Data distribution was checked by Normal probability plot and Kolmogorov-Smirnov normality test. For the comparison of two groups, student’s t-test was used if following normal distribution, otherwise Mann Whitney U-test was used. Paired t-test was used to test the mean difference between two sets of observations. Intraclass correlation coefficients (ICC) were calculated to determine the agreement between POCT and venous blood values. Qualitative variables were compared between the two groups using Chi-square test or Fisher’s exact test. For the comparison of more than two groups One-way analysis of variance followed by Bonferroni correction for multiple comparison was applied. Pearson’s correlation coefficient between study variables were calculated along with the assessment for the significance of these correlations. Odds Ratios (95% CI) were calculated for study variables associated with outcome.

**RESULTS**

A total of 197 children were screened, out of which 25 with diarrhoea, 4 with malabsorption, 7 with severe acute malnutrition and 3 with renal tubular acidosis were excluded. A total of 158 (66.4% boys) children with median (Q1,Q3) age of 11 (6-10) months were included in the study with outcomes available for 138 children, as others were still admitted at the end of study period. BUN and serum creatinine measurements were available for 28 children.

The disease wise distribution and proportion of electrolyte abnormalities is shown in Table 1.
### Table 1  Demographic and laboratory parameters of the study group (n=158)

| Parameter                      | Value n (%)  |
|--------------------------------|--------------|
| **Diagnosis**                  |              |
| Pneumonia                      | 56 (35.4%)   |
| Sepsis                         | 32 (20.2%)   |
| CHD                            | 32 (20.2%)   |
| Shock                          | 25 (15.8%)   |
| Seizures                       | 18 (11.4%)   |
| Meningitis                     | 6 (3.8%)     |
| Liver failure                  | 5 (3.2%)     |
| Others                         | 9 (5.7%)     |
| **Outcome (n=138)**            |              |
| Discharge                      | 100 (72.5%)  |
| Leave against advice           | 6 (4.3%)     |
| Death                          | 30 (21.7%)   |
| Abscond                        | 4 (2.9%)     |
| Acidosis                       | 73 (46.2%)   |
| Alkalosis                      | 3 (1.9%)     |
| Elevated Lactate               | 81 (51.3%)   |
| Ventilated                     | 28 (17.7%)   |
| †Duration of stay (d)          | 7 (4-10)     |
| ‡Duration of mechanical ventilation (hr) | 22 (18-25.7) |
| PRISM III, score*              | 5 (2-9)      |
| ‡pH                            | 7.32 ( 0.15) |
| †Bicarbonate (mEq/L)           | 16.9 (12-20) |

†Median (IQR); ‡Mean (SD); #the percentage of diagnoses adds to more than 100 as few patients had more than one diagnoses. CHD- congenital heart diseases; POCT- point of care testing; PRISM pediatric risk of mortality.
Hyponatremia and hypernatremia was found in 58 (37.7%) and 9 (5.7%) of the serum samples while hypokalemia and hyperkalemia was seen in 13 (8.3%) and 24 (15.2%) of the samples. The agreement between the laboratory and POCT device values (n=152) was good for all the above parameters as shown in Table 2.

The difference between sodium and potassium serum and gas values for different electrolyte ranges is also shown in Table 2. There was no significant difference in the proportion of sodium abnormalities between patients with PRISM III score >10 and <10 (P =0.16).

The odds of mechanical ventilation were not increased with abnormal sodium (OR 1.06 95% CI 0.4-2.4, P=0.87) or abnormal potassium (OR 1.3 95% CI 0.5-3.4, P=0.55).

The odds of death were not increased with sodium (OR, 95% CI 1.1, 0.5-2.5; P=0.79) and potassium abnormalities (OR, 95% CI 2.2, 0.89-5.7; P=0.08).

| Parameter | Laboratory value, mean (SD) | POCT value, mean (SD) | Interclass correlation (95% CI) | Mean difference (95% CI) | P value |
|-----------|-----------------------------|-----------------------|-------------------------------|--------------------------|---------|
| Sodium (meq/L) | 136.20 (7.3) | 133.6 (7.1) | 0.74 (0.64-0.84) | -2.56 (-3.64, -1.48) | **≤0.001 |
| Potassium (meq/L) | 4.60 (0.9) | 3.94 (0.8) | 0.71 (0.60-0.80) | -0.66 (-0.59, -0.73) | **≤0.001 |
| Sodium >145 meq/L | 152.86 (11.7) (n=9) | 149.46 (3.1) (n=9) | - | -3.4 (-12.85, 6.05) | 0.41 |
| Sodium 135-145 meq/L | 137.02 (2.1) (n=91) | 138.62 (2.0) (n=71) | - | 0.41 (-0.65, 1.47) | 0.43 |
| Sodium <135 meq/L | 130.21 (3.0) (n=58) | 128.94 (3.9) (n=78) | - | -1.27 (-2.41, -0.13) | *0.03 |
| Potassium >5.5 meq/L | 6.70 (0.4) (n=24) | 5.90 (0.4) (n=8) | - | -0.80 (-1.38, -0.23) | *0.02 |
| Potassium 3.5-5.5 meq/L | 4.51 (0.05) (n=121) | 4.03 (0.04) (n=111) | - | -0.48 (-0.6, -0.37) | **<0.001 |
| Potassium <3.5 meq/L | 2.89 (0.15) (n=13) | 2.75 (0.15) (n=39) | - | -0.14 (-0.51, 2.3) | 0.42 |

POCT: point of care testing; mean difference = POCT - laboratory value; *P<0.05; **P ≤0.01.
Patients with sepsis had higher odds of abnormal serum sodium compared to those without (OR, 95% CI 3.0, 1.3-6.7; P=0.006), unlike patients with CHD (OR, 95% CI 0.97, 0.4-2.1; P=0.95).

The odds of potassium abnormality were not significant in those with sepsis (OR 1.0, 95% CI 0.4-2.7, P=0.87) and or CHD (OR, 95% CI 1.3, 0.5-3.3, P=0.52).

The median (Q1, Q3) of lactate by POCT was 2.1 (1.3-3.4) mg/dL, range 0.8-17.2. Table 3 shows differences in various clinical and biochemical parameters in patients with or without hyperlactatemia. Children with hyperlactatemia had higher odds (OR, 95% CI) of shock (4.58, 1.6-12.9, P=0.002), acidosis (2.9, 1.51-5.59, P=0.001), mechanical ventilation (2.7, 1.1-6.6, P=0.02) with longer duration of ventilation (P=0.01) and death (3.1, 1.3-7.5 P= 0.01) compared to those with normal lactate.

Lactate levels had significant positive correlation with PRISM III score (r=0.45, P<0.001), while it negatively correlated with duration of stay (r=-0.14, P=0.09).

| Table 3 | Comparison of clinical parameters between normal and raised lactate (N=158) |
|---------|--------------------------------------------------------------------------------|
| Parameter | Normal lactate, n(%) (n=77) | Hyperlactatemia, n(%) (n=81) | P value |
| †Age (Months) | 11 (4.5,66) | 10 (3,39) | 0.78 |
| §Death | 8 (12.5%) (n=64) | 22 (29.7%) (n=74) | **0.01 |
| Shock | 5 (6.5%) | 20 (24.7%) | **0.002 |
| Sepsis | 13 (16.9%) | 19 (23.5%) | 0.94 |
| CHD | 15 (19.5%) | 17 (20.9%) | 0.87 |
| Ventilation | 8 (10.4%) | 20 (24.7%) | *0.02 |
| Acidosis | 25 (32.5%) | 48 (59.3%) | **0.001 |
| †Duration of stay (d) | 7 (4-10) | 7 (4,10) | 0.24 |
| †PRISM III | 4 (2,7) | 6 (2;11) | **<0.001 |
| †Duration of ventilation (hr) | 22 (18-40) | 22 (18-25) | **0.01 |
| ‡pH | 7.35 (0.11) | 7.29 (0.18) | 0.19 |
| ‡Bicarbonate (mEq/L) | 17 (5.7) | 15.4 (6.4) | **0.009 |

†Median (Q1,Q3); ‡Mean (SD); §Data not available in still admitted patients; *P<0.05; ** P ≤0.01; CHD- congenital heart diseases; PRISM pediatric risk of mortality.
DISCUSSION

The present study showed good agreement between the central laboratory and POCT for sodium and potassium. Lactate estimation by POCT was found to significantly predict illness and poor outcome.

The agreement between the laboratory and POCT device results for sodium is similar to earlier studies\(^1,6,16\), including one which used a similar method (ChemSTAT, Instrumentation Laboratories)\(^16\). Similar results were also reported for potassium earlier\(^6,16\) and better agreement by other studies\(^1,9\). It is postulated that the dilution and interaction of heparin in blood gas samples may decrease the electrolyte concentration in comparison to serum samples, as seen in the present study and also reported earlier\(^9,17\). There may be variability due to manually heparinizing the syringes for blood gas analysis which can introduce bias with the measurement of positively charged ions on a gas analyzer\(^3\).

The mean difference between the laboratory and POCT device sodium values was within the acceptable US CLIA limits\(^14\) for all ranges of sodium, unlike for potassium which was >0.5 mmol/L in the higher range. Hemolysis during collection of serum samples was potentially responsible for the higher serum potassium values. Studies have shown good association between lactate measured by serum and blood gas analyzers\(^7,13,18,19\) and handheld POC devices\(^20\).

A systematic review of over 3000 adult and pediatric patients demonstrated an advantage to measuring lactate in reducing mortality and duration of hospitalization in emergency settings\(^21\). Blood lactate levels at admission has consistently shown to be associated with mortality in sick children\(^16,21\).

However, unlike adults, sampling of sick children may be challenging in the emergency department and in states of shock. A significant percentage of children had hyperlactatemia as assessed by POCT in this study which was a predictor of severity of illness, outcome and need for ventilation, thus signifying its prognostic importance in both sepsis and non-sepsis conditions. A similar study demonstrated the role of POC measured lactate as a strong predictor of mortality in children with severe febrile illness\(^22\).

The reliability and advantage of clinical risk prediction of POC lactate was also concluded in umbilical cord samples (for perinatal hypoxia) compared by two separate handheld POC devices, blood gas machine and plasma lactate levels\(^21\). Arterial sample for lactate measurement which is considered as ideal for lactate measurement may be difficult and painful to obtain in sick children in the emergency. Venous lactate values have shown excellent agreement with arterial lactate during initial phase of sepsis in children\(^24\). Therefore, the utility of estimation of venous lactate by POCT device is further reiterated.

The present study was not powered sufficiently to conclude agreement between gas and blood samples, but showed acceptable difference for measurement of sodium and potassium at normal and extreme ranges. A lack of follow-up data of electrolyte measurements in the study population was a limitation. The serum lactate values were not measurable due to logistic issues and thus no comparison between POCT and laboratory lactate values could be made. There was no cost-effectiveness analysis for POCT in this study.

To conclude, POCT can be employed as an adjunct in the ICU and ED for rapid assessment of electrolytes, including lactate, which requires a smaller blood sample, and allows for quicker results, enabling faster decision making in sick children.
## What is already known?

1. Electrolyte abnormalities are common in sick children
2. Elevated lactate levels are associated with poor clinical outcomes
3. There is an increasing use of point-of-care devices for different laboratory parameters

## What this paper adds?

1. Point-of-care devices measured electrolytes in sick children with good correlation to serum values
2. Lactate measured by POCT was a good prognostic indicator for poor clinical outcomes

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(includes appropriate approvals or waivers)

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### Conflict of Interest:

None

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Point of care testing of serum electrolytes and lactate in sick children

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