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Clinical Utility of Blood Lactate Measurement in Patients with Sepsis

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Abstract Association between hyperlactatemia, organ dysfunctions, extended ICU stay and increased mortality has long been reported in cases of severe bacterial sepsis. It was also documented that elevated lactate levels provides assistance in early detection of patients at above mentioned risks and any probable adverse outcome. Therefore present study was undertaken to assess clinical utility of serum lactate measurement in patients with confirmed or suspected cases of sepsis and evaluation of its correlation in early identification of probable increased risk of organ dysfunction, extended intensive care unit (ICU) stay and/or any adverse outcome, such as mortality. Selected 266 patients were classified into hyperlactatemia and without hyperlactatemia. Hyperlactatemia is defined as Lactate ≥ 36.6 mg/dl. Characterization of involvement of systemic diseases and co-morbids in Sepsis patients' in both groups were documented and days of hospitalization and ICUs admissions were mentioned. Lactate was determined in serum by L-Lactate PAP (4-amino-antipyrine) colorimetric method on Roche's Cobas c501 chemistry analyzer. Initial venous lactate levels at the time of admission with suspected or confirmed sepsis were estimated followed by periodical estimation where applicable. The data is presented in mean ± SD and considered significant when $P < 0.05$. Data was analyzed using SPSS version 15 (USA) and compared among various age groups and gender. In present study we have observed more significant level of hyperlactatemia (≥ 36.6 mg/dl) in patients with sepsis, organ dysfunction (10.71%), SBI (25.00%) and admission to ICU (26.78%) as compared non-hyperlactatemia patients. Our data significantly correlated with clinical outcome, organ dysfunctions and prolong ICU stay advocating that an early detection of hyperlactatemia in sepsis patients may assist in early diagnosis of severity and probable prognosis.

Keywords Lactate, Sepsis, severe bacterial infection (SBI)

1. Introduction

In last few decades, despite gradual advances in diagnosis and management of sepsis, it remains a clinical condition of high mortality rate upto 25% to 50% [1-3]. Plethora of marked infection followed by sepsis, severe sepsis, Septic shock shall remain an important burden on clinicians and intensivist, besides availability of goal-directed therapies and some biomarkers for early recognition of sepsis [3-8. One of such biomarker is serum lactate; which is the end

product of anaerobic glycolysis and serves as an indicator of lactacidemia, perfusion, metabolic changes due to sepsis, bacterial load and critical illness [3, 9-15].

Several recent and past studies reported an association between hyperlactatemia and Increased mortality in cases of severe bacterial sepsis [3,16,17]. It was also documented that elevated lactate levels also provide assistance in early detection of patients at risk and any probable adverse outcome [3, 18].

Present study described clinical utility of serum lactate measurement in patients with confirmed or suspected cases of sepsis and evaluation of its correlation in early identification of probable increased risk of organ dysfunction, extended intensive care unit (ICU) stay and/or any adverse outcome, such as mortality.

2. Materials and Methods

2.1. Patients selection and Study Design: A total of 510 patients were screened for confirmed or suspected sepsis out of which 266 patients fall into inclusion criteria with confirmed presence of sepsis (pervious known history or currently admitted) or one of the related co-morbid indicator of suspected sepsis (3): temperature greater than 38^{o}C, heart rate greater than 90 beats/min, respiratory rate greater than 20 breaths/min, distorted psychological status. It was prospective cross-sectional observational study conducted during Study period was Dec 2014 to Dec 2016 at department of Biochemistry lab services and Chemical Pathology, and department of Clinical Microbiology, Liaquat National Hospital and Medical College, Karachi and Govt Lyari general Hospital-Karachi. Out of 266, n = 118 were females and n = 148 males within the age groups of 23-65 yrs in females and 27-66 yrs in males. Patients with age greater than 70 and less than 20, with recent history of surgeries, transplantation and diabetes, were excluded from the study. For retrieval of patient's demography, related clinical information, hospital admissions and Intensive care (ICU) stay, hospital information system, laboratory information system and electronic medical record were accessed and data documented. Clinical outcome was documented as type of Organ dysfunction, Blood culture with positive organism presence, Serious Bacterial Infections and Admission to Hospital, Admission to ICUs, Prior Admitted to hospital, and Treatments 1) IV antibiotics, 2) IV antibiotics + fluids and 3) oral antibiotics.

2.2. Patients grouping: Selected 266 patients were classified into hyperlactatemia and Without-Hyperlactatemia [3]. Hyperlactatemia is defined as Lactate ≥ 36.6 mg/dl. Characterization of involvement of systemic diseases and co-morbids that were noted in Sepsis patients' in both hyperlactatemia and non-hyperlactatemia groups and days of hospitalization and ICUs admissions were mentioned as Respiratory, Upper respiratory, Neurological, Renal, Hepatic, Cardiovascular and Hematological conditions.

2.3. Determination of Lactate: Lactate was determined in serum by L-Lactate PAP (4-amino-antipyrine) colorimetric method on Roche's Cobas c501 chemistry analyzer. The principle was based in the conversion of lactate into H_2O_2 and then to a purple colored end product after addition of TOOS (N-ethyl 2-OH-3-Sulphopropyl m-toluidine). Color intensity is directly proportional to increased lactate concentration in serum. Normal concentration of serum lactate is < 20 mg/dl. Initial venous lactate levels at the time of admission with suspected or confirmed sepsis were estimated followed by periodical estimation where applicable.

2.4. Statistical analysis: The data is presented in mean ± SD and considered significant when $P < 0.05$. Data was analyzed using SPSS version 15 (USA) and compared among various age groups and gender.

3. Results

Results are summarized in Tables 1 and 2. Out of 266 patients included in the study, 56 showed hyperlactatemia (Lactate ≥ 36.6 mg/dl) where as 210 were without hyperlactatemia. Number of hyperlactatemia patients falling in various categories of clinical outcome of both confirmed and suspected cases of Sepsis were noted to be Organ dysfunction= 6 (10.71%), blood culture with positive organism presence = 27 (48.21%), serious bacterial infections = 14 (25.00%), with admission to hospital = 23 (41.10%), admission to ICUs = 15 (26.78%), prior admission to hospital = 8 (14.28%), inclusive of under treatment with IV antibiotics = 24 (42.85%), IV antibiotics + fluids = 21 (37.50%) and oral antibiotics = 6 (10.71%). By comparison, in group of sepsis patients without hyperlactatemia (n = 210), subjects showed lower percentage of those either suffering from Organ dysfunction (n = 3; 1.4%), blood

culture with positive organism presence (n = 44; 20.95%), serious bacterial infections (n = 29; 13.80%), admission to hospital (n = 80; 38.09%) or to admission to ICUs (n = 34; 16.19%).

Observation of Systemic diseases and co-morbids involvements were noted in all sepsis patients and thus its characterization in both hyperlactatemia and non-hyperlactatemia groups and days of hospitalization and ICUs admissions were mentioned as Respiratory, Upper respiratory, Neurological, Renal, Hepatic, Cardiovascular and Hematological conditions. In hyperlactatemia group involvement of Respiratory system was noted in 11 patients (19.64%); Upper respiratory in 18 (32.14%), Neurological = 5 (8.9%), Renal = 6 (10.71%); Hepatic = 9 (16.07%); Cardiovascular = 12 (21.42%), and Hematological= 3 (5.35%). In non-hyperlactatemia group, similar systemic disease and organs dysfunctions were noted and specified as n = 101 (50.24%), n = 89 (44.27%), n = 13 (6.46%), n = 23 (11.44%), n = 45 (22.38%), 27 (13.43%) and 20 (9.95%), respectively.

Table 1: Confirmed and Suspected Sepsis patients' with *hyperlactatemia (n = 56) and without hyperlactatemia (n = 210)

Clinical Outcome	**N (%)** (**as compared to total number of patients in that group)**		**P < 0.05**
	Lactate ≥ 36.6 mg/dl (n = 56)	**Lactate ≤ 36.6 mg/dl (n = 210)**	
Organ dysfunction	6 (10.71)	3 (1.4)	0.01
Blood culture with positive organism presence	27 (48.21)	44 (20.95)	0.01
Serious Bacterial Infections	14 (25.00)	29 (13.80)	0.001
Admission to Hospital	23 (41.10)	89 (42.38)	0.001
Admission to ICUs	15 (26.78)	34 (16.19)	0.001
Prior Admitted to hospital Treatment	8 (14.28)	29 (13.80)	0.0001
1) IV antibiotics	24 (42.85)	85 (40.47)	0.001
2) IV antibiotics + fluids	21 (37.50)	65 (30.95)	0.001
3) oral antibiotics	06 (10.71)	17 (8.09)	0.01

*Hyperlactatemia is defined Lactate as ≥ 4.0 mmol/L or ≥ 36.6 mg/dl

Table 2: Involvement of systemic diseases and co-morbids in Sepsis patients' according to hyperlactatemia and non-hyperlactatemia and days of hospitalization and ICUs admissions

Diseases/Organ involvement	***Number of patients**	**Days Hospitalization/ICUs**
Hyperlactatemia (≥ 36.6 mg/dl)	N = 56 (% within group)	
• *Respiratory*	11 (19.64%)	5.15 ± 2.50
• *Upper respiratory*	18 (32.14%)	9.70 ± 5.25
• *Neurological*	5 (8.9%)	4.30 ± 3.10
• *Renal*	6 (10.71%)	10.15 ± 6.75
• *Hepatic*	9 (16.07%)	12.45 ± 5.50
• *Cardiovascular*	12 (21.42%)	10.25 ± 6.35
• *Hematological*	3 (5.35%)	7.30 ± 4.10
Non-Hyperlactatemia (≤ 36.6 mg/dl)	N = 201 (% within group)	
• *Respiratory*	101 (50.24%)	3.10 ± 2.45
• *Upper respiratory*	89 (44.27%)	7.45 ± 4.50
• *Neurological*	13 (6.46%)	3.35 ± 2.10
• *Renal*	23 (11.44%)	8.60 ± 5.15
• *Hepatic*	45 (22.38%)	9.75 ± 6.35
• *Cardiovascular*	27 (13.43%)	11.20 ± 7.10
• *Hematological*	20 (9.95%)	6.15 ± 3.15

*some patients also exhibited multiple disease/organs involvement

4. Discussion

In present study we have observed hyperlactatemia (≥ 36.6 mg/dl) more significantly in patients with sepsis, organ dysfunction (10.71%), SBI (25.00%) and admission to ICU (26.78%) than in non-hyperlactatemia patients. Nonetheless in both groups, systemic disease and organ dysfunction were similar and attributed to respiratory, upper respiratory, neurological, renal, hepatic, cardiac and hematological disorders. The results indicated a significant clinical utility of serum lactate measurements in patients either with suspected or confirmed cases of sepsis. Furthermore, our data significantly correlated with clinical outcome, organ dysfunctions and prolong ICU stay advocating that an early detection of hyperlactatemia in sepsis patients may assist in early diagnosis of severity and probable prognosis.

Earlier studies for measurement of lactate in sepsis patients demonstrated that lactate level is helpful in predicting outcome of acute conditions, especially serious bacterial infections (SBI) [12,19,20,21]. More importantly, in cases where initial episodes of SBI or

Sepsis is masked by co-morbidity, antibiotics or partial emergency treatments, indication of existence of hyperlactatemia proven to be a good indicator of proceeding severity and un favorable clinical outcome [12,15,21]. Previously, it was reported that elevated lactate level in sepsis patients is directly correlated with increased mortality and if treated at an early stage, will induce better outcome [3,13,15].

As observed in our study that a considerable number of hyperlactatemic patients developed organ dysfunction, earlier studies reported similar observations where chances of developing organ dysfunction were enhanced five folds in patients with hyperlactatemia [3, 22]. Association of serum lactate and systemic inflammatory response syndrome (SIRS) in cases of sepsis was also reported in pediatric patients where early detection of hyperlactatemia found significantly related to high risk of organ dysfunction, resuscitative therapies and critical illnesses [22]. Furthermore, it was also suggested that since lactate metabolism takes place in liver and kidneys, insufficiency of either or both also leads to hyperlactatemia and thus lactate assessment facilitates detection of shock processes [22].

5. Conclusion

In view of outcome of our study and evidences from other similar studies, it is, therefore concluded that lactate does provide important clinical utility and practical advantage in patients with sepsis or SBI/SIRS and facilitates urgent clinical decisions, minimizing risk and delays in treatment and management.

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