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Serum ammonia and serum lactate –predictingclinical outcome in critically ill children: A prospective study.

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ABSTRACT

Introduction: A significant number of children with systemic illness other than intrinsic liver disease show transient and early hepatic dysfunction related to hepatic ischemia and reperfusion injury and derangement of biochemical parameters related to circulatory failure, have prognostic importance. Serum ammonia and serum lactate was measured in critically ill patients and the hypothesis that hyperammonemia and hyperlactatemia is independently associated with an increased risk of hospital death was tested.

Methods: This observational study examined and measured serum ammonia and lactate of 61 critically ill patients (2 months- 12 years) admitted to pediatric intensive care unit (PICU), IPGME&R and SSKM Hospital, Kolkata, West Bengal, India from February 2018 – July2019. The relationship between level of this two parameters and hospital mortality was assessed.

Results: Higher lactate level was obtained in 26.7% and higher ammonia level in 60.7% of critically ill children and both are considered as a strong predictor of mortality (p value <0.019 and <0.038 respectively).

Conclusions: In critically ill children both hyperammonemia and hyperlactatemia are associated with increased risk of mortality. Hence, the current reference range for ammonia and lactate in critically ill may need to be re-assessed.

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Keywords: Hyperammonemia, Hyperlactatemia, critically ill children, prognosis.

Introduction

The liver is an orchestrator of metabolic arrangements and regardless of underlying pathological states, decrease hepatic microcirculation leads to disruption of biochemical milieu which affect about 50% of all intensive care patients. [(1)] Two prevalent biochemical abnormalities are hyperammonemia and hyperlactatemia. Higher blood ammonia and lactate level above normal reference range occur when their production exceeds clearance, when clearance capacity is decreased or more frequently when both occur simultaneously. [(2,3)] Serum serum lactate >2.5mmol/L are taken as abnormally high. [(4)] Serum lactate <2mmol/L are considered normal in critically ill individuals. [(5)] But in unstressed condition normal lactate concentration is 1 $\pm$0.5 mmol/L. [(6,7)] Hyperammonemia is usually defined as plasma level above 55 µmol/L in children above one month of age. [(8)] Critically ill children represent a uniquely vulnerable patient population characterized by their high susceptibility to a variety of life-threatening conditions. One of the major challenges in treating these patients lies in identifying and managing metabolic disturbances, which can have profound impacts on morbidity and mortality. Two metabolic biomarkers that have garnered substantial attention are hyperammonemia and hyperlactemia, which have been closely associated with adverse outcomes in critically ill children. Despite their clinical significance, the precise interplay between hyperammonemia, hyperlactemia, and mortality in critically ill children remains incompletely understood. Therefore, this observational study aims to investigate the underlying association linking these metabolic disturbances to adverse outcomes.

Methodology

Study design: This is a hospital based, prospective, observational study.

Place of study: This observational study was carried out at Pediatric Intensive Care Unit (PICU), Department of Pediatric Medicine, IPGME&R and SSKM Hospital, Kolkata, which is a tertiary care multispecialty hospital in Eastern India.

Study tools: One ml of EDTA blood for measuring serum ammonia, one ml of heparinized blood for measuring serum lactate, Cobas C 111 autoanalyzer for analyzing samples.

Study technique: After obtaining ethical clearance from the Institutional Ethics Committee, this study was conducted among the study population (2months-12years) after taking informed consent/assent (as applicable). During the first 15 months of study period all

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critically ill children admitted in PICU, satisfying inclusion and exclusion criteria, were thoroughly clinically examined. The term "critically ill" described as presence of any one of following five medical requirements or supports- a) mechanical ventilation, b) oxygen therapy >48 hours, c) inotrope infusion >24 hours, d) renal replacement therapy, e) blood/component transfusion

Free flow arterial blood samples were collected in separate tubes with prescribed temperature (2-8 ^{0}c) within 24 hours of admission for biochemical analysis. Samples were analyzed within10 minutes.

Statistical analysis: Data were collected, recorded, and compiled. Test of significance was analyzed using Statistical Package for Social Sciences (SSPS). This software used Statistica version6 and Graph Pad Prism version 5. p value <0.05 was considered significant. Outcome of this study was denoted by hospital mortality and length of stay (LOS) in PIC

Results and Analysis

A whole cohort of 61(n=61) was studied. Mean age of this cohort was 56.08 months. 39 children were discharged from PICU (discharged cohort n=39), 22 children died (expired cohort n=22). Mean length of stay (LOS) in PICU of total cohort was 9.41days. In our study most common initial clinical presentation was fever (74% cases) followed by respiratory illness (39% cases). Within the study population 43(70.5%) children were on mechanical ventilation, 55 (90%) children required prolonged O2 therapy either directly or post extubation and 31(51%) patients required inotrope support. These data revealed both overlapping of symptoms and therapeutic arrangements.

Regarding biochemical parameters, serum ammonia was elevated in 37 (60.7%) cases and serum lactate was raised in 16 (26.7%) cases. (Diagram -1).

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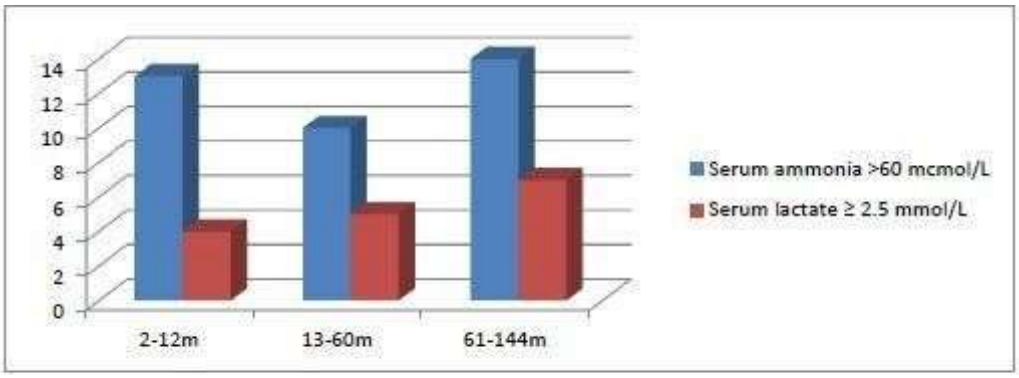
Diagram -1



Serum ammonia was increased in 37(60.7%) of cases and serum lactate was raised in 16(26.7%) cases.

Comparison of two parameters among discharged cohort and expired cohort revealed mean value of both serum ammonia and serum lactate were much higher in second group. Comparison was done by Student's unpaired t test and p value for both were < 0.05. Highserum ammonia and lactate above reference range were associated with increased risk ofhospital mortality. (Table -1)

Table 1

Showing comparison of serum ammonia and serum lactate between discharged and expired cohort

Parameters	Mean Value among discharged cohort	Mean Value among expired cohort	t-value	Degree of freedom(df)	p - value
Serum ammonia (µmol/L)	69.77	94.24	-2.127	59	**0.038**
Serum lactate (mmol/L)	1.90	2.70	-2.410	59	**0.019**

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Correlation between these biochemical parameters with length of PICU stay determined by Pearson's product moment correlation coefficient (r values) assuming linear correlation and we found that they did not have any correlation with LOS (r value -0.15 for both).

Discussion

Critical illness particularly shock and severe sepsis induces profound changes in the hepatic microcirculation. Decreased blood flow to liver leads to various biochemical derangements e.g., hyperammonemia and hyperlactatemia. Most affected primary organ systems resulting in PICU admission in our study was respiratory system in 24% of cases which was almost similar to earlier study conducted by Niederwanger et al [9] where 20.4% patient had respiratory involvement.

According to Abbas Q, Jamil MT, Khetpal V, Jafri L, Haque AU [(10)] hyperlactatemia was found in 33% cases where upper limit of serum lactate was taken as >4mmol/L and it was significantly associated with hospital death. But in our study,16 (26.7%) children had serum lactate level >2.5 mmol/L [(4)] and it was associated with increased risk of mortality (p value 0.019). The difference between this two studies could be due to variation of disease states,or duration of existing pathological conditions or time of measurement of lactate level.

Serum ammonia level was also found to be elevated in 37(60.7%) cases among total cohort and considered as a strong predictor of mortality (p value 0.038). Such observation with serum ammonia level was lacking after thorough review of related literature.

Conclusion

From this hospital based, prospective, observational study it can be concluded that early hepatic dysfunction is not rare in systemic diseases other than intrinsic liver disease. Serum lactate level >2.5mmol/L and serum ammonia >60µmol/L were a strong predictor of mortality, but they did not have any correlation with length of stay (LOS) in hospital. Early detection of biochemical alterations, related to hemodynamic changes in liver, may explore the scope of various therapeutic interventions in near future. Thus findings of this research will shed light on the association between hyperammonemia, hyperlactemia, and mortality in critically ill children, highlighting potential risk factors, prognostic implications, and therapeutic interventions. By expanding our knowledge in this field, healthcare professionals can make informed decisions, ultimately improving the critical care management and outcomes of these vulnerable patients.

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Limitations:

Being a single center, tertiary care-based study, all children had same ethnic origin. Hence conclusion drawn from this study may not be held true universally. Underlying undiagnosed primary disease might have some effect on biochemical alterations. Moreover, a few common PICU therapeutic intervention such as epinephrine, high volume hemofiltration (HVHF) with lactate- buffered replacement fluid can have effect on lactate level. Further multicentric study with a larger sample is required.

Conflict of Interest:

The authors declare that there is no conflict of interest.

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References:

1. Strassburg CP. Gastrointestinal disorders of the critically ill. Shock Liver. Best Pract Res Clin Gastroenterol. 2003; 17: 369-381.

2.Manikis P, Jankowski S, Zhang H, KhanRJ, Vincent JL: Correlation of serial blood lactate levels toorgan failure and mortality after trauma. Am J Emerg Med 1995,13: 619-622.

3.Vincent JL, DufayeP, BerreJ, LeemanM, Degaute JP, Khan RJ: Serial lactate determination duringcirculatory shock. Crit Care Med 1983,11:449-451.

4. Deshpande S A, Ward Platt M P. Acid-base and blood lactate in sick ventilatedbabies, Archives of Disease in Childhood 1997;76: F15–F20.

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5.Mizock BA: Lacticacidosis. Dis Mon 1989,35:233-300.

6. De Backer D: Lacticacidosis. Intensive Care Med 2003,29:699-702.

7.De Backer D: Lacticacidosis. Minerva Anestesiol 2003, 69: 281-284.

8. Savy et al: Hepatic Medicine: Evidence and Research 2018,10:105-115.

9. Niederwangeret al. Inflammatory and coagulatory parameters linked to survival incritically ill children with sepsis. Annals of Intensive Care (2018); 8:111: 2-10.

10. Abbas Q, Jamil M T, Khetpal V, Jafri L, Haque AU. Hyperlactetemia and its trends in critically ill children admitted in pediatric intensive care unit of a developing country. J Ayub Med Coll Abbottabad 2016; 28(4): 660-663.