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Original Research Article

Comparison of diagnostic and prognostic value of serum procalcitonin and serum lactate in pediatric sepsis

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ABSTRACT

Background: The clinical manifestations of sepsis are highly variable. The signs of both infection and organ dysfunction may be subtle, and thus the most recent international consensus guidelines provide a long list of warning signs of incipient sepsis. Lactic acid, which is a by-product of anaerobic metabolism, can be used as a marker of tissue hypoperfusion. It is being used widely. Procalcitonin has more recently been studied in children.
Methods: Totally 60 Children admitted with Septic Shock in PICU between Ages 3 Months to 12 Years were assessed for Serum Lactate & Serum Procalcitonin levels. Evaluation of the biomarkers was done on individual and combinational basis using receiver operating characteristics curve.
Results: Out of 60 children, male were 40, female were 20 children. In stage-1 serum lactate level was 47.83 (mg/dl) sensitivity is about 35.63 and specificity was 63.82 off p-value <0.065**.In stage -2 serum procalcitonin was 49.62 (mg/dl) sensitivity is about 37.77 and specificity was 69.28 off p-value <0.549**.In stage -3 serum procalcitonin was 52.89 (mg/dl) sensitivity is about 41.63 and specificity was 73.89 off p-value <0.651**
Conclusions: Early recognition of risk factors will help in timely appropriate therapy and thereby will help in reducing mortality and morbidity in pediatric septic shock. The results suggest that PCT is valid for auxiliary diagnosis of septic conditions in children and used as an indicator of the severity of patients.

Keywords: Septic shock, Serum lactate, Serum procalcitonin, Systemic inflammatory response syndrome (SIRS)

INTRODUCTION

In this epidemiologic study, the requirement of two or more SIRS criteria for the diagnosis of severe sepsis excluded a sizable group of patients in the ICU with infection and organ failure. These patients with SIRS-negative severe sepsis had substantial mortality and, over a period of more than a decade, had epidemiologic characteristics and changes that were essentially identical to those of patients with SIRS-positive severe sepsis, providing indirect empirical evidence that these two groups of patients represent separate phenotypes of the same condition.[1] The clinical manifestations of sepsis are highly variable, depending on the initial site of infection, the causative organism, the pattern of acute organ dysfunction, the underlying health status of the patient, and the interval before initiation of treatment.[2] The signs of both infection and organ dysfunction may be subtle, and thus the most recent international consensus guidelines provide a long list of warning signs of incipient sepsis.[3] Cardiovascular compromise is manifested primarily as hypotension or an elevated serum lactate level. After adequate volume expansion, hypotension frequently persists, requiring the use of vasopressors, and myocardial dysfunction may occur. There is no single diagnostic tool or clinical decision rule that is both highly sensitive and specific in recognizing sepsis in its early stages.[4] The best approach is a high

level of clinical suspicion, combined with the clinical history, vital signs, and physical examination.[5] Lactic acid, which is a by-product of anaerobic metabolism, can be used as a marker of tissue hypoperfusion. In adults with severe sepsis, an increased lactate level (>4 mol/L) is a negative prognostic indicator and should trigger aggressive septic resuscitation according to the Surviving Sepsis Campaign guidelines Procalcitonin has more recently been studied in children.[6]

METHODS

This was a prospective observational study carried in 60 children out between 2 years from 2016-July- 2018-March. Totally 60 Children Admitted in PICU between Ages 3 Months to 12 Years diagnosed with sepsis or septic shock were included. Children were excluded if they had chronic systemic inflammatory diseases, degenerative neurological diseases, and primary or acquired immunodeficiency diseases, were on corticoid therapy, no steroidal anti-inflammatories or antibiotics for more than 24 hours, had suffered traumas or burns or were in postoperative care. Written consent was obtained from parents or guardians before recruiting their children.

Inclusion criteria

- Children free from past history of infection,
- allergic to basic antibiotics,
- low weight.

Exclusion criteria

- Unwilling for the study,
- Ruled out of past medical illness.

Laboratory Assay

Three samples were collected during different stages

- Stage (1) 0-3 hours.
- Stage (2) 4-8 hours.
- Stage (3) 9-12 hours.

Once 12 hours had passed, another sample was taken and labeled T12 hours. The blood sample taken for PCT, lactate assay was 5 mL at T0 and 3 mL on subsequent occasions, from the central venous catheter.

After collection, the blood was immediately refrigerated and, no more than 8 hours later, the material was centrifuged so that the mediators could be assayed in plasma. The PCT assay was done using a two-step chemiluminescent enzyme immunoassay (The Lumipulse G B·R·A·H·M·S PCT assay).

Statistical analysis

Data were analyzed using SPSS software version 22 and MedCalc software version 15. Data were interpreted using descriptive and inferential statistics. The Chi-square test was used to test the statistical significance of the relationship between two variables. The area under the ROC curves of more than 0.5 indicates that the test predicts outcome better than no chance. Optimum cut off values was determined using the associated criterion. The curve represents the graphical relationship between sensitivity and 1-specificity.

RESULTS

Out of 60 children, the male was 40, female were 20 children. 26.7% (16) children were between 3-12 months .33.3% (20) children were between 13-60 months. 40% (24) children were between 61-144 months.

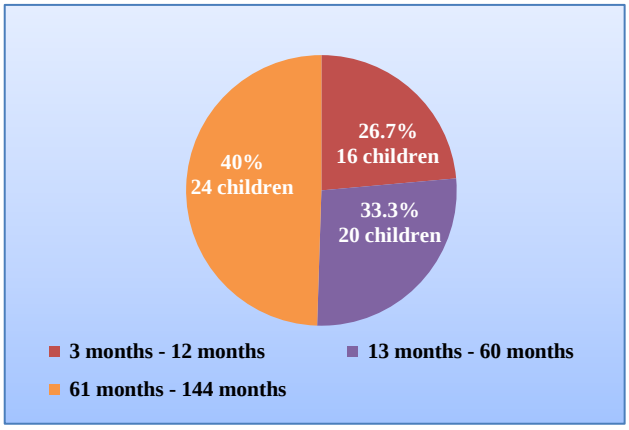

Figure 1: Age distribution among cases.

Of the total of 60 children, 36 had a negative culture (60.0%), majority was *Staphylococcus aureus* growth 7 [11.7%] children, E. coli was positive in 5 [8.3%] children, Klebsiella was positive in -4 [6.7%] children, Citrobacter was positive in 1 [1.7%] children, Acinetobacter was positive in 1 [1.7%] children, Pseudomonas sp. was positive 4[6.7%] children, *Burkholderia cepacia* positive in 1[1.7%] children, 1 sample had a fungus growth [1.7%].

Stage 1: 0-3 hours, stage (2) 4-8 hours, stage (3) 9-12 hours .CI: Confidence: p value <0.005** is considered to be statically significant. In stage-1 serum procalcitonin was 1.57 (ng/dl) sensitivity is about 22.60 and specificity was 77.82 off p value <0.005**.

In stage-2 serum procalcitonin was 2.83 (ng/dl) sensitivity is about 34.89 and specificity was 89.45 off p value <0.005**.

In stage-3 serum procalcitonin was 3.97 (ng/dl) sensitivity is about 59.76 and specificity was 91.89 off p value <0.005**. STAGE (1) 0-3 HRS, STAGE (2) 4-8 HRS, STAGE (3) 9-12 HRS .CI:

Confidence: p value <0.005 is considered to be statically significant. In stage-1 serum lactate level was 47.83

(mg/dl) sensitivity is about 35.63 and specificity was 63.82 off p value <0.065**In stage -2 serum procalcitonin was 49.62 (mg/dl) sensitivity is about 37.77 and specificity was 69.28 off p value <0.549**

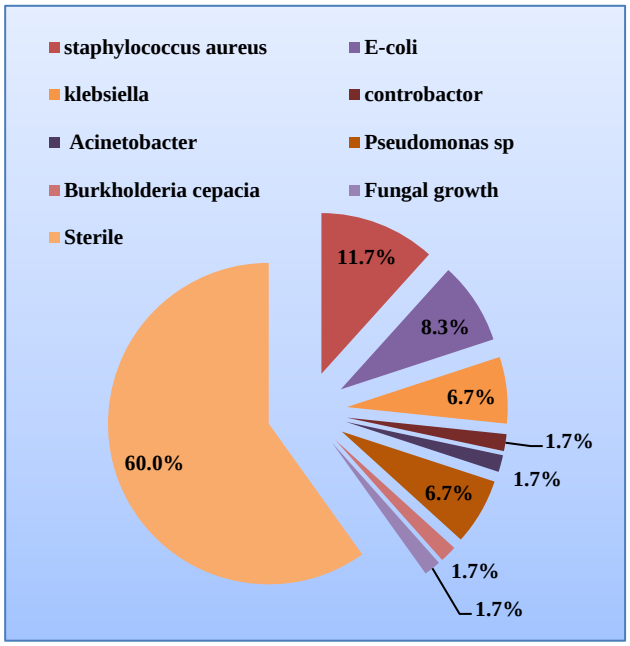

Figure 2: Culture sensitivity of different organism patterns in cases.

In stage -3 serum procalcitonin was 52.89 (mg/dl) sensitivity is about 41.63 and specificity was 73.89 off p value <0.651**.

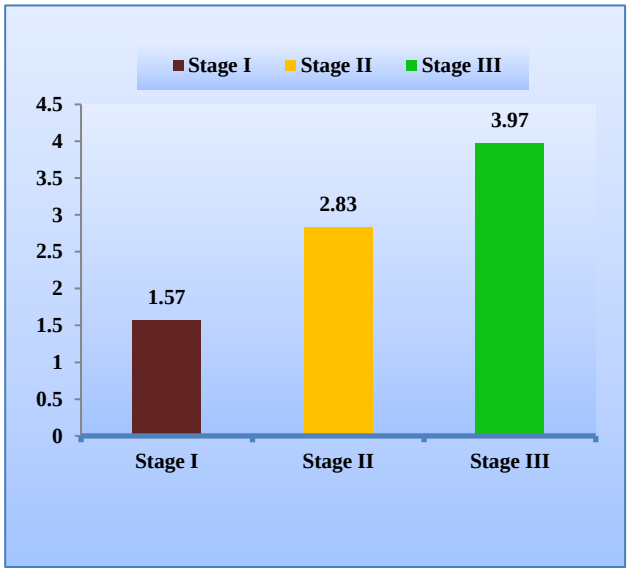

Figure 3: Serum procalcitonin level in 3 different stages of septic shock among children

Predicting value for serum lactate was 42.26 sensitivity was 78.3% and specificity was 73.1%. Predicting value for procalcitonin was 4.95 sensitivity was 81.8% and specificity was 75%.

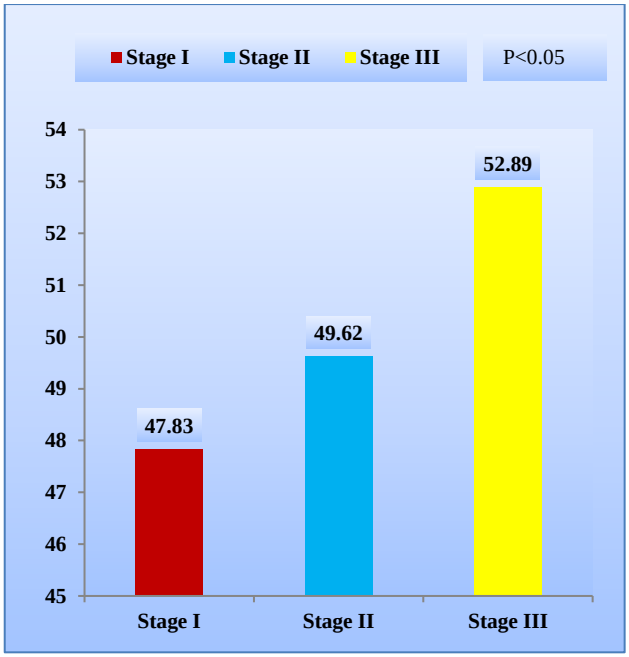

Figure 4 Serum lactate level in 3 different stages of septic shock among children.

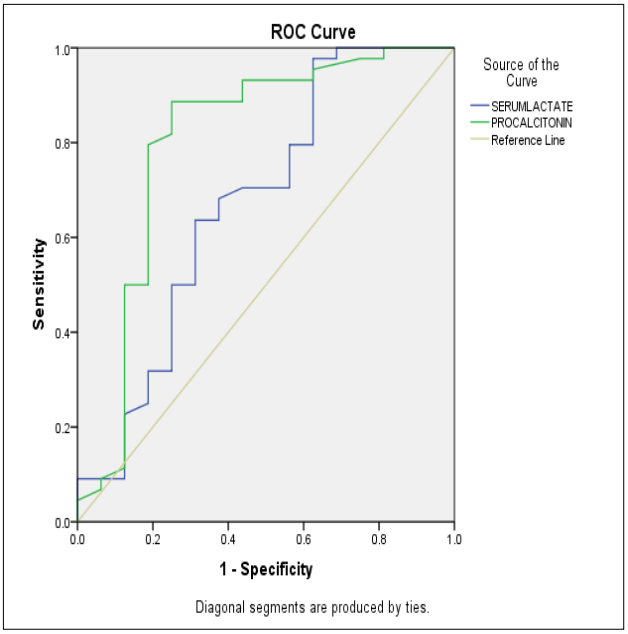

Figure 5: receiver operating characteristic curve.

DISCUSSION

According to the World Health Organization, more than two-thirds (68%) of the estimated 8.8 million deaths in children younger than 5 years worldwide in 2013 were caused by infectious diseases. This situation makes infection, often culminating in severe sepsis and septic shock, the most common cause of death in infants and children in the world In the United States, respiratory infections, and primary bacteremia are the most common infections leading to sepsis.[7] Bacteraemia predominates

in neonates, and respiratory illnesses are more common among older children. No specific cause is found in most children presenting to US-based emergency departments with undifferentiated sepsis. There is no single diagnostic tool or clinical decision rule that is both highly sensitive and specific in recognizing sepsis in its early stages.[8] The high levels last as long as the inflammatory process persists and tend to correlate with the outcome of the illness. Therapeutic immunoneutralization of animals with severe sepsis has been proven successful in two species. Such findings strongly indicate that PCT immunoneutralization in humans with these conditions offers considerable promise.[9] Moreover, the rapid onset of increased serum PCT with the advent of the illness and the very long-lasting duration of this elevation provide a broad clinical window for therapeutic intervention.[10] Furthermore, the ease and rapidity of PCT measurement allow for a swift documentation of the presence of the illness and permit the selection and stratification of the cases to be treated. Conceivably, not only sepsis but also SIRS might be amenable to such therapy.[11] JiayuanWet al study showed a significant association between plasma lactate level and the degree of organ dysfunction based on PELOD scores in 45 subjects with an average age of 48.7 months. Lactate level at 24 hours had a sensitivity of 30% and specificity of 25.8%. High lactate level, the presence of organ dysfunction and undernutrition were independently associated with poor outcome. This is comparable to the previous study conducted.[12] Kana ram Jat.et al in which lactate ≥ 5 moll/L or 45 mg /dl was significantly associated with poor outcome. In contrast to present study, Lapillonne A et al reported lactate level of ≥ 3 mol/L was a significant predictor of outcome.[13] Present study demonstrated that PCT was already capable of determining the severity of patients at the time of admission, differentiating children with sepsis from those with septic shock. Furthermore, we observed more elevated PRISM scores among patients with septic shock and higher PCT levels.[14] Misner M et al. conducted a study in surgical intensive care patients with severe sepsis in which two classes were considered, PCT-guided and control. For all patients, drug administration was based on the microbiological spectrum. When the clinical signs of infection improved and PCT level decreased to <35% of the initial value, the antibiotic treatment was discontinued in PCT-guided patients. In the control group, treatment was based on empirical rules. They observed that the PCT-based algorithm reduces the use of antibiotics as well as the expense of treatment.[15] The study also revealed that the relative risk for mortality increased with every day rise of the PCT value. PCT levels should be determined serially, it is used for monitoring the host response to the infection and the antibiotic treatment.

CONCLUSION

PCT is identified as part of the complex pro-inflammatory response of the innate immune system. PCT is widely reported as a useful biochemical marker to differentiate sepsis from other non-infectious causes. Serum PCT levels are elevated in patients with bacterial infections. The diagnosis of infection in critically sick patients is challenging as the current biomarkers are nonspecific. Our review showed that PCT is a more accurate diagnostic parameter for sepsis and a better predictor of mortality than lactate. PCT is a more reliable marker than other biomarkers.

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