

# Comparative Study of Procalcitonin/Albumin Ratio, Lactate /Albumin Ratio and CRP/Albumin Ratio in Pediatrics Sepsis Cases

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## ABSTRACT

**Introduction:** Sepsis is a life-threatening condition that happens when the body's immune system has an extreme response to an infection, causing organ dysfunction. Paediatric sepsis in India is a major public health crisis, causing high mortality (25–30%) and significant morbidity, largely driven by malnutrition, delayed care, and infection.

**Objective:** The present study was taken up to do a comparative study of PAR, LAR and CAR in paediatric sepsis cases and their significance with the conventional biomarker the C-reactive protein and procalcitonin.

**Material and methods:** A prospective observational study of 74 clinically diagnosed sepsis cases, admitted to paediatric ICU were analysed Along with sepsis panel, lactate, albumin, CRP and PCT were estimated at the time of admission.

**Results:** The study sample comprised 43 cases with sepsis and 31 cases with severe sepsis. The mean values of TLC, albumin, procalcitonin and C-reactive protein in severe sepsis were significantly higher in comparison to sepsis cases with p value <0.001. The values of PAR and CAR were significantly ( $p<0.001$ ) raised in severe sepsis cases. The rise in LAR was

statistically significant ( $p<0.05$ ) raised in severe sepsis cases as compared to sepsis cases. There was no significant correlation between CAR, LAR and PAR in both sepsis and severe sepsis cases.

**Interpretation and Conclusion:** PAR, CAR and LAR are independent indicators of systemic inflammation that aid in the severity assessment and prognostic prediction of sepsis-related outcomes.

**Keywords:** Albumin, CRP/albumin ratio, Lactate/albumin ratio, Procalcitonin/albumin ratio sepsis.

Sepsis in children is a rapidly progressive illness and a high index of suspicion is required for early identification of symptoms as the diagnosis may be easily missed or delayed [1]. High mortality in children has been attributed due to failures of early recognition of sepsis. Early interventions with rapid fluid administration, electrolyte balance, antibiotics therapy, oxygen supplementation and use of inotropes can improve the outcome of paediatric sepsis. Mortality from sepsis is not just related to the financial status or the availability of resources but rather to the adherence to treatment guidelines which is still very low, both in developing and under developed countries.

Sepsis in paediatric cases is associated with vascular endothelial dysfunction due to inflammation and tissue hypoxia [2]. The paediatric immune system is distinct from the adult phenotype, characterized by an underdeveloped innate response and a protracted period of immunologic maturation that continues throughout childhood into adolescence. Hemodynamic status is assessed using blood pressure, heart rate, pulse pressure, cardiac output and others which have been taken as surrogates for tissue perfusion. There has been longstanding interest to identify biomarkers to assist in the diagnosis of sepsis, with blood lactate, C-reactive protein (CRP), and procalcitonin (PCT) the most commonly used. In this regard, lactate can be considered as a biomarker for tissue hypoxia that indicative of abnormal perfusion and is used i as a marker of severity in sepsis. Increased lactate level in sepsis may be considered an early marker of a potentially reversible state [3]. Current paediatric sepsis guidelines do not endorse the routine measurement of lactate, thereby limiting its clinical application during the early stages of the disease Serum albumin is both a nutritional biomarker and an acute phase reactant in inflammatory states. Hypoalbuminemia is associated with higher mortality and adverse outcomes in paediatric patients with sepsis [4]. While C-reactive protein (CRP) and procalcitonin (PCT) are the most commonly used biomarkers for diagnosing bacterial infections, both have several limitations. Although they, have variable sensitivity and specificity, CRP has low accuracy as compared to PCT, which is a more specific biomarker of infection/inflammation and hence can aid clinicians in diagnosing sepsis.

Despite the known utility of inflammatory markers, there is a paucity of research within the Indian paediatric population evaluating the combined diagnostic accuracy of the Procalcitonin/Albumin (PAR), Lactate/Albumin (LAR), and CRP/Albumin (CAR) ratios in detecting

sepsis and its severity. The study evaluates the comparative efficacy of the PAR, LAR, and CAR in paediatric sepsis, assessing their clinical significance alongside conventional biomarkers such as CRP and (PCT).

## **MATERIALS AND METHODS**

The study was conducted at M.S. Ramaiah teaching hospital, Bangalore. A prospective cohort study was carried out to evaluate the significance of procalcitonin /albumin ratio (PAR), lactate /albumin ratio (LAR) and CRP/albumin ratio (CAR) in predicting the severity and outcome of sepsis in pediatric cases in association with lactate, albumin, C-reactive protein (CRP) and procalcitonin (PCT). The study was approved by the Institutional research and ethics committee and informed consent was taken from the study population before the collection of the sample. The study population consisted of 74 clinically diagnosed sepsis cases, admitted to pediatric ICU, aged between 1 month to 13 years of age with suspicion of sepsis based on the International Pediatric Sepsis Consensus Criteria for sepsis (2005) were recruited for the study [5]. Patients with non-infectious causes of SIRS, pneumonia and other conditions which can interfere with the study were excluded. Informed consent was taken from the parents/guardians as applicable. Demographic details, anthropometric measurements, clinical presentation, vitals and examination findings were recorded. Using aseptic precaution 3 ml of whole blood in EDTA vacutainer and 5 ml of venous blood sample in yellow vacutainer were collected at the time of admission to PICU. The sample in yellow vacutainer was allowed to stand for about 15 minutes for clotting and was then centrifuged at 5000 rpm. The serum sample was separated and stored at - 20° Celsius till estimation was done. Sepsis panel including total leukocyte count, platelet count, blood gas analysis including lactate, liver and kidney function tests were estimated. Chest X ray was done and paediatrics Sequential Organ Failure

Assessment score (pSOFA) at the time of admission were recorded [6]. Estimation of serum procalcitonin by ELISA automated kits, ELK Biotechnology and CRP - by immunoturbidimetric method, VITROS 5600 analyzer was done.

The study cases were clinically categorized into sepsis and severe sepsis according to International Pediatric Sepsis Consensus Criteria for sepsis (2005) [5]. All the cases were followed up for need for ventilation, length of ICU stays, discharge or death.

### Statistical Methods

The results were expressed as Mean  $\pm$  SD. Significance was assessed at 5% level of significance. Data was analyzed using SPSS

22 version software. Independent t- test was used as test of significance to identify the mean difference between two quantitative variables.

### RESULTS

A total of 74 cases were included of which 43 sepsis cases and 31 cases were severe sepsis (Fig 1). Demographic profiles, such as age compared between sepsis and severe sepsis cases did not show any statistical significance. The indicators of infection were compared between sepsis and severe sepsis cases. The mean PCT (3.64 ng/ml) and CRP (9.57 mg/dl) were higher in severe sepsis cases with statistical significance (p value <0.01) (Table 1).

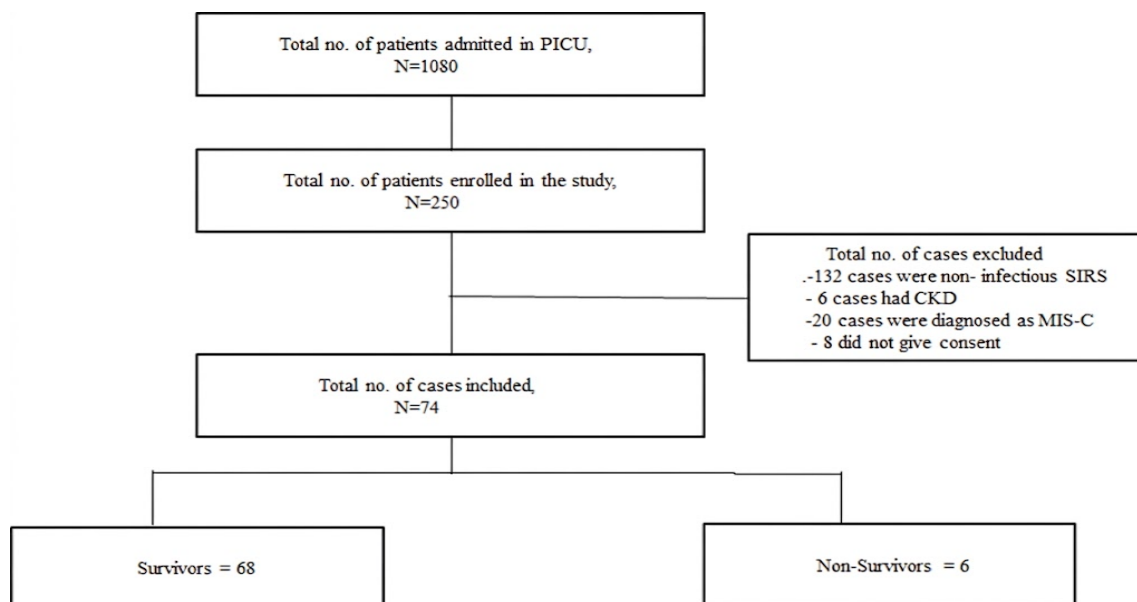


Figure 1: Flowchart of participants in the study

Table 1: - Distribution of subjects according to age group.

Age	Frequency	Percent
1-6months	13	17.57%
6-12months	9	12.16%
1-5yr	30	40.54%
6-10yrs	14	18.92%
>10yrs	8	10.81%
Total	74	100.0%

Comparative study of PAR, LAR and CAR in cases of sepsis and severe sepsis was taken up in the study. Along with these profiles, markers of inflammation including total leukocyte count (TLC), platelet count,

CRP, procalcitonin, albumin, lactate and other profiles were taken into consideration. Table 1 shows the demographic details of age distribution of cases. Nearly 40.54 % of

cases were in the age group between 1 to 5 years age group.

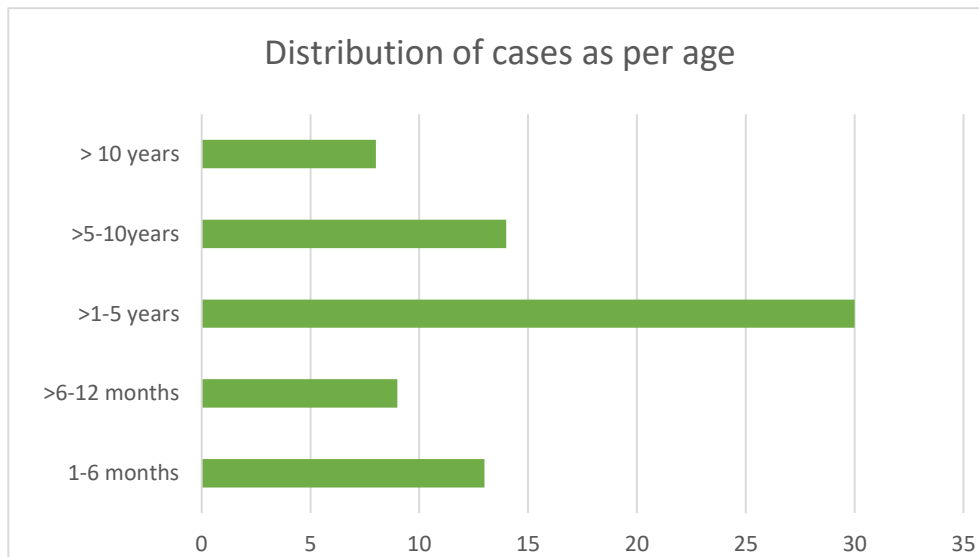


Figure 2: - Graph showing Distribution of subjects according to age group.

Table 2: - Distribution of subjects according to gender

Gender	Frequency	Percent
Female	31	42%
Male	43	58%
Total (N)	74	100.0%

Nearly 58 % of the sepsis cases were male population (Table 2).

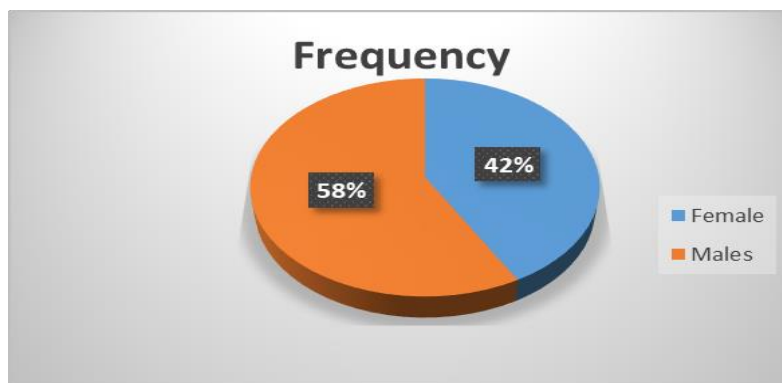


Fig 3: Distribution of sepsis cases according to gender

Table 3: - Distribution of subjects according to severity of sepsis

Diagnosis	Frequency	Percent
Sepsis	43	58 %
Severe sepsis	31	42%
Total (N)	74	100%

Of the cases included in the study 58% were sepsis cases and 42% were severe sepsis cases (Table 3).

**Table 4: - Comparison of various parameters between sepsis and severe sepsis.**

	Sepsis		Severe sepsis		p value
	Mean	SD	Mean	SD	
Age in yrs	4.01	3.26	4.93	4.04	0.13
TLC (10 <sup>3</sup> cells /cu.mm)	11.38	6.04	15.21	7.53	0.011
Platelets (lakhs/cu.mm)	2.38	0.85	1.82	1.16	0.013
CRP (>0.5 mg/dl)	4.67	4.14	9.57	6.63	<0.001
Lactate (mmol/L)	1.80	0.98	2.17	1.18	0.09
Albumin (g/dL)	2.91	0.61	2.47	0.74	<0.001
CRP/Albumin ratio (CAR)	1.61	1.50	4.59	4.29	<0.001
Lactate / Albumin ratio (LAR)	0.65	0.37	1.00	0.70	<0.05
Procalcitonin (PCT) (>2 ng/ml)	2.18	2.07	3.64	1.98	<0.001
PCT/Albumin ratio (PAR)	0.81	0.80	1.62	1.02	<0.001
Duration of ICU stay (days)	3.05	1.10	4.60	1.62	<0.001
N =	43		31		

The result analysis as in Table 4 shows comparison of inflammatory parameters between cases of sepsis and severe sepsis. There is age matched sample collection so that comparative study can be done across pediatric age group. There is significant rise in total leukocyte counts in both sepsis and severe sepsis cases. However, there is comparatively significant rise in TLC counts in severe sepsis cases (p=0.011), showing the increased severity of inflammation. Hematological parameters of infection such as leukocytosis and low platelets were deranged more in severe sepsis group compared to sepsis group and was found to be statistically significant.

The mean CRP value in sepsis cases was found to be 4.67 mg/dl while in severe sepsis group was 9.57 mg/dl which was also significant (p value <0.001). The rise in lactate level in severe sepsis is more as compared to sepsis cases but was not statistically significant. Lactate levels are found to be elevated in sepsis via, multiple mechanisms, including anaerobic metabolism from tissue hypoperfusion. There was significant decrease in serum albumin level in severe sepsis as compared to sepsis (p<0.001). Low albumin levels

may occur in children with sepsis due to increased microvascular permeability (associated with systemic inflammation), increased capillary leak and decreased hepatic synthesis.

CRP/albumin ratio (CAR) was found to be elevated in severe sepsis cases as compared to sepsis cases and was found to be highly significant (p<0.001). CAR is found to be significantly higher in severe sepsis, acting as a crucial marker for tracking clinical progression. Lactate/ albumin ratio (LAR) increased in severe sepsis cases as compared to sepsis cases (p<0.05). This elevated ratio reflects both higher lactate production from anaerobic metabolism and lower serum albumin (a negative acute-phase protein) due to increased capillary leakage.

Serum PCT was found to be significantly elevated in severe sepsis cases as compared to sepsis cases (p<0.001). PCT/albumin ratio (PAR) was found to be elevated in severe sepsis cases as compared to sepsis cases and was found to be highly significant (p<0.001). A higher PAR, reflecting both high inflammation (PCT) and low nutritional status (albumin), correlates with increased illness severity and poor prognosis in children.

**Table 5: - Pearson's correlation of various parameters in sepsis and severe sepsis.**

Correlation	Sepsis		Severe sepsis	
	r value	P value	r value	P value
CAR & LAR	-0.183	0.240	0.463	0.087*
CAR & PCT	-0.012	0.939	0.043	0.818
LAR & PCT	-0.148	0.344	-0.045	0.810
CRP & Albumin	0.122	0.436	-0.214	0.247

Lactate & Albumin	0.061	0.697	-0.116	0.534
CRP & LAR	-0.239	0.123	0.070	0.708
Lactate & CAR	-0.164	0.293	-0.024	0.898
PAR & CAR	-0.064	0.683	0.294	0.108
PAR & LAR	-0.001	0.995	0.191	0.303

There was no correlation between various parameters in sepsis and severe sepsis indicating they are independent of each other. (Table 5).

## DISCUSSION

Sepsis is a life-threatening condition that arises when the body's response to an infection triggers widespread inflammation, leading to acute organ dysfunction [7]. The study involves CRP, PCT, albumin and lactate as marker of inflammation and metabolic state of the body in sepsis cases. It also aims to evaluate the relationship between PAR, LAR and CAR across various degrees of sepsis. The result analysis of the study shows a definitive alteration in inflammatory markers i.e CRP, leukocyte count, platelet count, lactate, albumin and PCT level in severe sepsis cases in comparison to sepsis cases. Duration of stay in ICU in severe sepsis cases are more as compared to sepsis cases. Increase in total leukocyte count in severe sepsis is primarily due to the immune system's urgent and inflammatory response. There is comparatively decrease in platelet levels in severe sepsis cases as compared to sepsis cases (p=0.01) again consequent to inflammatory reaction. Decrease in platelet count in severe sepsis is driven by three main factors: widespread coagulation consumption, immune-driven destruction, and microvascular sequestration [8]. Platelet activation and adhesion to damaged endothelium is consequent to inflammatory response according to severity of infection.

The progression from sepsis to severe sepsis may be accompanied with higher bacterial load and /or intensified systemic inflammatory response, promoting increased synthesis of CRP in response to higher levels of proinflammatory cytokines like IL-6 and TNF-alpha [8]. Severe sepsis may be associated with dysregulated immune

reaction to infection compared to initial sepsis, instigating more extensive tissue injury and greater release of acute-phase reactants like CRP. CRP a non-specific, acute-phase reactant synthesized in liver that raises after exposure to an inflammatory trigger and decreases with the resolution of inflammation. Therefore, its diagnostic application is primarily confined to the assessment of inflammatory processes. Higher lactate levels in paediatric severe sepsis compared to sepsis are mostly caused by increased tissue hypoxia due to inadequate tissue perfusion, impaired cellular respiration or increased metabolic demand, or may be due to reduced clearance due to compromised hepatic and renal function [9]. However, lactate levels have been found to be elevated in certain circumstances not related to tissue hypoxia. Lower albumin levels in severe paediatric sepsis, compared to simple sepsis, are primarily due to increased capillary permeability (capillary leak syndrome) leading to extravasation into the interstitial space, along with increased catabolism and decreased hepatic synthesis. This is exacerbated by the inflammatory response and intense fluid resuscitation. Severe oxidative stress and capillary leak correlate with decreased serum albumin levels in sepsis [10]. Inflammation damages renal function, leading to proteinuria through the upregulation of glomerular infiltration and causing the leakage of albumin [11]. Previous studies have shown that the decreased serum albumin level (<3 gm/dl) is one of the risk factors for the increased mortality in sepsis. In the study mean albumin level in sepsis cases were 2.97 gm/dl and in severe sepsis cases 2.47 gm/dl. Low serum albumin was seen in severe sepsis group compared to sepsis group, which was also found to be statistically significant. Due to protein-rich fluid

extravasation caused by capillary dysfunction and other factors, hypoalbuminemia occurs more frequently in sepsis patients, especially in septic shock [12].

In the study serum PCT was found to be elevated in both sepsis and severe sepsis cases and was highly significant. PCT is one of the well characterised biomarkers that responds rapidly and with high specificity to the presence of bacterial infection. In healthy subjects, plasma levels of PCT are very low (0.05 ng/ml). In the course of bacterial infection, PCT values increase earlier than rise in CRP level is reported. High PCT levels in paediatric severe sepsis compared to sepsis are primarily due to the intensity of the systemic inflammatory response and pro inflammatory cytokine response and the direct, proportional relationship between PCT production and the severity of infection [13].

The high CRP/Albumin Ratio (CAR) in severe sepsis, compared to simple sepsis in paediatric cases, is due to the synergistic combination of a heightened inflammatory reaction (elevated CRP) and increased capillary permeability or decreased production (lowered albumin) [14]. Severe sepsis drives higher CRP production due to intense, systemic inflammation. Simultaneously, albumin, a negative acute-phase protein, drops rapidly due to increased vascular permeability, increased catabolism, and potential liver dysfunction, resulting in a higher ratio. These are inclusive of factors which contribute to rise in CRP levels and fall in albumin levels in sepsis cases. A higher CAR is strongly linked to greater mortality risks and the severity of the infection, making it a reliable indicator of deterioration in paediatric patients. Studies show that CAR is significantly higher in severe sepsis compared to mild sepsis acting as a crucial marker for tracking clinical progression.

A high lactate/albumin ratio (LAR) in paediatric severe sepsis, compared to sepsis is primarily driven

by profound microcirculatory dysfunction, tissue hypoxia, and increased severity of inflammation [15]. This elevated ratio reflects both higher lactate production from anaerobic metabolism and lower serum albumin (a negative acute-phase protein) due to increased capillary leakage. LAR is a combined biomarker for predicting mortality and assessing risk in paediatric patients, often considered better than lactate or albumin alone. Serum lactate and albumin are categorised as positive and negative acute phase reactants, respectively. Although lactate is a well-studied prognostic biomarker, its interpretation is complex due to the pathophysiology that can lead to elevation in lactate level. As such, the incorporation of albumin as a reflection of nutritional status in the LAR increases its use in prognostication of sepsis patients. The severe sepsis cases had a higher level of lactate and LAR. An elevated LAR—driven by high lactate (tissue hypoperfusion) and low albumin (inflammation)—indicates severe illness.

The combination of the two biomarkers in our study indicates that an elevated LAR may be a good surrogate of microcirculatory damage in children with sepsis. Thus, an increase in the LAR would more accurately reflect a pro-inflammatory condition [16]. The C-reactive protein (CRP)/albumin ratio (CAR) is a valuable, independent inflammatory marker indicating greater, bacterial infection burden. LAR is considered as a superior prognostic marker compared to CAR ratio for mortality and organ failure in paediatric sepsis, offering better sensitivity and specificity. While both reflect inflammation and metabolic stress, LAR has been reported to identify severe cases, with a ratio > 0.96-1.02, indicating higher risk.

CRP and procalcitonin, both are independent markers for the diagnosis of sepsis in children. The study show that PAR and CAR are independent predictors for neonatal sepsis. PAR is a valuable, sensitive biomarker for diagnosing paediatric and neonatal sepsis, offering

higher specificity than CRP, for early identification. PAR is often viewed as the "better" marker because PAR integrates the most specific bacterial signalling molecule (PCT) with a marker of systemic vulnerability [17]. While LAR, CAR, PAR, lactate, albumin, CRP and PCT did not correlate significantly in the study patients, but were significantly deranged across sepsis and severe sepsis cases. A deeper comprehension of the pathophysiology underlying dysregulated host responses and the subsequent failure to achieve homeostasis is essential to minimize adverse sepsis outcome.

The study has few limitations. The generalizability of these findings is limited because of the homogeneity of the study population's demographics and the reliance on data from a single tertiary care hospital. Serial inclusion of these inflammatory profiles in future study could provide a better understanding of sepsis prognosis. Longitudinal studies with larger sample sizes would provide a more comprehensive approaches for risk stratification and therapeutic intervention in paediatric sepsis. Conclusion: The study shows by integrating markers of systemic inflammation with indicators of nutritional and metabolic status—specifically albumin—the LAR, CAR, and PAR ratios offer superior prognostic value compared to individual markers. These composite indices facilitate more accurate severity assessments and outcome predictions in sepsis, establishing their utility as robust, independent indicators of the systemic inflammatory response.

#### **Declaration by Authors**

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