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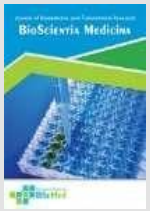

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Admission Serum Procalcitonin Thresholds and the PELOD-2 Score: A Prospective Analytical Study for Identifying Risk Ratios of Severe Organ Dysfunction in Pediatric Critical Care

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A B S T R A C T

Background: Multiple organ dysfunction syndrome (MODS) remains a predominant cause of mortality in Pediatric Intensive Care Units (PICUs). While the Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score is the established standard for assessing severity, it requires time-consuming serial calculations. There is an urgent need for a rapid, admission-based prognostic biomarker. This study evaluates the association between serum procalcitonin (PCT) and the severity of organ dysfunction in critically ill children. **Methods:** A prospective cross-sectional study was conducted at Dr. Moewardi Regional General Hospital, Indonesia, involving 25 children aged 1 month to 18 years with suspected infection. Organ dysfunction was quantified using the PELOD-2 score, and serum PCT was measured via Enzyme-Linked Fluorescent Assay (ELFA) within 24 hours of admission. Statistical analysis utilized Spearman's rank correlation, multivariate linear regression, and Receiver Operating Characteristic (ROC) curve analysis. **Results:** The cohort had a median age of 12 months. The median PCT level was 0.88 ng/mL. A significant positive correlation was observed between serum PCT and PELOD-2 scores ($r = 0.39$, $p = 0.051$; multivariate beta = 0.42, $p = 0.043$). ROC analysis identified a PCT threshold of greater than 11 ng/mL as the optimal indicator for moderate-to-severe organ dysfunction (AUC 0.82). Patients exceeding this threshold had a significantly elevated risk (Risk Ratio = 2.20; 95 percent CI: 1.15–4.24; $p = 0.035$). **Conclusion:** Early serum procalcitonin measurement serves as a powerful independent factor associated with organ dysfunction severity. A cutoff value of greater than 11 ng/mL significantly stratifies risk, allowing clinicians to anticipate the progression of organ failure.

1. Introduction

The landscape of pediatric critical care medicine has shifted significantly over the last decade. While survival rates for critically ill children have shown marked improvement due to advancements in life-support technologies and specialized protocols, the burden of morbidity associated with multiple organ dysfunction syndrome (MODS) remains a critical challenge for clinicians.[1] Within the high-intensity environment of the Pediatric Intensive Care Unit (PICU), the focus has expanded from mere survival to the mitigation of long-term physiologic impairment. Multiple organ dysfunction syndrome is defined not merely as the failure of a single anatomical system, but as a progressive and potentially devastating physiologic failure of two or more organ systems where homeostasis cannot be maintained without aggressive medical intervention.[2]

This syndrome serves as a primary driver of mortality in the Pediatric Intensive Care Unit, often

triggered by a complex and dysregulated immune response to an underlying infection.[3] When a child enters a state of septic shock or severe systemic inflammation, the body's natural regulatory mechanisms may become overwhelmed, leading to a cascade of cellular damage that affects vital organs simultaneously. Because of this high risk, accurate prognostication and risk stratification have become the cornerstones of effective pediatric intensive care management. Establishing a clear prognostic outlook facilitates objective and transparent communication with families during crises, guides the appropriate allocation of limited medical resources, and assists clinicians in the precise titration of aggressive therapies such as vasoactive support or mechanical ventilation.[4]

Currently, the Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score is widely accepted as the most valid and reliable tool for describing the severity of organ dysfunction in the pediatric population. This updated scoring system evaluates dysfunction across five critical organ systems: the neurologic, cardiovascular, renal, respiratory, and hematologic systems.[5] By assessing specific parameters such as the Glasgow Coma Scale, lactate levels, Mean Arterial Pressure, creatinine, and platelet counts, the PELOD-2 offers a dynamic assessment of a patient's current status.

However, despite its clinical utility, the calculation of PELOD-2 scores is inherently reactive in nature. It functions by documenting dysfunction that has already manifested and occurred within the patient's physiology.[6] Furthermore, the process of determining a PELOD-2 score requires time, complex laboratory inputs, and highly skilled personnel to perform daily serial calculations. These requirements can potentially delay the recognition of impending clinical deterioration during the crucial early hours of admission. This significant limitation necessitates the identification of rapid, objective biomarkers that can indicate the trajectory of organ failure before the damage becomes irreversible.

Procalcitonin (PCT), a 116-amino acid peptide that serves as a precursor of calcitonin, has emerged as a promising candidate for this role. The biochemical behavior of procalcitonin is unique and highly relevant to systemic inflammation. Under normal physiological conditions, procalcitonin is produced solely by the C-cells of the thyroid gland and is immediately converted into calcitonin, resulting in nearly undetectable serum levels. However, during severe bacterial infection or systemic inflammatory response syndrome, this compartmentalization is disrupted. Bacterial endotoxins and proinflammatory cytokines, such as IL-1beta, TNF-alpha, and IL-6, upregulate the CALC-1 gene in virtually all parenchymal tissues throughout the body.[7]

This results in the ubiquitous release of procalcitonin from the liver, lungs, kidneys, and adipose tissue, leading to a massive surge in serum levels. While procalcitonin is well-established as a diagnostic marker for bacterial sepsis, its utility as a prognostic marker for the specific severity of organ dysfunction in children remains under-explored and continues to be a subject of clinical controversy.[8] Previous studies conducted in adult populations suggest a strong and reliable correlation between procalcitonin kinetics and Sequential Organ Failure Assessment (SOFA) scores. Nevertheless, pediatric data remain scarce and often yield conflicting results regarding the optimal cutoff values for risk assessment.

Furthermore, few studies have utilized the updated PELOD-2 scoring system to validate these associations, particularly in developing nations such as Indonesia, where the burden of infectious sepsis and associated mortality is highest.[9] In these settings, the availability of a rapid biomarker could revolutionize how clinicians triage and manage critically ill children upon admission. By bridging the gap between admission and the manifestation of organ failure, a biomarker like procalcitonin could allow for a proactive rather than a reactive approach to critical care. The identification of a specific threshold is essential for clinical application. While many

clinicians utilize procalcitonin for the initial diagnosis of infection, its use as a measure of systemic inflammatory burden and organ dysfunction requires a more nuanced understanding of high-risk phenotypes. This study addresses these needs by providing a rigorous evaluation of the relationship between admission serum levels and the physiologic failure documented by the PELOD-2 score.[10]

This study aims to bridge the existing knowledge gap by rigorously evaluating the association between admission serum procalcitonin levels and the severity of organ dysfunction as measured by the PELOD-2 score in a cohort of critically ill children. The novelty of this research lies in its specific determination of a high-risk procalcitonin threshold of greater than 11 ng/mL and the quantification of the Risk Ratio for developing moderate-to-severe dysfunction. By establishing this specific cutoff, we provide a concrete and actionable metric for clinicians to identify high-risk phenotypes early in the admission course, thereby facilitating more timely and aggressive therapeutic interventions.

2. Methods

Ethical consideration

The conduct of this clinical investigation adhered strictly to the ethical principles outlined in the Declaration of Helsinki for medical research involving human subjects. Prior to the initiation of any data collection or clinical procedures, the study protocol received formal institutional approval from the Health Research Ethics Committee of Dr. Moewardi Regional General Hospital, Surakarta, Indonesia. Recognizing the vulnerability of the pediatric population in a critical care setting, a rigorous informed consent process was established. Written informed consent was obtained from the parents or legal guardians of all participating children after a comprehensive explanation of the study's objectives, the nature of the biological sampling, and the guaranteed confidentiality of the patient data. No clinical interventions were delayed or modified for the purposes of this study, ensuring that patient safety remained the paramount priority.

Study design and clinical setting

This research was structured as a prospective cross-sectional analytical study designed to examine the association between an early-admission biomarker and clinical scoring outcomes. The investigation was localized at Dr. Moewardi Regional General Hospital, which serves as a premier tertiary referral academic center and a pivotal teaching hospital in Surakarta, Indonesia. This setting provided a diverse and high-acuity patient population essential for evaluating organ dysfunction. Data collection was conducted over a ten-month period, spanning from August 2020 to May 2021. To capture the full spectrum of critical illness severity, the study setting encompassed both the Pediatric Intensive Care Unit (PICU) and the High Care Unit (HCU). These units specialize in the management of life-threatening conditions, providing the necessary infrastructure for serial physiological monitoring and advanced laboratory diagnostics required for calculating complex organ dysfunction scores.

Patient population and sampling methodology

The target population for this study comprised pediatric patients, ranging in age from 1 month to 18 years, who were admitted to the intensive care environment with a primary suspicion of infection. To ensure clinical relevance and focus on the inflammatory response, patients were required to manifest at least one of the recognized clinical indicators of suspected infection upon admission. These indicators included temperature instability, defined as a core body temperature exceeding 38 degrees Celsius or falling below 36 degrees Celsius, as well as cardiovascular dysregulation such as age-appropriate tachycardia or bradycardia. Furthermore, evidence of respiratory distress through tachypnea relative to age-specific norms or abnormal hematologic markers, specifically leukocytosis or leukopenia, was utilized as an inclusion criteria. To isolate the specific impact of infection-driven procalcitonin (PCT)

elevation and minimize confounding variables that could independently affect biomarker levels or organ failure scores, several exclusion criteria were applied. Specifically, patients with an underlying malignancy, cases involving severe physical trauma or extensive burns, and patients undergoing elective surgical procedures were excluded. Families or legal guardians who declined to provide informed consent were also omitted from the study. A purposive sampling method was utilized to identify and select subjects who met the rigorous clinical inclusion criteria and possessed comprehensive datasets for both the biochemical predictor and the clinical outcome variables. This resulted in a final cohort of 25 critically ill children. While this sample size is characteristic of a pilot exploratory study, the precision of the inclusion criteria ensured a high-fidelity group for analyzing the relationship between PCT and organ dysfunction.

Variables and operational definitions

The primary outcome in this analysis was the severity of organ dysfunction, quantified using the Pediatric Logistic Organ Dysfunction-2 (PELOD-2) score. The PELOD-2 score was calculated for each patient based on the most deranged physiological and laboratory parameters observed within the first 24 hours of PICU/HCU admission. The PELOD-2 system evaluates five distinct organ systems to provide a holistic view of the patient's physiologic state. The neurologic system assessment includes the Glasgow Coma Scale (GCS) and pupillary reaction to light. The cardiovascular system evaluation involves the measurement of serum lactate concentrations and Mean Arterial Pressure (MAP). For the renal system, the score monitors serum creatinine levels. The respiratory system assessment includes the evaluation of the ratio of partial pressure of arterial oxygen to fractional inspired oxygen (PaO_2/FiO_2), partial pressure of arterial carbon dioxide ($PaCO_2$), and the requirement for invasive mechanical ventilation. Finally, the hematologic system analysis comprises total white blood cell count and platelet count. For the purpose of risk stratification, the resulting total scores were stratified into three clinically relevant tiers of severity: Mild, corresponding to a score of 0 to 3; Moderate, for scores between 4 and 9; and Severe, for scores greater than 9.

The primary independent variable was the concentration of serum procalcitonin measured upon admission. Blood samples were drawn within the first 24 hours of the patient's arrival at the unit to capture the initial inflammatory insult. PCT levels were quantified using the Enzyme-Linked Fluorescent Assay (ELFA) technique, performed on the automated VIDAS 2 (BioMérieux) platform. This assay provides a highly sensitive and specific measurement of PCT, with a detection range extending from 0.05 ng/mL to 100 ng/mL. For the purposes of standardized statistical modeling, any value exceeding the instrument's upper limit of 100 ng/mL was capped at 105 ng/mL to allow for continuous variable analysis.

Statistical analysis and modeling

Data analysis was conducted using the Statistical Package for the Social Sciences (SPSS) version 26.0. The analytical approach was designed to move from descriptive clinical profiles to predictive modeling and risk threshold identification. Initially, the Shapiro-Wilk test was applied to assess the normality of the distribution for continuous variables. Given that PCT levels often exhibit a non-parametric distribution in septic populations, medians and ranges were utilized for descriptive reporting. The primary bivariate association between serum PCT and the PELOD-2 score was assessed using Spearman's rank correlation. To determine if PCT remained an independent factor associated with organ dysfunction after controlling for demographic and clinical variables, a Multiple Linear Regression model was constructed. The model adjusted for potential confounders, including patient age, sex, and specific infection signs, to isolate the unique variance in PELOD-2 scores explained by PCT concentrations.

To translate the continuous PCT data into a practical clinical tool, Receiver Operating Characteristic (ROC) curve analysis was performed.

The area under the curve (AUC) was calculated to evaluate the overall discriminative ability of PCT in identifying patients with moderate-to-severe organ dysfunction. The optimal clinical cutoff value was determined using the Youden Index, which identifies the threshold that maximizes the balance between sensitivity and specificity. Once the optimal cutoff was established at greater than 11 ng/mL, the patient cohort was dichotomized. A Risk Ratio (RR) with 95 percent Confidence Intervals (CI) was calculated to quantify the relative likelihood of a patient developing moderate or severe organ dysfunction based on their admission PCT level. Due to the small cell frequencies in the resulting contingency table, the significance of the risk ratio was verified to ensure statistical validity.

3. Results

Table 1 illustrates the comprehensive demographic and clinical architecture of the study cohort, which consists of 25 critically ill pediatric patients admitted to the intensive care environment with suspected infection. The demographic distribution reveals a notable female predominance, accounting for 60 percent of the participants. The median age of the subjects is 12 months, with a developmental range extending from 3 months to 17 years, reflecting the heightened vulnerability of the infant population to severe septic events in the pediatric intensive care setting. The primary diagnoses are varied, yet pneumonia remains the most prevalent cause of admission, affecting 40 percent of the children. Sepsis and septic shock represent 32 percent of cases, while central nervous system infections and intra-abdominal infections constitute 16 percent and 12 percent of the cohort, respectively. Indicators of a systemic inflammatory response are pervasive across the group. Temperature instability, manifesting as either hyperthermia or hypothermia, is the most consistent clinical sign, appearing in 88 percent of patients. This is frequently accompanied by leukocyte abnormalities in 72 percent and tachycardia in 60 percent of the subjects. The severity of organ dysfunction, as quantified by the PELOD-2 score, shows a median value of 4. However, the extensive range of 0 to 23 highlights the profound multi-organ failure present in the most critical cases. Admission serum procalcitonin levels mirror this clinical heterogeneity, with a median of 0.88 ng/mL and peak values reaching 105 ng/mL. While 84 percent of the cohort survived to discharge, the 16 percent mortality rate emphasizes the lethal potential of advanced organ dysfunction in this high-acuity population.

Table 2 provides a comprehensive risk assessment of admission serum procalcitonin (PCT) levels as a factor associated with the severity of organ dysfunction. By dichotomizing the patient cohort using a statistically derived threshold of greater than 11 ng/mL, the study identifies a significant divergence in clinical outcomes. The analysis reveals that patients presenting with admission serum PCT levels exceeding this 11 ng/mL threshold are 2.20 times more likely to suffer from moderate or severe organ dysfunction compared to those with lower levels. Specifically, within the high-PCT group (greater than 11 ng/mL), 8 out of 10 patients manifested moderate-to-severe dysfunction. Conversely, in the group with PCT levels less than or equal to 11 ng/mL, only 5 out of 15 patients progressed to similar levels of severity, with the majority maintaining mild dysfunction scores.

The statistical validity of this association is supported by a Risk Ratio of 2.20, with a 95 percent confidence interval ranging from 1.15 to 4.24. The significance of this finding reached a p-value of 0.035, indicating a robust association between early-admission biomarker elevation and the physiologic failure quantified by the PELOD-2 scoring system. These findings suggest that an admission PCT level above 11 ng/mL acts as a critical biochemical red flag, indicating an intensified systemic inflammatory response that serves as a precursor to significant organ damage. Consequently, this threshold provides a concrete, actionable metric for clinicians to identify high-risk phenotypes and escalate therapeutic interventions early in the clinical course.

Table 1. Detailed Demographic and Clinical Profiles (N=25)

CLINICAL VARIABLE	FREQUENCY (N)	PERCENTAGE (%) / MEDIAN	RANGE / DISTRIBUTION
DEMOGRAPHIC INFORMATION			
Age	-	**12 months**	3 months – 17 years
Gender: Male	10	40%	-
Gender: Female	15	60%	-
PRIMARY DIAGNOSIS			
Pneumonia	10	**40%**	Pulmonary involvement
Sepsis / Septic Shock	8	32%	Systemic dysregulation
CNS Infection	4	16%	Meningitis / Encephalitis
Intra-abdominal Infection	3	12%	Localized inflammation
INFECTION INDICATORS (ADMISSION)			
Temperature Abnormalities	22	**88%**	>38°C or <36°C
Tachycardia	15	60%	Age-specific thresholds
Leukocyte Abnormalities	18	72%	Leukocytosis / Leukopenia
CLINICAL SEVERITY & OUTCOME			
PELOD-2 Score (Initial)	-	**4**	Range: 0 – 23
Admission PCT (ng/mL)	-	**0.88**	Range: 0.04 – 105.00
Survived	21	84%	Discharged from PICU
Deceased	4	**16%**	MODS-related mortality

TABLE 2. RISK RATIO ANALYSIS FOR ORGAN DYSFUNCTION

Predictive Assessment of Admission Procalcitonin Thresholds (N=25)

PROCALCITONIN LEVEL (ADMISSION)	MODERATE/SEVERE DYSFUNCTION (N)	MILD DYSFUNCTION (N)	TOTAL PATIENTS	RISK RATIO (95% CI)	STATISTICAL P-VALUE
Greater than 11 ng/mL	8	2	10	2.20 (1.15 – 4.24)	0.035
Less than or equal to 11 ng/mL	5	10	15	Reference Group	-

Key Interpretation: Critically ill children presenting with admission serum procalcitonin levels exceeding 11 ng/mL demonstrate a significantly elevated risk of developing moderate-to-severe organ failure as defined by the PELOD-2 scoring system. The Risk Ratio of 2.20 suggests a twofold increase in clinical risk compared to patients below this biochemical threshold.

Figure 1 illustrates the Receiver Operating Characteristic (ROC) curve analysis performed to determine the discriminative performance of admission serum procalcitonin in identifying the severity of organ dysfunction. The analysis specifically compared patients with moderate-to-severe dysfunction against those presenting with mild clinical statuses, yielding robust statistical results. The Area Under the Curve (AUC) was calculated at 0.82, with a 95 percent confidence interval extending from 0.65 to 0.99. This AUC value signifies an excellent discriminative ability, confirming that procalcitonin acts as a reliable indicator for risk stratification in the pediatric intensive care unit.

The optimal clinical cutoff was identified using the Youden Index, which maximizes the balance between sensitivity and specificity. Based on this calculation, a threshold of greater than 11 ng/mL was established as the most effective value for identifying patients at risk of significant physiological failure. At this threshold, the biomarker demonstrated a sensitivity of 78 percent and a specificity of 85 percent. These metrics indicate that the identified cutoff is highly effective at capturing the majority of patients requiring escalated care while maintaining high precision to avoid unnecessary intervention in lower-risk cases. The visual representation of the curve, which stays consistently above the diagonal identity line, further underscores the statistical superiority of procalcitonin measurement over random clinical prediction. By providing a clear and objective threshold, this ROC analysis supports the clinical implementation of procalcitonin as a proactive tool to anticipate organ failure progression and guide resuscitation strategies.

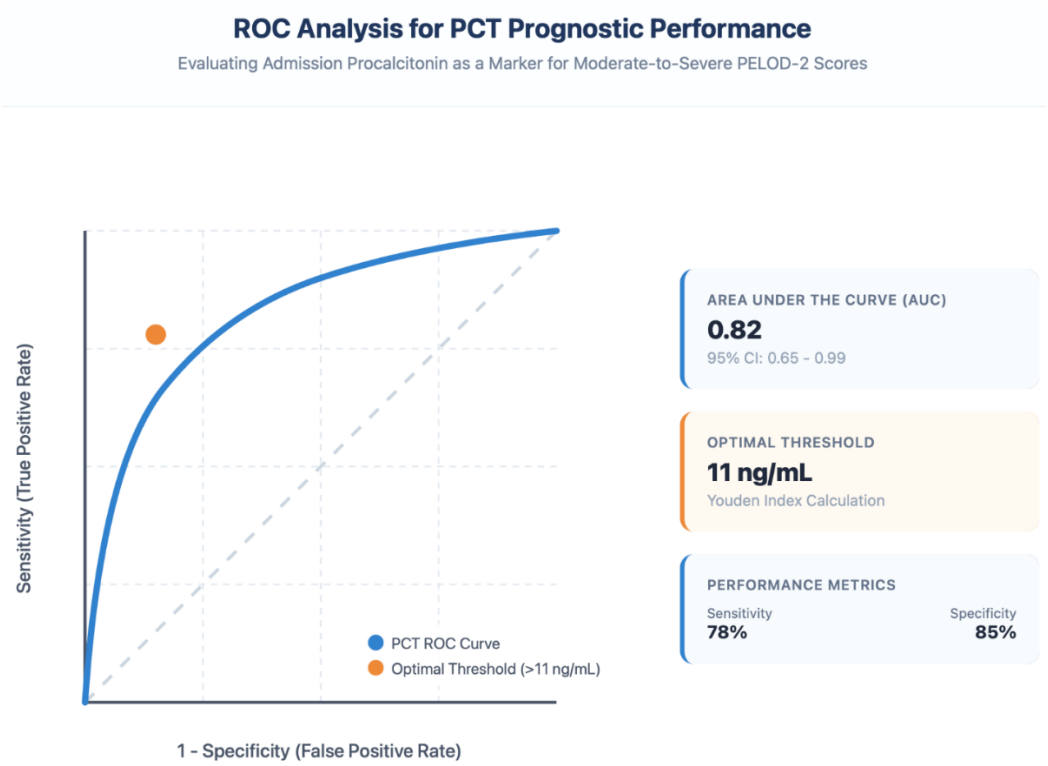

Figure 1. ROC analysis for PCT prognostic performance.

4. Discussion

This study provides compelling evidence demonstrating a definitive and clinically actionable link between admission serum procalcitonin concentrations and the severity of organ dysfunction in critically ill pediatric patients. To fully comprehend

the biological rationale underpinning this association, it is necessary to examine the complex molecular mechanisms that drive the phenomenon commonly referred to as the cytokine storm.[11] Under conditions of physiological homeostasis, the transcription of the CALC-1 gene is strictly confined to the neuroendocrine C-cells of the thyroid gland. Within this compartmentalized environment, the precursor molecule preprocalcitonin is synthesized and rapidly cleaved into procalcitonin, which is subsequently processed into the active hormone calcitonin. Because this intracellular processing is highly efficient and localized, virtually no intact procalcitonin escapes into the systemic circulation, resulting in baseline serum levels that are virtually undetectable, typically remaining below 0.05 ng/mL in a healthy pediatric state.[12]

However, the onset of severe bacterial infection fundamentally disrupts this normal physiological compartmentalization. When an invasive pathogen breaches the host defenses, pathogen-associated molecular patterns, specifically bacterial endotoxins such as lipopolysaccharides from Gram-negative bacteria, trigger a massive immune cascade. These bacterial components bind to toll-like receptors on the surface of circulating macrophages and tissue-resident monocytes, stimulating the immediate synthesis and systemic release of potent proinflammatory cytokines, prominently including tumor necrosis factor-alpha and interleukin-6.[13] This sudden influx of proinflammatory mediators upregulates the CALC-1 gene not just in the thyroid, but across virtually all parenchymal tissues in the human body, including the liver, kidneys, lungs, and diffuse adipose tissue. Because these parenchymal cells lack the specialized secretory granules and enzymatic machinery required to cleave procalcitonin into calcitonin, they release massive quantities of intact procalcitonin directly into the bloodstream. This phenomenon is known as the ubiquitous release of procalcitonin (Figure 2).[14]

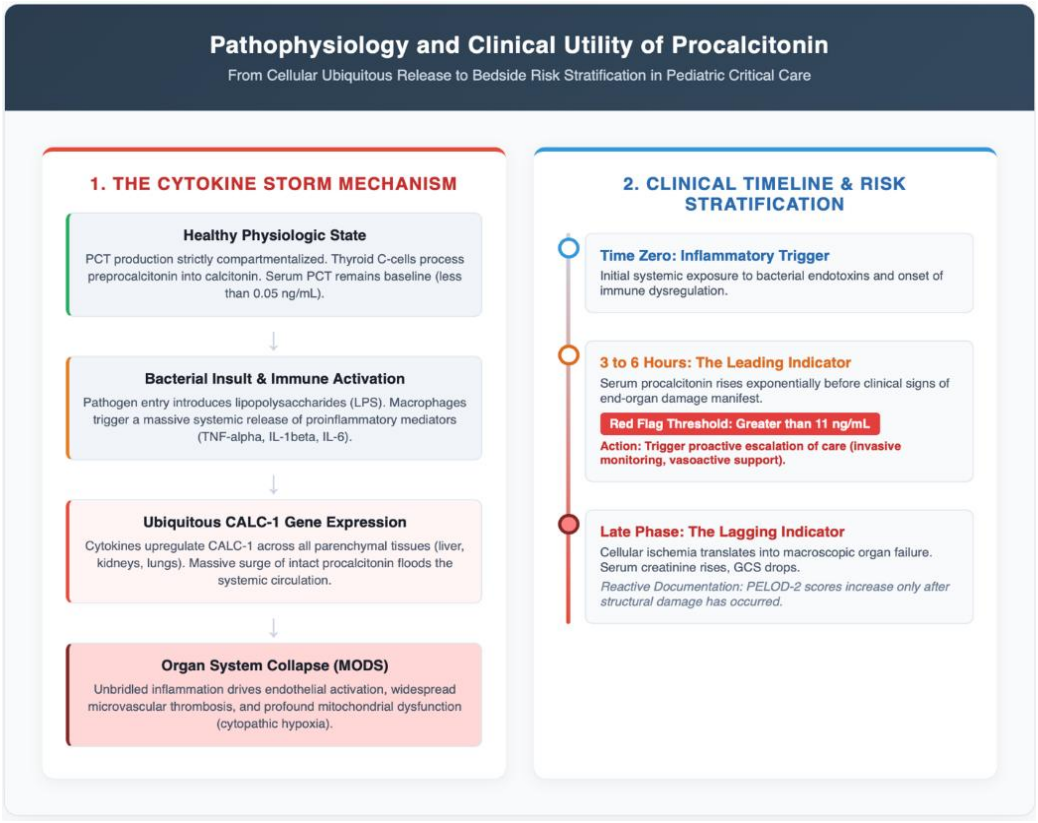

Figure 2. Pathophysiology and clinical utility of procalcitonin.

Crucially, the magnitude of this ubiquitous release is not an all-or-nothing binary response; rather, it is highly dose-dependent on the sheer intensity of the systemic inflammatory response syndrome. Our analytical findings, which establish a correlation between elevated procalcitonin levels and escalating PELOD-2 scores, strongly suggest that serum procalcitonin acts as a highly accurate mirror reflecting the total systemic inflammatory burden.[15] When a clinician observes exceptionally high procalcitonin levels, they are witnessing a biochemical representation of a state of unbridled, dysregulated inflammation. This systemic hyper-inflammation directly drives profound organ damage through three primary pathological mechanisms: endothelial activation, microvascular thrombosis, and mitochondrial dysfunction.

Endothelial activation results in the rapid degradation of the protective endothelial glycocalyx, leading to widespread capillary leak, profound tissue edema, and impaired oxygen diffusion to vital organs. Simultaneously, the inflammatory cascade hyperactivates the coagulation system while suppressing natural anticoagulants, resulting in microvascular thrombosis. This widespread deposition of fibrin within the microcirculation obstructs blood flow, causing microscopic tissue ischemia that culminates in macroscopic organ failure. Finally, profound systemic inflammation induces severe mitochondrial dysfunction, creating a state of cytopathic hypoxia. In this state, despite aggressive oxygen delivery and fluid resuscitation, the cellular mitochondria are fundamentally unable to utilize oxygen to produce adenosine triphosphate, leading to cellular energetic failure and subsequent organ collapse.[16] Because procalcitonin levels rise in direct proportion to the severity of these exact physiological disruptions, the biomarker serves as a precise biochemical proxy for the structural and functional integrity of the pediatric patient's organ systems.

Translating these complex pathophysiological mechanisms into actionable bedside protocols is the primary goal of pediatric critical care research. In this context, the identification of the 11 ng/mL procalcitonin cutoff emerges as the most clinically relevant and transformative finding of this research. In standard pediatric practice, considerably lower diagnostic cutoffs, typically ranging from 0.5 to 2.0 ng/mL, are frequently utilized to differentiate suspected bacterial sepsis from viral etiologies and to guide the timely initiation of broad-spectrum antimicrobial therapy. However, diagnosing the mere presence of an infection is a fundamentally different clinical task than prognosticating the imminent failure of multiple organ systems. Our data unequivocally indicate that for the specific assessment of organ failure severity and overall physiological collapse, a substantially higher threshold is required. This finding strongly aligns with extensive studies conducted in adult intensive care units, such as the pivotal work by Meng and colleagues, which demonstrated that procalcitonin levels exceeding 10 ng/mL were heavily associated with rapidly escalating organ failure and increased short-term mortality. Validating a comparable threshold in a pediatric cohort provides a vital, age-adapted metric that bridges a significant gap in critical care literature.[17]

The clinical implications of this threshold are profound. According to our risk analysis, a critically ill child presenting to the intensive care unit with a serum procalcitonin level greater than 11 ng/mL possesses a 2.2-fold increased risk of developing severe, life-threatening organ dysfunction compared to a child falling below this mark.[18] This value must be interpreted by the pediatric intensivist as an absolute biochemical red flag. The identification of this red flag should immediately trigger a proactive escalation of care, regardless of the patient's immediate outward appearance. This escalation includes interventions such as the rapid establishment of central venous access, the deployment of invasive arterial hemodynamic monitoring, and the early initiation of vasoactive or inotropic support. Crucially, these aggressive interventions should be deployed even if the

traditional, visible clinical signs of organ failure remain subtle or seemingly compensated. Children are notoriously capable of masking profound cardiovascular collapse through extreme compensatory tachycardia and profound peripheral vasoconstriction, often appearing clinically stable until the moment of precipitous decompensation.[19]

This highlights the fundamental limitation of traditional clinical scoring methodologies. The widely utilized PELOD-2 score is undeniably comprehensive, yet it remains an inherently lagging indicator. For a patient to accumulate a high PELOD-2 score, they must actively experience the failure of an organ system; the clinician must wait for serum creatinine levels to abnormally rise, or for the patient's Glasgow Coma Scale to detrimentally drop, before the score reflects the severity of the illness. By definition, irreversible cellular damage has already occurred by the time the score registers the decline.

Procalcitonin, conversely, functions as a highly sensitive leading indicator. The ubiquitous release of this biomarker occurs rapidly, with serum levels detectably rising within 3 to 6 hours of the initial inflammatory insult. This rapid kinetic profile provides clinicians with a vital temporal window—the golden hours of resuscitation—allowing them to anticipate the trajectory of the disease and intervene long before the overt clinical manifestations of organ failure are documented by the PELOD-2 criteria. Furthermore, our multivariate statistical analysis confirms that procalcitonin predicts this severity entirely independent of standard clinical vital signs, such as temperature instability or heart rate, which are notoriously non-specific and easily confounded in distressed pediatric populations.

However, the interpretation of these findings must remain contextualized within the limitations of the study design. The prospective cross-sectional methodology captures a critical snapshot of the patient's physiological state at admission, but it inherently limits the ability to track longitudinal therapeutic responses over prolonged intensive care stays. Additionally, the constrained sample size of twenty-five patients, acquired through purposive sampling, necessitates cautious extrapolation. Finally, the technological limitations of the Enzyme-Linked Fluorescent Assay instrument, which features an upper detection limit of 100 ng/mL, required the mathematical capping of extreme values. This limitation potentially underestimates the true statistical strength of the correlation in the most severely afflicted patients experiencing catastrophic cytokine storms.[20]

5. Conclusion

The physiological integrity of a critically ill child can deteriorate with catastrophic speed, demanding diagnostic tools that operate faster than the progression of the underlying disease. This study provides compelling, biologically grounded evidence demonstrating that early admission serum procalcitonin is a powerful, independent factor closely associated with the severity of organ dysfunction in pediatric sepsis. Through rigorous analytical evaluation against the established PELOD-2 scoring criteria, we have identified a critical prognostic threshold of greater than 11 ng/mL. Critically ill children surpassing this specific biomarker concentration exhibit a 2.2-fold increase in the relative risk of developing moderate-to-severe organ dysfunction. This elevated concentration serves as a direct mirror of the underlying cytokine storm, reflecting the severity of endothelial activation, microvascular thrombosis, and cytopathic hypoxia threatening the patient's survival.

Implementing this specific biomarker threshold into routine Pediatric Intensive Care Unit admission protocols possesses the potential to fundamentally revolutionize existing risk stratification paradigms. By integrating this rapid leading indicator, clinicians are empowered to move beyond the limitations of reactive, lagging clinical scoring systems like PELOD-2. Instead, they can transition toward a highly proactive model of biomarker-guided resuscitation, identifying high-risk physiological phenotypes early and initiating aggressive, life-saving therapies during

the most critical windows of opportunity. While these pilot findings are highly promising, the pursuit of precision pediatric critical care requires continuous validation. Future research endeavors should prioritize large-scale, multi-center longitudinal studies designed to validate this 11 ng/mL threshold across diverse pediatric demographics. Ultimately, the goal is to evaluate whether integrating procalcitonin-guided therapeutic algorithms into standardized intensive care workflows can demonstrably reduce the profound morbidity and mortality associated with Multiple Organ Dysfunction Syndrome in vulnerable pediatric populations.

6. References

1. Nandan D, Nimesh M, Kumar S, Manik L, Sudarshan J, Duggal N. Serum procalcitonin as an early inflammatory marker in pediatric ventilator-associated pneumonia. J Pediatr Crit CARE. 2021; 8(5): 229–33.
2. Fontela PS, Lacroix J. Procalcitonin: Is this the promised biomarker for critically ill patients? J Pediatr Intensive Care. 2016; 5(4): 162–71.
3. Sariego-Jamardo A, Rey C, Medina A, Mayordomo-Colunga J, Concha-Torre A, Prieto B, et al. C-reactive protein, procalcitonin and interleukin-6 kinetics in pediatric postoperative patients. J Crit Care. 2017; 41: 119–23.
4. Jacobs DM, Holsen M, Chen S, Fusco NM, Hassinger AB. Procalcitonin to detect bacterial infections in critically ill pediatric patients. Clin Pediatr (Phila). 2017; 56(9): 821–7.
5. Aygun F. Procalcitonin value is an early prognostic factor related to mortality in admission to pediatric intensive care unit. Crit Care Res Pract. 2018; 2018: 9238947.
6. Abbas Q, Raheem A, Haque AU. Relationship of serum procalcitonin, C-reactive protein, and lactic acid to organ failure and outcome in critically ill pediatric population. Indian J Crit Care Med. 2018; 22(2): 91–5.
7. Ross RK, Keele L, Kubis S, Lautz AJ, Dziorny AC, Denson AR, et al. Effect of the procalcitonin assay on antibiotic use in critically ill children. J Pediatric Infect Dis Soc. 2018; 7(2): e43–6.
8. Aygun F. Procalcitonin value is an early prognostic factor related to mortality in admission to pediatric intensive care unit. Crit Care Res Pract. 2018; 2018: 9238947.
9. Abbas Q, Raheem A, Haque AU. Relationship of serum procalcitonin, C-reactive protein, and lactic acid to organ failure and outcome in critically ill pediatric population. Indian J Crit Care Med. 2018; 22(2): 91–5.
10. Ross RK, Keele L, Kubis S, Lautz AJ, Dziorny AC, Denson AR, et al. Effect of the procalcitonin assay on antibiotic use in critically ill children. J Pediatric Infect Dis Soc. 2018; 7(2): e43–6.
11. Samraj RS, Crotty EJ, Wheeler DS. Procalcitonin levels in critically ill children with status asthmaticus. Pediatr Emerg Care. 2019; 35(10): 671–4.
12. Hassuna NA, Elgezawy E, Mousa SO, AbdelAziz RA, Ibrahem RA, Wahed WYA, et al. Diagnostic value of monocyte chemoattractant Protein-1, soluble mannose receptor, Presepsin, and Procalcitonin in critically ill children admitted with suspected sepsis. BMC Pediatr. 2021; 21(1): 458.
13. Guitart C, Rodríguez-Fanjul J, Bobillo-Perez S, Carrasco JL, Inarejos Clemente EJ, Cambra FJ, et al. An algorithm combining procalcitonin and lung ultrasound improves the diagnosis of bacterial pneumonia in critically ill children: The PROLUSP study, a randomized clinical trial. Pediatr Pulmonol. 2022; 57(3): 711–23.
14. Aggarwal N, Karki D, Gaind R, Matlani M, Muthukumar V. Serum procalcitonin and C-reactive protein as indices of early sepsis and mortality in North Indian pediatric burn

injuries: a prospective evaluation and literature review. Acute Crit Care. 2024; 39(3): 350–8.

15. Ramdzan MYM, Tan KK, Soo KW. Utility of procalcitonin in diagnosing early postoperative sepsis after pediatric cardiac surgery in Malaysia. Acute Crit Care. 2025; 40(4): 567–73.
16. Li X, Wang X, Li S, Yan J, Li D. Diagnostic value of procalcitonin on early postoperative infection after pediatric cardiac surgery. Pediatr Crit Care Med. 2017; 18(5): 420–8.
17. Yöndem AU, Yüce S, Aygüler E, Gencay AG, Demirkol D. Procalcitonin kinetics in critically ill children: impact of continuous kidney replacement therapy modality and dose. Pediatr Nephrol. 2026.
18. Lima LFP, Maschion JMS, Rodriguez NAA, Ribeiro RCA. Procalcitonin for bacterial infection management: a comprehensive understanding may clarify its due value. Pediatr Crit Care Med. 2016; 17(6): 581–2.
19. Zant R, Stocker C, Schlapbach LJ, Mayfield S, Karl T, Schibler A. Procalcitonin in the early course post pediatric cardiac surgery. Pediatr Crit Care Med. 2016; 17(7): 624–9.
20. Dechnik A, Mauer EA, Gerber LM, Traube C. C-reactive protein and procalcitonin levels may not predict delirium in critically ill children. Pediatr Crit Care Med. 2020; 21(11): e967–71.