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Original article

Serum amyloid A and proadrenomedullin as early markers in critically ill children with sepsis

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Background: Proadrenomedullin (proADM), the most stable part of adrenomedullin (ADM), serves as an indirect marker of ADM levels. Serum amyloid A (SAA) is a protein produced primarily in the liver during acute inflammation.

Purpose: To assess the role of SAA and proADM, individually and in combination, as diagnostic and prognostic markers in pediatric sepsis.

Methods: This prospective case-control cohort study included 65 critically ill children admitted to the pediatric intensive care unit (PICU) and 31 controls. The study grouped the cases by confirmed diagnosis of sepsis, severe sepsis, or septic shock. All children included in this study underwent PICU scoring, routine laboratory investigations, and specific serum biomarker assessments (SAA and proADM).

Results: The mean SAA and proADM levels were significantly higher in the patients versus controls. Both markers were elevated in patients with sepsis, with even higher levels observed in those with severe sepsis and septic shock. SAA demonstrated greater sensitivity for predicting mortality than proADM (61% vs. 52%, respectively). When used together, the sensitivity of the 2 tests for predicting mortality increased to 70%. The 2 tests exhibited fair specificity (57%).

Conclusion: SAA and proADM are promising biomarkers for diagnosing and predicting outcomes of pediatric sepsis.

Key words: Amyloid A, Biomarkers, Child, Critically ill, Proadrenomedullin

Key message

Question: Are serum amyloid A (SAA) and proadrenomedullin (proADM) levels early markers in critically ill children with sepsis?

Finding: This prospective case-control study included 65 critically ill children with sepsis admitted to the pediatric intensive care unit and 31 controls. SAA and proADM levels were significantly higher in patients versus controls.

Meaning: SAA and proADM are promising biomarkers for diagnosing and predicting outcomes in pediatric sepsis.

Introduction

Pediatric sepsis is a severe and potentially fatal condition involving organ dysfunction caused by an abnormal host response to infection. Septic shock, a severe subset of sepsis, is characterized by profound circulatory and cellular/metabolic disturbances that significantly elevate mortality risk.[1)]

Prompt identification of pediatric septic shock through source detection, assessment of inflammatory markers, and biomarker analysis, along with initiating aggressive reatment, can potentially reverse shock symptoms.[2)]

Distinguishing bacterial sepsis from other sources of systemic inflammatory response syndrome (SIRS) in critically ill children is a complex task. Diagnosing sepsis typically involves identifying suspected infections alongside the presence of 2 or more SIRS criteria.[3)]

Biomarkers serve as valuable tools in determining the presence or absence of bacterial infections. Using multiple biomarkers rather than a single one can enhance infection specificity and improve the accuracy of distinguishing true bacterial sepsis from other SIRS causes.[4)]

Adrenomedullin (ADM) is a highly potent peptide that induces vasodilation and is produced during sepsis. However, accurately measuring ADM is technically difficult due to its short half-life ($t_{1/2}$=22 minutes), causing it to be rapidly

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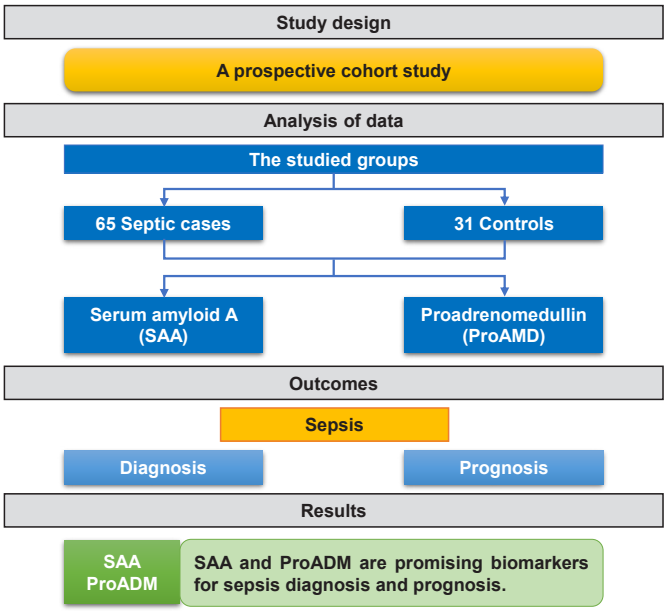

Graphical abstract

eliminated from the blood stream. Proadrenomedullin (proADM), the most stable part of ADM, serves as an indirect marker for ADM measurement.[5]

Serum amyloid A (SAA) is a protein produced primarily in the liver during the acute phase of inflammation, with its serum concentration potentially increasing up to 1,000-fold during acute inflammatory responses.[6] Consequently, this study aimed to evaluate the roles of proADM and SAA as biomarkers in pediatric sepsis.

Methods

1. Study design

This was a prospective case-control cohort study conducted on 65 critically ill children admitted to the pediatric intensive care unit (PICU) at Menoufia University Hospital. Additionally, 31 apparently healthy children, matched for age and sex with the patients, served as controls. The study spanned from October 2020 to September 2021. The study included children aged 1 month to 16 years with a confirmed diagnosis of sepsis, severe sepsis, or septic shock at the time of admission to the PICU. The diagnoses were based on definitions provided by the American College of Critical Care Medicine and the International Pediatric Sepsis Consensus Congress (IPSCC).[7] Exclusion criteria were (1) patients without blood samples collected within 24 hours of PICU admission for marker measurement, (2) patients not meeting the diagnostic criteria for sepsis and (3) patients with chronic diseases, such as amyloidosis, atherosclerosis, systemic lupus erythematosus, rheumatoid arthritis, pericarditis, or inflammatory bowel disease, which could influence SAA measurements.

2. Patient groups

The patients were categorized into 3 groups: sepsis group: comprising 23 patients (11 males and 12 females), severe sepsis group: comprising 18 patients (10 males and 8 females) and septic shock group: comprising 24 patients (12 males and 12 females). In addition, a control group included 31 apparently healthy children (15 males and 16 females).

Sepsis is defined as a systemic response to an infectious stimulus defined by 2 or more of the following factors, leading to infection: (1) body temperature>38°C or <36°C, (2) heart rate>90 beats/min, (3) respiratory rate>20 breaths/min or carbon dioxide pressure ($PaCO_2$) <32 mmHg, and (4) white blood cell count>12,000/mm^3 or <4,000/mm^3, or >10% immature (band) formation in the total blood count. Severe sepsis is defined as sepsis plus the following: cardiovascular impairment, acute respiratory distress syndrome, or 2 or more other organ impairments. Septic shock is defined as a subset of severe sepsis known as sepsis-induced hypotension that persists despite adequate fluid replacement. The definitions were based on the IPSCC.[7]

3. Study outcomes

The primary outcome was sepsis diagnosis, and secondary outcomes were sepsis prognosis, PICU stay length and correlation between clinical and laboratory characteristics with serum biomarkers.

Methods

All children included in this study underwent the following: comprehensive history-taking, thorough general and localized physical examinations and the implementation of PICU scoring systems in form of disseminated intravascular coagulation (DIC) score,[8] pediatric index of mortality-2 (PIM2) is a more rapid technique for which scores are estimated within 1 hour of in-person contact with the patient, and scores correspond to a predicted mortality rate[9] and pediatric sequential organ failure assessment scale (pSOFA) is used to assess organ dysfunction. Depending on the patient's baseline risk level, a pSOFA score of 2 or greater corresponds to a 2- to 25-fold greater risk of death than patients with pSOFA scores was less than 2.[10]

All patients underwent routine investigations at the time of admission, which included a complete blood count, random blood sugar measurement, electrolyte analysis, liver and kidney function tests, C-reactive protein levels, blood culture, and coagulation studies (prothrombin time and international normalized ratio). Additionally, specific serum biomarkers were assessed, with single measurements of SAA and proADM performed for all patients within 24 hours of admission to the PICU. These biomarkers were also measured for the control group using the quantitative SAA ELISA Kit (Catalogue No. 201-12-1226) and the Human ProADM ELISA Kit (Catalogue No. 201-12-2196).

The authors declare review and approval of the study by the research ethical committees in the faculty of medicine, Menoufia University. Freely given, informed, written consent to participate in the study was obtained from

Table 1. Demographic and clinical characteristics of patient groups

Variable	Sepsis (N=23)	Severe sepsis (N=18)	Septic shock (N=24)	Test	*P* value
Age (mo)				1.20[a]	0.547
Mean±SD	17.5±24.5	26.1±38.6	15.8±18.2		
Median (IQR)	8.0 (3.0–36.0)	15.5 (6.0–24.0)	9.5 (4.8–19.0)		
Sex, n (%)				0.25[b]	0.882
Male	11 (47.8)	10 (55.6)	12 (50.0)		
Female	12 (52.2)	8 (44.4)	12 (50.0)		
Weight (kg)				1.66[a]	0.44
Mean±SD	8.8±8.1	11.4±9.0	9.0±5.0		
Median (IQR)	10.9 (7.6–14.8)	13.5 (10.2–16.0)	11.8 (7.2–14.0)		
Height (cm)				1.73[a]	0.42
Mean±SD	73.4±22.3	80.9±25.9	75.8±16.9		
Median (IQR)	73.0 (67.0–97.0)	88.5 (75.2–102.5)	84.0 (68.5–97.5)		
BMI (kg/m^2)				1.20[a]	0.55
Mean±SD	16.1±3.8	16.6±4.1	15.2±3.5		
Median (IQR)	17.4 (14.6–18.7)	16.7 (15.1–18.3)	16.0 (14.9-17.4)		
DIC score				10.80[a]	**0.005**
Mean±SD	2.6±0.8	2.7±1.3	4.2±2.0		
Median (IQR)	2.0 (2.0–3.0)	2.0 (2.0-3.0)	3.5 (2.75–7.0)		
pSOFA score				14.71[a]	**<0.001**
Mean±SD	4.7±1.8	5.6±3.2	8.1±3.5		
Median (IQR)	5.0 (3.0–5.5)	5.0 (4.0–6.0)	8.0 (5.0–10.0)		
PIM2 score				10.70[a]	**0.005**
Mean±SD	13.5±13.2	18.2±24.6	36.3±27.1		
Median (IQR)	8.8 (7.4–13.8)	10.6 (6.6–15.1)	34.7 (17.6–49.9)		
PICU stay (day)				0.53[a]	0.767
Mean±SD	11.1±13.0	9.8±7.0	8.3±4.3		
Median (IQR)	7.0 (4.0–11.5)	9.0 (4.2–12.0)	7.5 (5.8–9.2)		
MV, n (%)				3.8[b]	0.146
Yes	10 (43.5)	13 (56.5)	9 (50.0)		
No	9 (50.0)	17 (70.8)	7 (29.2)		
MV duration (hr)				0.12[a]	0.94
Mean±SD	205.7±191.8	153.7±92.4	160.9±82.3		
Median (IQR)	120.0 (96.0–258.0)	132.0 (96.0–216.0)	144.0 (120.0–216.0)		

SD, standard deviation; IQR, interquartile range; BMI, body mass index; DIC, disseminated intravascular coagulation; pSOFA, Pediatric Sequential Organ Failure Assessment; PIM2, Pediatric Index of Mortality 2; PICU, pediatric intensive care unit; MV, mechanical ventilation.
[a]Kruskal-Wallis rank-sum test. [b]Chi-square test.
Boldface indicates a statistically significant difference with $P<0.05$.

participants parents. Participants were informed about objectives of the study. Ethical approval number was 7/2020PEDI30.

Data were collected, organized, and analyzed statistically using IBM SPSS Statistics ver. 20.0 (IBM Co., USA). The Student *t* test was employed to compare 2 groups with normally distributed quantitative variables, whereas the Mann-Whitney U test was utilized for comparing 2 groups with nonnormally distributed quantitative variables. The chi-square test was applied to evaluate the association between 2 qualitative variables. Pearson correlation coefficient (*r*) was used to measure the relationship or rank-order correlation between variables. Receiver operating characteristic (ROC) curve analysis was used to evaluate the ability to differentiate between affected (diseased) and normal cases.

Results

This study included 65 children diagnosed with sepsis, with ages ranging from 4.0 to 24.0 months and a mean age of 22.8 months. Additionally, 31 apparently healthy children, matched by age and sex with the patients, were enrolled as a control group.

There were significant differences in DIC, PIM2, and

Table 2. Laboratory characteristics by patient group

Variable	Sepsis (N=23)	Severe sepsis (N=18)	Septic shock (N=24)	Test[a)]	*P* value
Hemoglobin (gm/dL)	2.52	0.284		2.52	0.284
Mean±SD	10.5±1.6	11.6±2.6	10.2±3.2		
Median (IQR)	10.4 (9.8–11.2)	11.4 (10.3–12.3)	10.0 (8.5–12.6)		
WBC (1,000/μL)	1.68	0.432		1.68	0.432
Mean±SD	14.1±8.1	19.3±11.5	17.8±15.4		
Median (IQR)	11.0 (8.4–16.8)	15.4 (12.4–28.2)	11.7 (7.5–25.0)		
Platelets (1,000/μL)	15.25	<0.001		15.25	**<0.001**
Mean±SD	174.3±61.63	142.44±59.01	96.33±68.23		
Median (IQR)	170.0 (110.5–221.0)	136.5 (107.5–195.5)	86.0 (50.8-129.2)		
ANC (1,000/mL)	1.76	0.416		1.76	0.416
Mean±SD	8.2±5.4	11.9±8.4	9.5±8.1		
Median (IQR)	7 (4.1–10.1)	11.2 (4.4-17.0)	7.9 (3.3–13.8)		
CRP (mg/dL)	0.96	0.61		0.96	0.61
Mean±SD	37.1±35.8	41.2±64.8	56.2±71.1		
Median (IQR)	24.0 (6.0-70.5)	16.8 (4.2–39.8)	34.1 (6.0–80.2)		
Base deficit (mEq/L)	3.39	0.183		3.39	0.183
Mean±SD	-5.1±8.5	-3.3±9.0	-8.4±9.1		
Median (IQR)	-3.0 (-8.0 to 1.8)	-2.5 (-6.0 to 1.9)	-5.5 (-14.6 to -3.5)		
Prothrombin time (sec)	4.28	0.118		4.28	0.118
Mean±SD	15.6±2.7	15.8±2.3	18.4±5.4		
Median (IQR)	15.7 (13.2–17.4)	15.4 (14.1–17.0)	17.0 (14.1–21.2)		
INR	4.26	0.119		4.26	0.119
Mean±SD	1.3±0.3	1.2±0.3	1.5±0.5		
Median (IQR)	1.2 (1.0-1.5)	1.1 (1.0-1.3)	1.4 (1.1–1.9)		
AST (U/L)	1.18	0.554		1.18	0.554
Mean±SD	32.3±15.0	37.4±22.1	123.2±159.3		
Median (IQR)	27.0 (21.0–44.5)	32.5 (22.8–43.0)	31.0 (19.8-202.8)		
ALT (U/L)	1.59	0.453		1.59	0.453
Mean±SD	27.0±22.3	29.6±19.5	96.2±140.2		
Median (IQR)	18.0 (12.0–31.5)	23.0 (16.2–39.5)	19.5 (13.5–128.2)		
Creatinine (mg/dL)	2.12	0.347		2.12	0.347
Mean±SD	0.5±0.6	0.5±0.4	0.6±0.6		
Median (IQR)	0.2 (0.2–0.4)	0.3 (0.2-0.6)	0.3 (0.2–0.9)		
Total serum bilirubin (mg/dL)	16.08	<0.001		16.08	**<0.001**
Mean±SD	0.4±0.3	0.3±0.2	2.6±7.3		
Median (IQR)	0.4 (0.3–0.5)	0.2 (0.2–0.4)	0.6 (0.4-1.0)		

SD, standard deviation; IQR, interquartile range; WBC, white blood cell; ANC, absolute neutrophil count; CRP, C-reactive protein; INR, international normalized ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase.
[a)]Kruskal-Wallis rank-sum test.
Boldface indicates a statistically significant difference with $P<0.05$.

pSOFA scores among the sepsis subgroups. These scores were highest in the septic shock group compared to the severe sepsis and sepsis groups, consistent with the increasing severity of the condition (Table 1). Platelet counts and total serum bilirubin levels also showed significant differences among the subgroups, with platelet counts markedly lower in septic shock cases and total bilirubin levels elevated in the same group (Table 2).

The mean levels of SAA and proADM were significantly higher in patients compared to the control group. Significant differences in SAA and proADM levels were observed between the control and sepsis subgroups, as well as among the sepsis subgroups. Levels of SAA and pro ADM were notably higher in the septic shock group than in controls or other subgroups, correlating with disease severity (Table 3; Fig. 1A and B).

Regarding clinical characteristics, both SAA and proADM demonstrated significant positive correlations with PIM2, DIC, and pSOFA scores, as well as the PICU stay. While proADM correlated positively with hospital stay and DIC scores. In terms of laboratory parameters, both SAA and proADM exhibited significant positive correlations with blood urea levels and negative correlations with platelet counts. Additionally, proADM was positively correlated with alanine aminotransferase levels (Table 4).

Both biomarkers demonstrated good sensitivity for predicting sepsis, with SAA at 68% and proADM at 66%. proADM was more specific (65%) compared to SAA (55%). Combining the 2 tests improved sensitivity for predicting sepsis to 77%, with an overall accuracy of 69%. SAA demonstrates greater sensitivity in predicting mortality compared to proADM, with rates of 61% versus 52%. When both tests are used together, the sensitivity for predicting mortality increases to 70%. However, both tests exhibit fair specificity at 57% (Table 5; Fig. 2A and B).

Discussion

Early and accurate diagnosis and risk stratification are

Table 3. Serum biomarker levels of patients versus controls

Biomarker	Controls (n=31)	Sepsis (n=23)	Severe sepsis (n=18)	Septic shock (n=24)	Test[a)]	*P* value[a)]	Test[b)]	*P* value[b)]	Survivors	Nonsurvivors	Test[c)]	*P* value[c)]
SAA (μg /mL)					-2.91	**0.002**	6.55	**0.038**			0.773	0.08
Mean±SD	7.8±4.2	9.1±5.0	13.4±5.7	14.4±9.5					11.7±6.7	12.5±7.9		
Median (IQR)	6.2 (5.2–8.5)	6.1 (5.6–12.1)	12.5 (9.7–18.5)	10.2 (6.7–24.9)					9.2 (5.7–16.0)	10.0 (5.8-18.7)		
ProADM (ng/mL)					-2.97	**<0.001**	12.01	**0.002**			0.162	1.96
Mean±SD	89.9±37.1	105.7±59.4	146.3±70.0	185.0±80.5					127.1±63.1	156.7±83.2		
Median (IQR)	73.5 (63.8–09.0)	71.1 (62.9–163.1)	152.7 (93.0–194.2)	204.9 (111.0–236.4)					111.3 (67.2–186.4)	159.6 (71.9-230.9)		

SAA, serum amyloid A; SD, standard deviation; IQR, interquartile range; ProADM, proadrenomedullin.
[a)]Kruskal-Wallis rank-sum test and *P* value: between the sepsis subgroups (sepsis, severe sepsis, septic shock) and controls. [b)]Kruskal-Wallis rank-sum test and *P* value: among the sepsis subgroups (sepsis, severe sepsis, septic shock). [c)]Kruskal-Wallis rank-sum test and *P* value: between survivors and nonsurvivors.
Boldface indicates a statistically significant difference with *P*<0.05.

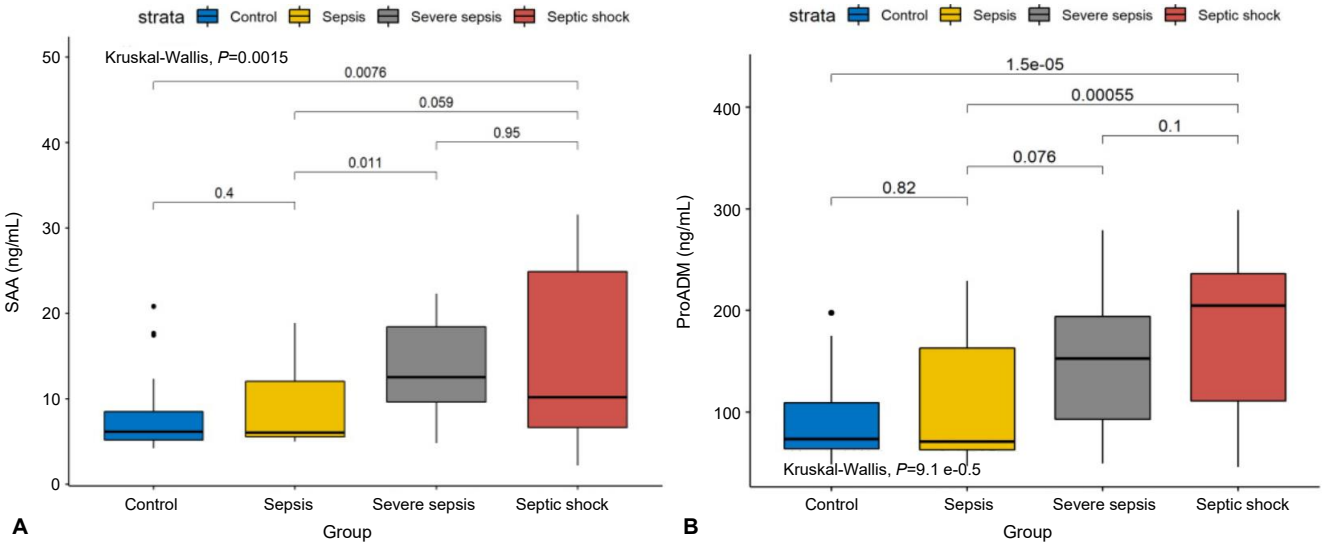

Fig. 1. (A) Serum amyloid A (SAA) levels by patient subgroup. (B) Serum proadrenomedullin (proADM) levels by patient subgroup.

critical for the optimal care of critically ill patients. The use of easily measurable circulating biomarkers can enhance timely assessment, severity classification, and mortality prediction in septic patients.[11] However, to date, no single biomarker or combination of biomarkers has reliably distinguished sepsis from trauma or tissue damage. Many sepsis biomarkers either rise too slowly or drop too quickly, making it challenging for clinicians to detect developing sepsis or rule it out as a cause of deterioration.[12]

ADM plays an important role in immune modulation, metabolic regulation, and vascular tone. The stable midregional fragment of proADM reflects the levels of rapidly degraded active ADM.[13,14] SAA, an acute-phase reactant synthesized in the liver, increases significantly during inflammation, making it a key marker of systemic inflammation.[15]

The pediatric pSOFA score is widely used to track the severity of organ dysfunction and predict PICU outcomes, thanks to its simplicity and reliance on routinely available clinical parameter.[16] Similarly, the PIM2 is a robust tool for estimating mortality risk at PICU admission and facilitates ongoing quality assessments.[17,18]

This study evaluates the diagnostic and prognostic roles of SAA and proADM in pediatric sepsis that has been less

Table 4. Correlation between clinical and laboratory characteristics and serum biomarkers

Characteristic	SSA		ProADM	
	r	*P* value	*r*	*P* value
Age (mo)	0.03	0.78	0.024	0.81
Weight (kg)	0.09	0.40	0.07	0.47
Height (cm)	0.10	0.36	0.11	0.27
BMI (kg/m^2)	0.05	0.64	-0.06	0.57
PIM2 score	0.24	0.02	0.25	0.01
pSOFA score	0.34	<0.001	0.33	<0.001
DIC score	0.19	0.06	0.26	0.01
PICU stay (day)	0.23	0.03	0.24	0.02
Hospital stay (day)	0.12	0.25	0.22	0.03
WBC (1,000/μL)	0.05	0.66	0.13	0.19
Platelets (1,000/μL)	-0.34	<0.001	-0.36	0.001
Hemoglobin (gm/dL)	-0.07	0.52	-0.13	0.22
ANC (1,000/mL)	0	0.98	0.07	0.47
CRP (mg/dL)	0.03	0.76	0	0.97
Creatinine (mg/dL)	0.02	0.81	0.16	0.13
Urea (mg/dL)	0.21	0.04	0.22	0.03
PT (sec)	0.01	0.94	0.14	0.16
INR	0.12	0.25	0.15	0.15
AST (U/L)	0.13	0.20	0.18	0.08
ALT (U/L)	0.13	0.22	0.26	0.01
Bilirubin (mg/dL)	-0.02	0.86	0.01	0.95
Base deficit (mEq/L)	0.12	0.25	0.07	0.48

SAA, serum amyloid A; ProADM, proadrenomedullin; r, Pearson correlation coefficient; BMI, body mass index; PIM2, pediatric index of mortality 2; pSOFA, pediatric sequential organ failure assessment; DIC, disseminated intravascular coagulation; PICU, pediatric intensive care unit; WBC, white blood cell; ANC, absolute neutrophil count; CRP, C-reactive protein; PT, prothrombin time; INR, international normalized ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Table 5. Validity of biomarkers for predicting sepsis and mortality

Parameter	AUC	*P* value	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
Prediction of sepsis								
SAA	0.684	0.004	6.50	68%	55%	76%	45%	64%
ProADM	0.688	0.003	90.0	66%	65%	80%	48%	66%
SAA+proADM	-	-	-	77%	52%	77%	52%	69%
Prediction of mortality								
SAA	0.522	0.773	9.88	61%	57%	44%	73%	58%
ProADM	0.606	0.162	124.8	52%	57%	43%	66%	55%
SAA+proADM	-	-	-	70%	50%	43%	75%	57%

AUC, area under curve; PPV, positive predictive value; NPV, negative predictive value; SAA, serum amyloid A; ProADM, proadrenomedullin.

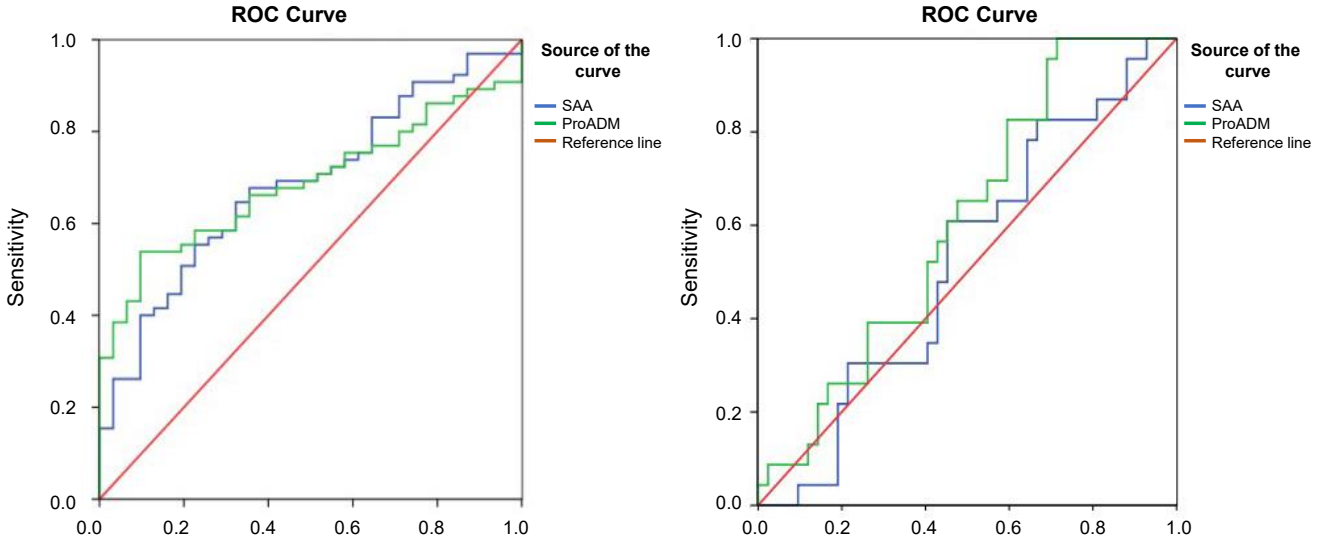

Fig. 2. (A) ROC curve of SAA and proADM for predicting sepsis. (B) ROC curve of SAA and proADM for predicting mortality. proADM, proadrenomedullin; ROC, receiver operating characteristic; SAA, serum amyloid A.

studied compared to their roles in adult and neonatal sepsis.[19] SAA is an acute-phase reactant that responds rapidly to inflammatory cytokines such as interleukin (IL)-1, IL-6, and tumor necrosis factor-α. While mild SAA elevation is common in viral infections or localized inflammation, its significant elevation often signals bacterial infections.[20]

In this study, SAA levels were significantly higher in septic patients than in controls (P<0.004), and levels increased progressively from sepsis to septic shock (P=0.038). However, no significant differences were observed between survivors and nonsurvivors (P=0.08). This aligns with findings by Yahia et al.,[19] who reported elevated SAA levels in septic children and higher levels in nonsurvivors than survivors (P<0.001). Other studies, such as those by Abo-Hagar et al.,[21] and Yu and Li[22] corroborated the role of SAA in distinguishing sepsis severity.

Regarding proADM, the current study found significantly higher levels in patients compared to controls (P< 0.003), with levels increasing across sepsis subgroups (P= 0.002). However, proADM levels did not differ significantly between survivors and nonsurvivors (P=1.96). These findings are consistent with Solé-Ribalta et al.,[23] who observed a gradual increase in proADM levels from sepsis to septic shock among pediatric patients. Similar trends were noted in adult studies, such as those by Angeletti et al.[24] and Andaluz-Ojeda et al.[25]

The ROC analysis in this study demonstrated moderate predictive accuracy for both biomarkers in diagnosing sepsis, with SAA achieving an area under curve (AUC) of 0.684 (sensitivity 68%, specificity 55%) and proADM an AUC of 0.688 (sensitivity 66%, specificity 65%). Combining the 2 markers improved sensitivity to 77%, with an overall accuracy of 69%. Previous studies have reported varied results for SAA and proADM, likely due to differences in infection control measures, sample sizes, and patient populations.[19,26-28]

For mortality prediction, SAA was slightly more sensitive (61%) than proADM (52%), but combining the 2 markers improved sensitivity to 70%. Despite this, their standalone predictive abilities were limited. These findings mirror observations by Suberviola et al.[29] and Valenzuela-Sánchez et al.,[30] who reported that ProADM levels alone were insufficient for predicting mortality in adults. Notably, Guignant et al.[31] found that ProADM's predictive accuracy improved after 5–7 days, suggesting that serial measurements might enhance its utility.

In conclusion, while SAA and proADM are valuable for diagnosing sepsis, their ability to predict mortality in pediatric patients is limited when used individually. Combining the 2 biomarkers modestly improves diagnostic sensitivity but does not significantly enhance mortality prediction. Serial measurements of these biomarkers may improve their predictive utility in clinical practice.

This study has some limitations that should be considered. First, only a single measurement of proADM and SAA levels was taken at admission, and serial measurements of these biomarkers over time could provide more valuable insights into their role in sepsis diagnosis and prognosis. Second, this was a single-center study, and results may be influenced by local practices or patient demographics. Therefore, we recommend conducting further multicenter studies with larger sample sizes to validate and expand upon these findings.

In conclusion, SAA and proADM are promising biomarkers for diagnosing and predicting outcomes in pediatric sepsis. Both markers are elevated in sepsis patients, with even higher levels observed in those with severe sepsis and septic shock. SAA demonstrates greater sensitivity in predicting mortality compared to proADM, with rates of 61% versus 52%. When both tests are used together, the sensitivity for predicting mortality increases to 70%. However, both tests exhibit fair specificity at 57%.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

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