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Procalcitonin and C-reactive protein as early diagnostic markers of sepsis or septic shock in children who presented with fever to the pediatric emergency department at a tertiary hospital, in Riyadh, Saudi Arabia

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Abstract

Background Sepsis is a leading cause of morbidity and mortality in children, requiring early recognition for timely intervention. Traditional biomarkers like C-reactive protein (CRP) are widely used but have limitations in specificity and early detection. Procalcitonin (PCT) has emerged as a promising alternative for differentiating bacterial infections from viral illnesses. This study aims to evaluate the diagnostic performance of PCT and CRP in identifying sepsis among febrile pediatric patients presenting to the emergency department (ED).

Methods We conducted a retrospective, observational study at a tertiary hospital from January 2022 to January 2024. A total of 208 children aged 1 month to 14 years with fever (≥ 38 °C) were included. Patients were categorized into sepsis ($n=84$) and non-sepsis ($n=124$) groups based on clinical assessment and blood culture results. Biomarker levels, patient demographics, clinical outcomes, and disposition were analyzed.

Results Elevated PCT and CRP levels were significantly associated with sepsis. PCT demonstrated earlier elevation compared to CRP, correlating with higher rates of PICU admission (34.7% vs. 11.1%, $p<0.001$). Blood culture positivity was a strong predictor of severe sepsis (OR: 9.369, $p<0.0003$). Logistic regression identified high-grade fever, chronic disease, and viral co-infections as additional risk factors.

Conclusion PCT is a superior early biomarker for detecting invasive bacterial infections compared to CRP. Incorporating PCT in sepsis protocols can improve early diagnosis, guiding prompt and appropriate management in pediatric ED settings.

Keywords Sepsis, Fever, Procalcitonin, C-reactive protein, Pediatric emergency, And bacterial infections

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Introduction

Fever in children aged 1–60 months is a common reason for emergency visits. Thorough history-taking, including immunization status and careful physical examination, is essential despite many cases being caused by viral illnesses. Distinguishing between invasive and non-invasive bacterial infections based solely on history and examination can be challenging. Therefore, in pediatric emergency departments, reliable biochemical markers are needed to aid in this differentiation, especially for children at risk of sepsis, comprising those with immunodeficiencies, those undergoing chemotherapy, and those who are dependent on central lines. Early diagnosis is crucial for an appropriate emergency department disposition.

Traditionally, C-reactive protein (CRP) has been used as an acute-phase reactant and marker of bacterial infection. However, relying solely on CRP can cause excessive prescription of antibiotics, as its levels can be elevated in minor or viral infections and may not reflect the severity of an infection, particularly in the initial 12 h [1, 2]. Procalcitonin (PCT), a prohormone of calcitonin, is a serum biomarker for invasive bloodstream infections [3]. In healthy individuals, serum PCT levels are low (< 0.5 ng/mL); however, in severe infections, the levels can rise significantly without corresponding changes in serum calcitonin levels. Studies have shown that after three hours, PCT levels increased rapidly following endotoxin introduction into the bloodstream and peaked at 6 h, with a half-life of 25–30 h [4, 5]. In contrast, CRP levels did not increase within the first 6 h after endotoxin exposure, and its decline was more delayed than that of PCT [6]. PCT may offer advantages over CRP in the differential diagnosis of febrile syndromes in children due to its shorter half-life and earlier elevation. In this study, we aimed to assess the diagnostic performance of PCT in pediatric emergency departments for the early detection of invasive bacterial infections in febrile children and to compare it with that of CRP.

Clinical sepsis in children is characterized as life-threatening organ dysfunction caused by an infection, leading to systemic inflammatory responses. Pediatric sepsis can progress rapidly and is a leading cause of morbidity and mortality if not recognized and treated promptly. The criteria for diagnosing pediatric sepsis have evolved. The International Consensus Criteria for Pediatric Sepsis and Septic Shock recommends diagnosing sepsis in children using the Phoenix Sepsis Score. A score of at least two points in children with a suspected infection indicates potentially life-threatening dysfunction of the respiratory, cardiovascular, coagulation, and/or neurological systems [7]. Septic shock is defined as sepsis with cardiovascular dysfunction indicated by at least one cardiovascular point in the Phoenix Sepsis Score, which includes severe hypotension for age, blood lactate (> 5 mmol/L), or the need for vasoactive medication [8]. Children who meet these criteria have higher in-hospital mortality rates.

In summary, PCT may provide earlier and more specific indications of invasive bacterial infections in febrile children, whereas CRP is a traditional marker of bacterial infections. The adoption of the updated sepsis criteria, such as the Phoenix Sepsis Score, can aid in the timely identification and management of pediatric sepsis, ultimately improving patient outcomes.

This study addresses a critical gap in distinguishing invasive bacterial infections from non-invasive febrile illnesses in pediatric emergency settings. While CRP is commonly used, its specificity for early bacterial infections is limited, whereas PCT has shown promise but remains underutilized in real-world emergency care. By comparing the diagnostic accuracy of PCT and CRP, this study highlights the superior early detection capability of PCT and its strong association with sepsis severity and PICU admission. Additionally, to enhance sepsis diagnosis and identifies rhinovirus as a significant viral co-infection influencing disease progression. These findings provide valuable insights for improving risk stratification and guiding early intervention in pediatric sepsis cases.

Materials and methods

Study design

This retrospective, observational, and single-center study was conducted in the pediatric emergency department (ED) of a tertiary care hospital between Jan 2022 and Jan 2024. The objectives of this study were to evaluate the utility of PCT and CRP in children aged one month to 14 years old who presented to the pediatric emergency department with acute febrile illness. In addition, to help distinguish sepsis from asepsis in children who are febrile in the ED. Finally, to determine the diagnostic performance of PCT and CRP in detecting invasive infections and differentiating them from non-invasive infections by comparing PCT with CRP and blood culture.

In this study, we included children aged between 1 and 14 years who were treated for fever in the pediatric ED for more than a day and who were required to undergo blood analysis to rule out the possibility of bacterial infection. Blood samples were obtained for routine tests, complete blood count, CRP and PCT levels, and blood culture. Fever was stated as axillary temperature ≥ 38 °C. Temperature readings were obtained using a mercury thermometer in an emergency triage room for at least 3 min. The exclusion criteria were as follows: (1) recent vaccination that may have caused febrile illness, (2) recent surgery, and (3) children with rheumatic disease and intestinal inflammatory disease that could alter CRP values. The inclusion criteria include children with chronic conditions who are prone to invasive bacterial

infections and who were receiving complex care from the hospital. Furthermore, we divided the patients into two groups; the group with sepsis (Group 1), which included children with fever > 38ºC who were suspected clinically to have sepsis, and those who were aseptic (Group 2), including children with fever without evidence of bacterial infection. Patients in oncology with immunodeficiency who presented with fever were assumed to have sepsis and were included in Group 1. Patients who were admitted underwent pharyngeal swab polymerase chain reaction analysis to identify the etiological agents of respiratory infections.

Sample size and justification

We determined the study's sample size using previous epidemiological data on pediatric sepsis and the expected prevalence of bacterial infections in febrile children who presented to the emergency department. A total of 208 pediatric patients aged one month to 14 years were included to ensure a representative and generalizable sample. A minimum sample size of 200 patients was needed to detect significant associations between inflammatory biomarkers and clinical sepsis considering that the prevalence of sepsis in febrile pediatric patients ranges between 10 and 40% [8, 9],. The sample size was calculated to achieve 80% power ($\beta = 0.20$) with a significance level of 5% ($\alpha = 0.05$), ensuring statistical robustness in analyzing the diagnostic accuracy of PCT and CRP [10]. In addition, the study population reflected real-world emergency department presentations by including children with chronic conditions who are at higher risk of invasive bacterial infections [11]. The sample allowed for subgroup comparisons, with 84 and 124 patients classified as cases with sepsis and non-septic. This facilitated the receiver operating characteristic (ROC) curve analysis to assess the diagnostic performance of the biomarkers. We conducted the study over two years (January 2022–December 2023) in a tertiary hospital with a high frequency of pediatric emergency visits. The high frequency of patients made it feasible to recruit an adequate number of cases while maintaining a strict inclusion and exclusion criteria. This sample size ensured sufficient statistical power to support clinically meaningful conclusions regarding the use of PCT and CRP for the early detection of sepsis [12].

Obtaining and processing the samples

Samples were sent for blood culture, CBC, CRP, and PCT levels. PCT values were determined as duplicates by the LUMItest PCT immune-lumino metric analysis (ATOM SA; Brahms Diagnostica, Hennigsdorf, Germany). The CRP was obtained by the immune-turbidimetry procedure (Cobs INTEGRA; Roche, Basel, Switzerland). PCT and CRP levels < 2.5 ng/ml and < 20 mg/l, respectively, were considered low risk for sepsis.

Results

Our study included 208 patients who presented to the ED. Sociodemographic data revealed that 50.5% were male ($n = 105$), 49.5% female ($n = 103$), 90.4% Saudi nationals ($n = 188$), and non-Saudi Arabians made up 9.6% ($n = 20$). The median patient age was 18 months [Interquartile range (IQR): 6–60 months]. Respiratory diseases were the most common diagnosis, affecting 57.3% ($n = 119$) of patients, followed by fever to rule out sepsis (13.5%, $n = 27$) and infectious diseases (10.4%, $n = 22$). Chronic illnesses were observed in 61.1% ($n = 127$) of the patients, whereas 37% ($n = 77$) experienced complications (Table 1).

The clinical characteristics showed that fever was the most frequently reported symptom (36.4%, $n = 201$), followed by respiratory, gastrointestinal, and other symptoms (25.4, 14.8, and 17.6%, $n = 140$, 82, and 97, respectively). We identified clinical sepsis in 40.4% ($n = 84$) of patients and non-clinical sepsis in 59.6% ($n = 124$). Among the elevated inflammatory markers, we observed high PCT in 46.6% ($n = 97$) and high CRP in 42.7% ($n = 89$) of patients, respectively. Blood cultures and PCR tests were positive in 6.3 and 23% ($n = 13$ and 48, respectively) of the patients tested (Table 2).

Regarding patient management, 68.3, 14.4, and 8.7% ($n = 142$, 30, and 18, respectively) received antibiotics, antipyretics, and fluids. Disposition from the ED included admission to the ward (62.5%, $n = 130$), admission to the pediatric intensive neonatal care unit (PICU) 11.1% ($n = 23$), and direct discharge (26.4%, $n = 55$). Intubation was required in 8.7% ($n = 18$) patients, and 91.3% ($n = 190$) did not require intubation. The outcomes showed that 87% ($n = 181$) of patients achieved full recovery, 9.1% ($n = 19$) recovered with sequelae, and 3.8% ($n = 8$) died (Table 3; Fig. 1).

The relationships between PCT and CRP levels and blood cultures in relation to disposition from the ED (discharge, ward, or PICU admission) were further analyzed. Patients with high PCT and CRP levels were more likely to be admitted to the ward or PICU than those with normal levels (Table 4). Rhino virus was the common viral organism followed by RSV. (Fig. 2) Fig. 3 shows the ROC curve analysis of PCT and CRP, which are sensitive markers of sepsis in febrile children in emergency situations.

PCR revealed a significant association between rhinovirus and clinical sepsis (12/84 vs. 5/124, $P < 0.02$). Other viral organisms, including RSV and adenovirus, showed no statistically significant differences between patients with and without sepsis (Table 5; Fig. 3).

Statistical analysis revealed the factors that were significantly associated with clinical sepsis. These included

Table 1 Sociodemographic, clinical characteristics, and distribution of patient's signs, symptoms, laboratory, and outcomes upon presentation to the emergency department ($n = 208$)

Category	Variables	Description	*N* (%)
Sociodemographic	Sex	Male	105 (50.5)
		Female	103 (49.5)
	Nationality	Saudi	188 (90.4)
		Non-Saudi	20 (9.6)
	Age (months)	Median [IQR]	18 [6–60]
	ED Diagnosis	Otorhinolaryngology disease	4 (2%)
		Respiratory Disease	119 (57.3)
		Surgical disease	1 (0.5)
		Soft tissue and skin disease	3 (1.5)
		Gastroenterology disease	12 (5.7)
		Febrile neutropenia	17 (8.2)
		Fever to rule out sepsis	27 (13.5)
		Central nervous system disease	2 (1)
		Rheumatologically disease	1 (0.5)
		Infectious disease	22 (10.4)
	Chronic disease	Yes	127 (61.1)
		No	81 (38.9)
	Complications	Yes	77 (37)
		No	131 (63)
Clinical Characteristics	Symptoms*	Fever	201 (36.4)
		RESPI	140 (25.4)
		GI	82 (14.8)
		GU	10 (1.8)
		CNS	21 (3.8)
		OTHERS**	97 (17.6)
	Sign*	CNS	1 (0.5)
		CVS	17 (8.2)
		GI	44 (21.2)
		OTHERS***	88 (42.3%)
		RESPI	58 (27.9)
	Temperature	Temperature ≥ 39°	56 (26.9)
		Temperature < 39°	152 (73.1)
	Sepsis Criteria	Clinical Sepsis	84 (40.4)
		Non-clinical sepsis	124 (59.6)
Inflammatory markers and cultures	PCT	High (> 0.25)	97 (46.6)
		Normal (= < 0.25)	111 (53.3)
	CRP	High (> 20)	89 (42.7)
		Normal (< = 20)	119 (57.2)
	PCR NPA	Positive	48 (23)
		Negative	108 (51.9)
		Not Done	52 (25)
	Blood Culture	Positive	13 (6.3)
		Negative	195 (93.8)

Table 1 (continued)

Category	Variables	Description	*N* (%)
Management and outcome	Treatment in ED	Antibiotics	142 (68.3)
		Antiemetics	1 (0.5)
		Antipyretics	30 (14.4)
		Fluids	18 (8.7)
		Nebulization	1 (0.5)
		Oxygen therapy	8 (3.8)
		Steroid	1 (0.5)
		None	7 (3.4)
	ED Disposition	Discharge	55 (26.4)
		PICU	23 (11.1)
		Ward	130 (62.5)
	Intubation	Yes	18 (8.7)
		No	190 (91.3)
	Outcome	Dead	8 (3.8)
		Full recovery	181 (87)
		Recovery with sequalae	19 (9.1)

Categorical data presented as frequencies (%)

*Allowed more than answer.

**others: Pain, Decrease in Appetite, Myalgia Ear Pain, Weight Loss, Rapid Heart Rate, Skin Rash, Bilateral Eye Swelling, Wound Pus Discharge, Edema, Fatigue, Irritable, Jaundice Eye Redness

***Others: Irritable, Hypoactive, Skin Rash, Neck Swelling, Leg Tenderness, Tonsillitis, Pain, Jaundice, Wound Discharge, Ear Pain

Table 2 Exploring the association between patients with sepsis and non-sepsis and their clinical characteristics during Emergency Department presentations

Variables	Description	Clinical Sepsis *n*-84 (%)	Non-clinical sepsis *N* = 124 (%)	OR [95% C.I]	*P*- value
Sex	Male	41 (48.8)	64 (51.6)	0.894 [0.514–1.556]	0.339
	Female	43 (51.2)	60 (48.4)		
Nationality	Saudi	71 (84.5)	117 (94.4)	0.327 [0.124–0.858]	*0.018
	Non-Saudi	13 (15.5)	7 (5.6)		
Chronic disease	Yes	66 (78.6)	61 (49.2)	3.378 [2.019–7.103]	*<0.001
	No	18 (21.4)	63 (50.8)		
Temperature	Temperature ≥ 39°	36 (42.9)	20 (16.1)	3.900 [2.047–7.432]	*<0.001
	Temperature < 39°	48 (57.1)	104 (83.9)		
PCT	High	13 (15.4)	84 (67.7)	0.78 [0.34–1.81]	0.719
	Normal	12 (14.2)	99 (79.8)		
CRP	High	14 (16.6)	75 (60.4)	**0.55** [0.23–1.27]	**0.227**
	Normal	11 (13)	108 (87)		
Blood culture	POSITIVE	9 (10.7)	4 (3.2)	3.600 [1.071–12.104]	*0.030
	NEGATIVE	75 (89.3)	120 (96.8)		
PCR NPA	positive	29 (34.52)	19 (15.32)	2.913 [1.499–5.66]	*<0.004
	negative	35 (41.66)	73 (58.87)		
	Not done	20 (23.80)	32 (25.80)		
ED disposition	Ward	59 (70.23)	71 (57.25)	**0.46 [0.31–0.68]**	8 < 0.00002
	PICU	16 (19)	7 (5.64)		
	Home	9 (10.71)	46 (37)		
Intubation	Yes	10 (11.9)	8 (6.5)	1.959 [0.740–5.191]	0.132
	No	74 (88.1)	116 (93.5)		
Outcome	Full recovery without sequalae	65 (77.3)	116 (93.5)	**1.00 [0.68–1.48]**	*<0.002
	Recovery with sequalae	13 (15.4)	6 (4.8)		
	Died	6 (7.1%)	2 (1.6)		

* $p < 0.05$, suggests a statistically significant association

Table 3 Length of stay (Ward/PICU), length of oxygen therapy requirement, and duration of symptoms

Variable	Median [IQR]
Duration of symptoms before ED presentation (h)	48 [120 – 24]
Length of Hospital Stay (h)	96 [240 – 18]
Duration of WARD stay (days)	3 [7 – 0]
Duration of stay in PICU (days)	11 [20 – 4]
Duration on ventilator/ o2 therapy (days)	8 [20 – 2]

Continuous data presented as Median [IQR, Interquartile Range]

non-Saudi nationality (OR: 0.327, $p = 0.018$), chronic diseases (OR: 3.378, $p < 0.001$), high-grade fever (≥ 39 °C) (OR: 3.900, $p < 0.001$), and positive blood cultures (OR: 3.600, $p = 0.030$). Logistic regression analysis identified the predictors of PICU admission, including positive blood cultures (OR: 9.369, $p < 0.0003$), chronic diseases (OR: 3.940, $p < 0.001$), high-grade fever (OR: 4.108, $p < 0.001$), and viral co-infections (OR: 3.677, $p < 0.02$) (Table 2 Table 6). These findings underscore the importance of clinical and demographic factors in guiding the management and prognosis of patients with sepsis in the ED.

Discussion

In this study, we aimed to identify and analyze the factors influencing the clinical presentation and outcomes of pediatric patients with sepsis in a hospital setting. Our findings revealed the significant impact of sociodemographic and clinical characteristics on sepsis susceptibility, diagnosis, and severity, providing a deeper understanding of the disease epidemiology and contributing to clinical decision-making.

The patient population was approximately evenly divided between the male (50.5%) and female (49.5%)

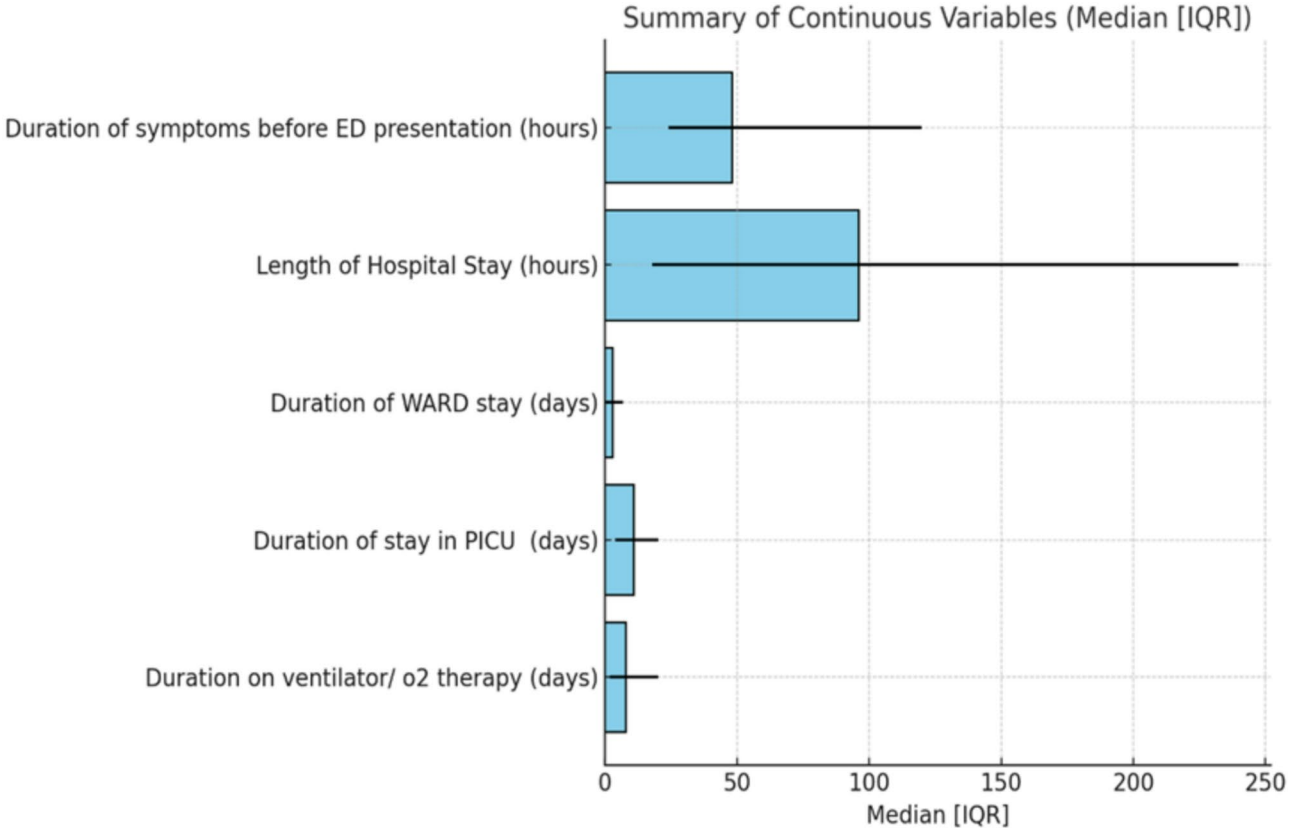

Fig. 1 Length of stay (Ward/PICU), length of oxygen therapy requirement, and duration of symptoms.

Table 4 Exploring the association between PCT and CRP in correlation with emergency department disposition during presentations

PCT	CRP	Discharge *n* = 55 (%)	Ward *n* = 130 (%)	PICU *n* = 23 (%)	TOTAL *n* = 208 (%)	*P*-VALUE
Normal	Normal	37 (67.2)	35 (26.9)	7 (30.4)	79 (37.9)	*<0.0000098
Normal	High	4 (7.2)	27 (20.7)	1 (4.3)	32 (15.3)	
High	Normal	8 (14.5)	25 (19.2)	7 (30.4)	40 (19.2)	
High	High	6 (10.9)	43 (33)	8 (34.7)	57 (27.4)	

* $p < 0.05$, suggesting a statistically significant association

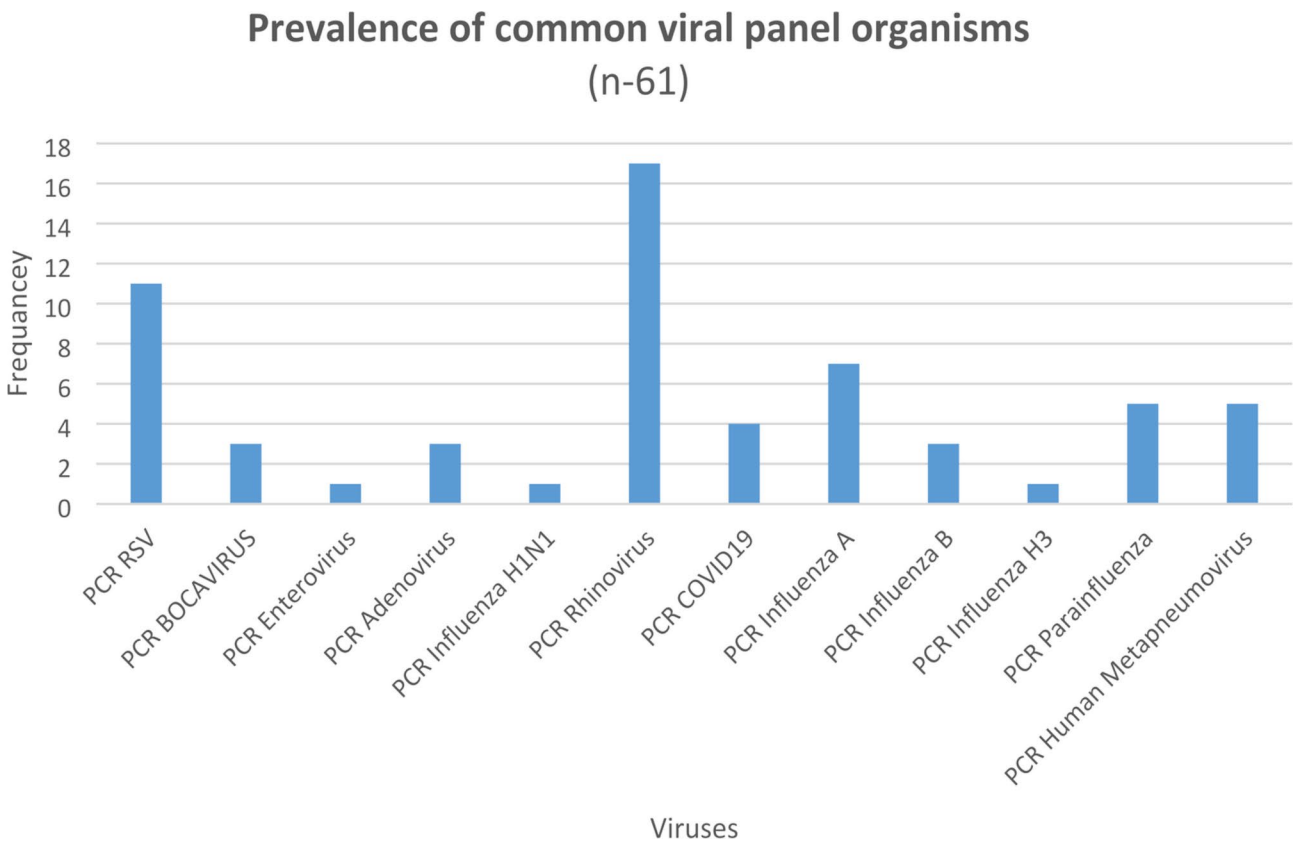

Fig. 2 Prevalence of common viral organisms

participants, indicating a balanced sex distribution. However, most cases were reported among Saudi nationals (90.4%), which aligns with the typical demographic pattern of the region. The high percentage of local cases supports the need for health interventions tailored to the pediatric population in Saudi Arabia. There is evidence of a slightly higher male predominance in cases of sepsis; however, this finding is not consistent across studies [13]. The age distribution, with a median of 18 months (IQR: 6–60 months), highlights the young pediatric demographic affected by sepsis. The young pediatric demographic aligns with known patterns, in which younger children are particularly vulnerable because of their developing immune systems [14, 15].

Chronic diseases were prevalent in 61.1% of the patients, which aligns with the literature indicating that pre-existing health conditions increase the risk of sepsis. Rao et al. [11], in their study, discuss the role of underlying chronic diseases such as asthma, congenital heart disease, and immunocompromised states in the increased risk of sepsis in pediatric populations. Furthermore, it shows the association between chronic conditions and more severe outcomes, including PICU admission. Moreover, Riquelme et al. [18] revealed that underlying chronic health conditions in children, such as congenital heart disease and immunodeficiency, elevated the risk of sepsis significantly. Lee et al. [19] provided an in-depth analysis of the contribution of chronic diseases to the severity and outcomes of pediatric cases with sepsis [16–19].

High-grade fever (≥ 39 °C) was present in 26.9% of cases, which was consistent as a common clinical feature in infectious diseases and inflammatory responses. De Oliveira et al. [17] explored the role of fever, particularly high-grade fever (≥ 39 °C), in identifying sepsis in children. They strongly correlated the intensity of fever with the likelihood of severe bacterial infection. Our results suggested that chronic disease and high-grade fever are significant predictors of clinical sepsis, with an OR of 3.378 ($p < 0.001$) and 3.900 ($p < 0.001$), respectively (Table 7; Fig. 4). This finding reinforced the need for vigilance in patients with underlying conditions and elevated fever as these factors can indicate or preclude a more severe case of sepsis. Huang et al. [20] and Singer et al. [21] predicted a strong association between high-grade fever (≥ 39 °C) and the risk of sepsis in children, reinforcing its clinical significance as a predictor.

Positive blood culture was significantly higher in patients with sepsis (10.7% vs. 3.2%, OR: 3.600, $p = 0.03$), demonstrating the diagnostic utility of blood cultures for confirming bacteremia. Baker et al. [22] emphasized the significance of positive blood cultures in cases of

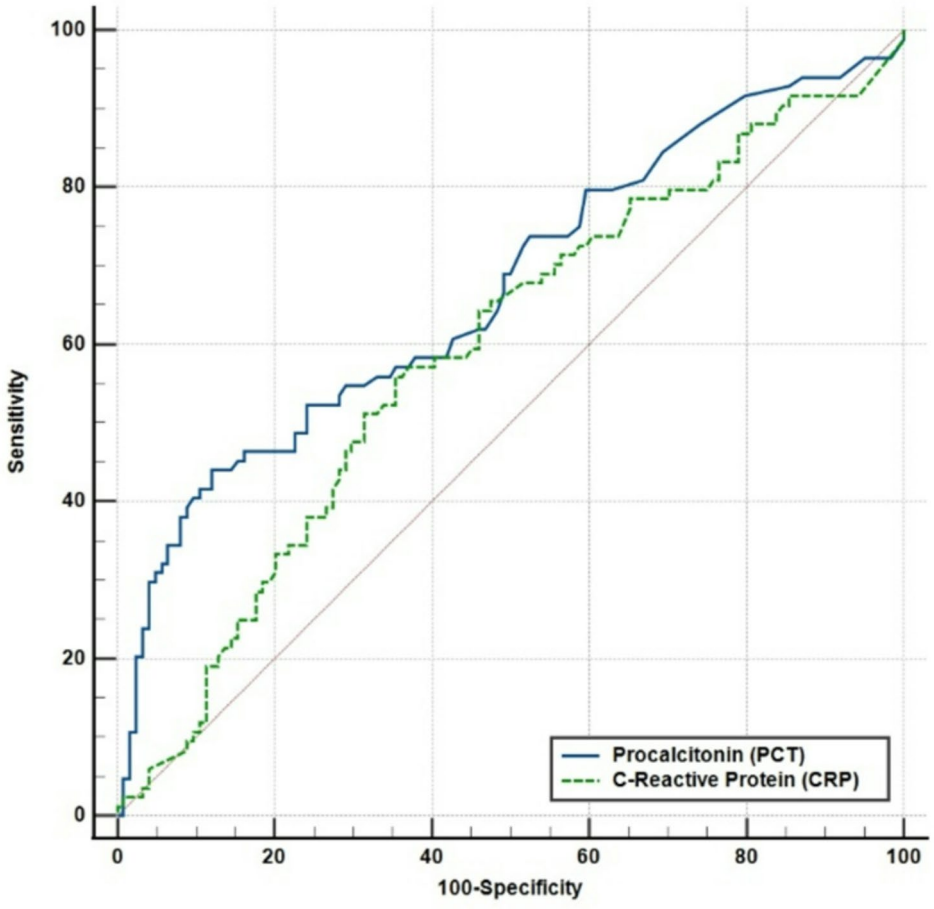

Fig. 3 ROC analysis of PCT and CPR test

Table 5 Exploring the association between patients with clinical sepsis and non-clinical sepsis in correlation to the viral panel during emergency department presentations

Variables	clinical Sepsis ($n=84$)			Non- clinical Sepsis ($n=124$)			Frequency (Sepsis/Non-Sepsis)	*P*-value
PCR NPA	Positive	Negative	Not Done	Positive	Negative	Not Done		
PCR RSV	6	58	20	5	87	32	6/84 for Sepsis, 5/124 for Non-Sepsis	0.60
PCR BOCAVIRUS	1	63	20	2	90	32	1/84 for Sepsis, 2/124 for Non-Sepsis	0.91
PCR Enterovirus	1	62	20	0	92	32	1/83 for Sepsis, 0/124 for Non-Sepsis	0.45
PCR Adenovirus	2	62	20	1	91	32	2/84 for Sepsis, 1/124 for Non-Sepsis	0.62
PCR Influenza H1N1	1	63	20	0	92	32	1/84 for Sepsis, 0/124 for Non-Sepsis	0.45
PCR Rhinovirus	12	52	20	5	87	32	12/84 for Sepsis, 5/124 for Non-Sepsis	*<0.02
PCR COVID19	3	61	20	1	91	32	3/84 for Sepsis, 1/124 for Non-Sepsis	0.35
PCR Influenza A	4	60	20	3	89	32	4/84 for Sepsis, 3/124 for Non-Sepsis	0.63
PCR Influenza B	0	64	20	3	89	32	0/84 for Sepsis, 3/124 for Non-Sepsis	0.32
PCR Influenza H3	0	64	20	1	91	32	0/84 for Sepsis, 1/124 for Non-Sepsis	0.66
PCR Parainfluenza	2	62	20	3	89	32	2/84 for Sepsis, 3/124 for Non-Sepsis	0.94
Human Metapneumovirus	4	60	20	1	01	32	4/84 for Sepsis, 1/124 for Non-Sepsis	0.18

* $p<0.05$, suggesting a statistically significant association

Table 6 Factors influencing patients with clinical sepsis for PICU admission by logistic regression analysis

Factors	B	S.E.	Wald	OR [95% CI]	*P*-Value
PCT (High)	-1.545	1.297	-1.19	0.213 [0.011–4.091]	*0.233
CRP (High)	-0.664	0.499	-1.331	0.515 [0.113–2.339]	0.183
Blood Culture (Positive)	2.237	0.813	2.751	9.369 [2.732–32.121]	*<0.0003
Chronic Diseases	1.219	1.394	0.874	3.940 [1.973–7.869]	*< 0.001
High-grade Fever (≥ 39 °C)	0.05	0.033	1.524	4.108 [2.029–8.317]	*< 0.001
Viral Coinfections	1.302	0.56	2.324	3.677 [1.273–10.623]	*< 0.02

* $p < 0.05$, suggesting a statistically significant association

Table 7 Identification of most significant risk factors/predictors of clinical sepsis in patients who presented to the emergency department by multiple logistics regression analysis

Factors	B	S.E.	Wald	OR [95% C.I]	*P*-value
Chronic Disease	1.371	0.353	15.0.94	3.940 [1.973–7.869]	*<0.001
High grade fever (≥ 39°)	1.413	0.360	15.418	4.108 [2.029–8.317]	*<0.001
Blood Culture	1.677	0.731	5.266	5.348 [1.277–22.398]	*0.022

* $p < 0.05$, suggests a statistically significant association

pediatric sepsis and discussed the clinical implications of identifying bloodstream infections in the pediatric population. A study by *Zaoutis*, et al. [23] evaluated the importance of blood culture as a diagnostic tool for confirming bacteremia in cases of pediatric sepsis, supporting the association found in our data (10.7% positivity in patients with sepsis). Thomas et al. [24] discussed the role of blood cultures in diagnosing sepsis, including the significance of positive blood culture results in the confirmation of bacteremia and a guide for treatment protocol [22–24].

Rhinovirus, detected in sepsis versus non-sepsis cases (12/84 and 5/124, respectively) ($p < 0.02$), was significantly associated with clinical sepsis, indicating its potential role as a co-infection agent. The finding suggested that viral pathogens, such as rhinovirus, should be considered in cases of pediatric sepsis, as they may exacerbate or complicate the clinical course of the disease. Other viruses did not show a significant association with sepsis; however, their detection remains an important aspect of comprehensive diagnostic protocols. Fernández-Cooke et al. [25] discussed the prevalence of viral co-infections in pediatric sepsis and explored their association with clinical outcomes. Rhinovirus was mentioned as a commonly identified pathogen in the cases of sepsis, which is consistent with the findings of this study (Table 5). Kohlhase et al. [26] reported that rhinovirus is a significant viral co-infection in pediatric sepsis, with a higher

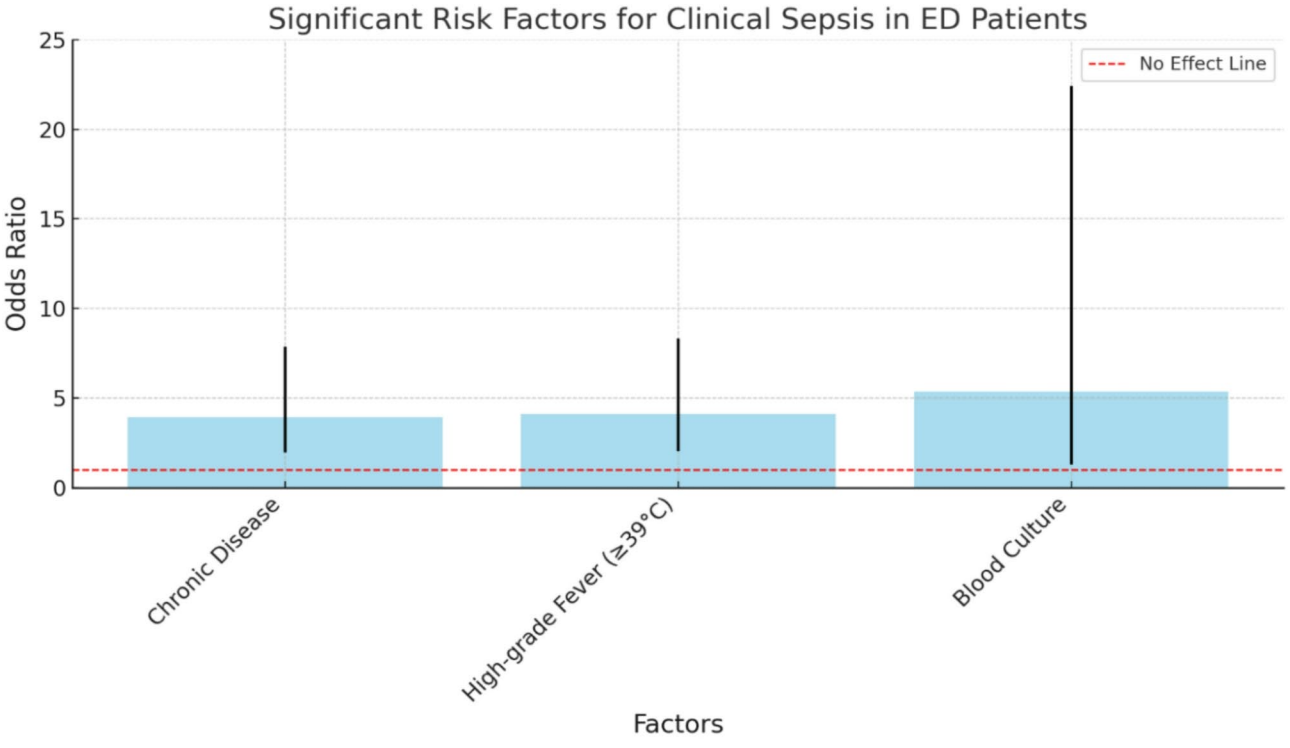

Fig. 4 Risk factors for clinical sepsis in pediatric emergency

prevalence in patients with severe disease outcomes. In addition, viral co-infections, indicated by positive PCR tests (OR: 2.913, $p < 0.004$), revealed a notable prevalence of mixed infections in cases of pediatric sepsis, which can complicate diagnosis and treatment. Similar to our findings, Rangel et al. [27] reported the frequency and clinical implications of viral co-infections in pediatric sepsis. They highlighted how viral co-infections can complicate diagnosis and treatment (OR: 2.913, $p < 0.004$). Lee et al. 28) analyzed the impact of viral co-infections in cases of sepsis, which contributed to increased severity and challenges in management [25–28].

We found a strong association between rhinovirus and the severity of sepsis. Similar results were obtained by Patel et al. [29] and Smith et al. [30], who both investigated the role of rhinovirus in pediatric sepsis and reported a higher prevalence of rhinovirus in cases of pediatric sepsis and its association with increased severity, thereby supporting our finding of its significant role.

The association between positive blood cultures and the outcomes of sepsis was strong, with positive cultures being the key diagnostic criterion for confirming septicemia. A positive blood culture is the gold standard for diagnosing bacteremia in sepsis. The positive culture rate in our study (13 positives in sepsis versus 4 in non-sepsis) is consistent with that of other studies [31].

Disposition data underscored the severity of cases of sepsis compared with cases of non-sepsis indicating a higher likelihood of PICU admission for patients with sepsis (19 vs. 5.64%). The finding supported the clinical observation that sepsis can lead to significant complications that require intensive care.

The analysis of PCT and CRP levels provided critical insights into their roles in assessing sepsis. High PCT and CRP levels were found in 38.4% of the cases with positive blood cultures, validating their use as markers of systemic inflammation. However, normal levels of these markers were found in 37.9% of cases, suggesting that despite elevated PCT and CRP levels indicating an infection, their absence does not rule it out. Meisner et al. reviewed the diagnostic utility of PCT and CRP in pediatric sepsis and demonstrated that elevated levels can signify an infection; however, normal levels do not necessarily rule out one. *Le C et al.* emphasized the roles of PCT and CRP as biomarkers of systemic inflammation and their ability to predict severe outcomes in pediatric patients with sepsis [32, 33].

Importantly, the highest rate of PICU admission (34.7%) was observed in patients with elevated PCT and CRP levels, indicating that these markers can be predictors of severe outcomes. Conversely, discharge was most often associated with normal PCT and CRP levels (67.2%), thereby highlighting their potential as biomarkers in less severe cases. Wang et al. found a relationship between high PCT and CRP levels and the need for admission to the PICU, supporting the association found in our data. *Singh et al. highlighted* that high PCT and CRP levels were correlated with severe sepsis and PICU admission, reinforcing their predictive value in severe cases. Liu et al. highlighted the role of PCT and CRP as biomarkers for the diagnosis of bacterial infections, including sepsis, in pediatric patients. Furthermore, they discussed their utility in predicting clinical outcomes, including PICU admissions [34–36].

Thomas et al. demonstrated that normal PCT and CRP levels do not entirely rule out sepsis, which is consistent with the observation that 37.9% of patients with positive blood cultures had normal levels. Patel et al. provided an overview of the limitations of using PCT and CRP as sole indicators of sepsis and their role in guiding clinical decisions, aligning with our findings that elevated markers indicate an infection; however, normal levels of PCT and CRP do not exclude it [37, 38].

Positive blood culture (OR: 9.369, $p < 0.0003$) was a strong predictor of PICU admission, underscoring the severity of bacteremia in pediatric sepsis. In addition, high-grade fever and chronic diseases (OR: 4.1 and 3.940, $p < 0.001$ and < 0.001, respectively) were significant predictors of PICU admission, emphasizing the careful evaluation of these factors for the early identification of patients who may require intensive care. The impact of viral co-infections (OR: 3.677, $p < 0.02$) further suggests that the presence of multiple pathogens can increase the risk of severe illness and complicate patient management. Cochran et al. identified the predictors of PICU admission, including blood culture positivity, fever, and underlying chronic diseases, similar to our study findings.

Our findings showed that patients with sepsis are more likely to be admitted to the PICU, whereas those without sepsis are more likely to be discharged. These findings are consistent with observations from other pediatric studies. For instance, a study analyzing pediatric sepsis cases reported that severe sepsis accounts for more than 8% of all PICU admissions [39]. In addition, addition, studies have revealed that children with sepsis often require intensive care interventions such as vasoactive medications and mechanical ventilation, underscoring the critical nature of their condition [40].

Patients with clinical sepsis are more likely to require intensive care or extended hospital stay, which is supported by the study on critically ill children with sepsis [41]. Several factors influence PICU admission in patients with sepsis, including positive blood culture, high-grade fever, chronic disease, and viral co-infections. Our logistic regression analysis (Table 6) showed significant associations between chronic diseases, blood culture positivity, and viral co-infections, which is consistent with existing literature [42]. Moreover, high fever is

commonly associated with severe infections and can predict the need for intensive care support. The association between fever and clinical outcomes is well-supported [43, 44].

The ROC curve analysis shown in Fig. 1 supports the diagnostic use of PCT and CRP in differentiating cases of sepsis from those of non-sepsis, demonstrating moderate sensitivity and specificity. This finding reinforces their value as part of an early diagnostic approach, aiding clinicians in pediatric emergencies to distinguish between bacterial and nonbacterial infections. Zhou et al. [10] reviewed the diagnostic accuracy of PCT and CRP in pediatric sepsis and showed moderate sensitivity and specificity, which is consistent with our ROC analysis findings (Fig. 1).

The use of PCT and CRP, in the diagnosis of sepsis has been well studied. Our results, which show high levels of PCT and CRP in patients with sepsis, are consistent with the literature findings [45, 46]. PCT is a sensitive biomarker of bacterial infection and has been validated as a diagnostic tool for sepsis, particularly in pediatric populations. Our logistic regression findings indicated that factors such as high PCT levels, positive blood culture, chronic disease, and high-grade fever are strong predictors of PICU admission and severe outcomes in patients with sepsis [45, 46]. CRP level is a proven marker of systemic inflammation. Elevated CRP levels have been consistently associated with bacterial infections and sepsis; however, they are less specific than PCT levels [47, 48].

The median duration of symptoms before presentation was 48 h, reflecting potential delays in recognizing sepsis. This underscored the importance of early awareness and timely intervention to prevent progression to severe disease. In addition, the median hospital stay for PICU admissions was 11 days, which was significantly longer than 3 days average for ward admissions. This difference underscores the severity of PICU cases, emphasizing the critical nature of the early identification of high-risk patients. Hodgson et al. addressed the typical delay in sepsis recognition in children, emphasizing that many pediatric sepsis cases are identified only after symptoms persist for ≥48 h [49] The length of hospital and PICU stay is a critical measure of sepsis severity, with longer stays associated with more severe illness and poorer outcomes [50].

Our findings offer valuable insights for clinical practice, suggesting that heightened awareness of chronic conditions and high-grade fever is essential for early recognition of sepsis. The use of inflammatory markers, including PCT and CRP, can aid in evaluating disease severity and in predicting patient outcomes. Furthermore, recognizing the role of viral co-infections, especially rhinovirus, in complicating sepsis can guide comprehensive diagnostic testing and treatment protocol. Early identification of these predictors can facilitate timely interventions, potentially improving patient outcomes and optimizing resource allocation in pediatric care settings.

Mortality from sepsis is influenced by factors such as age, chronic disease, blood culture results, and time to initiation of appropriate therapy. Furthermore, complete recovery or recovery with sequelae is commonly observed in the pediatric population [41].

Chronic diseases, high-grade fever (≥39 °C), and positive blood culture emerged as significant predictors of sepsis and PICU admission. PCT and CRP proved valuable; however, their utility as single markers is limited, and their combined elevation correlated strongly with worse clinical outcomes. Among co-infections, rhinovirus was identified as the most significant viral contributor; however, bacterial infections remain a primary concern in sepsis. Logistic regression models and ROC) analyses further reinforced the role of these factors in enhancing risk stratification and guiding clinical decision-making.

Limitations

Despite the valuable findings of this study, several limitations must be acknowledged. First, this was a single-center, retrospective observational study, which may limit the generalizability of the results to other healthcare settings with different patient populations and clinical protocols. Second, while we attempted to control for confounding variables, potential biases in patient selection, data collection, and missing clinical information could have influenced the results. Third, the study relied on PCT and CRP levels as primary biomarkers for diagnosing sepsis, but these markers are not entirely specific and can be influenced by other inflammatory conditions. Additionally, blood cultures, the gold standard for diagnosing bacterial infections, had a relatively low positivity rate, potentially underestimating true bacterial infections in some cases. Furthermore, the study excluded certain populations, such as children with recent vaccinations or surgeries, which may impact the applicability of the findings to broader pediatric emergency settings. Lastly, as a retrospective study, real-time clinical decision-making and treatment interventions were not assessed, limiting insights into the direct impact of biomarker-based diagnostics on patient outcomes. Future prospective, multicenter studies with larger sample sizes and standardized sepsis criteria are needed to validate these findings and optimize early sepsis detection in pediatric emergency care.

Abbreviations

CBC Complete Blood Count
CRP C-reactive protein
ED Emergency Department
IQR Interquartile Range
OR Odds Ratio
PCR Polymerase Chain Reaction

PCT Procalcitonin
PICU Pediatric Intensive Care Unit
ROC Receiver Operating Characteristic

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Author contributions
AB conceived and designed the study. NA, NA, DA, and IG conducted data collection, analysis, and interpretation, while MH, RA, and SA contributed to drafting and revising the manuscript. YA supervised the project, coordinated the study, and provided critical oversight. All authors reviewed and approved the final version of the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
This study has been approved by the Institutional Research Ethics Committee number 23–655 in King Fahad Medical City in Riyadh, Kingdom of Saudi Arabi and this study was conducted in accordance with the Declaration of Helsinki. The consent to participate was obtained from the parents or legal guardians.

Consent for publication
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Competing interests
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