


# Procalcitonin for Predicting Sepsis in Infants in the Emergency Department: A Retrospective Study

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**Background:** Among children younger than 5 years, infectious conditions account for the majority of pediatric emergency department visits. Due to nonspecific presentation, early identification of Sepsis and serious bacterial infection is challenging. Procalcitonin (PCT) level has been examined as a marker of sepsis. It has been shown to have advantages over other inflammatory markers.

**Aim:** This study aimed to evaluate the association between high PCT levels and positive blood, urine, or cerebrospinal fluid (CSF) cultures in all infant patients suspected of having sepsis/Serious bacterial infections (SBIs) clinically or using the Pediatric Early Warning as integration between elevated PCT and culture-proven infections with PEWS to improve early risk stratification and guide clinical decision-making in a tertiary.

**Methods:** This retrospective cross-sectional study included all patients aged 28 to 90 days whose PCT was obtained simultaneously with blood, urine, or CSF cultures and a viral nasopharyngeal aspirate, taken under suspicion of sepsis/SBIs, from January 2020 to December 2021. All statistical analyses were performed using the SPSS software (IBM) version 27.0.1.

**Findings:** This study included 352 patients. In total, 205 (58.2%) were between 28 and 60 days old, while 147 (41.8%) were aged 60–90 days. The association between the PCT levels and blood culture outcomes was not statistically significant. However, the association between PCT levels and positive urine culture was statistically significant ( $p = 0.008$ ). In addition, the analysis revealed a nonsignificant association between PCT levels and respiratory viral infection.

**Conclusion:** In this cohort, as a single center, PCT level is not a predictor of positive blood or CSF culture results. In contrast, high PCT levels are significantly associated with positive urinary culture results. The study was conducted at a single center with small sample size which may affect the generalizability of its findings. Future multicenter research with large sample size is required to validate the study findings.

**Keywords:** PCT, bacteremia, urinary tract infection, sepsis, serious bacterial infections, biomarkers

## Introduction

Sepsis is a major concern in all age groups. The World Health Organization classifies sepsis as a “life-threatening organ dysfunction caused by a dysregulated host response to infection.” It is a reversible cause of major global health and financial burdens. Bacterial sepsis in pediatric patients can be described using many different criteria, ranging from clinical scores (Pediatric Index of Mortality, Organ Failure Assessment) that consider the systemic manifestations of a child (ie., systolic blood pressure, temperature instability, delayed capillary refill)<sup>1</sup> to a biochemical definition incorporating inflammatory markers, the use of gold standard diagnostic tests, and positive cultures from infection sources.<sup>2</sup> However, identifying sepsis in young patients can be challenging. The management of sepsis in pediatric populations is commonly initiated despite the unknown probability of infection if there is evidence of a systemic inflammatory response.<sup>3</sup>

In 2015, deaths of approximately 50% of all neonatal patients and those aged < 5 years of age were due to infectious causes.<sup>4</sup> Procalcitonin (PCT), a precursor of calcitonin typically produced by neuroendocrine cells, is upregulated during sepsis and expressed in multiple extrathyroidal tissues,<sup>5,6</sup> and is believed to be a reaction to the endotoxins produced by bacterial infections and to the immune system inflammatory response (interleukin 1 and 2 and tumor necrosis factor Alpha).<sup>7</sup> PCT, as a molecular biomarker for sepsis, was first described in the literature in 1993.<sup>8</sup> Since then, several studies have examined PCT level as a marker of sepsis. It has advantages over other inflammatory markers, such as cytokines and C-reactive protein (CRP). One advantage is the kinetic profile of PCT, which increases within 4–12 h of stimulation. Additionally, it drops by half daily once the infection is controlled with antimicrobial therapy or the immune system.<sup>5,9</sup> Another advantage of PCT is its higher specificity for bacterial infections compared with other biomarkers. PCT has the potential to discriminate between infectious and noninfectious inflammatory responses. One study showed that PCT level > 1 ng/mL had 43% sensitivity and 96% specificity toward bacterial infections, and a level < 0.1 ng/mL had a remarkably high sensitivity to exclude bacteremia.<sup>10–12</sup> Moreover, PCT can be used as a marker of bacterial load and the severity of bacterial infection.<sup>13,14</sup> Six meta-analyses were performed to examine the accuracy of PCT for diagnosing infections in different populations. Four of these studies favored PCT as an accurate biomarker,<sup>15–18</sup> whereas one showed a moderate benefit.<sup>13</sup> In contrast, another meta-analysis showed a null effect in larger studies.<sup>14</sup> Literature supports PCT as a valuable biomarker for infants aged 28–90 days in conjunction with clinical appearance and urinalysis to determine the risk of bacterial infection, reduce admission rate, and strengthen antibiotic stewardship. The globally recognized clinical practice guidelines for this age group recommend using PCT for risk stratification.<sup>15,17</sup> Although global efforts exist, few regional studies have examined the use of PCT for risk stratification, considering regional differences in epidemiology and clinical practice, with the diagnostic performance varying across infection sources (blood, urine, and cerebrospinal fluid).

Early identification of sepsis and serious bacterial infections in infants remains challenging due to non-specific clinical manifestations, especially during rapid emergency assessment. As sepsis represents a significant global health burden and is associated with high mortality. In Local context, most existing studies reported the prevalence of sepsis mortality rates ranges from 30–50% in intensive care setting.<sup>18,19</sup>

This study aimed to evaluate the association between elevated procalcitonin levels and positive blood, urine, or cerebrospinal fluid cultures in infants with suspected sepsis or serious bacterial infections presenting to the emergency department. Nasopharyngeal aspirates for viral causes of fever were also analyzed separately to account for potential confounding, rather than being used as primary outcomes.

## Materials and Methods

### Study Design

This is a retrospective, observational, cross-sectional cohort study at a single center over one year, January 2020 - December 2021.

### Study Settings

The study was conducted at a tertiary care center at King Abdullah Specialist Children's Hospital (KASCH) in Riyadh, Kingdom of Saudi Arabia. KASCH is a tertiary care hospital with approximately 100,000 annual visits to the pediatric emergency department.

### Study Population

The study included infants aged 28–90 days who presented to the emergency department with suspected sepsis or serious bacterial infection (SBI) based on clinical manifestations such as fever, lethargy, respiratory distress, or an elevated Pediatric Early Warning Score (PEWS).

Patients were included if serum procalcitonin (PCT) levels and blood, urine, or cerebrospinal fluid (CSF) cultures were obtained during the same visit. Importantly, inclusion was based on clinical suspicion rather than confirmed culture results, reflecting real-world emergency department decision-making.

Exclusion criteria included patients with malignancy, hematological disorders, organ transplantation, immunosuppressive therapy, missing clinical data, or absence of simultaneous PCT and culture testing.

A total of 447 patients were identified, of whom 95 were excluded based on the predefined criteria.

## Data Collection and Variables

Data were obtained from the biochemistry and microbiology laboratories to identify patients with simultaneous PCT and culture testing, followed by retrospective extraction of clinical data from electronic medical records (BestCare system).

Collected variables included: Serum PCT levels, Blood, urine, and CSF culture results; clinical presentation (eg., fever, lethargy, mottling); Pediatric Early Warning Score (PEWS); and Viral testing results, including respiratory multiplex PCR and COVID-19 PCR-NAAT. A PCT level  $>0.05$  mcg/L was defined as elevated, while a level  $\leq 0.05$  mcg/L was considered normal.

## Outcome Measures

The primary outcome was the association between elevated PCT levels and positive bacterial cultures (blood, urine, and CSF). Secondary outcomes included: Association between PCT levels and viral test results (respiratory multiplex PCR and COVID-19 PCR-NAAT), Distribution of microorganisms identified in positive cultures.

## Statistical Analysis

Data were analyzed using IBM SPSS Statistics. Descriptive statistics were presented as frequencies and percentages for categorical variables. Associations between PCT levels and categorical variables (culture results and viral testing) were assessed using the chi-squared test or Fisher's exact test, as appropriate. Binary logistic regression analysis was performed to evaluate predictors of elevated PCT levels, including positive blood and urine cultures. Results were reported as adjusted odds ratios (AORs) with corresponding p-values. Multinomial logistic regression was used for analyses involving multiple categorical outcomes. Statistical significance was set at  $p \leq 0.05$ , with a 95% confidence interval (CI).

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Additionally, the study received approval from our local Institutional Review Board (IRB), in accordance with the guidelines of the King Abdullah International Medical Research Center (KAIMRC) (IRB number NRC22R/039/01), ensuring that all ethical guidelines were adhered to during the study's conduct—data collection from January 2020 to December 2021, retrospectively after the IRB approval.

## Results

The study included 352 patients, predominantly aged 60–90 days (41.8%) and male (55.4%), with most having no comorbidities (60.8%), while 15.3% had prematurity or neonatal conditions. A first fluid bolus was administered in 17.3% of patients and a second in 5.4%. ICU admission was required in 31.5% of cases, the mean hospital stay was  $6 \pm 12$  days, and overall survival was high at 98.9% with a mortality rate of 1.1% (Table 1).

All patients included in this study who underwent laboratory investigations, including those for PCT, erythrocyte sedimentation rate (ESR), CRP, white blood cell (WBC), and antineutrophil count levels, were reviewed. "PCT" had a mean level of 1.926, with a standard deviation of 15.638. Among the study participants, 303 (86.3%) had a PCT level in the range 0–0.5, followed by 11 (3.1%) participants with a PCT level in the range 0.5–1, and 5 (1.4%) participants with a PCT level in the range 1–1.5. A notable number, 32 (9.1%), had PCT values  $> 1.5$ . Most participants had missing ESR (64.8%) and CRP (40.9%) results. Among those tested, the majority had values  $< 20$ ; The mean WBC count was  $12 \pm 6$ , and most participants had ANC  $< 4000$  (59.1%) (Table 2).

## Culture-Proven and PCT Levels

Most blood cultures were negative (93.5%), with limited Gram-positive (5.7%) and Gram-negative (0.6%) growth; urine cultures were also largely negative (84.7%) with small proportions of *E. coli* (5.5%) and *Klebsiella* (4.0%), while no positive CSF cultures were identified and over half were not performed (57.7%) (Table 3).

**Table 1** Demographic and Clinical Characteristics

		<b>N (%)</b>
Age, days	28–60	205 (58.2%)
	60–90	147 (41.8%)
Sex	Male	195 (55.4%)
	Female	157 (44.6%)
Associated commodities	None	214 (60.8%)
	Neurological or neuromuscular	8 (2.3%)
	Gastrointestinal	12 (3.4%)
	Metabolic	1 (0.3%)
	Cardiovascular	49 (13.9%)
	Renal or urological	21 (6.0%)
	Premature/neonatal	54 (15.3%)
	Other congenital/genetic defect/metabolic	23 (6.5%)
Fluid bolus	Once	61 (17.3%)
	Twice	19 (5.4%)
	More than 2	12 (3.4%)
	Not given	260 (73.9%)
ICU admission	Yes	111 (31.5%)
	No	241 (68.5%)
Final outcome	Survived	348 (98.9%)
	Died	4 (1.1%)
Length of stay (days)	Mean ± Std. Dev	6 ± 12
Viral respiratory panel	Not done	134 (38.1%)
	Negative	67 (19.0%)
	Positive	151 (42.9%)

**Abbreviations:** n, frequency; %, percentage; ICU, intensive care unit.

**Table 2** Laboratory Investigation Results of the Study Subjects

<b>Variable</b>	<b>Value</b>
<b>PCT (ng/mL), Mean ± Std. Dev.</b>	1.926 ± 15.638
<b>ESR (mm/h), Mean ± Std. Dev.</b>	5 ± 13
<b>CRP (mg/L), Mean ± Std. Dev.</b>	13.29 ± 31.89
<b>WBC (<math>10^9/L</math>), Mean ± Std. Dev.</b>	12.10 ± 6.00
<b>ANC (<math>10^9/L</math>), Mean ± Std. Dev.</b>	4.27 ± 3.54

(Continued)

**Table 2** (Continued).

Variable	Value
<b>PCT category, n (%)</b>	
0–0.5	303 (86.3%)
0.5–1	11 (3.1%)
1–1.5	5 (1.4%)
> 1.5	32 (9.1%)
<b>PCT level, n (%)</b>	
Normal 0–0.5	303 (86.3%)
High >	84 (13.6)
<b>ESR category, n (%)</b>	
Not done	228 (64.8%)
< 20	91 (25.9%)
≥ 20	33 (9.4%)
<b>CRP category, n (%)</b>	
Not done	144 (40.9%)
< 20	160 (45.5%)
≥ 20	48 (13.6%)
<b>ANC (<math>10^9/L</math>) category, n (%)</b>	
Not done	10 (2.8%)
< 4000	208 (59.1%)
≥ 4000	133 (37.8%)

**Abbreviations:** n, frequency; %, percentage; ESR, erythrocyte sedimentation rate (mm/h); CRP, C reactive protein (mg/L); WBC, white blood cell; ANC, antineutrophil count.

**Table 3** Blood, Urine, and CSF Culture Results of the Study Subjects

	n (%)
<b>Blood culture</b>	
<b>Gram positive</b>	<b>20 (5.7%)</b>
<i>Staphylococcus aureus</i>	3 (0.9%)
<i>Staphylococcus hominis</i>	10 (2.8%)
<i>Staphylococcus epidermidis</i>	4 (1.1%)
<i>Corynebacterium falsenii</i>	1 (0.3%)
<i>Staphylococcus capitis</i>	1 (0.3%)
<i>Streptococcus viridans group</i>	1 (0.3%)
<b>Gram negative</b>	<b>2 (0.6%)</b>
<i>Salmonella species</i>	2 (0.6%)
<b>Negative culture</b>	<b>329 (93.5%)</b>
<b>Not done</b>	<b>1 (0.3%)</b>
<b>Urine culture</b>	
<i>Escherichia coli</i>	19 (5.5%)
<i>Klebsiella</i>	14 (4.0%)
Negative	294 (84.7%)
Not done	16 (4.6%)
Others	4 (1.1%)

(Continued)

**Table 3** (Continued).

	n (%)
<b>CSF culture</b>	
Positive GP	0 (0.0%)
Positive GN	0 (0.0%)
Negative	149 (42.3%)
Not done	203 (57.7%)

**Abbreviations:** n, frequency; %, percentage; GP, Gram-positive bacteria; GN, Gram-negative bacteria; CSF, cerebrospinal fluid.

PCT levels were predominantly within the normal range across all groups. Among patients with positive blood cultures, most had normal PCT levels (77.3%) compared with elevated levels (22.7%), while a similar pattern was observed in those with negative cultures (86.9% vs 13.1%), with no statistically significant association ( $p=0.203$ ). In urine culture analysis, although normal PCT levels were more frequent in both positive (69.7%) and negative (88.1%) cases, a statistically significant association was identified ( $p=0.008$ ). No positive CSF cultures were detected. Regarding clinical outcomes, the majority of both survivors (86.5%) and non-survivors (75.0%) had normal PCT levels, with no significant association between PCT and survival ( $p=0.446$ ) (Table 4).

The relationship between PCT levels and the results of various culture tests was comprehensively explored. Regarding blood culture GP and GN bacteria, a larger proportion of individuals with normal PCT levels (80.0% and 50.0%, respectively) showed bacterial growth, compared with those with high PCT levels (20.0% and 50.0%,

**Table 4** Association Between Procalcitonin Levels, Culture Results from Blood, Urine, and Cerebrospinal Fluid, and Patient Survival Outcomes

		Procalcitonin Level		
		Normal (< 0.05 mcg/L)	High (> 0.05 mcg/L)	p-value
		n (%)	n (%)	
<b>Blood culture</b>	Positive	17 (77.3%)	5 (22.7%)	0.203
	Negative	285 (86.9%)	43 (13.1%)	
<b>Blood culture</b>	GP	16 (80.0%)	4 (20.0%)	0.277
	GN	1 (50.0%)	1 (50.0%)	
	Negative	285 (86.9%)	43 (13.1%)	
	Not done	1 (100.0%)	0 (0.0%)	
<b>Urine culture</b>	Positive	23 (69.7%)	10 (30.3%)	0.008*
	Negative	258 (88.1%)	35 (11.9%)	
<b>Urine culture</b>	<i>E. coli</i>	9 (47.4%)	10 (52.6%)	< 0.001*
	<i>Klebsiella</i>	14 (100.0%)	0 (0.0%)	
	Negative	258 (88.1%)	35 (11.9%)	
	Not done	14 (87.5%)	2 (12.5%)	
	Others	3 (75.0%)	1 (25.0%)	
<b>CSF culture</b>	Positive	0 (0.0%)	0 (0.0%)	–
	Negative	119 (79.9%)	30 (20.1%)	
<b>Final outcome</b>	Survived	300 (86.5%)	47 (13.5%)	0.446
	Died	3 (75.0%)	1 (25.0%)	

**Notes:** \* $p < 0.05$ ; significant; Fisher exact test.

**Abbreviations:** n, frequency; %, percentage; GP, Gram-positive bacteria; GN, Gram-negative bacteria; CSF, cerebrospinal fluid.

respectively). Among those with negative blood culture results, a substantial majority had normal PCT levels (86.9%), compared with those with high levels (13.1%). The calculated p-value (0.277) suggested no statistically significant association between PCT levels and blood culture outcomes (Table 4).

Regarding urine culture results, participants with normal PCT levels showed a higher prevalence of growth for *Klebsiella* (100%) and other bacteria (75.0%) compared with those with high PCT levels (0.0% and 25.0%, respectively). However, for *E. coli* growth, 52.6% had high PCT levels, whereas 47.4% had normal PCT levels. The p-value (< 0.001) indicated a statistically significant association between PCT levels and urine culture outcomes.

Univariate logistic regression demonstrated that *E. coli* was the only organism significantly associated with elevated PCT levels ( $p < 0.001$ ), with patients showing over eightfold higher odds of high PCT (OR=8.241), while no significant associations were observed for other organisms; clinically, this suggests that elevated PCT may be a useful indicator of *E. coli* infection, particularly in urinary tract infections (Table 5).

Logistic regression analysis indicated that the association between PCT levels and blood culture outcomes was not statistically significant, with an AOR of 1.822 (95% CI: 0.576–5.762). In contrast, positive urine culture results were significantly associated with higher PCT levels, exhibiting an AOR of 3.366 (95% CI: 1.466–7.730) and a p-value of 0.004, indicating a robust statistical relationship (Table 6).

## Viral Infection and PCT Levels

Among screened patients, 42.9% tested positive for viral infections, 19.0% were negative, and 38.1% were not tested; human rhinovirus/enterovirus (19.6%) was the most common, followed by respiratory syncytial virus (10.2%) and SARS-CoV-2 (6.3%), reflecting a diverse viral distribution (Figure 1).

**Table 5** Association of Bacterial Growth in Blood and Urine with High PCT Levels: Univariate Logistic Regression

		p-value	OR	95% CI for OR	
				Lower	Upper
Blood culture	Gram positive	0.500	1.48	0.46	0.48
	Gram negative	0.322	3.32	0.30	37.36
	Negative	Ref			
Blood culture (by organism)	<i>Streptococcus pyogenes</i> (Group A)	0.999	10,720,878,502.557	–	–
	<i>Staphylococcus hominis</i>	0.999	0.000	–	–
	<i>Staphylococcus epidermidis</i>	0.496	2.212	0.23	21.74
	<i>Salmonella</i> species	0.999	0.000	–	–
	<i>Staphylococcus aureus</i>	0.999	0.000	–	–
	Others	0.173	3.318	0.59	18.66
	Negative	Ref			
Urine culture	<i>E. coli</i>	< 0.001*	8.241	3.14	21.64
	<i>Klebsiella</i>	0.999	0.00	–	–
	Others	0.438	2.472	0.25	24.41
	Negative	Ref			

**Notes:** P-values were obtained using univariate logistic regression analysis. A p-value <0.05 was considered statistically significant. \*statistically significant.

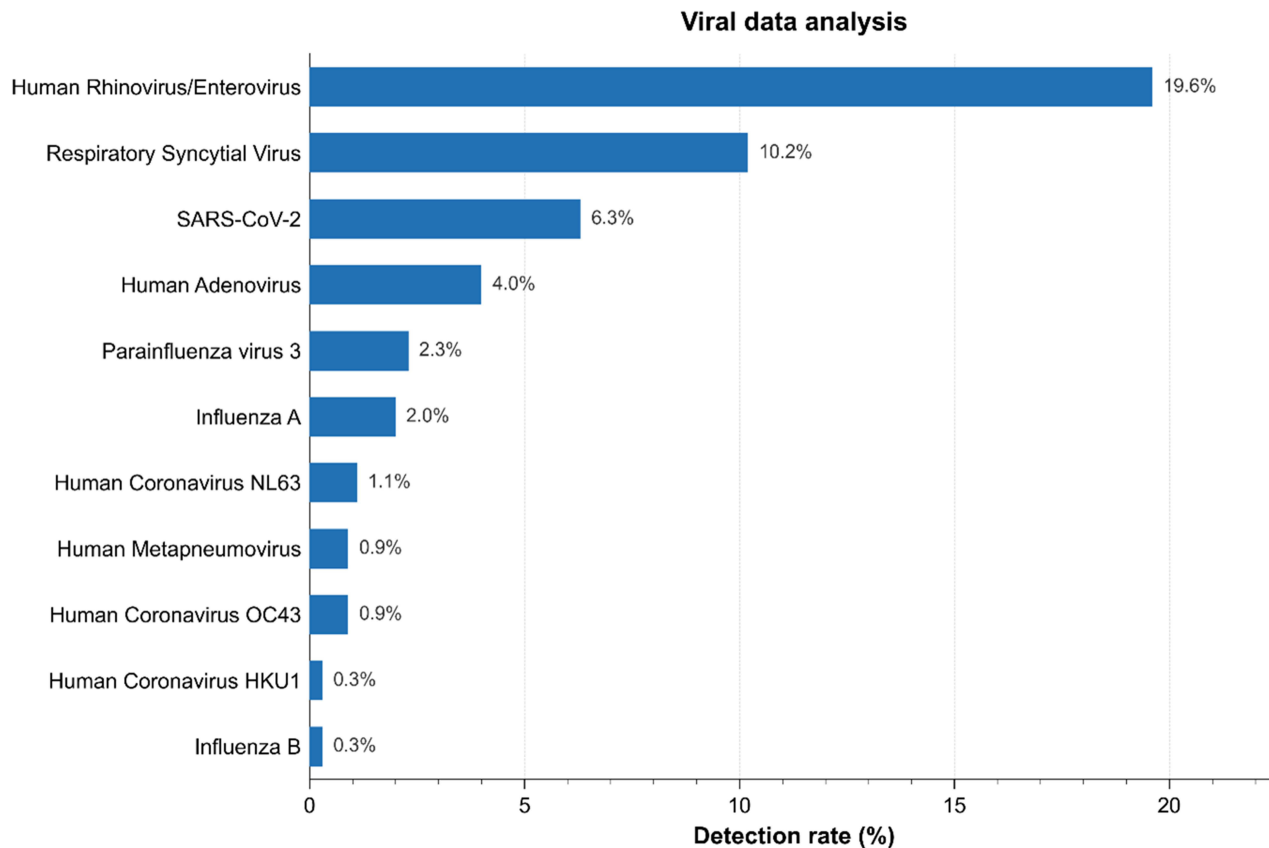
**Abbreviations:** Ref, reference group; OR, odds ratio; CI, confidence interval.

**Table 6** Predictive Value of Procalcitonin for Blood and Urine Culture Outcomes

	p-value	AOR	95% CI for AOR	
			Lower	Upper
<b>Blood culture</b>				
Positive	0.307	1.822	0.576	5.762
Negative	–	Ref.	–	–
<b>Urine culture</b>				
Positive	0.004*	3.366	1.466	7.730
Negative	–	Ref.	–	–

**Notes:** P-values were obtained using univariate logistic regression analysis. A p-value <0.05 was considered statistically significant. \*statistically significant.  
**Abbreviations:** CI, confidence interval; AOR, adjusted odds ratio.

Univariate logistic regression showed no statistically significant association between viral organisms and PCT levels; however, human rhinovirus/enterovirus demonstrated a borderline association (p=0.059), with approximately twofold higher odds of elevated PCT (OR=2.28) (Table 7).



**Figure 1** Distribution of detected viral pathogens among study patients.

**Table 7** Prediction of the Type of Organisms with Respect to High PCT Level

		<i>p</i> -value	Odds ratio (OR)	95% CI for OR	
				Lower	Upper
<b>Human coronavirus NL63</b>	Yes	0.999	0.00	–	–
	No	Ref			
<b>Influenza A</b>	Yes	0.509	1.77	0.33	9.63
	No	Ref			
<b>Influenza B</b>	Yes	1.00	0.00	–	–
	No	Ref			
<b>Human adenovirus</b>	Yes	0.643	0.69	0.15	3.23
	No	Ref			
<b>Parainfluenza virus 3</b>	Yes	0.999	0.00	–	–
	No	Ref			
<b>Human coronavirus OC43</b>	Yes	0.529	2.19	0.19	24.99
	No	Ref			
<b>Human metapneumovirus</b>	Yes	0.075	9.15	0.80	104.78
	No	Ref			
<b>Human coronavirus HKU1*</b>	Yes	1.00	0.00	–	–
	No	Ref			
<b>Human rhinovirus/enterovirus</b>	Yes	0.059	2.28	0.97	5.34
	No	Ref			
<b>SARS-Cov-2</b>	Yes	0.189	0.36	0.08	1.65
	No	Ref			
<b>Respiratory syncytial virus</b>	Yes	0.379	0.62	0.22	1.78
	No	Ref			

**Notes:** \* “HK” denoting its origin in Hong Kong and “U1” indicating its unique strain designation.

**Abbreviations:** Ref, reference group; CI, confidence interval; OR, odds ratio.

## Discussion

This study investigated the role of PCT as a single biomarker for predicting sepsis in infants aged 28–90 days. Although literature over the last decade has identified the utility of PCT in predicting bacteremia and mortality in the pediatric population, the use of PCT as a sole biomarker for identifying sepsis remains controversial, especially for young infants, as the biomarker is limited in its ability to distinguish bacterial infections, viral respiratory infections, and noninfectious autoimmune diseases.<sup>20,21</sup> The study defined the cutoff limit for high PCT levels to detect serious or invasive bacterial infections in children with fever without an apparent clinical focus, based on a published systematic review, as  $> 0.05$  mcg/L.<sup>22</sup> This review examined PCT levels based on culture results for the study group without focusing on the clinical picture. PCT levels were high in 13% of study patients.

## Bacteremia and PCT Level

The prevalence of bacteremia in the study patients was 6.25%. Bacteremia was observed in 1.4% of patients with high PCT levels in the total patient population, whereas 4.8% of patients with bacteremia exhibited normal PCT levels. This

study revealed no significant association between positive blood culture results and high PCT levels. The findings from this study are consistent with the existing literature regarding the limited utility of PCT as a biomarker and standalone test for diagnosing bacteremia in infants.<sup>23</sup> The sensitivity of PCT as a diagnostic tool for sepsis in infants remains unclear.<sup>10,24</sup> However, studies have demonstrated the effectiveness of PCT in ruling out bacteremia, thereby playing a key role in antibiotic stewardship by minimizing unnecessary antibiotic therapy.<sup>25</sup> The literature supports using the PCT threshold of 0.05 mcg/L for risk stratification in infants with bacteremia; however, this cutoff should not replace clinical judgment.<sup>26,27</sup> This study findings illustrate this point, and the prediction of the likelihood of bacteremia in relation to PCT levels was not statistically significant. This highlights the limited diagnostic utility of PCT as a single biomarker in this cohort and PCT alone should not be relied upon to predict bacteremia in young infants; it is best used as an adjunct to clinical assessment and other diagnostic tools.

## Urinary Tract Infection and PCT Level

The prevalence of positive urine cultures in this study was 9.5%. Among patients with elevated PCT levels, 30% had a positive urine culture. These results suggest that PCT levels may serve as a promising biomarker for predicting UTIs. In agreement with the study findings, the literature reports that PCT is a potential biomarker for identifying UTI and differentiating pyelonephritis from lower UTI.<sup>28,29</sup> In this study, we investigated the utility of elevated PCT levels in relation to the bacterial pathogens responsible for UTIs. Findings revealed that high PCT levels were significantly associated with an increased risk of UTI, particularly when the causative pathogen is *E. coli*. This finding was consistent with a retrospective study that showed a positive correlation between bacterial pathogens and PCT levels, as well as between PCT and CRP levels, and an association with UTIs caused by *E. coli*.<sup>30</sup> Although findings from this study regarding PCT as a potential biomarker for UTIs are promising, its clinical utility as a standalone diagnostic measure requires further investigation. The integration of PCT with other biomarkers and point-of-care urine dipstick tests may enhance its effectiveness in screening and diagnosing UTIs. Additional studies are essential to validate this approach and determine the most effective combinations for clinical practice.<sup>31,32</sup>

## Viral Respiratory Infections and PCT Level

In the current study, the relationship between high PCT and respiratory viral infections was investigated among 42.9% of infants who tested positive on a viral PCR test. The utility of high PCT levels in the context of viral infections remains undetermined, despite the evidence that they are present in human rhinovirus/enterovirus infections. However, this association was not statistically significant. Moreover, the findings contrast with the existing literature, indicating that PCT levels are typically low during viral infections and are higher and more specific for bacterial infections.<sup>33,34</sup> This underscores that PCT can effectively guide antibiotic therapy by reducing unnecessary antibiotic use in patients diagnosed with viral respiratory infections.<sup>35,36</sup>

The findings of the current study indicate that procalcitonin (PCT) is more effective for risk stratification than for definitive diagnosis. Within this single-center cohort, PCT exhibited limited utility in predicting bacteremia. However, its association with urinary tract infections, particularly those caused by *E. coli*, suggests a potential role in informing early clinical decision-making. Clinical judgment remains essential, and PCT results should be interpreted within the broader clinical context.

## Implications and Limitations

The study has several limitations, primarily due to its single-center design, which may restrict the generalizability of the findings. Additionally, repeat blood cultures obtained during the patients' admissions were not considered, which could reflect either the progression of the illness or infections acquired in a hospital setting. Furthermore, the relatively small sample size may have limited the statistical power of the findings and the robustness of the conclusions. A notable limitation is the low percentage of study patients who had positive blood cultures, even when clinically identified as having sepsis. While the focus was on examining the predictive value of procalcitonin (PCT) levels for bacteremia, urinary tract infections (UTIs), and meningitis, the overall diagnostic utility was not comprehensively assessed. Consequently, additional studies with larger

sample sizes and multicenter collaborations are warranted to validate these findings and further elucidate the role of PCT in the diagnostic framework for bacteremia, UTIs, and meningitis.

## Conclusion

The study did not identify a significant association between procalcitonin (PCT) levels and positive blood or cerebrospinal fluid culture results, which limits the utility of PCT as a standalone predictor of bacteremia or meningitis. However, elevated PCT levels were significantly associated with urinary tract infections, especially those caused by *Escherichia coli*, indicating a more specific role for PCT in identifying clinically relevant bacterial infections.

These findings suggest that PCT is better used as an adjunct to clinical assessment to differentiate the source of infection, particularly to facilitate early recognition of urinary tract infections, rather than as a broad marker for predicting sepsis in young infants. However, the findings were found from single center study which may affect their generalizability. Therefore, future prospective multicenter studies with larger sample sizes are required to validate these findings and to clarify the role of PCT within integrated clinical algorithms for infection stratification and antibiotic stewardship.

## Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of King Abdullah International Medical Research Center, Riyadh, Saudi Arabia (IRB approval NO.: NRC22R/039/01) on January 26, 2022. Patient or parental consent was waived, as no personally identifiable information was shared or published.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors declare no conflicts of interest in this work.

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