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RESEARCH

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Role of STREM-1 for early prediction of ventilator-associated pneumonia in pediatrics

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Abstract

Background TREM-1 (setting off receptor imparted on myeloid cells-1) is an immunoreceptor. Neutrophils, monocytes/macrophages, and endothelial cells all express TREM-1. This work aimed to evaluate the role of STREM-1 in ventilator-associated pneumonia (VAP) early prediction in pediatrics.

Methods This case–control research involved 56 children aged from 1 month to 5 years old, who were admitted to the pediatric intensive care unit (PICU) and needed mechanical ventilation (MV), from January 2023 to June 2023. Subjects were equally allocated into two groups: VAP group and non-VAP group.

Results There was significantly elevated serum STREM-1 after 72 h than at admission between both groups. There was significantly elevated STREM-1, procalcitonin (PCT), and C-reactive protein (CRP) after 72 h in the VAP group compared to the non-VAP group. There was a positive correlation between PCT and CRP after 72 h. STREM-1 at admission and after 72 h area under the curve (AUC) was 0.641 (0.502 to 0.765), 1.000 (0.936 to 1.000), with best cut-off value for prediction of VAP was > 185, > 230 with sensitivity 53.6%, 100% and specificity 67.9%, 100%, respectively.

Conclusion Serum sTREM-1 concentration is a reliable biomarker for predicting VAP in pediatrics received MV.

Keywords Pneumonia, Pediatrics, STREM-1, Mechanical ventilation

Introduction

Ventilator-associated pneumonia (VAP) is one of the most prevalent healthcare-associated infections (HAIs) in the pediatric intensive care unit (PICU) and has been linked with higher morbidity and duration of hospital stay [1].

VAP resulted from microbial infiltration of the lower respiratory tract and lung parenchyma and occurs in approximately 15–20% of children who have been intubated for more than 48 h which is given through an endotracheal tube or tracheostomy [2, 3]. Gram-negative bacilli are the plurality of VAP in the patients [4].

Yet early assumption for VAP could add to advantageous contravention and treatment. No suitable marks for diagnosis of VAP in pediatrics have been seen up until this point. Due to the obscurity of clinical and radiological symptoms, as well as the monotony, prominence, and efficacy of tissue culture as the ideal diagnostic standard, the early diagnosis of VAP remains problematic [5].

Multiple blood markers have been evaluated for their capacity to help in VAP diagnosis and representation in the past. Interleukin-6 (IL-6), C-reactive protein (CRP), and procalcitonin (PCT) are inflammatory cytokines with clinical significance as prognostic or predictive disease markers. In particular, PCT has been shown to be beneficial in directing antibiotic therapy [6].

TREM-1 is an immunoreceptor. Neutrophils, monocytes/macrophages, and endothelial cells all express

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TREM-1. It exacerbates the inflammatory response caused by the activation of toll-like receptors (TLR) [7].

One of the two types of TREM-1, dissolvable TREM-1 (STREM-1), has been identified as a novel and potent marker of pneumonia [8].

Patients and methods

This case–control research involved 56 children aged from 1 month to 5 years old, who were admitted to PICU and needed mechanical ventilation (MV) from January 2023 to June 2023, at Ain-Shams University's Hospitals.

Ethical considerations

1 An approval by ethical guidelines of the Faculty of Medicine's Research Ethics Committee at Ain Shams University was done before the study (NO. FWA00017585).
2 A written informed consent was obtained from patients or their legal guardians.
3 All the data of the patients and results of the research are confidential and the patients have the right to keep it or withdraw from the study at any time.
4 The researcher explains the aim of the research to the patient.

Immunocompromised cases receiving chemotherapy and/or radiotherapy were excluded from the study.

Study tools

Subjects were equally allocated into two groups: the VAP group and the non-VAP group.

All children underwent full history taking, full clinical examination and vital signs (e.g., temperature, oxygen saturation, heart rate) were monitored and fate of the patients, duration of MV, and ICU stay. VAP was diagnosed according to the CDC definition. Routine care of the ventilated patient was applied using VAP bundle care. Immediately following MV, a chest X-ray was applied and subsequent X-rays were applied every 1–3 days. Laboratory investigations, e.g., CBC, ABG, AST, ALT, urea, creat, sputum, and blood cultures were done. Blood specimens were taken at the beginning (0 h) and after (72 h) of MV. At room temperature, blood samples were centrifuged at 2000 rpm for 5 min, and the supernatant serum was collected and stored at − 80 °C. The following inflammatory biomarkers were done: STREM-1, CRP, and PCT. STREM-1 was measured by ELISA catalog No:201–12-0311, Shanghai Sunred Biological Technology Co., Ltd., Shanghai, China.

Statistical analysis

The statistical analysis was conducted using SPSS version 23. (Inc., Chicago, IL, USA). Comparing quantitative data provided as mean standard deviation (SD) for parametric data and as median with interquartile range (IQR) for non-parametric data using an independent samples *t*-test. Qualitative variables were reported as numbers, and percentages were compared using the chi-square test or Fisher's exact test. The degree of relationship between two sets of variables was established using Pearson's correlation coefficient (*r*) test. The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to examine the data for normality. P value ≤ 0.05 was judged statistically significant.

Results

Table 1 outlines the demographics of the patients studied. Insignificant differences existed between the two groups regarding age (months), sex, underlying disease about septic shock, CNS infection, cardiac patients postoperative, Hb, and platelets. Regarding WBCs, there was a significant difference between the two groups (Table 2).

There was an elevated STREM-1 (pg/ml) at 72 h compared to admission between the two groups (Table 3).

There was an elevated STREM-1, PCT, and CRP after 72 h in the VAP group than in the non-VAP group (Table 4).

There was an insignificant correlation between STREM-1 (pg/ml), PCT, and CRP at admission in the VAP group. However, There was a positive correlation between PCT and CRP after 72 h (Table 5).

No correlation was observed between STREM-1 (pg/ml), PCT, and CRP at admission and after 72 h in the non-VAP group, as seen in Table 6.

The receiver operating characteristics (ROC) curve was calculated for sTREM- at admission and 72 h after admission and the area under the curve (AUC) was 0.641 (0.502 to 0.765), 1.000 (0.936 to 1.000), with best cut-off (CO) value for prediction of VAP was > 185, > 230 with sensitivity 53.6%, 100% and specificity 67.9%, 100%, respectively. As regards PCT, AUC was 0.582 (0.443 to 0.713), 0.970 (0.885 to 0.997), and the best CO value for prediction of VAP was > 0.88, > 1.21 with sensitivity 53.6%, 92.9% and specificity 46.4%, 96.4%, respectively. As for the CRP

Table 1 Demographic data of the studied patients

Parameters		*n* = 56
Age (months)		29.61 ± 16.32
Sex	Female	17 (30.4%)
	Male	39 (69.6%)

Table 2 Comparison between the non-VAP and VAP group according to demographic data, underlying diseases, Hb, WBCs, platelets, sputum culture, and blood culture

Parameters		Non-VAP ($n=28$)	VAP ($n=28$)	Test	*P*-value
Age (months)		29.14 ± 5.51	30.07 ± 7.37	− 0.211	0.834
Sex	Female	9 (32.1%)	8 (28.6%)	0.084	0.771
	Male	19 (67.9%)	20 (71.4%)		
Underlying diseases					
Septic shock (*n*, 23/56)		11 (39.3%)	12 (42.9%)	0.074	0.786
CNS infection(*n*, 20/56)		10 (35.7%)	10 (35.7%)	0.000	1.000
Cardiac patients(*n*, 7/56)		4 (14.3%)	3 (10.7%)	0.163	0.687
Postoperative(*n*, 6/56)		3 (10.7%)	3 (10.7%)	0.000	1.000
Laboratory tests					
Hb		11.36 ± 1.73	11.64 ± 1.57	0.420	0.520
WBCs		8.39 ± 2.36	10.01 ± 2.94	− 2.276	0.027
Platelets		337.57 ± 58.33	364.68 ± 63.88	1.175	0.103
Sputum culture + ve		7 (25.0%)	12 (42.9%)	1.991	0.158
Blood culture + ve		10 (35.7%)	12 (42.9%)	0.299	0.584

Table 3 STREM-1 (pg/ml) comparison between non-VAP and VAP at admission and after 72 h

STREM-1 (pg/ml)			Paired sample *t* -test		
	At admission	**At 72 h**	**MD ± SD**	***t* -test**	***p* -value**
Non-VAP ($n=28$)	181.04 ± 7.66	209.89 ± 10.85	28.85 ± 4.90	− 12.08	< 0.001**
VAP ($n=28$)	184.36 ± 8.67	318.86 ± 25.23	134.50 ± 22.87	26.523	< 0.001**

**Highly Significant

Table 4 Comparison between non-VAP and VAP group according to STREM-1 (pg/ml), PCT, and CRP

	Non-VAP ($n=28$)	**VAP ($n=28$)**	***T* test**	***P* -value**
STREM-1 (pg/ml)				
At admission	181.04 ± 7.66	184.36 ± 8.67	− 1.519	0.135
At 72 h	209.89 ± 10.85	318.86 ± 25.23	− 20.99	**< 0.001****
PCT				
At admission	0.86 ± 0.12	0.90 ± 0.08	− 1.61	0.113
At 72 h	1.01 ± 0.21	1.41 ± 0.15	− 8.195	**< 0.001****
Amount of change	0.15 ± 0.04	0.51 ± 0.03	13.400	**< 0.001****
CRP				
At admission	3.52 ± 0.90	3.78 ± 0.83	− 1.128	0.264
At 72 h	7.24 ± 0.82	14.56 ± 1.89	− 18.82	**< 0.001****
Amount of change	3.72 ± 0.63	10.78 ± 1.83	19.302	**< 0.001****

**Highly Significant

AUC 0.568 (0.429 to 0.700), 1.000 (0.936 to 1.000), and the best CO value for prediction of VAP was > 3.6, > 9 with sensitivity 67.9%, 100% and specificity 57.1%, 100%, respectively. STREM-1 and CRP are the most significant predictors of PCT, as seen in Fig. 1.

Discussion

In our research, there was no significant difference between the VAP group and the non-VAP Group regarding STREM-1 (pg/ml) at admission and there was a highly statistically significant increase among

Table 5 Correlation between STREM-1, PCT, and CRP at Admission and after 72 h in the VAP group using Pearson's correlation coefficient (*r*)

		STREM-1 (pg/ml) at admission	**PCT at admission**	**CRP at admission**
STREM-1 (pg/ml) at admission	*r*-value		0.195	0.219
	p-value		0.321	0.263
PCT at admission	*r*-value	0.195		−0.048
	p-value	0.321		0.808
CRP at admission	*r*-value	0.219	−0.048	
	p-value	0.263	0.808	
		STREM-1 (pg/ml) at 72 h	**PCT at 72 h**	**CRP at 72 h**
STREM-1 (pg/ml) at 72 h	*r*-value		−0.015	−0.137
	p-value		0.940	0.485
PCT at 72 h	*r*-value	−0.015		**0.403***
	p-value	0.940		**0.033**
CRP at 72 h	*r*-value	−0.137	**0.403***	
	p-value	0.485	**0.033**	

*Highly Significant

Table 6 Correlation between STREM-1, PCT, and CRP at admission and after 72 h in the non-VAP group, using Pearson's correlation coefficient (*r*)

Non-VAP group		**STREM-1 (pg/ml) at admission**	**PCT at admission**	**CRP at admission**
STREM-1 (pg/ml) at admission	*r*-value		0.044	−0.235
	p-value		0.824	0.228
PCT at admission	*r*-value	0.044		0.259
	p-value	0.824		0.184
CRP at admission	*r*-value	−0.235	0.259	
	p-value	0.228	0.184	
		STREM-1 (pg/ml) at 72 h	**PCT at 72 h**	**CRP at 72 h**
STREM-1 (pg/ml) at 72 h	*r*-value		0.186	0.126
	p-value		0.317	0.524
PCT at 72 h	*r*-value	0.186		0.205
	p-value	0.317		0.295
CRP at 72 h	*r*-value	0.126	0.205	
	p-value	0.524	0.295	

the VAP group than the non-VAP group regarding STREM-1 (pg/ml) after 72 h.

This agreed with Zhao et al. (2020) [5] that the increase in serum STREM-1 as well as the increase in serum PCT after 72 h of MV may serve as a predictor of VAP in newborns, MV alone may result in ventilator-associated lung injury (VALI) and increase the production of numerous inflammatory cytokines and may elevate STREM-1 level in non-VAP group with MV.

Gibot et al. (2009) [9] demonstrated that elevated STREM-1 in septic cases reduced as their condition improved.

This is in agreement with [10] who revealed that STREM-1 served as a reliable indicator of bacterial infection.

Studies [11, 12] demonstrated that STREM-1 was detected in high concentrations in BAL samples from individuals with bacterial lung infections; hence, it may be employed as a reliable early marker for VAP and reliably differentiate VAP from non-pulmonary illnesses.

El Nady et al. (2019) [13] reported that sTREM 1 was greater in children with pneumonia than in the control group, although the difference was not significant.

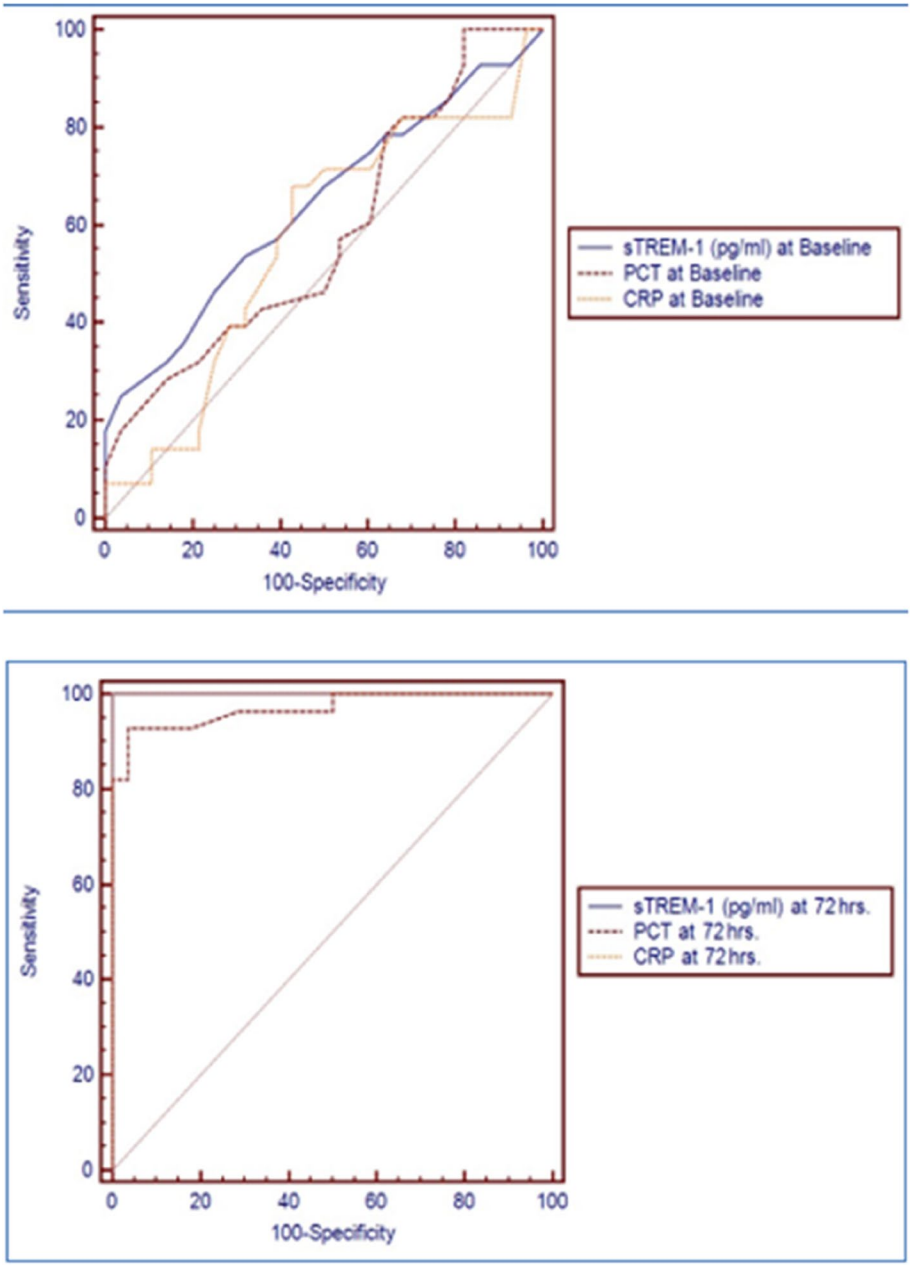

Fig. 1 STREM-1 (pg/ml), PCT, and CRP at admission (**A**) and after 72 h (**B**)

Yang et al. (2021) [14] reported that serum and bronchoalveolar lavage fluid STREM-1 were significantly elevated in the neonatal VAP group than controls. Bellos et al. (2018) [15] revealed that STREM-1 may be a useful biomarker for predicting sepsis.

There are various probable explanations for the discrepancy between this prior study's results and our own. First, the emphasis of the current research was on juvenile patients, while the majority of prior studies exclusively included adult participants. In addition, the underlying disorders may vary among research populations, which may influence the study's findings. In addition, the STREM-1 was assessed by ELISA in the current investigation, while in prior studies they were determined by Western blotting [16].

The present study showed that there was no significant difference between the VAP group and the non-VAP group as regards PCT at admission and there was a significant increase in the VAP group than non-VAP one as regards PCT after 72 h.

Tsao et al. (2020) [17] concluded that serum PCT levels ≥ 1 ng/ml have been linked to persistent infection in MV children. This value alone may lead to infective VAP overdiagnosis, particularly with decreased values.

According to Nandan et al. (2021) [18] who revealed that in conjunction with SCPIS, the increasing PCT levels higher than 10 ng/ml has very elevated sensitivity and specificity for infection. The impact of non-VAP clinical entities simultaneously elevating serum PCT is nullified by the administration of several agents. It may be utilized as a VAP screening test, that has the distinct benefit of producing findings quickly and objectively.

On the other hand, Ericksen et al. (2019) [19] reported that PCT did not distinguish between pediatric patients with viral bronchiolitis and those with bronchiolitis with concurrent bacterial pneumonia.

ROC curve was performed for STREM-1 at admission and demonstrated an AUC of 0.641 (0.502 to 0.765) with *P* value 0.059. The best CO value for the prediction of VAP was > 185 with sensitivity 53.6% and specificity 67.9%. Also, the PCT demonstrated an AUC of 0.582 (0.443 to 0.713) with *P* value 0.288. The best CO value for the prediction of VAP was > 0.88 with sensitivity 53.6% and specificity 46.4%. As for the CRP and demonstrated an AUC of 0.568 (0.429 to 0.700) with *P* value 0.389. The best CO value for the prediction of VAP was > 3.6 with sensitivity 67.9% and specificity 57.1%, and at 72 h, the ROC curve was performed for STREM-1 and demonstrated an AUC of 1.000 (0.936 to 1.000) with *P* value < 0.001. The best CO value for the prediction of VAP was > 230 with sensitivity 100% and specificity 100%. Also, the PCT demonstrated an AUC of 0.970 (0.885 to 0.997) with *P* value < 0.001. The best CO value for the prediction of VAP was > 1.21 with sensitivity 92.9% and specificity 96.4%. As for the CRP and demonstrated an AUC of 1.000 (0.936 to 1.000) with *P* value < 0.001. The best CO value for the prediction of VAP was > 9 with sensitivity 100% and specificity 100%, while the STREM-1 and CRP were the most significant predictor of PCT, with *p*-value ($p < 0.05$).

Hillas et al. (2010) [20] discovered almost the opposite conclusion, namely that CRP levels did not aid in predicting the occurrence of VAP and disease progression.

To determine CRP's sensitivity, its diagnostic value was compared to a variety of other indicators. Since it is a "indirect" infection marker, its sensitivity and specificity are not 100% and vary [21, 22].

El-Sheikh et al. (2022) [23] reported that CRP was significantly elevated in neonates with VAP than those without VAP.

El Nady et al. (2019) [13] showed high notable difference with CRP in cases with pneumonia than controls.

In clinical practice, CRP is often used as an indicator of infection severity by measuring inflammation. Healthy individuals have modest serum CRP levels, but patients with autoimmune illness, tissue necrosis, and viral disease have dramatically higher CRP levels [24, 25].

Póvoa et al. (2006) [26] reported that CRP may serve as an indication for the early diagnosis and prognosis prediction of VAP.

This is in accordance with El Nady et al. (2019) [13] who reported that there was no significant correlation between TREM-1 and CRP. STREM-1 has shown greater specificity and sensitivity than CRP [27].

Conclusion

Serum STREM-1 concentration is a reliable biomarker for predicting VAP in pediatrics received MV.

Abbreviations

TREM-1	Receptor imparted on myeloid cells-1
MV	Mechanical ventilation
CRP	C-reactive protein
PCT	Procalcitonin
VAP	Ventilator-associated pneumonia
HAIs	Healthcare-associated infections
ICU	Intensive care unit
IL-6	Interleukin-6
PICU	Pediatric intensive care unit
CDC	Centers for Disease Control and Prevention
CBC	Complete blood count
ABG	Arterial blood gas analysis
ELISA	Enzyme-linked immunosorbent assay
SD	Standard deviation
IQR	Inter-quartile range
ROC	Receiver operating characteristics
AUC	Area under the curve
CO	Cut-off
VALI	Ventilator-associated lung injury
SCPIS	Simplified Clinical Pulmonary Infection Score

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Authors' contributions

M E selected the patients; reviewed their images; did the interventional procedure; and collected, tabulated, and analyzed the data. T A A, M A A, and S M M supervised the management of the cases, interpreted the patient data, and wrote the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

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Declarations

Ethics approval and consent to participate

Uploaded with submission files.

Consent for publication

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Competing interests
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