

VALIDATION OF NOVEL SEPSIS SUB-PHENOTYPES USING TRAJECTORIES OF VITAL SIGNS AT ALEXANDRIA PEDIATRIC INTENSIVE CARE UNIT

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Introduction

Sepsis is a major global health threat, particularly for children, contributing to significant morbidity and mortality. The WHO recognizes it as a leading cause of death in pediatric intensive care units (PICUs), with mortality rates exceeding 50% in developing countries. Sepsis is caused by an abnormal immune response to infection, leading to life-threatening organ dysfunction. Early diagnosis and treatment are essential for improving outcomes. Recent studies suggest that identifying sub-phenotypes could enable more personalized management strategies. These sub-phenotypes may display distinct baseline characteristics, laboratory abnormalities, and patterns of organ dysfunction. However, data on sepsis remains limited, and understanding of its sub-phenotypes—distinct classifications based on responses to treatment—remains incomplete and are areas of ongoing research. Identifying these sub-phenotypes could improve diagnosis, intervention timing, and monitoring.

Aim of the work

This study aims to validate novel sepsis sub-phenotyping based on vital signs trajectories in pediatric severe sepsis and correlate these sub-phenotypes with clinical outcomes, complications, PICU stay length, and mechanical ventilation need.

Patients and Methods

This study retrospectively collected the data of all patients (n=116) with a primary diagnosis of severe sepsis and septic shock admitted to PICU in Alexandria University Children’s Hospital in the last five years from 1st March 2018 to 28th February 2023 (Figure 1). The 116 included patients were divided into four groups according to fever and hypotension as follows:Group A A: Fever AND Hypotension Group (n=20). Group B B: Fever NO Hypotension Group (n=40).Group C C: No Fever NO Hypotension Group (n=40).Group D D: No Fever BUT Hypotension Group (n=16).

Results

In the present study, the age of the total studied children (n=116) ranged from 0.08 to14.00 years, with a median (IQR) of 0.50 (0.17 – 1.67) years, with 50.86% males. The median (IQR) of PELOD-2 was 9 (5.00-14.50), and the median (IQR) of PIM3 was 39.00 (16.20-66.50). In the study, 40.52% of the children had chronic illnesses, with the most common being cardiac and gastrointestinal conditions, each affecting 8.62% of the participants. The observed PICU mortality rate was 45.69% related to septic shock. Common primary infections were pneumonia (32.76%) and gastrointestinal infections (28.48%). Complications included respiratory failure (48.28%), metabolic issues (32.76%), multi-organ failure (18.10%), renal insufficiency (16.38%), and disseminated intravascular coagulation (15.52%).The four groups were matched with no statistically significant difference in sex, admitting diagnosis, chronic illness, complications, PIM-3, PELOD-2, laboratory investigations, causative organisms, nor treatment, need for supportive measures: MV, inotropes, dialysis nor invasive procedure. There was no statistically significant difference in the length of PICU stay among the four groups. The study found that over the first 6 hours of PICU admission, the feverish groups (A and B) showed a declining temperature trend, likely due to antipyretic use. Regarding blood pressure, Group A exhibited an upward trend, possibly from vasopressor use, while Group D had fluctuating blood pressure that did not increase despite vasopressor treatment. The PIM-3, PELOD-2, need for MV were significant risk factors for mortality, while all other factors were not significant.

Table (1): Variable studied regarding mortality

	Outcome		Test of significance p value
	Discharged (n=63)	Deceased (n=53)	
Age (months)			
- Min - Max	1.00 - 162.00	1.50 - 168.00	Z _(Mw) =1.11 p=.21 NS
- Mean ± S.D.	18.21 ± 34.34	29.12 ± 45.60	
- Median (IQR)	6.00 (2.00 - 18.00)	6.00 (2.50 - 30.00)	
Sex			C ² _(df=1) =0.000, p=.987 NS OR=0.994 95% CI: (0.479 - 2.064 NS)
- Male	32/59 (54.24%)	27/59 (45.76%)	
- Female	31/57 (54.39%)	26/57 (45.61%)	
PIM- 3			Z _(Mw) =2.245 p=.025*
- Min - Max	1.30 - 100.00	1.20 - 113.00	
- Mean ± S.D.	36.44 ± 29.00	48.40 ± 29.01	
- Median (IQR)	26.80 (10.50 - 63.00)	47.00 (21.60 - 66.50)	
PELOD-2			Z _(Mw) =5.140 p<.001*
- Min - Max	0.00 - 22.00	1.00 - 30.00	
- Mean ± S.D.	7.22 ± 5.27	14.26 ± 7.50	
- Median (IQR)	6.00 (3.00 - 10.00)	12.00 (9.00 - 19.00)	
Temperature (°C)			Z _(Mw) =0.587 p=.557 NS
- Min - Max	35.00 - 39.50	35.00 - 40.00	
- Mean ± S.D.	37.45 ± 0.81	37.55 ± 1.10	
- Median (IQR)	37.60 (37.00 - 38.00)	37.60 (36.80 - 38.40)	
Mean arterial blood pressure (mmHg)			Z _(Mw) =0.114 p=.910 NS
- Min - Max	27.33 - 89.67	33.00 - 80.33	
- Mean ± S.D.	57.54 ± 12.90	56.96 ± 12.27	
- Median (IQR)	58.33 (48.33 - 66.00)	56.33 (49.00 - 67.33)	
Length of PICU Stay (days)			Z _(Mw) =1.626 p=.104 NS
- Min - Max	2.00 - 70.00	1.00 - 36.00	
- Mean ± S.D.	13.83 ± 10.84	11.38 ± 9.17	
- Median (IQR)	10.00 (6.00 - 20.00)	8.00 (4.00 - 17.00)	
Need for Mechanical Ventilation			C ² _(df=1) =7.623, p=.006* OR=3.462 95% CI: (1.396 - 8.581 NS)
- No	24/32 (75.00%)	8/32 (25.00%)	
- Yes	39/84 (46.43%)	45/84 (53.57%)	
Duration of Mechanical Ventilation (days)			Z _(Mw) =1.714 p=.086 NS
- n	39	45	
- Min - Max	2.00 - 23.00	1.00 - 35.00	
- Mean ± S.D.	7.36 ± 5.28	10.87 ± 8.90	
- Median (IQR)	6.00 (3.00 - 10.00)	9.00 (4.00 - 14.00)	
Chronic illness (Yes/No)			C ² _(df=1) =0.336, p=.562 NS OR=1.246 95% CI: (0.592 - 2.622 NS)
- No	39/69 (56.52%)	30/69 (43.48%)	
- Yes	24/47 (51.06%)	23/47 (48.94%)	

Conclusion

In conclusion, sepsis had high incidence and mortality, with PIM-3, PELOD-2, and mechanical ventilation as key mortality risk factors. Phenotypic categorization and sub-phenotyping based on vital sign trajectories were inconsistent, lacked distinct outcomes or treatment responses, and underscored the need for caution in relying solely on temperature and blood pressure to assess sepsis outcomes.