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Research Article

Interleukin (6, 10): Can be used as a Prediction tool for Multiple organ Dysfunction Syndrome in Critically ill Pediatric Patients?

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Abstract:

Objectives: This study aims to determine the best cut-off level of interleukin 6,10 levels for the prediction of multiple organ dysfunction syndrome in critically ill pediatric patients.

Methods: A case-control study included 110 critical pediatric patients who were admitted to the PICU at Al Azhar University Hospitals from March 2023 to February 2024 and 68 approximate-general children matched Sex and age were recruited from other departments of our hospital as a control group. Full history taken, Thorough clinical examination, the incidences of organ dysfunctions in the studied critically ill pediatric patients, Determined the levels of Interleukin 6 and 10 measured using for both critically ill children's patients and general patients using ELISA Kit Human IL-6, 10.

Results: critically ill patients who suffered from coagulation abnormalities were more common than other incidences (n=62, 56.36%) followed by those who suffered from acute liver injury (n=59, 53.64%), Interlukine-6 and 10 levels were significantly higher in the critically ill patients (252.3±171, 185.12±72.16 pg/mL respectively) than those in the general patients (64.15±50.01, 35.40±11.90 pg/mL respectively), Also, interleukin-10 levels were significantly lower among children who had post-CAR T cell/chemotherapy, and post-bone marrow transplantation (Median=144.76, and 163.44 respectively). ROC (receiver operating characteristic) analysis showed that interleukin10 levels could be used as good tool for diagnosis of critically ill patients with an area under a curve of 0.879 (p <.001) at 95% CI of (0.830-0.927), using a cut-off of >239 pg/mL with 92.5% sensitivity and 79.4% specificity as compared to interleukin 6 which at 95% CI (0.968-1), using a cut-off of >178.5 pg/mL with 97.4% sensitivity and 62% specificity. In conclusion, The IL-6 and IL-10 levels were significantly different between critically ill patients with organ injury. The IL-6 and IL-10 levels were higher in critically ill patients with organ injury compared to general patients. The interleukin-10 levels could be used as a good tool for the diagnosis of critically ill patients with a cut-off of >239 pg/mL with 92.5% sensitivity and 79.4% specificity as compared to interleukin 6.

Keywords: diagnostic tool; organ dysfunction; interleukin 6, 10; Pediatric critical illness

Introduction

Pediatric critical illness encompasses severe conditions affecting the airways, breathing, circulation, or consciousness. These life-threatening situations often arise abruptly, making early intervention crucial. **(Kortz et al., 2022)**. While the global impact of pediatric acute critical illness is significant, its true extent remains undetermined due to various

challenges **(Ruth et al., 2020)**. Pediatric Multiple Organ Dysfunction Syndrome (MODS) is a serious condition characterized by the simultaneous impairment of two or more organs. This systemic inflammatory response can lead to widespread organ dysfunction **(Arias et al., 2024)**.

Pediatric multiple organ dysfunction syndrome (MODS) has been defined as the presence of two or more concurrent organ dysfunctions **(Badke et al., 2022; Southard-Goebel et al., 2023)**. The pathophysiology of MODS is characterized by a severe, systemic, uncontrolled inflammatory process that leads to multiple organ system dysfunctions **(Fan et al., 2022)**. Various underlying conditions can contribute to MODS, with sepsis being the most common. Other risk factors include trauma, burns, pancreatitis, metabolic disorders, and post-transplant complications **(Bose et al., 2021)**. MODS is a significant concern in pediatric intensive care, affecting over 25% of admissions and contributing to a substantial number of deaths **(Sanchez-Pinto et al., 2020; Killien et al., 2022; Gaugler et al., 2023)**.

Excess humoral mediators leak into the bloodstream, triggering a systemic inflammatory response syndrome (SIRS). This dysregulated immune response is a key factor in the development of multiple organ dysfunction **(Balkrishna et al., 2023)**. Early prediction of MOD could enhance critical care and patient outcomes. **(Ishikawa et al., 2021)**. A cytokine storm, characterized by the excessive release of various cytokines, plays a crucial role in the inflammatory response and the development of MOD in critically ill patients **(Shimazui et al., 2021)**.

The interleukin-1 (IL-1) family of cytokines and their receptors are unique players in the immune system **(Migliorini et al., 2020)**. They are primarily linked to innate immunity and form a complex network regulating innate and adaptive immune responses **(Teufel et al., 2022)**. This diversity allows IL-1 family members to influence a wide range of immune responses, from maintaining homeostasis to contributing to various diseases such as cancer, autoimmune disorders, infections, inflammation, and metabolic dysfunctions **(Behzadi et al., 2022, Fernández-Sarmiento et al., 2022)**. Elevated plasma levels of IL-1 and nitric oxide metabolites have been associated with increased mortality in pediatric MODS **(Broderick and Hoffman, 2022)**. Additionally, genetic variations in TNF-α, IL-1β, and IL-1ra have been linked to the severity of sepsis **(Liang et al., 2024)**.

Interleukin-6 (IL-6) is a crucial immune regulator involved in various diseases, including autoimmune disorders, chronic inflammation, and cancer **(Rose-John et al., 2023)**. Normally, IL-6 levels in the blood are very low, but they can dramatically increase during inflammation or severe conditions like sepsis **(Rose-John, 2023)**. IL-6 is produced by immune cells in response to infection or injury, and its production is amplified by other inflammatory cytokines like IL-1β and TNF-α. High levels of IL-6 are associated with severe illness and the risk of multiple organ failure **(Andruszkow et al., 2014, Gidon et al., 2021, Akkaya et al., 2022)**. This study aims to identify the optimal IL-6 level that can accurately predict the development of multiple organ dysfunction syndrome in critically ill children.

Patients and Methods

Study design

A case-control study was conducted involving 110 critically ill pediatric patients admitted to the PICU at Al Azhar University Hospitals between March 2023 and February 2024. A control group of 68 children, matched for sex and age, was recruited from other departments within the same hospital.

Patients' selection criteria

This study included critically ill children aged 1 month to 18 years who met the criteria for severe disease and were expected to stay in the PICU for more than 7 days. Complete clinical information was essential for inclusion. Children were excluded if they refused blood tests, were receiving immunomodulatory drugs prior to hospitalization, had a pre-existing inflammatory disease, or lacked parental consent.

Patients diagnoses

The diagnosis of multiple organ dysfunction syndrome (MODS) in the study participants was made based on international guidelines and/or criteria established by the Chinese Abdominal Intensive Care Association, (2021), McDonag et al. (2021), Pickkers et al. (2021), Liu et al. (2022).

All patients were subjected to the following:

Full history datils included the history of age, sex, present illness, history, nutritional history, and the presence of chronic illness e.g. a genetic syndrome predisposing to mechanical ventilation and VAP.

Thorough clinical examination*:* This included local and general examination with emphasis on detecting any change in chest examination and respiratory secretions or change in vital signs. Initial leukemia, relapsed leukemia, Post-CAR T cell/chemotherapy, post-bone marrow transplantation, sepsis, severe pneumonia, severe encephalitis, myocarditis, arthritis and hemophagocytic syndrome, and solid tumors.

The incidences of organ dysfunctions in the studied critically ill pediatric patients such as acute gastrointestinal injury (AGI), acute respiratory distress syndrome (ARDS), acute liver injury (ALI), acute liver failure (ALF), acute kidney injury (AKI), and acute myocardial injury (AMI).

Determined the levels of Interleukin 6 and 10 measured using as Sandwich ELISA for both critically ill children's patients and general patients using ELISA Kit Human IL-6, 10 (Fine Biotech comp, Wuhan, 430074, Hubei, China).

Outcomes of the study

This study aimed to evaluate the levels of interleukin-6 (IL-6) and interleukin-10 (IL-10) in critically ill pediatric patients and assess their association with clinical findings and organ dysfunction. The primary objective was to determine the optimal cutoff values for IL-6 and IL-10 to predict the development of multiple organ dysfunction syndrome (MODS) in this population.

Ethics approval and consent to participate.

Informed consent was obtained from parents or caregivers of all study participants, who were informed about the potential benefits and risks of the study. The study protocol was approved by the ethical committee of Faculty of Medicine, Al-Azhar University (Assiut), (RESERACH/AZ.AST./5/207/12/2024) and was conducted in accordance with the Declaration of Helsinki and relevant national and institutional guidelines.

Sample size estimation

Indeed, Zhu et al. et al. (2024) reported that the best cutoff value for IL-10 was 279.45 pg/mL and IL-6 was 1,425.6 pg/mL for predicting cardiac

arrest patients with a sensitivity of 0.875 and 0.625, respectively. To detect the null hypothesis, a sample size of 178 child patients (critically ill children's patients and general patients) would be required, with a drop-out rate of 10% and a research power of 80%.

Statistical analysis

The statistical analysis was performed using Microsoft Excel 2019 and SPSS v. 25. Descriptive statistics, including relative frequencies, were used to summarize categorical variables. To compare groups, independent t-tests, Mann-Whitney U tests, and Chi-square tests (including Fisher's exact test and Monte Carlo simulations) were employed. Receiver operating characteristic (ROC) curve analysis was utilized to determine the optimal cutoff values for IL-6 and IL-10 in predicting MODS. Statistical significance was set at a p-value of less than 0.05.

Results

In our study, Figure 1 depicts a flowchart of 186 pediatric patients. 8 patients were excluded from the research, with 5 of them not meeting inclusion criteria and 3 patients declined to participate. Out of the 178 patients who were willing to participate, 110 Critically ill children's patients and 68 general patients matched age and sex as the control group, (Figure 1).

In our study between the critically ill patients and general patients according to age and gender, we observed that there was no significant difference among the studied groups (P>0.05), (Table 1).

In the current study according to initial leukemia, relapsed leukemia, post-cart cell/chemotherapy, post-bone marrow transplantation, sepsis, severe pneumonia, severe encephalitis, myocarditis, arthritis, and hemophagocytic syndrome, and solid tumors. there was no significant difference between the studied groups (P>0.05), (Table 2)

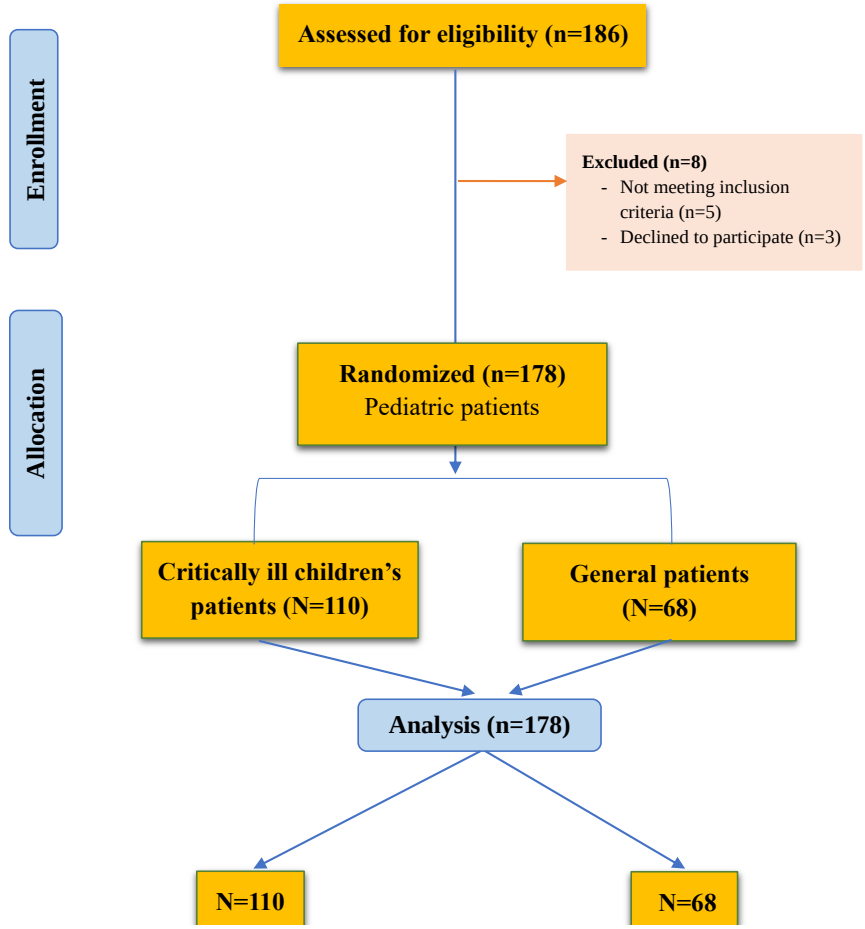

Figure 1: Flowchart of the studied pediatric patients.

	Group C (n=110)	Group G (n=68)	test	*P value*
Age/year				
Mean ±SD	6.28±2.09	6.81±2.71	t=49.50	0.142
Median (Range)	6 (2.35-11.41)	6.90 (1.80-12.02)		
Gender				
Male	71(64.55%)	43 (63.24%)	X^2=0.031	0.860
Female	39 (35.45%)	25 (36.76%)		

Group C (critically ill patients), Group G (general patients), Independent t-test (t), Chi-square test (X^2)

Table 1: Demographic data among the studied patients.

	Group C (n=110)	Group G (n=68)	X^2	*P value*
Initial leukemia	7 (6.36%)	6 (8.82%)	0.37	0.540
Relapsed leukemia	10 (9.09%)	4 (5.88%)	FE=0.59	0.441
Post-CAR T cell/chemotherapy	22 (20%)	17 (25%)	0.61	0.433
Post-bone marrow transplantation	5 (4.55%)	3 (4.41%)	*FE*=0.002	0.967
Sepsis	28 (25.45%)	16 (23.53%)	0.08	0.772
Severe pneumonia	1 (0.91%)	0	*FE*=0.61	0.432
Severe encephalitis	20 (18.18%)	7 (10.29%)	2.03	0.154
Myocarditis	3 (2.73%)	2 (2.94%)	*FE*=0.007	0.933
Arthritis and hemophagocytic syndrome	19 (17.27%)	8 (11.76%)	0.99	0.320
Solid tumors	1 (0.91%)	0	*FE*=0.61	0.432

Group C (critically ill patients), Group G (general patients), Chi-square test (X^2), Fisher's exact test (FE)

Table 2: Thorough clinical examination among the studied patients.

In the current study, critically ill patients who suffered from coagulation abnormalities were more common than other incidences (n=62, 56.36%) followed by those who suffered from acute liver injury (n=59, 53.64%), also, acute myocardial injury, acute gastrointestinal injury, neurological abnormalities, and acute kidney injury were observed in 43 (39.09%), 37 (33.63%), 35 (31.81%) and 23 (20.9%) critically ill patients respectively, while, the lowest common were Cardiac arrest (n=5, 5.54%), acute liver failure (n=4, 3.63%), and acute respiratory distress syndrome (n=2, 1.81%), (Figure 2).

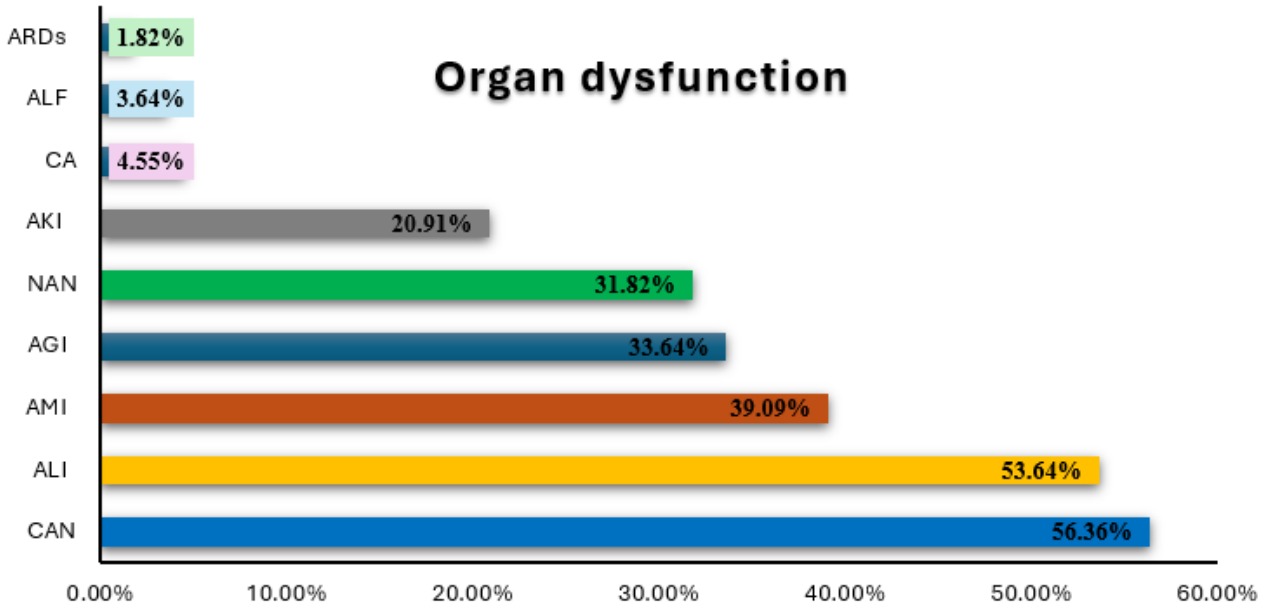

Figure 2: The incidences of organ dysfunction in the studied critically ill pediatric patients. Group C (critically ill patients), Group G (general patients), Coagulation abnormalities (CAN), acute liver injury (ALI), acute myocardial injury (AMI), acute gastrointestinal injury (AGI), Neurological abnormalities (NAN), acute kidney injury (AKI), Cardiac arrest (CA), acute liver failure (ALF), acute respiratory distress syndrome (ARDS).

In the present study, there was a significant difference between the studied patient groups regarding interleukin-6 and 10 levels (p<0.001). Interlukine-6 and 10 levels were significantly higher in the critically ill patients (252.3±171, 185.12±72.16 pg/mL respectively) than those in the general patients (64.15±50.01, 35.40±11.90 pg/mL respectively), (Figure 3).

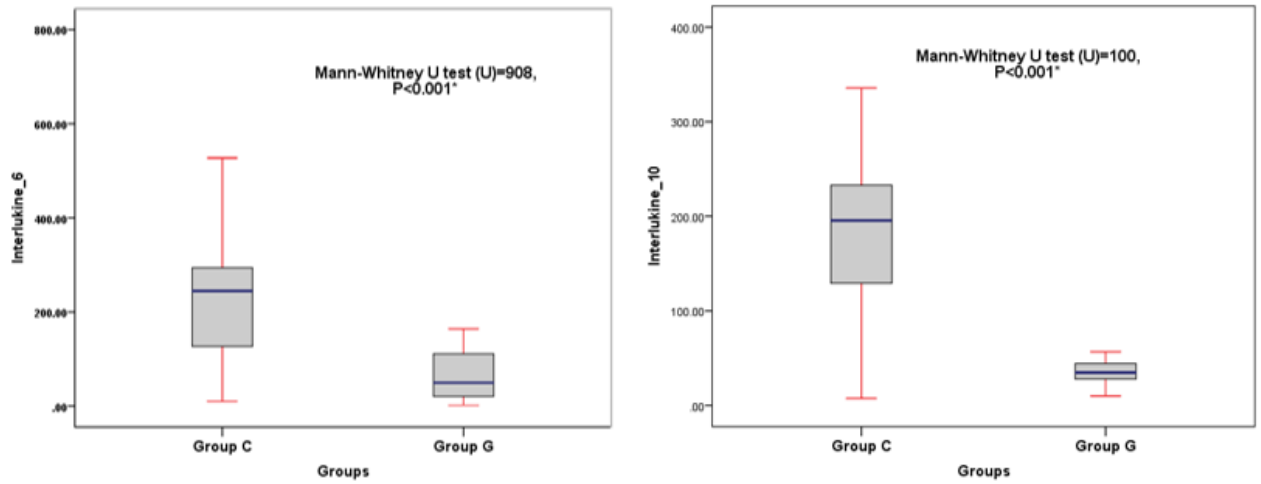

Figure 3: Interlukine-6, 10 levels among the studied patient groups. *Significant.

In the current studies, there was no significant association between interleukin-6,10 levels and gender, relapsed leukemia, sepsis, myocarditis, arthritis, hemophagocytic syndrome, and solid tumors (p>0.05). Interleukin-6 levels were significantly higher among children who had Initial leukemia and severe encephalitis (Median=525, 282.50 respectively) compared to those children who hadn't initial leukemia and severe encephalitis (Median=144.76243, 234.50 respectively). Also, interleukin-10 levels were significantly lower among children who had post-CAR T cell/chemotherapy, and post-bone marrow transplantation (Median=144.76, and 163.44 respectively) compared to those who didn't post-CAR T cell/chemotherapy, and post-bone marrow transplantation (Median=203.50, 200, respectively), (Table 4)

	No	Group C (n=110)			
		Interleukin-6 Median (range)	*UP value*	Interleukin-10 Median (range)	*UP value*
Gender					
Male	71	243(10-743)	0.488	187(7.55-300)	0.389
Female	39	252(28-703)		205.45(57.74-335.74)	
Initial leukemia					
No	103	243(10-743)	0.030*	193.25(7.55-335.74)	0.497
Yes	7	525(76-703)		205.45(133-273.51)	
Relapsed leukemia					
No	100	239(10-743)	0.055	191.88(7.55-335.74)	0.632
Yes	10	275(127-703)		207.22(47-295)	
Post-CAR T cell/chemotherapy					
No	88	245(10-743)	0.673	203.50(7.55-335.74)	0.024*
Yes	22	244(24.50-555)		144.76(45-283)	
Post-bone marrow transplantation					
No	105	235(10-743)	0.080	200(7.55-335.74)	0.045*
Yes	5	278(245.22-555)		163.44(45-189.36)	
Sepsis					
No	82	243.50(10-743)	0.714	203.26(7.55-335.74)	0.371
Yes	28	255.50(19-629)		174.87(45-295)	
Severe pneumonia					
No	109	244(10-743)	0.582	197.91(7.55-335.74)	0.092
Yes	1	278.00		145.00	
Severe encephalitis					
No	90	234.50(15-743)	0.045*	198.07(7.55-335.74)	0.895
Yes	20	282.50(10-703)		186.72(45-295)	
Myocarditis					
No	107	245.22(15-743)	0.716	190.52(7.55-335.74)	0.204
Yes	3	219(10-502)		223(205.45-274.71)	
Arthritis and hemophagocytic syndrome					
No	91	235(10-743)	0.819	189.36(7.55-335.74)	0.953
Yes	19	256.23(24.50-703)		206.71(45-289.35)	

Solid tumors					
No	109	244(10-743)	0.236	193.25(7.55-335.74)	0.655
Yes	1	527.25		217.98	

For Group C (critically ill patients), the association between interleukin 6, 10 levels and clinical examination was performed using the Mann-Whitney U test, *Significant.

Table 4: The association between interleukin 6, 10 levels and clinical examination among the studied critically ill pediatric patients.

In the present study, there was no significant relationship between Interlukine-6 and 10 levels in critically ill patients and organ functions (acute respiratory distress syndrome, acute liver injury, acute liver failure, acute kidney injury, acute myocardial injury, neurological abnormalities, coagulation abnormalities, and cardiac arrest), (p>0.05), (Table 5).

	No	**Group C (n=110)**			
		Interlukine-6 Median (range)	***U P value***	**Interlukine-10** Median (range)	***U P value***
Acute gastrointestinal injury					
No	73	234(10-743)	0.302	190.52(47-335.74)	0.894
Yes	37	260(15-703)		198.24(7.55-300)	
Acute respiratory distress syndrome					
No	108	244.6(10-743)	0.014*	195.58(7.55-335.7)	0.647
Yes	2	332.5(219-446)		152.58(82.16-223)	
Acute liver injury					
No	51	246(10-743)	0.636	187(7.55-289.65)	0.673
Yes	59	243(23-703)		197.91(45-335.74)	
Acute liver failure					
No	106	245.61(10-743)	0.737	198.07(7.5-335.72)	0.177
Yes	4	215(127-278)		122.14(45-223)	
Acute kidney injury					
No	87	246(10-743)	0.673	190.52(47-335.74)	0.971
Yes	23	235(28-629)		204.53(7.55-269)	
Acute myocardial injury					
No	67	244(15-743)	0.776	204.53(7.55-313)	0.205
Yes	43	245.22(10-593)		184.09(45-335.74)	
Neurological abnormalities					
No	75	235(10-703)	0.633	202(47-335.7)	0.220
Yes	35	252(19-743)		181(7.55-295)	
Coagulation abnormalities					
No	48	243.5 (19-743)	0.756	178.5(7.55-335.74)	0.488
Yes	62	250.5 (10-703		203.265(45-313)	
Cardiac arrest					
No	105	244 (10-743)	0.824	193.25(7.55-335.74)	0.813
Yes	5	255 (178-333)		229.91(85.49-260)	

Group C (critically ill patients), acute gastrointestinal injury (AGI), acute respiratory distress syndrome (ARDS), acute liver injury (ALI), acute liver failure (ALF), acute kidney injury (AKI), and acute myocardial injury (AMI). The association between interleukin 6, 10 levels and organ dysfunctions were performed using the Mann-Whitney U test.

Table 5: The association between interleukin 6, 10 levels and organ dysfunctions among the studied critically ill pediatric patients.

ROC (receiver operating characteristic) analysis showed that interleukin10 levels could be used as good tool for diagnosis of critically ill patients with an area under a curve of 0.879 (p <.001) at 95%CI of (0.830-0.927), using a cut-off of >239 pg/mL with 92.5% sensitivity and 79.4% specificity as compared to interleukin 6 which at 95% CI (0.968-1), using a cut-off of >178.5 pg/mL with 97.4% sensitivity and 62% specificity (Table 6, Figure 4).

	Area	*Cutoff value* >	*P value*	*Sensitivity %*	*Specificity %*	*95%CI*
Interlukine-6	0.879	239	<0.001*	92.5%	79.4%	(0.830-0.927)
Interlukine-10	0.987	178.5	<0.001*	97.4%	62%	(0.968-1)

Confidence interval (CI), *significant

Table 6: The cut-off value interleukin 6,10 levels for a prediction of multiple organ dysfunction syndrome in critically ill pediatric patients.

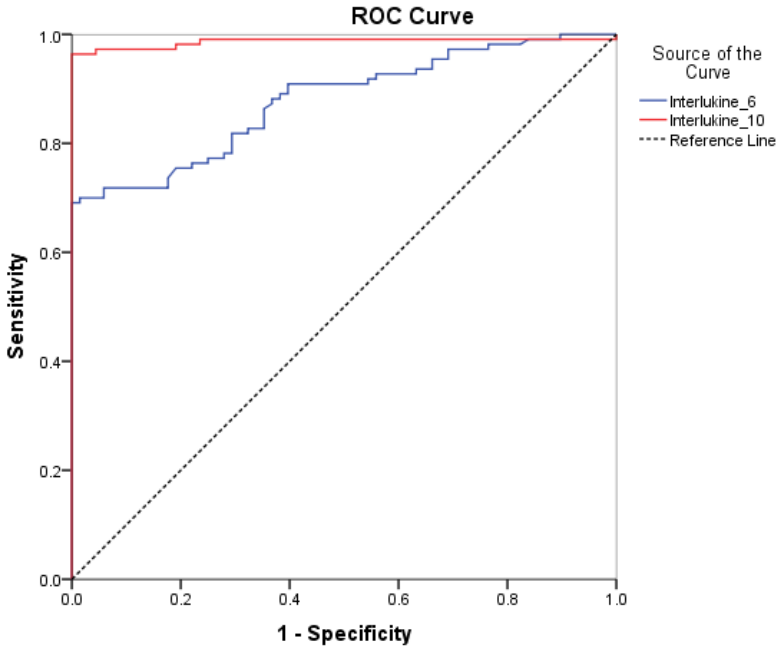

Figure 4: ROC curve analysis of interleukin 6,10 levels for a prediction of Multiple organ dysfunction syndrome in critically ill pediatric patients.

Discussion

Multiple organ dysfunction syndrome (MODS) is a significant cause of morbidity and mortality in children undergoing cardiac surgery with cardiopulmonary bypass (CPB), (Benscoter et al. 2023). Early prediction of MODS is crucial for timely intervention and improved patient outcomes **(**Typpo et al. 2009, Gourd and Nikitas, 2020**)**. While various biomarkers have shown promise **(**Pandey et al. 2015, Novak et al. 2023**),** this study focuses on the diagnostic potential of interleukin-6 (IL-6) and interleukin-10 (IL-10) levels in critically ill children with MODS.

In the current study according to initial leukemia, relapsed leukemia, post-cart cell/chemotherapy, post-bone marrow transplantation, sepsis, severe pneumonia, severe encephalitis, myocarditis, arthritis, and hemophagocytic syndrome, and solid tumors. there was no significant difference between the studied groups. Also, coagulation abnormalities were more common (56.36%), followed by acute liver injury (53.64%), acute myocardial injury, acute gastrointestinal injury, neurological abnormalities, and acute kidney injury were observed in 39.09%, 33.63%, 31.81%, and 20.9% patients respectively. Zhu et al. (2024) showed that AKI and ALI happened in critically ill patients with the occurrence of 23.5% and 56%, in line with previous studies (Jettonet al. 2017, Kaddourah et al. 2017). Badke et al. (2022) found three common combinations of organ dysfunctions were associated with a significant portion of mortality and persistent MODS in our cohort. These included Cardiovascular and liver dysfunction: Linked to 75% of deaths, Respiratory and hematologic dysfunction: Linked to 75% of deaths, Respiratory and renal dysfunction: Linked to 75% of deaths and has been previously associated with fluid overload in critically ill children, potentially leading to respiratory failure and increased mortality. Additionally, the following combinations were linked to persistent MODS, Neurologic and respiratory dysfunction: Linked to 36.3% of persistent MODS cases and Hematologic and immunologic dysfunction: Linked to 36.3% of persistent MODS cases, Endocrinologic and respiratory dysfunction: Linked to 36.3% of persistent MODS cases (Alobaidi et al. 2018, Barhight et al. 2022).

Another study by Weiss et al. (2015) found that 30% of children developed new or worsening MODS after sepsis diagnosis. Similarly, Villeneuve et al. (2016) reported an incidence of 19.6% and 20.1% for new and progressive MODS, respectively, using different diagnostic criteria. This suggests that the choice of criteria may not significantly impact the sample size of a randomized controlled trial focused on new or progressive MODS. Benscoter et al. (2023) have developed a new risk prediction model to assess the likelihood of MODS after pediatric cardiac surgery with CPB. If validated prospectively, this model could help identify high-risk patients and guide interventions to improve outcomes by preventing postoperative organ dysfunction.

The current study found significantly higher levels of interleukin-6 (IL-6) and interleukin-10 (IL-10) in critically ill patients compared to a control group. These findings align with previous research demonstrating elevated levels of various cytokines, including IL-6, IL-10, and IL-17A, in critically ill patients compared to healthy individuals. This suggests a strong association between cytokine levels and disease severity (Dhar et al. 2021, Jarczak et al. 2022, Zhang et al. 2022). In the context of sepsis, elevated IL-6 and IL-10 levels have been linked to progressive organ dysfunction, but they may not help identify specific bacterial types. However, these cytokines have been shown to correlate with the severity of organ dysfunction and can be useful predictors of sepsis prognosis (Zhang et al. 2022).

In the current study, Interleukin-6 levels were significantly higher among children who had Initial leukemia and severe encephalitis. Also, interleukin-10 levels were substantially lower among children who had post-CART cell/chemotherapy, and post bone marrow transplantation. Also, there was no significant relationship between Interlukine-6 and 10 levels in critically ill patients and organ functions (acute respiratory distress syndrome, acute liver injury, acute liver failure, acute kidney injury, acute myocardial injury, neurological abnormalities, coagulation abnormalities, and cardiac arrest). A previous study by Mu et al. (2021) suggested that IL-10 may contribute to the development of acute kidney injury (AKI), consistent with Zhu et al.'s (2024) findings of elevated IL-10 in patients with acute kidney injury. Additionally, research has focused on the "IL-6/IL-10 ratio" as a potential biomarker for disease severity. de Brito et al. (2016) demonstrated the clinical value of this ratio in early diagnosis of severe pneumonia. The ratio can reflect the balance between pro-inflammatory and anti-inflammatory responses during sepsis, which is crucial for understanding disease progression. IL-6, a multifunctional cytokine, is produced by macrophages and endothelial cells in response to inflammatory stimuli. It plays a role in various immune processes, including B-cell differentiation, T-cell activation, and the regulation of innate immune cell responses. Elevated IL-6 levels have been linked to increased disease severity and poor outcomes in clinical settings (Zhang et al. 2022).

Several studies have investigated the diagnostic potential of early IL-6 and IL-10 levels in severe infections. Vanska et al. (2012) found that a combination of IL-10 and procalcitonin (PCT) was effective in predicting severe febrile neutropenia. Persson et al. (2005) suggested that lower IL-6 levels in the early stages of neutropenic fever could indicate a milder infection.

In patients without progressive organ failure, elevated IL-6 and IL-10 levels were observed after both Gram-positive and Gram-negative bacterial infections, suggesting that these cytokines may not be highly specific for distinguishing between bacterial types in non-severe sepsis (Zhang et al. 2022). Similarly, in the non-NPMODS group, IL-6 elevation was primarily associated with worsening organ failure rather than specific bacterial types. While IL-6 elevation was linked to organ failure, IL-10 levels showed some differences between Gram-positive and Gram-negative bacterial infections, suggesting a potential role in identifying bacterial types (Zahar et al. 2011). However, other factors such as disease severity and organ dysfunction often have a greater impact on sepsis prognosis than the specific type of infecting organism.

ROC analysis showed that interleukin10 levels could be used as good tool for diagnosis of critically ill patients with an area under a curve of 0.879 ($p < .001$) at 95%CI of (0.830-0.927), using a cut-off of >239 pg/mL with 92.5% sensitivity and 79.4% specificity as compared to interleukin 6 which at 95% CI (0.968-1), using a cut-off of >178.5 pg/mL with 97.4% sensitivity and 62% specificity. ROC curves were plotted to assess the prediction value of the selected cytokines for organ injury. Another study reported significant differences in IL-10 between critically ill patients and general patients were indicated (Zhu et al. 2024). The AUC for IL-10 (more than 279.45 pg/mL) in predicting cardiac arrest was the largest (AUC =0.913, sensitivity =0.875, specificity =0.927), followed by the IL-6 (more than 1,425.6 pg/mL) for cardiac arrest (AUC =0.754, sensitivity =0.625, specificity =0.844). L-10, according to existing research, is a cytokine that suppresses the immune response (Fiorentino et al. 1991, Del Prete et al. 1993, Couper et al. 2008, Deng et al. 2012, Hombach et al. 2012).

Interestingly, while IL-10 is generally considered an anti-inflammatory cytokine, in this context, elevated levels were associated with severe tissue damage and predicted cardiac arrest. This suggests a complex role for IL-10 in the inflammatory response, potentially involving both protective and harmful effects (Steensberg et al. 2003, Tanaka et al. 2016). IL-6, on the other hand, is typically considered a pro-inflammatory cytokine. While it can induce anti-inflammatory responses through negative feedback mechanisms, excessive IL-6 levels can contribute to severe inflammation and adverse outcomes. The combination of IL-6 and IL-10 has been explored as a potential biomarker for disease severity. While some studies have shown promise, the results may vary depending on the specific disease and patient population (Dhar et al. 2021). Further research is needed to fully understand the complex interplay between these cytokines and their role in critical illness.

Conclusions

In conclusion, coagulation abnormalities and acute liver injury were the most common organ dysfunctions observed in the critically ill patient group. Significantly higher levels of IL-6 and IL-10 were detected in critically ill patients compared to the general patient group. Notably, IL-10 emerged as a valuable biomarker for the diagnosis of critical illness, with a cutoff value of >239 pg/mL demonstrating high sensitivity (92.5%) and specificity (79.4%). These findings highlight the potential of IL-10 as a diagnostic tool for identifying critically ill patients and guiding clinical decision-making.

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