

FREQUENCY OF MULTIORGAN DYSFUNCTION SYNDROME (MODS) ON DAY 0 IN PATIENTS ADMITTING TO PICU AND ITS ASSOCIATION WITH RISK FACTORS FOR MORTALITY

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(Received, 05th June 2025, Revised 18th June 2025, Accepted 16th July 2025, Published 20th July 2025)

ABSTRACT

Background: Multiorgan dysfunction syndrome (MODS) has been recognized as a leading contributor to death and disability in the PICU. Several definitions have been discussed in multiple studies. **Objective:** This study aims to evaluate the current incidence of MODS using Pediatric Organ Dysfunction Information Update Mandate 2022 (PODIUM) on Day 0 of admission to PICU and its associations with risk factors for mortality. **Study design:** It was a prospective descriptive study. **Setting:** The study was conducted in children (age: 1mo-15yrs) admitted to the PICU of Children Hospital, Korangi, Karachi. **Duration of study:** The study was conducted over 6 months, from December 2024 to May 2025. **Methods:** A total of 396 patients were eligible for the study. Data collection was conducted using demographic data (age, gender), pertinent clinical variables, and the presence or absence of MODS as an outcome and disposition as either alive or expired. Logistic regression was applied for the assessment of risk factors of mortality in the presence of MODS. **Results:** A total of 396 patients were eligible for the study. Median age IQR was 9(5-24) and male gender 60.1%(n=238). The most common diagnostic category was sepsis (56.3%). PODIUM was observed in 34%(n=134). The frequency of Respiratory, Cardiovascular, and Neurologic dysfunction was reported to be 68.2%, 29%, and 20.7% respectively. The most common diagnostic category was sepsis (56.3%). The most common system contributing to mortality was cardiovascular, followed by neurologic. The use of vasoactive drugs and mechanical ventilation is one of the predictors of mortality on multivariate logistic regression analysis. The overall mortality was 8.3% and the case fatality rate was 21.6% (29/134). **Conclusion:** The incidence of PODIUM on day 0 was one-third of patients in our cohort. It was also observed that higher mortality is associated with >3 organ involvement.

Keywords: Organ Dysfunction, PICU, Critically Ill, Mortality, Children

INTRODUCTION

The term Multi-Organ Dysfunction Syndrome (MODS) was adopted to describe the organ dysfunction rather than failure. It is a final common pathway towards mortality, long-term functional impairment, or disability in critically ill children. It is characterized by concurrent failure of two or more organ systems. However, defining single and multiple organ dysfunctions is challenging as there is no 'gold standards' that exist (1-4).

Previously, various diagnostic criteria, such as Pediatric Logistic Organ Dysfunction (PELOD), 2005- International Pediatric Sepsis Consensus Conference (IPSSC), Pediatric Risk of Mortality (PRISM), have been developed and used over the years. However, over the past decade, pediatric critical care practices have undergone significant evolution, necessitating recent research and data to support the new advances in the field. In response to these, the Pediatric Organ Dysfunction Information Update Mandate 2022 (PODIUM) convened a group of over 90 international experts to develop an updated set of diagnostic criteria for single and multiple organ dysfunction (5).

However, there are limited studies on MODS in critically ill children in low-middle income countries (LMICs), either due to the high burden of infectious diseases, malnutrition, or limited healthcare resources. Therefore, the incidence and predictors of MODS in the pediatric population remain poorly understood. So, this identification is crucial for high-risk patients and designing appropriate interventions. In this study, we aim to evaluate the current incidence of MODS. It will contribute to the literature by providing valuable insights for new professionals and researchers regarding its association with other variables, such as risk factors and mortality in our population.

METHODOLOGY

We conducted a prospective descriptive study of critically ill children admitted to the closed multidisciplinary Pediatric Intensive Care Unit (PICU) of Children's Hospital of Korangi under the management of Sindh Institute of Child Health and Neonatology (SICHN). It is a public sector, free-of-cost organization working for neonatal and pediatric healthcare under the provincial government of Sindh. We included all children aged 1 month to 15 years admitted to PICU between December 2024 and May 2025. Patients were excluded who remained in PICU for <24 hours, i.e., either left the hospital, shifted to the ward, or expired. We included the patient demographics, primary and secondary diagnosis, outcome (survival or mortality), and the components of Pediatric Organ Dysfunction Information Mandate (PODIUM) (5).

Using the PODIUM criteria, we evaluated PICU admission to assign organ dysfunction for neurologic, respiratory, cardiovascular, renal, hematology, hepatic, coagulation, gastrointestinal, endocrine, and immune. MODS was defined as two or more dysfunctional organs out of 10 (Table 1) (5). The sample size was calculated using the software OpenEpi with assumptions of Confidence Interval: 95%, frequency of MODS: 32% (3), margin of error: 5% and required sample size of 339. A non-probability consecutive sampling technique was used. This study followed the STROBE guideline. IRB approved the study with the number (SICHN/IRB-007/2024). Data was collected using REDCap software. Analysis was done using SPSS Version 26. Frequency and percentages were reported for all categorical variables. Mean \pm SD or Median (IQR) were reported for all continuous data. Normality was assessed using the Shapiro-Wilk test. Association of

[Citation: Izhar, Z., Haque, A.U., Majeed, A.A, Ali, S.R. (2025). Frequency of multiorgan dysfunction syndrome (MODS) on day 0 in patients admitting to PICU and its association with risk factors for mortality. *Pak. J. Inten. Care Med.* 5(2), 2025: 115. doi: <https://doi.org/10.54112/pjicm.v5i02.115>]

MODS with other variables was assessed using Chi-square. All statistically significant risk factors were assessed utilizing multivariate logistic regression. PODIUM Score was assessed using receiver operating characteristic (ROC) curve analysis.

RESULTS

A total of 396 patients admitted to the PICU were enrolled in this study. Their Median (IQR) age was 9 (5-24) months, and the gender distribution showed a male predominance with 238 (60.1%). MODS was observed in 134(34%) patients (Fig;1). The majority of patients were diagnosed with sepsis at the time of admission, 223(56.3%), followed by septic shock in 57(14.4%), while very few were admitted due to cardiovascular disease (CVS). ICU interventions included VAD 79(19.9%), and MV support 95(23.9%) respectively (Table 1). The patients who developed MODS had many risk factors; therefore, confounding of risk variables was possible. To address this, all statistically significant risk factors were assessed utilizing multivariate logistic regression to overcome the confounding. This revealed that patients with comorbidities had significantly higher odds of developing MODS (adjusted odds ratio (aOR) = 5.45; 95% CI (2.44-12.16)) compared to those without comorbidities. Similarly, sepsis was associated with a 4.49-fold increase in the likelihood of MODS (aOR = 4.49; 95% CI (1.04-19.42)), whereas septic shock markedly elevated the risk (aOR = 146.94; 95% CI (10.86-1987.71)). Mechanical ventilation (MV) was also a significant predictor, with supported patients exhibiting 11.94 times higher odds of MODS (aOR = 11.94; 95% CI (5.23-27.38)). Furthermore, mortality was 5.37 times more likely among patients with MODS (aOR = 5.37; 95% CI (1.28-22.59)) (Table 3). Lastly, the predictive capability of the PODIUM Score was assessed using receiver operating characteristic (ROC) curve analysis. The area under the curve (AUC) was 0.84, indicating good discrimination for mortality prediction (Fig. 4).

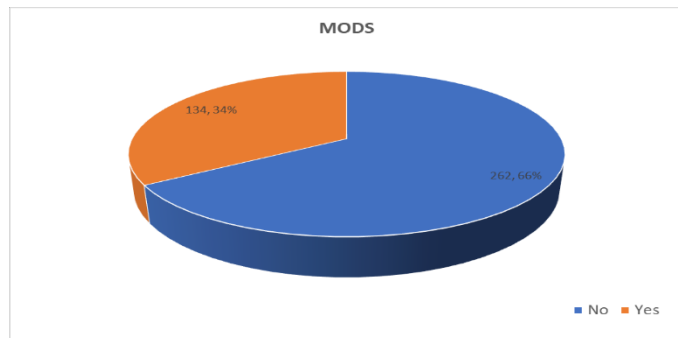


Figure 1: Percentage of Multiorgan Dysfunction

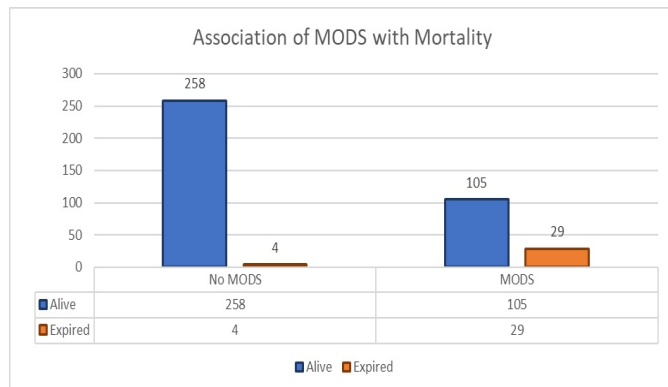


Figure 2: Association of MOS with Mortality

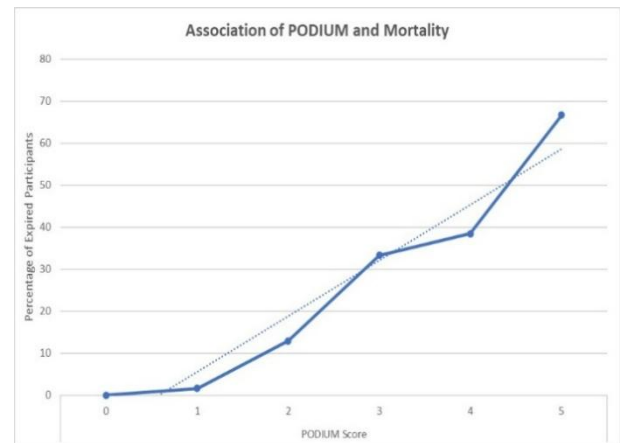


Figure 3: Association of PODIUM Score with Mortality

Table 1: Characteristics of Study Participants

Variables	n (%)
Age (Months)	
Median (IQR)	9(5-24)
Min-Max	1-156
Gender	
Male	238 (60.1)
Female	158 (39.9)
Co-Morbid	
Diagnostic Category	n (%)
Resp	50 (12.6)
CVS	20 (5.1)
Sepsis	223 (56.3)
Septic Shock	57 (14.4)
Misc.	23 (5.8)
Organ Dysfunction	
CVS	115 (29)
Respiratory	270 (68.2)
CNS	82 (20.7)
Hem	36 (9.1)
Renal	20 (5.1)
Hepatic	38 (9.5)
Coagulation	22 (5.6)
ICU-Intervention	
MV	95 (4)
VAD	79 (19.9)
Mortality	33 (8.3)

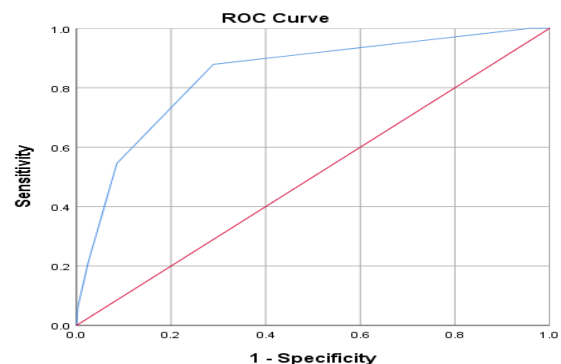


Figure 4: ROC curve analysis of the PODIUM Score for mortality prediction

Table 2: Association of MODS with Participant Characteristics, Diagnostic Categories, and Interventions

MODS			
Variables	No n (%)	Yes n (%)	p-value
Gender			
Male	167(63.7)	71(53)	0.039 [†]
Female	95(36.3)	63(47)	
Age (Months)			
≤60	238(90.8)	127(94.8)	0.168 [†]
>60	24(9.2)	7(5.2)	
Comorbidity			
No	224(85.5)	106(79.1)	0.106 [†]
Yes	38(14.5)	28(20.9)	
Diagnostic Criteria			
Resp	37(14.1)	13(9.7)	0.210 [†]
CVS	4(1.5)	16(11.9)	<0.001 ^{**†}
CNS	18(6.9)	5(3.7)	0.206 [†]
Sepsis	181(69.1)	42(31.3)	<0.001 ^{**†}
Septic Shock	2(0.8)	55(41)	<0.001 ^{**†}
Misc.	20(7.6)	3(2.2)	0.030 ^{*†}
VAD			
No	255(97.3)	62(46.3)	<0.001 ^{**†}
Yes	7(2.7)	72(53.7)	
MV			
No	248(94.7)	53(39.6)	<0.001 ^{**†}
Yes	14(5.3)	81(60.4)	
*P value<0.05, **P value <0.001, † Pearson Chi-Square			

*P value<0.05, **P value<0.001, [‡] Pearson Chi-Square**Table 3: Multivariate logistic regression analysis of risk factors for MOD**

Variables	Adjusted OR (95% CI)	P value
Gender	0.9(0.48-1.69)	0.754
Comorbidity	5.45(2.44-12.16)	<0.001**
Respiratory	3.17(0.69-14.47)	0.137
CVS	7.93(0.94-67.05)	0.057
Neuro	5.2(0.82-33.02)	0.08
Sepsis	4.49(1.04-19.42)	0.044*
Septic Shock	146.94(10.86-1987.71)	<0.001**
VAD	1.29(0.22-7.47)	0.776
MV	11.7(5.23-27.38)	<0.001**
Mortality	5.37(1.28-22.59)	0.022*

CI: Confidence Interval, Ref: Reference Category, OR: Odds Ratio, *Significant Value <0.05, A **Significant Value <0.001

Area Under the Curve

Test Result Variable(s): podium_2				
Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.841	.037	.000	.770	.913

The test result variable(s): podium_2 has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

DISCUSSION

We demonstrated that the incidence of MODS on day 0 was 34%, which was consistent with the recent published studies conducted by Sanchez *et al* in the US (6) and Iqbal *et al* in Pakistan (33%) (7),

respectively. In 2016, another study from PICU on 800-plus patients showed MODS in 180 (21.4%) and 314 patients (37.3%), using the Proulx and Goldstein diagnostic criteria, respectively (8). It was reported to be much higher, up to 57%, in a study done by Scott *et al* in 2017 (4). In 2003, Tantalean *et al* reported a population of patients with a MODS incidence of 56.5% (9).

And, we also identify that the presence of MODS on day 0 of PICU admission is associated with high mortality outcome. In a 6-month study, a total of 1415 patients were admitted, out of which 396 fulfilled the criteria. Median age on admission of our study population was 9 months, while it is 5.5 years (1.5-12.7) higher in a study conducted in 2020 by Nelson *et al* (10) and also reported as 4.6 years (interquartile range (IQR) 1.4–11.6) by the same author in 2022(6). Most of the patients were male, comprising 60% of the study population, almost similar numbers were shared in a study conducted by Iqbal *et al* in Pakistan (60.4%)(7) and a lower number of about 54.8% by Nelson *et al* (10). The nearby number was 56.5%, as reported by Hamshary *et al*. (11).

The most common diagnostic category at the time of admission was infection-related illnesses, and it was the leading diagnosis that accounted for 290 (73%), followed by respiratory illnesses 50 (12.6%). In 2017, Hamshary *et al* reported a lower incidence of sepsis, approximately 45%, as a cofactor for MODS using PRISM III vs PELOD for mortality prediction (11). Typpo *et al* reported higher numbers of Respiratory dysfunction, occurring in 34% of patients admitted to PICU, which was followed by cardiovascular (20.9%) and neurologic dysfunction (10.6%) (3). It did not match with a study done by Giri *et al* which showed the most common diseases needing PICU admissions were Neurological 31% (32 cases), followed by Respiratory 26.2% (27 cases), & other infectious diseases (including Sepsis, TB, Enteric fever etc.) comprising 11.8% (12 cases) in 2019 (12).

In our study, most of the population fell under 5 years, but we did not find the age-specific relation for single or cumulative organ dysfunction. In comparison to a study done by Nelson *et al*, who have age-specific diagnoses for organ dysfunction, infants <1 year of age had a higher cumulative incidence of respiratory and cardiovascular dysfunction, and school-aged children older than 6 years had a higher cumulative incidence of renal, endocrine, and immune dysfunction (2022) (6). The number of organ dysfunctions has a close relationship with mortality. We observed that the higher the number of organ dysfunctions, the higher the mortality rate. The highest mortalities were seen with >3 organ involvement. Scott *et al* reported mortality rates <5% in patients with little to no organ dysfunction and mortality >80% in children with the most severe and highest number of organ dysfunction (4). Similarly, Typpo *et al* reported that the patients who had three or more dysfunctional organ systems had the worst functional outcomes with a mortality rate of 16.2% (3).

Respiratory dysfunction was the most common, occurring in 68.2% of patients in our cohort, but septic shock and sepsis had the highest association with mortality, 41% and 31.3% respectively. In 2017, Travis *et al* compared the pSOFA and Sepsis-3 for MODS and reported that a lower number of patients, 14.1% were classified as having sepsis, and only 4% as septic shock, with mortality rates of 12.1% and 32.3% respectively (13).

We found that MODS-positive patients required more ICU interventions compared to MODS-negative patients, including Vasoactive drugs (VAD) in 53.3% and Mechanical ventilation (MV) in 60.4% of the MODS population. In 2020, Lower results were reported by Carlton *et al*, where 39.7% of patients were mechanically ventilated, 13.2% received vasopressors (14). Ventilated patients with MODS are 35 times more likely to die as compared to non-ventilated patients with MODS, with an OR of 35.616 and a p-value of 0.002 (11). Costa *et al* described the population with MODS using the

PRISM score and reported the use of mechanical ventilation and vasoactive drugs in 63% and 35% of patients, respectively (15). Few studies have included fluid overload as a predictor for mortality, as Chen *et al* reported that both early fluid overload and PICU-acquired daily fluid overload were independent risk factors associated with mortality (16).

The adjusted odds ratio and significant p-value of <0.001 were documented in patients with septic shock, which was 146.94 (10.86-198.71), followed by CVS of 7.93 (0.94-67.05) with a p-value of 0.057.

The overall mortality of PICU admissions was 8.3%, very close to the study conducted by Sanchez *et al* (6-10%) (6) and by Typo *et al* (10.3%) (2), respectively. But the case fatality rate of MODS positive was 21.6% which is lower than the case fatality rate reported as 45.3% by Giri *et al* (12) and much lower rate of 6.4% documented by Nelson *et al* (2), this huge difference in numbers might be due to resource availability as highest numbers were reported in LMICs like Pakistan and Nepal.

The strength of this study was that it represented the first evaluation of PODIUM organ dysfunction criteria in our region and its association with the outcome in the first 24 hours in the entire country. This study was single-center-based, thus not representing the entire population of PICU patients throughout the country. Our study population consisted of medical patients only. Moreover, we did not report the immune system as an organ dysfunction in our cohort.

CONCLUSION

The incidence of MODS based on the PODIUM consensus definition on day 0 was one-third of patients in our cohort. It was also observed that higher mortality is associated with more than 3 organ involvement, and septic shock and sepsis were the most common ones contributing to mortality.

DECLARATIONS

Data Availability Statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (SICHN/IRB-007/2024)

Consent for publication

Approved

Funding

Not applicable

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

ZOYA IZHAR (Postgraduate Resident)

Conception of Study Design, Data collection, Data entry, Review of manuscript, and Manuscript drafting

ANWAR UL HAQUE (Professor & HOD)

Methodology, Critical Input, and Final Approval of Manuscript

AQSA ABDUL MAJEED (Research Associate)

Data entry, Result Analysis

SYED REHAN ALI (Supervisor)

Critical Review.

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[Citation: Izhar, Z., Haque, A.U., Majeed, A.A., Ali, S.R. (2025). Frequency of multiorgan dysfunction syndrome (MODS) on day 0 in patients admitting to PICU and its association with risk factors for mortality. *Pak. J. Inten. Care Med*. 5(2), 2025: 115. doi: <https://doi.org/10.54112/pjicm.v5i02.115>]

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