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## **Prediction of mortality on seventh day with PELOD scoring on day-0 and day-2 in children with multi organ dysfunction syndrome in a tertiary care PICU**

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**Abstract**---Background: In a PICU set up the reported incidence of MODS is 11-56% and the Odds of death in children with MODS 11.3. In a resource limited setting, mortality prediction becomes important within the first 3 days of PICU stay for financial burden plays a big role in these decisions. The PELOD score has been validated as an outcome measure when recorded daily. In this study, validation of the PELOD score on just 2 days i.e. at baseline (day 0) and after 48hrs (day 2) and the difference between the two was studied to predict short term mortality as an outcome by the end of 7 days. Aim: Prediction of mortality on seventh day with PELOD scoring on Day-0 and Day-2 in children with Multi Organ Dysfunction Syndrome in a tertiary care PICU. Materials & Methods: A prospective longitudinal observational cohort study was carried out in a 20 bedded Indian PICU. Inclusion criteria included children age 1 month to 12 years, the presence of MODS and a PICU stay > 24 hrs. Once an inclusion criterion is met data was collected from the patients in PICU & entered in EXCEL 2013 for calculation of PELOD & PRSIM. In PELOD score

Six organ systems are considered, each with up to 3 variables (total 12 variables). Each variable is assigned points (0, 1, 10 or 20) based on the level of severity. PELOD scores were recorded on both Day 0 and Day 2 and the cohort were followed up to seven days to assess the outcome – survival/non-survival. Results: Among the 75 children in the study population, 36 were non-survivors and 39 were survivors. The overall mortality from MODS was 48%. The PELOD score among non survivors was found to be significantly higher as compared to survivors on Day 2 ( $p=0.000$ ). The rise in scores from Day 0 to Day 2 was also found to be significant ( $p=0.000$ ). High scorers on Day 2 were found to have a significantly higher risk of mortality as compared low scorers. The discriminative ability and calibration were found to be good for both day 2 and the rise in scores from day 0 to day 2 thereby validating the study. Conclusion: The PELOD score on Day 2 and the rise in score from Day 0 to Day 2 are valid outcome measures that predict short term mortality within 7 days. In addition, a high score on Day 2 increased the chance of mortality 23.8 times. Therefore, the use of the PELOD score on Day 0 and Day 2 is sufficient as predictors of short-term PICU mortality.

**Keywords**---multi organ dysfunction syndrome (MODS), severe inflammatory response system (SIRS), pediatric logistic organ dysfunction score (PELOD), mortality.

## Introduction

MODS is a reversible disorder, however the final outcome is dependent on the severity of MODS itself. Determinants of the severity of MODS include the severity of illness at onset and the progression of the illness (12) and not just number of organ systems involved as described by previous studies (1-3,5,6,8,13). In an Indian setting, most of the times MODS is sepsis related. It usually follows the sequence of Severe Inflammatory Response System (SIRS), sepsis, septic shock and onto MODS (14-19). Under this wide spectrum of Sepsis there are septic shock, Dengue shock syndrome, MISC, Rickettsial fever and Falciparum malaria that are among the leading causes of sepsis leading on to MODS. Other predisposing causes include burns and post-operative patients especially in those with hospital acquired sepsis.

Several scoring systems have been described to assess the severity of MODS. Some are the Pediatric Logistic Organ Dysfunction Score (PELOD) (7,10,20,21), Pediatric Multi Organ Dysfunction Score (PEMOD) (7) and the Sequential Organ Dysfunction Score (SOFA) (22). Of these only one descriptive score is validated to estimate the severity of cases of multiple organ dysfunction syndrome in PICUs, namely, the Pediatric Logistic Organ Dysfunction score (PELOD) (10). In the PELOD score, the data required to calculate this score are collected daily from baseline to discharge from the PICU or up to 2 hrs before death in the PICU. The original PELOD score was never intended to be an indicator of mortality, and was initially designed as a tool to assess the severity of illness as a means of baseline /outcome measure in clinical studies (20,23). The PELOD score can be used to

describe the clinical outcome of patients during their stay in a PICU when scored as a daily PELOD score (dPELOD) for at least 7 days (Days 1,2,5,6,12, 16 and 18) (12). Aim of this study is “Prediction of mortality on seventh day with PELOD scoring on Day-0 and Day-2 in children with Multi Organ Dysfunction Syndrome in a tertiary care PICU”.

### **Review of literature**

Organ dysfunction is well known as a predisposition to mortality (29,30). Which organ system gets involved first also determines risk for mortality (For example, some children develop coagulation abnormalities early, while others develop renal dysfunction). The severity of organ dysfunction and the number of organ systems involved also determine severity and as a consequence mortality (27,28). Similar studies by Wilkinson et.al in 1986 among 831 children showed a mortality rate of 50% with 3organ system involvement and 62% with 4 (8).

In 1999 Leteurtre et al developed two MODS scoring systems. The Pediatric Logistic Organ Dysfunction Score (PELOD) score was derived using the approach developed by Le Gall et al, i.e. using logistic regression to determine the severity levels and relative weights for the Logistic Organ Dysfunction System (LODS). The Pediatric Multiple Organ Dysfunction Score (PEMOD) score was derived using the method developed by Marshall et al. For each of the six organ systems involved PEMOD had one variable while the PELOD included several variables. Severity levels and relative weights of organ dysfunction were determined according to the mortality rates (PEMOD) or logistic regression (PELOD) (5,23,24).

Tantalean et al in2003 among 276 children showed that those with 3 organ systems had a mortality of 38.8%, those with 4 organ system mortality of 84%and 5 with a mortality of 100% (5). Most recently in March 2012, Lola Purnama Dewi et al from Indonesia used the PELOD score to predict mortality among children ( 60% within the age group of 1-5 ) with Dengue shock syndrome (DSS). The study looked at the PELOD score only on Day 1 of 81 children admitted with DSS. The mean PELOD scores among survivors was 11 (2-32) with a p <0.001 and that of non survivors was 33 (13-44) with a p < 0.001. The scores showed a good discriminative ability with AUC 0.97. Of the 14 children who died, they found that hepatic dysfunction was present in 8 (53.3%) and 9 (60%) with hematological involvement, emphasizing that the severity of certain organ system dysfunction associated with certain disease conditions may be the cause of mortality in those subjects (45). A well developed and well-validated quantitative score can take into account the independent weight of each variable that is integrated into it.

### **Meterials and Methods**

This is a Prospective, Observational, Longitudinal Cohort Study conducted in Pediatric Intensive Care Unit, Institute Of Women And Child Health, Niloufer Hospital from 6 -10 -2020 to 30 -12- 2021.

**Inclusion Criteria**

- Age 1 month to 12 years
- Presence of Pediatric MODS (>1 organ system failure) irrespective of cause
- PICU stay with MODS >24hrs
- Signed consent for the study by parents/ guardian

**Exclusion Criteria**

- PICU stay < 24 hrs
- Discharge against medical advice (DAMA) prior to 7 days duration will not be included in the Study

**Case Definition**

Multiple Organ Dysfunction Syndrome (MODS): Any patient with at least 2 or more organ system dysfunction as defined by the American College of Critical Care Medicine (ACCM) /Society of Critical Care Medicine (SCCM). The sample size was calculated based on a pilot study, calculated for a 80% level of significance and a hazard ratio of 7.

**PELOD Score**

The original PELOD score is calculated with data collected over the entire PICU stay (using the most abnormal value of each variable during the entire PICU stay), taking into account six organ systems (neurologic, cardiovascular, renal, respiratory, hematologic and hepatic) each with up to 3 variables (total 12 variables). Each variable is assigned points (0, 1, 10 or 20) based on the level of severity. The maximum score that can be attained is 71. Levels of severity and relative weights of each organ dysfunction were determined by means of logistic regression (10). The PELOD score is tabulated below.

Table.1

Organ System Variables	Points by level of severity for each system			
	0	1	10	20
<b>Respirator</b> % PaO <sub>2</sub> /FiO <sub>2</sub> ; PaCO <sub>2</sub> ; Ventilation	>70 and ≤90 and no ventilation	Ventilation	≤70 or >90	
<b>Cardiovascular:</b> Heart Rate: <12yr, >12yr; Systolic BP: 1 mo- 1 yr, 1-12 yr, > 12yr	≤195, ≤150 and		>195, >150 or 35- 75,45-85,55- 95	<35, <45, <55
<b>Neurologic:</b> GCS; Pupillary reaction	12-15 and both reactive	7-11	4-6 or both fixed	3
<b>Hepatic:</b> ALT; PT(INR)	<950 and >60 or < 1.4	≥950 and ≤60 or ≤1.4		
<b>Renal:</b> Creatinine 7 day – 1 yr; 1-12 yr, >12 yr	<0.62, <1.13, <1.5 9		≥0.62, ≥1.13, ≥1.59	
<b>Hematologic:</b> WBC count Platelet count	>4,500/cmm and 35,000 cells/cmm	≥1.5-4.4 or <35,000	<1.5	

The PELOD score over the entire PICU stay cannot be calculated before discharge, therefore, it cannot be used to characterize and follow the severity of organ dysfunction on a daily basis. Measurements repeated daily may provide more useful information. This formed the basis of the daily PELOD (dPELOD) score. The dPELOD score is also calculated in the same way, the highest value through each day for each variable is used to calculate the total score.

### Study Procedure

Before commencing the study the “Institutional Ethics Committee” clearance was taken. Patients fulfilling inclusion criteria were thus included in the study after informed consent. Once included, they were scored with the PELOD score on day 0 (i.e. the day of diagnosis of MODS). These patients were then scored with the PELOD again on day 2. For the PELOD score, six organ systems (neurological, cardiovascular, renal, respiratory, hematological and hepatic) are considered, each with up to 3 variables (total 12 variables). Each variable is assigned points (0, 1, 10 or 20) based on the level of severity. Levels of severity and relative weights have been determined by logistic regression. The maximum number of points for an organ is 20, and the maximum PELOD score is 71. All patients were followed up for 7 days from the day of diagnosis of MODS to determine the Day 7 outcome (Survivor or Non-survivor). Discharge against Medical Advice prior to 7 days duration was considered as a Non-survivor for analysis. Other data including demographic data like system(s) involved, age and

sex of the patient was recorded. Day of death /DAMA within the follow up period of 7 days were also recorded.

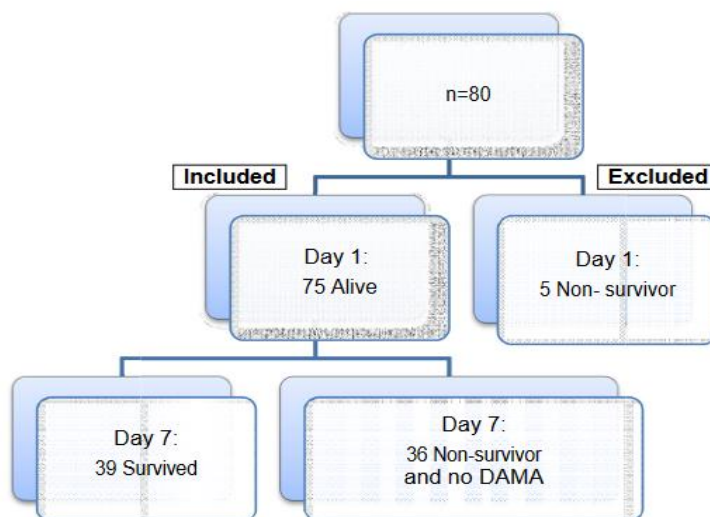
### Data Management and Statistical Analysis

Data was entered into an excel sheet and after cleaning transferred to a statistical software SPSS 17.0 that was used for the analysis of data. Microsoft Word and Excel, along with SPSS have been used to generate graphs and tables. Results are expressed as frequencies and percentages for categorical variables and as medians and interquartile ranges for numerical variables. A p value of  $< 0.05$  was considered statistically significant.

### Results

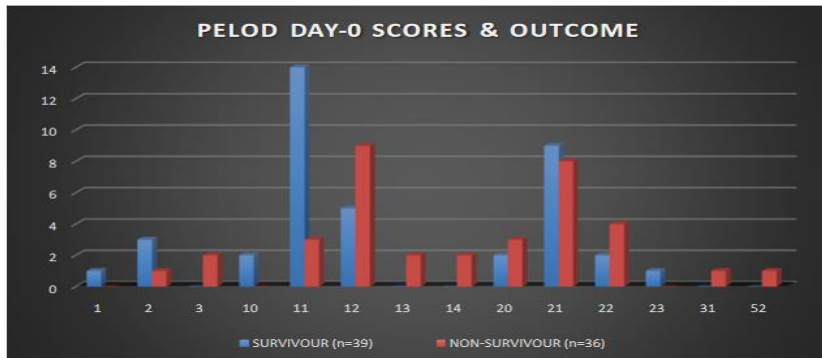
A total of 80 patients were included in the study, recruited on day 0 of Diagnosis of MODS after informed consent was taken .They were scored for PELOD scores. The patients were then scored again on day 2 with the PELOD score. Five patients could not be scored on Day 2 as they died on Day 1 within 24 hours of MODS diagnosis and they were excluded from the study. The remaining 75 patients were then followed upon day 7 to look at the primary outcome variable, i.e; survival vs non-survival. Of the 75 recruited children who met the inclusion criteria 39 were survivors and 36 were non-survivors and there were no cases who were discharge against medical advice (DAMA), with an overall mortality of 48.

Fig.1



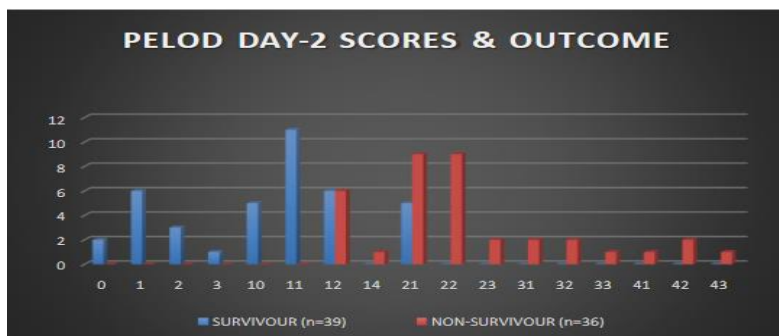
The median PELOD score among survivors on Day 0 was 11.0 with interquartile range between 11 and 21 and a standard deviation of 6.2, while that of non-survivors was 14.0 with interquartile range between 12 to 21 and a standard deviation of 8.7.

Figure 2: Day- 0 PELOD scoring and mortality



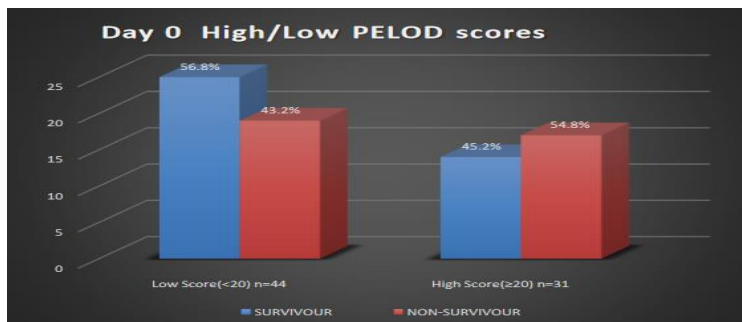
Statistical analysis using the Mann Whitney test, which is a non-parametric test used for skewed data gave a p value of 0.347 which is not statistically significant. The area under the receiver operator curve (AUC) was found to be 0.647 (p =0.054) which is not statistically significant. The calibration of the score was however good with (p =0.327). Comparing the scores on Day 2, survivors had a median score of 11 with inter-quartile ranges between 2 and 12 with a standard deviation of 6.4 while non- survivors had a median score of 22 with inter-quartile range between 21 and 29 with a standard deviation of 8.5.

Figure 3: Day 2 PELOD scoring and mortality



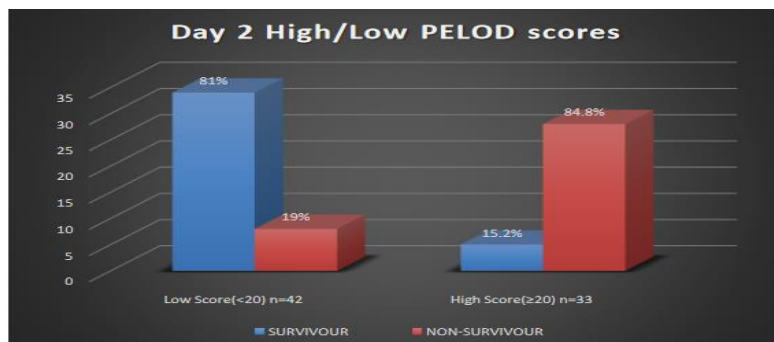
PELOD Scoring on day-2 if more than 22 is associated with 100% mortality and less than 12 is associated with 100% survival in our study. This was statistically significant with a p=0.000. The AUC for day 2 score was 0.946 (p=0.000) being statistically significant and the calibration (p= 0.283) good. Therefore, the Day 2 PELOD score was found to be of significance as an indicator of mortality by day 7 of MODS diagnosis and not a Day 0 score. Patients were further categorized into High (PELOD  $\geq$ 20) and Low (PELOD <20) scorers on day 0 and day 2. Further comparison of outcomes was done to determine if a high score on day 0 or day 2 was an indicator of mortality. There was no significant association between high score at day 0 and mortality. 43.2% with low scores on Day 0 died compared to 54.8% with high score (p=0.320). The odds ratio of death was 1.6 (95% confidence interval: 0.6, 4.03).

Figure 4: Day 0 High / Low Scores and Mortality



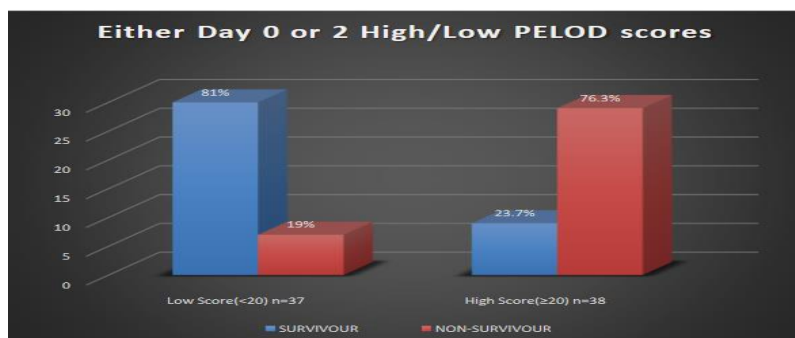
However on day 2, there was a significant association between high score and death. 19% with low scores died compared to 84.8% with high score ( $p=0.000$ ). The odds ratio of death was 0.224 (95% confidence interval:0.12,0.45).

Figure 5: Day 2 High / Low Scores and Mortality



Comparison of overall high scorers, i.e. children who had a high score either on day 0 or day 2, versus those with low scores and mortality was also analyzed.

Figure 6: Either Day 0 or 2 High/Low Scores and Mortality



There was a significant association between high score either at day 0 or day 2 and death. 19% with low scores died compared to 76.3% with high score ( $p=0.000$ ). The odds ratio of death was 0.25 (95% confidence interval:0.12,0.5).

## Discussion

Reported incidence of MODS in children admitted to PICUs varies from 11%–56% (1,5) and reported mortality from MODS varies from 11%–57% (10,11). In this study, among 61 children with MODS the overall mortality rate was 47.6%. In New Delhi, Khilnani P et al showed similar mortality rates of 49.2% among the 184 patients with MODS (46) and in Anu Thukral's New Delhi study had a similar mortality rates of 57.34% among 190 children with MODS (13). Wilkinson et al in 1986 showed a mortality rate of 54% (8), while Tantalean et al showed a mortality rate of 41.7% (5). Anu Thukral et al, in addition to increased mortality rates in association to increased number of organ system involvement showed, that the PELOD scores in each group proportionately increased.(13) This was found to be similar in comparison to this study results.

Table.2

Number of Organ dysfunction	Present study				Anu Thukral et al		
	Patients (%)	PELOD D0	PELOD D2	Mortality rates (%)	Patients (%)	PELOD score	Mortality rates (%)
2	32	13.5	10.1	22 (18.2%)	76(36.3)	7.8	12 (15.7)
3	34	17	17.4	37 (59.5%)	70(33.1)	16.6	27 (38.5)
4	7	15.1	27.6	10 (80%)	32(15.6)	24.5	20 (62.5)
5	2	13.5	23	2 (100%)	10 (4.9)	35.1	7 (70)
6	-	-	-	-	2 (1.0)	33	2 (100)

A sub-analysis of the scores, categorized children into High (PELOD  $\geq$ 20) and Low (PELOD < 20) scorers on day 0 and day 2 was compared with their outcomes. High scorers on day 2 had a significant association with mortality ( $p = 0.002$ ). This is probably due to the rise in score reflected in a high score on Day 2, therefore emphasizing that the initial score may not be as useful an indicator as a rise in score. Children with an overall high score on either day 0 or day 2 had a significant association with mortality by day 7 from MODS.(ref figures 4,5,6).

## Merits

The study design was a prospective, observational, longitudinal cohort study of children with MODS. This study was able to grade MODS severity from its time of onset, both at baseline and after 48 hrs, looking for short term mortality among children with MODS. This study also stratified patients into high ( $\geq$ 20) and low (<20) scores associated with mortality. Worsening of score or the rise in score was also looked for by means of comparing the scores on day 0 and day 2, thereby analysis was done in more than one way to best assess the severity of MODS using the PELOD score. The discriminative ability of the score on Day 0, Day 2

and the difference in scores was also assessed using the AUC (area under the receiver operator curve). The scores were also checked for calibration. Thereby an attempt was made to validate the scores.

### **Demerits**

All our children were assessed only after they reached the PICU. No scoring was done in the Pediatric Emergency. Scores of the PELOD were probably influenced by the emergency treatments prior to shifting the child to the PICU, especially influencing initial scores. This might be the reason for why day 1 scores were not reflective of the severity of MODS and not predictive of mortality as the child's score might have been higher if scored in Emergency or in the ward prior to stabilization. Limiting the setting to the PICU alone could have been a bias factor. The study period was 7 days for each patient. Patients were not followed up through their entire duration of stay in PICU. This restricted the follow up of patients and the final outcome of patients beyond 7 days was not documented as a part of this study design. Hence this study is only valid for short term mortality and not mortality beyond 7 days.

### **Recommendations**

Based on this study recommendations are that a PELOD score can be done at baseline (Day of Diagnosis of MODS) called the day 0 score and another after 48hrs (day 2). The scores on day 2 if high or if there is a worsening of scores especially in the setting of the presence of a High Score ( $\geq 20$ ) implies bad prognosis. And it can be used as a predictor of early PICU mortality ( $\leq 7$ days). In a resource limited setting where costs of PICU care are expensive the financial burden on the family is heavy such a mortality score is an objective tool for assessment of severity of MODS and helps to prognosticate the patient as early predictor of mortality within 7 days. Based on the predictive function it can also allow timely detection of potential risks, which can then be prevented promptly.

### **Conclusion**

Day 2 PELOD score was found to be significant as an indicator of mortality by day 7 of MODS diagnosis and not a Day 0 score. PELOD score on day-2 if  $< 12$  had 100% survival rate; if  $> 22$  had 100% mortality. The presence of a high score  $\geq 20$  implies a worse outcomes either on day 0 or on day 2, especially so on day 2 as a predictor of mortality. One can thus assess the severity of MODS just by looking at the scores and thereby predicting the outcome. This concluded that the PELOD score is a valid outcome measure of death both on day 2 and in association with a rise in score; a high score on day 2 by itself to be used to estimate the severity of MODS and as a predictor of short term mortality ( $\leq 7$ days) in critically ill children with MODS.

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