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ORIGINAL ARTICLE

Incidence of new morbidity in children on discharge from pediatric intensive care unit of a developing country.

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ABSTRACT… Objective: To determine the incidence of newly acquired morbidity, its categorization, and to identify the associated risk factors among children upon being discharged from the PICU. **Study Design:** Prospective Longitudinal Cohort study. **Setting:** Multidisciplinary PICU of Aga Khan University Hospital. **Period:** October 2022 to March 2023. **Material & Methods:** Patients who were readmitted to the PICU, deceased, or lost to follow-up during the study were excluded. The functional status was assessed using FSS at baseline, PICU discharge, and at 3 months to measure newly acquired morbidity and dysfunction. All data was collected on a structured proforma. Categorical variables were presented as absolute values and percentages, and continuous variables were expressed as means ± SD or medians with interquartile range or proportions as applicable and considered statistically significant level if p value is ≤ 0.05. **Results:** A total 96 patients were discharged alive from PICU and 85 of them were included in this study. The mean age was 5.27 ± 5.01 years. The major diagnostic categories were acute respiratory illnesses (25.89%), cardiovascular disorders (21.18%), and neurological disorders (16.47%). 43.53% of the patients underwent surgical intervention. The mean PRISM score at admission was 4.32 ± 5.84. The incidence of morbidity was 40% (34/85) at PICU discharge and 5.8% at 3 months. Longer duration of vasoactive medications, arterial catheterization, mechanical ventilation and PICU stay were associated with new morbidity in critically ill children on discharge from PICU. **Conclusion:** At PICU discharge, the incidence of new morbidity among critically ill pediatric patients was 40%, which reduced to 5.8% at 3 months. Patients with hemodynamic instability, longer duration of inotropic support and those on prolonged mechanical ventilation had longer PICU stay and exhibited increased risk for new morbidity development. The majority of patients (>82%) exhibited either good functional status or mild dysfunction upon discharge.

Key words: Dysfunction, Functional Status, Functional Status Score, Intensive Care, Morbidity, Pediatric Critical Care, Pediatric Intensive Care.

INTRODUCTION

Pediatric Intensive Care Unit (PICU) is a highly specialized area, where critically ill or injured patients require complex critical care interventions. With the ongoing progress in knowledge, practices, and technology, the mortality in PICU has decreased significantly. Most of the PICUs in the developed world report low mortality rates (2-4%).[1] However, PICU survivors undergo a diverse spectrum of physical, cognitive, neurodevelopmental, emotional, and social challenges that adversely impact their health-related quality of life.[2] This has prompted the intensivists to focus on PICU and post-PICU interventions, aimed at reducing the morbidity among survivors.[3-5] The short term and long-term outcome of PICU survivors has not been well elaborated due to lack of availability of reliable and efficient assessment tools suitable for a diverse range of pediatric patients. Reliable assessment of pediatric outcomes can be quite challenging, especially with the diversity of diseases, their severity, and variable age-grouped patients.

Functional status scale (FSS) is a new tool, which has been developed through formal consensus process, by pediatric healthcare professionals of the Collaborative Pediatric Critical Care Research

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Network (CPCCRN) from the Eunice Kennedy Shriver National Institute of Child Health and Human Development. FSS is an efficient, reliable and objective tool, which assesses functional status, in six different domains; mental status, sensory functioning, communication, motor functioning, feeding, and respiration. Each domain is graded on a scale ranging from normal (score 1) to very severe dysfunction (score 5). The overall FSS score varies from 6 (representing the best) to 30 (representing the worst).[5] New morbidity refers to an increase in cumulative FSS score of ≥3 points or an increase of 2 points in a single domain. Different functional status categories that have been defined by Pollock et al[6] are: normal function (6-7), mildly dysfunctional (7-8), moderate dysfunction (10-15), severe dysfunction (16-20), and very severe dysfunction (25-30). In a recent study, the FSS corresponds to the Pediatric Overall Performance Category (POPC) and Pediatric Cerebral Performance Category (PCPC); however, it estimates the functional status more precisely.[7] Recently, FSS has been used to assess the functional status at hospital discharge in neonatal and pediatric patients treated with ECMO and in patients with traumatic brain injury.[8,9]

PICU is expanding in Pakistan and more children are surviving after critical illness; however, there is dearth of data regarding the occurrence of newly acquired morbidity among PICU survivors in low-middle-income countries such as Pakistan. Moreover, no significant work has been done on the type and domain of disability. Our study was primarily focused on determining the incidence of new morbidity at and 3 months after PICU discharge with respect to individual domains of disability, while the secondary outcome was to categorize the functional level, based on FSS score and to determine the association of new morbidity with PICU supportive therapies.

MATERIAL & METHODS

This prospective single-center study included all children aged 1 month to 18 years who met the inclusion criteria and were admitted to our PICU between October 2022 and March 2023 and were followed up during this time period. The study protocol was reviewed and approved by the institutional ethical committee (Ref: 2022-7765-23070).

This prospective longitudinal cohort study was conducted at Multidisciplinary PICU of Aga Khan University Hospital.

Inclusion Criteria – All children (1mo -18 yr.) admitted in PICU (> 24 hours length of PICU stay).
Exclusion Criteria– Readmission to PICU during the study period. Patients who either deceased or were not able to be followed up throughout the study.

FSS is a tool used to evaluate six areas of functioning: mental status, sensory functioning, communication, motor functioning, feeding, and respiratory. Scoring is conducted on a scale from 1 (normal function) to 5 (very severe dysfunction), with the overall FSS score ranging from 6 to 30.

Morbidity

is characterized by a change of ≥3 points in FSS aggregate and change of 2 points in a single domain of FSS from the baseline.

Primary Outcome

- To determine the incidence of new morbidity among the PICU survivors at discharge and at 3 months from the baseline.

Secondary Outcome

- To determine the severity of dysfunction by dividing the cohort into 5 groups, based on the FSS score i.e., normal function (6-7), mild dysfunction (8-9), moderate dysfunction (10-15), severe dysfunction (16-20), and very severe dysfunction (21-30) at PICU discharge and at 3 months.
- To determine the association of new morbidity with PICU supportive therapies, like mechanical ventilation, non-invasive ventilation, inotropes, renal replacement therapy, length of PICU stay and length of hospital stay.

Sample Size Calculation

In a previous study on PICU patients, the incidence of new morbidity was 3.5%. The sample size of 52 was obtained, based on a 95% confidence interval and a 5% margin of error. Considering 10-15% probability of dropout, the final sample size was 75.

Data Collection

The collected data included, demographic variables like age & gender, clinical variables like admitting diagnosis, co-morbidity, disease severity based on PRISM-III score, ICU interventions like use of invasive and noninvasive mechanical ventilation, vasoactive medications, renal replacement therapy, and FSS on admission, discharge and at 3 months. All data was collected on a structured proforma. FSS scoring was done by the principal investigator/co-investigator. Functional Status Scale scores were done 3 times. The first-time for the pre-illness as baseline, second time on PICU discharge and third time at 3 months period, and was noted on data collection sheet. The first reading was done retrospectively by interviewing the parents on admission, second reading was done prospectively by the principal investigator/co-investigator, and third reading was done on telephone follow-up with the parents by the principal investigator/co-investigator. All the data was collected after taking written informed consent and assent in patients ≥ 7 years (where applicable: if the patient is conscious and able to give assent). The parents were explained about the procedure of patient's assessment, data collection and follow up in a separate room in PICU to maintain the confidentiality. They were given the written consent form to sign and the contact number was taken by the principal investigator.

Statistical Analysis

All the statistical analyses were performed using the statistical software STATA version 17.0. Categorical variables were expressed as absolute values and percentages, while continuous variables were presented as mean ± standard deviation (SD) or medians with interquartile range, as appropriate. To compare the mean values between participants with and without morbidity, t-test was employed. For categorical variables, their association with morbidity was assessed using either the Chi-square test or Fisher's exact test, as applicable. A p-value less than 0.05 was considered statistically significant.

RESULTS

The study comprised a total of 96 enrolled patients. The final analysis comprised 85 patients, as 11 patients were excluded, with one lost to follow-up, and 10 others experienced mortality during the research period as shown in Figure-1. An overview of the demographic and clinical characteristics of the eligible patients is shown in Table-I.

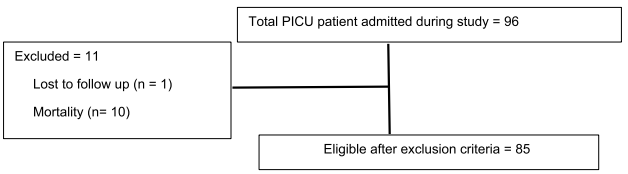

Figure-1. Data flow diagram

The mean age of the study population was 5.27 ± 5.01 years and 51.8% were male. Almost 2/3rd (61.17%) of the total patients were under 5 years. The PRISM score had a mean value of 4.32 ± 5.84. The main diagnostic categories were: respiratory illnesses (25.89%), cardiovascular diseases (21.18%) and neurological disorders (16.47%). 43.53% patients required surgical intervention. Figure-2 shows the distribution of surgical procedures.

The new onset morbidity at PICU discharge was calculated to be 40% (n=34), with 32 patients having a change in FSS of ≥3 scores and 2 patients had a change of 2 scores in a single domain of FSS. Morbidity was 5.8% at three months after PICU discharge. We categorized the change in FSS as normal (6-7), mild (8-9), moderate (10 -15), severe (16-20) and very severe (21-30) at different stages of illness as demonstrated by Figure-3.

There was statistically significant association observed in patients with new onset morbidity and the median length of PICU stay, duration of vasoactive medications, arterial line and mechanical ventilation as shown in Table-II.

Variables	n (%)
Age, years, (mean ± SD)	5.27±5.01
<1 year	19 (22.35%)
1-5 years	33 (38.8%)
>5 years	33 (38.8%)
Gender (Male)	44 (51.8%)
Admitting Diagnostic categories	
Respiratory	22 (25.89%)
Cardiovascular	18 (21.18%)
CNS	14 (16.47%)
GI-Liver	10 (11.76%)
Infection Diseases	8 (9.41%)
Metabolic	5 (5.88%)
Oncology	4 (4.70%)
Miscellaneous	4 (4.70%)
PRISM score (Mean± SD)	4.32 ± 5.84
Length of hospital stay, days, Median(IQR)	12.00 (6.00-21.00)
Length of PICU stay, days, Median(IQR)	3.00 (2.00-5.00)
PICU Interventions	
Vasoactive medications	28 (32.94%)
Renal Replacement Therapy	2 (2.35%)
Central Venous Catheterization	35 (41.18%)
Arterial Catheterization	36 (42.35%)
Mechanical Ventilation	39 (45.88%)
BiPAP	5 (5.88%)
High Flow Nasal Cannula	39 (45.88%)
Morbidity at PICU discharge	34 (40%)
Morbidity at 3 months	5 (5.8%)

SD: Standard deviation, BiPAP: Bi-level Positive Airway Pressure, CNS: Central nervous system CVS: Cardiovascular system, GI: Gastrointestinal, PRISM: Pediatric Risk of Mortality, PICU: Pediatric intensive care unit

Table-I. Demographic and clinical variables (n=85)

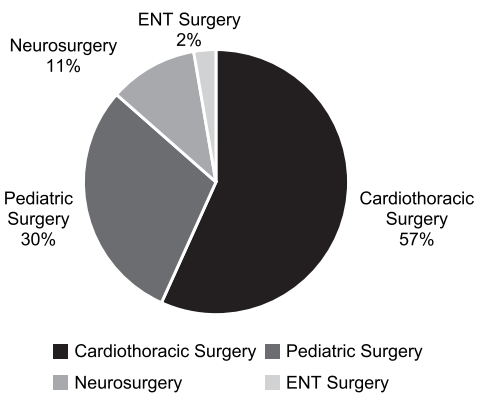

Figure-2. Distribution of surgical procedures

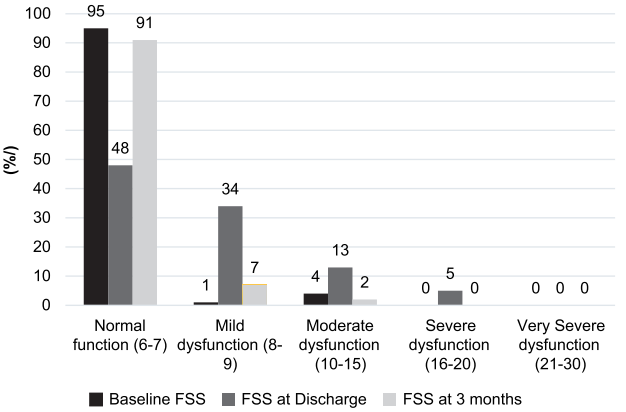

Figure-3. Functional status scale categories

DISCUSSION

In our cohort, a 40% incidence of new morbidity upon PICU discharge was observed, which subsequently decreased to 5.8% at 3-month after PICU discharge, which is similar (36%) to that reported by Dannenberg et al.[10] Another study by William et al[9] on 325 patients with primary neurological diagnosis also reported 35% new disability, while a study conducted on pediatric trauma patients by Umar Z mentioned 11% new morbidity.[11] A similar study by Haque et al[12] in a tertiary care hospital of Pakistan showed the incidence of morbidity at PICU discharge to be 12.2% among 155 patients; Holding et al[13] mentioned 16% new functional impairment whereas Alvarez et al[1] reported 3.56% morbidity upon PICU discharge, and 0.7% at the time of hospital discharge, in a cohort of 842 patients. The incidence of morbidity in our study is higher as compared to the previously published reports from multidisciplinary PICUs. Several factors contribute to this high morbidity. Our hospital, being one of the country's largest referral centers, receives critically ill complex patients, mainly with multi-organ dysfunction syndrome (MODS). Moreover, our intensive care includes both the PICU and the PCICU with 21% of our study population comprising of post-op cardiac surgery patients. Furthermore, due to limited number of PICU beds and a higher turnover of patients; patients are discharged earlier from PICU to be shifted to the HDU, under the care of general pediatrician, resulting in high morbidity on PICU discharge.

Characteristics	No-morbidity N=51	Morbidity N=34	P-Value
Age, years, (mean ± SD)	5.51±4.76	4.90±5.40	0.59
<1 year	9 (17.65%)	10 (29.41%)	0.14
1-5 years	18 (35.29%)	15 (44.12%)	
>5 years	24 (47.06%)	9 (26.47%)	
Gender			0.79
Female	24 (47.06%)	17 (50.00%)	
Male	27 (52.94%)	17 (50.00%)	
Length of hospital stay, days, Median (IQR)	10.00 (5.00-20.00)	16.00 (8.00-23.00)	0.11
Length of PICU stay, days, Median (IQR)	2.00 (1.00-4.00)	3.50 (2.00-7.00)	0.005
Vasoactive Drugs			0.19
No	37 (72.55%)	20 (58.82%)	
Yes	14 (27.45%)	14 (41.18%)	
Duration of vasoactive Drugs, (days), Median (IQR),	2.00 (1.00-3.00)	3.50 (2.00-5.00)	0.047
Renal replacement therapy (n=2)			0.080
No	51 (100.00%)	32 (94.12%)	
Yes	0 (0.00%)	2 (5.88%)	
Duration of renal replacement therapy (days)		6.50 (3.00-10.00)	-
Central venous catheter (n=33)			0.072
No	34 (66.67%)	16 (47.06%)	
Yes	17 (33.33%)	18 (52.94%)	
Duration of central venous catheter (days)	2.50 (1.00-5.00)	4.00 (3.00-5.00)	0.19
Arterial line (n=35)			0.11
No	33 (64.71%)	16 (47.06%)	
Yes	18 (35.29%)	18 (52.94%)	
Duration of arterial Line, (days)	2.00 (1.00-3.00)	5.00 (2.00-13.00)	0.004
Mechanical ventilation (n=39)			0.53
No	29 (56.86%)	17 (50.00%)	
Yes	22 (43.14%)	17 (50.00%)	
Duration of mechanical ventilation (days)	0.00 (0.00-1.00)	5.00 (2.00-11.00)	<0.001

Table-II. Risk factors for increased morbidity from baseline to PICU discharge

As far as the individual FSS domains are concerned, the highest change in scores, in our study population, was observed in "feeding" and "respiration" as shown in Figure-4.

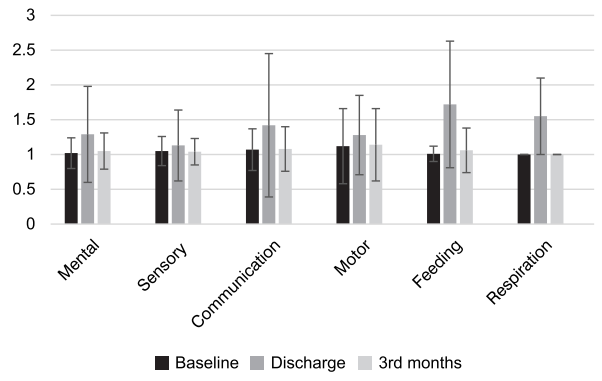

Figure-4. FSS score (mean ± SD) of individual domains at baseline, PICU discharge and at 3 months

This is similar to a Brazilian study by Pereira et al[14], which reported the highest scores in "motor" "feeding" and "respiratory" domains. Another study on primary neurological disorders has reported the highest change in the "motor" and "feeding" components.[9]

We have also categorized FSS into normal, mild, moderate, severe, and very severe dysfunction as published in many clinical reports. The majority of our patients had normal to mild dysfunction; moderate dysfunction was observed in only 13% of our patients at PICU discharge and 2% at 3 months. This has also been observed in another report from Pakistan[12] and a study on neonatal and pediatric patients treated with ECMO.[15] Moderate dysfunction was the most frequently reported category in several studies.[1,10,16]

Many studies on FSS in the pediatric population have determined certain risk factors which were significantly associated with the incidence of morbidity such as high PRISM score on admission, younger age group, and specific diagnostic categories like neurological disorders, prolonged PICU stay, and use of mechanical ventilation. The results demonstrated a significant association of new onset morbidity with a median length of PICU stay, duration of vasoactive drugs, arterial line duration, and mechanical ventilation. Most of the studies have calculated FSS at hospital discharge only. We have calculated the morbidity at PICU discharge (40%) which declined to (5.3%) at 3 months, which can be related to early discharge from PICU so it can be an overestimation of FSS scores. On the contrary, an increase in morbidity has been reported from 9.1% at discharge to 14.3% at 6 months by Pinto et al.[17]

The strengths of our study are that we have calculated and categorized not only the morbidity at PICU discharge but also after 3 months of critical illness, while many other studies have only reported short term morbidity. We have also analyzed the individual domains of FSS to assess which functional domains are affected the most in the critical illness. This study had some limitations. Firstly, since it was a prospective study conducted at a single center, the findings may not be applicable to a broader population. Additionally, the sample size was small, which could affect the generalizability of the results. Valuable insights can be gained from future multicenter studies with larger sample sizes involving different pediatric intensive care units in Pakistan. These research endeavors have the potential to identify the factors that can mitigate the development of new morbidities, optimize the treatment provided to critically ill children, and assess the long-term functional status of these patients.

CONCLUSION

Our study determined a morbidity incidence of 40% in critically ill pediatric patients upon PICU discharge, which declined to 5.8% after 3 months. Patients with hemodynamic instability, with longer duration of vasoactive medications, and prolonged mechanical ventilation and longer PICU stay were found to be at an elevated risk for new morbidity development. A considerable proportion of patients (>82%) attained good functional status or mild dysfunction at the time of discharge.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Iram Iqbal	Synopsis & Manuscript writing, data collection.	
2	Muhammad Farrukh Qazi	Statistical analysis.	
3	Muhammad Abid Shah	References writing.	
4	Awais Abbas	References writing.	
5	Qalab Abbas	Review and proof reading of manuscript.	
6	Naveed ur Rehman	Synopsis & manuscript writing, daa collection, review, proof reading.