RESEARCH PAPER

Risk Factors of Delirium in Children in Pediatric Intensive Care Unit

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Received: May 27, 2022;
Initial review: July 19, 2022;
Accepted: August 18, 2022.

Objectives: To determine the prevalence of delirium and its risk factors among children admitted to a Pediatric intensive care unit (PICU). **Method**: A descriptive study in which consecutive patients admitted to the PICU over a period of 12 months were screened daily for delirium using the Cornell Assessment of Pediatric Delirium (CAPD) score. Treatment-related and demographic variables were collected and analyzed. The statistically significant risk factors for delirium were analyzed by multivariable logistic regression for independent associations. **Results:** Among the 476 screened patients, 96 (20.2%) developed delirium. The independent risk factors associated with the development of delirium were respiratory failure (P<0.001), administration of benzodiazepines during PICU stay (P<0.001), and presence of multiple (≥2) risk factors for delirium (P<0.001). The mean length of PICU stay was significantly higher among delirious subjects with P<0.001. **Conclusion:** Delirium is a frequent complication in critically ill children, and recognition of associated factors may assist in early diagnosis and focussed management.

Keywords: *Benzodiazepine, Outcome, Respiratory failure, Unconscious.*

***Published online*: August 26, 2022; *PII:* S097475591600449**

Delirium is a manifestation of acute cerebral dysfunction due to a serious underlying illness. It has been linked to increased mortality, prolongation of hospital stay, and long-term disabilities [1]. The pathophysiology of delirium is com-plex and involves multiple factors, including alterations in cerebral blood flow, energy metabolism, neurotransmission, and disordered cellular homeostasis. It is a result of the synergism of three events: the underlying disease itself, adverse effects of the treatment, and the highly stressful intensive care environment [1].

The available pediatric studies [2,3] have found a varying prevalence of delirium in critical patients, ranging from 17.3% to 25%. The various risk factors found to be associated with the development of delirium in these studies are age ≤2 years, developmental delay, the severity of illness, mechanical ventilation, and administration of vasopressors, benzodiazepines, anticholinergics and narcotics, and use of physical restraints [2,3]. We studied the prevalence of delirium in the pediatric intensive care unit (PICU) and the associated risk factors.

METHODS

This descriptive study was conducted at a public sector tertiary care hospital, after obtaining approval from the institutional ethical committee. Between 1 April, 2020 to 31 March, 2021, all patients with ages ranging from 1 month to 14 years, admitted to the PICU for at least 24 hours were included in the study, after taking informed consent from a guardian of the child. Demographic data, including age, sex, and developmental status were collected at admission in the PICU.

All children included in the study were screened once daily by observing the patient over the entire duty shift by a single investigator, using the Richmond Agitation-Sedation Scale (RASS score), followed by the Cornell Assessment of Pediatric Delirium (CAPD score) for assessment of delirium during their entire PICU stay. The RASS is a validated scale in critical pediatric patients for accurate assessment of awareness in mechanically ventilated and spontaneously breathing patients [4]. The RASS score ranges from –5 (unarousable), through 0 (alert and calm), to +4 (combative). It was used to assess the level of awareness and classify the subtype of delirium in this study. The CAPD is a rapid, observational screen, validated for the detection of delirium in PICU setting. It consists of eight items that correlate with the diagnostic domains of awareness and cognition from the DSM-5, and also includes psychomotor symptoms. It has a high over-all sensitivity (94.1%) and specificity (79.2%) for critically ill patients. In developmentally delayed patients, it has low specificity (51.2%) but high sensitivity (96.2%) [5].

As per the calculated scores, subjects were categorized into 'Comatose' (subjects with a RASS score of -4 or -5 at any point of time during their PICU stay, who were under

deep sedation or unarousable to verbal or physical stimulation and therefore impossible to assess for delirium), 'Delirious' (CAPD score ≥9 at any point of time during their PICU stay) or 'Non-delirious'. Comatose patients were excluded from the study. The subtype of delirium was categorized based on the RASS score of the delirious patient, as Hypoactive delirium (RASS score of 0 to -3), Hyperactive delirium (RASS score of +1 to +4), or Mixed delirium (RASS score crossing both sides of 0).

The risk factors for the development of delirium assessed clinically for individual subjects over their PICU stay were the presence of significant developmental delay (clinical assessment and/or developmental problems that led to severe impairment in the ability to communicate with caregiver in age-appropriate ways), respiratory failure (presence and persistence of any of the following: respiratory acidosis, SpO2 < 90% or PaO2 < 60 mm Hg, tachypnea, increased work of breathing) [6], cardiac failure (based on clinical and radiological criteria) [7], shock [8], cyanotic spells, renal failure [9], and administration of benzodiazepines during PICU stay. Duration of delirium was defined as the number of days for which the patient was delirious during the PICU stay.

Statistical analysis: The statistical tests used were the chi-square test and Fisher exact test for analysis of risk factors, and unpaired t-test for comparison of PICU length of stay. *P* value <0.05 was considered statistically significant in univariate analyses. All factors which were found to be significantly associated with the development of delirium in univariate analysis were entered in the multivariable logistic regression analysis to identify independent associations.

Table I Characteristics of Children Admitted in the PICU and Enrolled in the Study

Characteristics	*Delirious (n=96)*	*Non-delirious (n=380)*	*P value*
Male sex	55 (57.3)	210 (55.3)	0.73
Age			
<2 y	55 (57.3)	144 (37.9)	0.001
2-5 y	14 (14.6)	108 (28.4)	
6-10 y	18 (18.7)	81 (21.3)	
>10 y	9 (9.4)	47 (12.4)	
Developmental delay	40 (41.6)	43 (11.3)	<0.001
Respiratory failure	40 (41.6)	3 (0.8)	<0.001
Cardiac failure	9 (9.4)	23 (6.1)	0.25
Shock	34 (35.4)	8 (2.2)	<0.001
Cyanotic spells	2 (2.1)	4 (1.1)	0.34
Renal failure	2 (2.1)	2 (0.6)	0.18
Benzodiazepine administration	55 (57.3)	26 (6.9)	<0.001
Multiple risk factors for delirium	79 (82.3)	44 (11.6)	<0.001
Outcome of PICU stay			
Discharge	50 (52.1)	325 (85.5)	<0.001
Death	38 (39.6)	9 (2.4)	
Other	8 (8.3)	46 (12.1)	

Data expressed as n (%). PICU pediatric intensive care unit.

RESULTS

We screened a total of 534 children for eligibility during the study, of which, parents of 11 children refused consent and 47 children had coma (GCS<8). Thus, 476 children (55.6% males) were enrolled, of which 20.2% (*n*=96) screened positive for delirium (**Table I**). The most common subtype of delirium was the hypoactive type (44.8%) followed by hyperactive (29.2%) and mixed types (26%).

The risk factors that were found in a significantly higher proportion in delirious patients were age less than 2 years (*P*=0.001), developmental delay (*P*<0.001), respiratory failure (*P*<0.001), shock (*P*<0.001), administration of benzodiazepines during PICU stay (*P*<0.001), and presence of multiple (≥2) risk factors (*P*<0.001) (**Table I)**

In the multivariate logistic regression analysis, independent risk factors found to be associated with the development of delirium were respiratory failure (*P*<0.001), administration of benzodiazepines during PICU stay (*P*<0.001), and presence of multiple (≥2) risk factors (*P*<0.001) (**Table II**). The mean (SD) length of PICU stay was significantly higher in delirious subjects as compared to non-delirious subjects [5.75 (2.71) and 2.74 (1.61) days; *P*<0.001, respectively].

DISCUSSION

We found the incidence of delirium to be 20.2% among children in the PICU. The independent risk factors found to be associated with the development of delirium were respiratory failure, administration of benzodiazepines during PICU stay, and presence of multiple (≥2) risk factors for delirium.

Delirium is a commonly occurring condition in critically ill patients, as they are predisposed to environmental and

Table II Multivariate Logistic Regression Analysis of Risk Factors Associated With the Development of Delirium

Characteristics	*Adjusted OR (95% CI)*	*P value*
Age <2 y	1.21 (0.54-2.71)	0.62
Developmental delay	1.75 (0.72-4.24)	0.21
Respiratory failure	14.03 (3.24-60.74)	<0.001
Shock	2.21 (0.66-7.31)	0.19
Benzodiazepine administration	7.31 (3.31-16.11)	<0.001
Multiple risk factors	6.30 (2.33-17.04)	<0.001

WHAT THIS STUDY ADDS?

- Delirium is a common phenomenon in the PICU, and is commonly associated with respiratory failure and benzodiazepine administration.

metabolic risk factors for delirium such as disturbed sleep, immobility, infections, withdrawal, noise disturbances, and sensory overload [10]. The findings of our study are in accordance with the range of prevalence of delirium in previous pediatric studies [2,3]. The varying prevalence of delirium among these studies may be due to different patient populations, varying reasons for admission, use of different tools for diagnosis of delirium, differences in sedation practices, or other unknown factors. Among the subtypes of delirium, incidence of hypoactive delirium was found to be similar (46%) in another study [2], but they reported the incidence of hyperactive delirium as only 8%, which is in contrast to our study. Another study that was performed among adult medical ICU patients concluded that mixed delirium was the most common subtype (54.1%) [11]. The risk factors found to be associated with delirium in our study are consistent with previous pediatric and adult studies [1-3,12,13]. A two-times longer length of PICU stay was reported among delirious subjects in one study [2], and few other studies have reported similar results [1,13].

The limitations of the study include assessment of delirium could be performed only once daily, so any fluctuations or diurnal variations in the state of delirium could not be analyzed. The tool for diagnosis of delirium which is used in this study was CAPD, which is a well-validated screening tool for pediatric patients with high sensitivity, but its specificity is low in developmentally delayed children, which could lead to an under-diagnosis of delirium in that subset of patients [5]. The causality of association for the risk factors of delirium also could not be established.

To conclude, delirium is a lesser known but prevalent condition in the PICU. It is associated with risk factors like respiratory failure and administration of benzodiazepines and it also leads to a longer length of PICU stay. Further multi-institutional studies on various aspects of delirium, including its effects on patient outcomes and long-term neurocognitive impairment, are required to improve our understanding of pediatric delirium. Another area of future research could be focused on the evaluation of interventions to reduce the incidence of delirium, as well as its effect on patient outcomes.

Ethics clearance: IEC, Gandhi Medical College, Bhopal; No. 530/MC/IEC/2020, dated Jan 04, 2020.
Contributors: BM: Acquisition and interpretation of data, data analysis, drafting the article, and literature review; UP: Concept, interpretation of data and data analysis, drafting the article, literature review, and revising the article critically for important intellectual content; AA: Drafting the article, literature review, and revising the article critically for important intellectual content; JS: Interpretation of data and data analysis, literature review, and revising the article critically for important intellectual content. All the authors approved the final manuscript.
Funding: None; *Competing interests*: None stated.

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