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Delirium among pediatric patients admitted to open-heart surgery intensive care unit: A cross-sectional study investigating a common challenge and concern, and its inciting factors

Mohammadreza Mirzaaghayan[1], Sara Memarian[1], Alireza Abdshah[2], Mojgan Ghavami[3], Ghazale Roozbahani[4], Fatemeh Naseri[5], Mohammad Sajjad Jolani[2], Masood Ghahvechi[1], Behdad Gharib[1]

[1] Children's Medical Center, Tehran University of Medical Sciences, Tehran, Iran
[2] School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3] Cardiovascular Research Institute, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran
[4] School of Nursing, Tehran University of Medical Sciences, Tehran, Iran
[5] School of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background: Delirium is a common challenge in pediatric open heart surgery intensive care units (OH-ICU). It is believed that emergence of delirium can lead to extended hospitalization periods. Therefore, we decided to investigate the association between delirium and its inciting factors in OH-ICU.

Methods: This was a cross-sectional study on 92 pediatric patients admitted to OH-ICU of "Children's Medical Center" in Tehran, Iran, for more than 48 hours. To screen for delirium, the Cornell Assessment of Pediatric Delirium (CAPD ≥ 9) was utilized. Demographics, length of stay, development of complications, delirium, and factors associated with delirium were recorded.

Results: We observed 34 (37%) cases of delirium in patients in OH-ICU. We had 51% male patients and 49% female ones, with a median age of 8 (0.2-144) months.

Corresponding Author: Behdad Gharib
Email: behdad_gharib@hotmail.com

The median length of mechanical ventilation was 11.5 hours (2-405) and they stayed in the hospital for a median of 4 days (2-31). The most common cardiac abnormality was ventricular septal defect (18%), associated with tetralogy of Fallot (TOF) (10%). Most of the patients (71%) experienced no adverse events during their stay; however, among those who did, vomiting and post-operation chorea were the most prevalent. Among the patients in our study, age [adjusted odds ratio (AOR) = 0.91], weight (AOR = 1.34), and sex (AOR = 0.31 for boys vs. girls) were significantly associated with delirium.

Conclusion: We observed delirium in 37% of the patients. Development of delirium in patients admitted to pediatric intensive care unit (PICU) was associated with younger age, female sex, and higher weight.

Introduction

Delirium is an acute-onset disturbance in attention, awareness, and cognition that tends to accompany poorer outcomes including increased duration of stay, prolonged use of ventilation, lower health-related quality of life (HRQOL), higher morbidity and mortality, and higher healthcare costs.[1-6] Although the exact pathophysiology of delirium is unknown, different theories, including neuroinflammatory theory, neurotransmitter theory, and oxidative stress theory exist and they agree that dysregulations in neurotransmitters including acetylcholine, melatonin, dopamine, norepinephrine, glutamate, serotonin, histamine, and gamma-aminobutyric acid (GABA) result in symptoms of delirium.[7,8] The prevalence of delirium seems to vary widely in different settings. It has been reported to be 27.2% in patients who were admitted to a pediatric intensive care unit (PICU) following an elective surgery,[9] 67.4% in children who underwent non-invasive ventilation,[10] 49% following cardiac bypass surgery,[11] and 18.8% in children with cancer.[12] To establish the diagnosis of delirium, an assessment of the children regarding the presence of delirium criteria, based on the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5), is made. Besides, tools including the Cornell Assessment of Pediatric Delirium (CAPD) and Pediatric Confusion Assessment Method for ICU (pCAM-ICU) have made the detection of this complication easier.[3,13] Earlier detection of delirium can help with effective management.[14] Non-pharmacological approaches mainly focus on managing sensory stimuli, improving the sleep-wake cycle, and involving families in the care process of their children. In pharmacological management, antipsychotics, both typical and atypical, are generally used.[3]

Due to the nature of congenital heart disease, patients experience a combination of hypoxia, insufficient nutritional intake, oxidative stress, cardiopulmonary bypass, and blood transfusions. Eventually, these factors lead to a higher risk of delirium in this particularly vulnerable population.[8]

Thus, these results emphasize the importance of screening for delirium in pediatric patients. To develop an effective screening program and preventive strategies, comprehensive knowledge of the risk factors of delirium is crucial. Therefore, we designed this study aiming to assess the prevalence and risk factors of delirium in children following cardiac surgery.

Materials and Methods

This cross-sectional study was conducted in the open heart surgery intensive care unit (OH-ICU) of one of the largest pediatric medical centers in Iran, Children's Medical Center, Tehran University of Medical Sciences, Tehran, from March 2022 to August 2022. The study involved 92 patients who were eligible based on the inclusion criteria including a minimum of two-day stay in the OH-ICU, being extubated, not receiving any sedation at the time of study, and normal baseline mental status.

Patients were assessed using the CAPD. It is designed to detect delirium in pediatric patients. This observational tool assesses the behaviors of patients regarding consciousness and cognition and is adapted for each age group. It consists of eight questions, all of which are scored based on the frequency of symptoms, occurring as never, rarely, sometimes, often, or always. If the sum of scores is ≥ 9, the patient is recorded as delirious.[15] In our study, the nurses performed the assessment near the end of their shift, twice on each day, once morning (6 AM) and once evening (6 PM), recorded the patients' scores, and documented those with scores of 9 or greater (≥ 9) as delirious.

We calculated the patients' risk of their surgery based on the Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) score, which is a well-known tool utilized to assess the risk associated with the procedure.[16,17]

The demographic data (age, gender) and other variables including type of heart disease, duration of intubation, duration of ICU stay, sites of central vein catheters involved, and adverse outcomes

were recorded. Adverse outcomes we aimed to record included vomiting (more than 2 vomiting events after the first 48 hours), post-operation chorea, prolonged open sternotomy (open-sternum, kept for more than 24 hours), chylothorax, mediastinitis, pneumonia, diarrhea, paralysis, seizure, thrombosis, sepsis, and any other events that occurred in the intensive care unit (ICU). Moreover, we categorized the age like the study by Traube et al.,[15] into groups of less than 2 years, 2-5 years, and more than 5 years old, to get a better picture of age distribution.

Sample size was calculated by considering alpha = 0.05, expected prevalence (p) = 0.2 (based on literature), and precision (d) = 0.1. We concluded that the sample of 62 patients would be sufficient. The data were then analyzed using chi-square (or Fisher's exact test where appropriate) and t-test (or Mann-Whitney U where appropriate). We also performed a multivariate logistic regression to investigate the adjusted effect of independent factors in association with delirium. The data were analyzed using SPSS software (version 28, IBM Corporation, Armonk, NY, USA). A P-value of 0.05 was set as the cut-off for significance and two-sided tests were performed.

The study was reviewed and approved by the Ethics Committee of Tehran University of Medical Sciences with the code "IR.TUMS.CHMC.REC.1398.101", and there are no conflicts of interest to report.

Results

Patient characteristics: We included 92 patients in our study with an average of 25 [standard deviation (SD) = 32.7] and a median of 8 (0.2-144) months of age. We had 45 female and 47 male patients. The patients spent an average of 5.97 (SD = 5.97) and a median of 4 (2-31) days in the OH-ICU and had an average of 32.8 (SD = 61.8) with a median of 12 (2-405) hours on mechanical ventilation support. The most common central vein access utilized in these patients was femoral vein (right and left accesses) in 76 (83%) of the patients, followed by jugular and supra- and infra-clavicular vein accesses.

RACHS-1 score among the patients was an average of 2.32 (SD = 0.79) with a median of 2 (1-6). Among all the patients, 34 (37%) developed delirium, while 58 (63%) did not develop delirium during the course of their admission. Most of the patients did not develop any complications (65 patients, 71%); however, the most common

complications were post-op chorea in 6 (6.5%) patients, vomiting in 5 (5.4%) patients (which was defined as more than 2 vomiting events after the first 48 hours), and prolonged open sternotomy (open-sternum, kept for more than 24 hours) in 4 (4.3%) patients. The details of the characteristics of the patients are listed in table 1, categorized by their delirium status, along with their statistical comparison.

Univariable analysis: Among the 47 male patients, 13 developed delirium, and among the 45 female patients, 21 developed delirium. The difference between the two was not significant (P = 0.061, chi-square test).

The mean age of the patients with delirium was 12 months (SD = 16.5) with a median of 5.75 (0.2-72) and the mean age of patients without delirium was 32.6 (SD = 37.3) with a median of 15 months (0.3-144). The difference between the ages of the two groups was statistically significant (P = 0.004). We also categorized the patients' age into three categories. 65.2% of patients were younger than 2 years of age, while 18.5% were 2 to 5 years old, and 16.3% were older than 5 years old. Among those without delirium, 56.9% were younger than 2 years old; however, among those with delirium, 79.4% were younger than 2 years old (P = 0.023).

Additionally, the mean weight of the patients with delirium was 6.98 kilograms (kg) (SD = 4.81) with a median of 5.45 and the mean weight of those without delirium was 10.5 kg (SD = 7.59) with a median of 9. The difference between the weights of the two groups was statistically significant (P = 0.009).

RACHS-1 score was also calculated for each patient, and the difference between the two groups of patients was not significant (P = 0.361).

There were also different central venous access points used in the patients, and the proportion of patients developing delirium was not correlated with the points of access (P = 0.920).

Several complications were experienced during the patients' stay as explained. There was no significant correlation between developing complications and the presence of delirium in the patients during their stay in the OH-ICU (P = 0.172).

The median duration of ventilation among the 34 patients with delirium was 14.5 hours (4-405), and the median duration of ventilation among those without delirium was 7.5 hours (2-191). The difference between the two groups was statistically significant (P = 0.007).

Table 1. Characteristics of patients based on their delirium status

Variable		Without delirium (n = 58)	With delirium (n = 34)	Total (n = 92)	P (test)
Age (month)	Mean ± SD	32.60 ± 37.30	12.00 ± 16.50	25.00 ± 32.70	0.004
	Median (range)	15.00 (0.30, 144.00)	5.75 (0.20, 72.00)	8.00 (0.20, 144.00)	(Mann-Whitney)
Age groups (year) [n (%)]	0-2	33 (56.9)	27 (79.4)	60 (65.2)	0.023
	2-5	11 (19.0)	6 (17.6)	17 (18.5)	(Fisher's exact)
	More than 5	14 (24.1)	1 (2.9)	15 (16.3)	
Sex [n (%)]	Girl	24 (41.4)	21 (61.8)	45 (48.9)	0.061 (χ^2)
	Boy	34 (58.6)	13 (38.2)	47 (51.1)	
RACHS-1 score	Mean ± SD	2.28 ± 0.89	2.38 ± 0.60	2.32 ± 0.79	0.361
	Median (range)	2.00 (1.00, 6.00)	2.00 (1.00, 4.00)	2.00 (1.00, 6.00)	(Mann-Whitney)
Weight (kg)	Mean ± SD	10.50 ± 7.59	6.98 ± 4.81	9.15 ± 6.87	0.009
	Median (range)	9.00 (2.20, 44.00)	5.45 (2.60, 25.00)	7.00 (2.20, 44.00)	(Mann-Whitney)
Site of central vein access [n (%)]	Femoral	47 (81.0)	29 (85.3)	76 (82.6)	0.920
	Jugular	6 (10.3)	3 (8.8)	9 (9.8)	(Fisher's exact)
	Supra- or infra-clavicular	5 (8.6)	2 (5.9)	7 (7.6)	
Complications [n (%)]	None	42 (72.4)	23 (67.6)	65 (70.7)	0.172
	Vomiting	5 (8.6)	0 (0)	5 (5.4)	(Fisher's exact)
	Post-operation chorea	2 (3.4)	4 (11.8)	6 (6.5)	
	Prolonged open sternotomy	3 (5.2)	1 (2.9)	4 (4.3)	
	Other	6 (10.3)	6 (17.6)	12 (13.0)	
Duration of ventilation (hour)	Mean ± SD	20.80 ± 34.30	53.10 ± 88.40	32.80 ± 61.80	0.007
	Median (range)	7.50 (2.00, 191.00)	14.50 (4.00, 405.00)	11.50 (2.00, 405.00)	(Mann-Whitney)
Duration of OH-ICU stay (day)	Mean ± SD	4.86 ± 5.84	7.79 ± 5.80	5.97 ± 5.97	< 0.001
	Median (range)	3.00 (2.00, 31.00)	6.00 (2.00, 24.00)	4.00 (2.00, 31.00)	(Mann-Whitney)

RACHS-1: Risk adjustment for congenital heart surgery-1; OH-ICU: Open heart surgery intensive care unit; SD: Standard deviation

Among the 34 patients who developed delirium during their ICU stay, the median of admission was 6 days (2-24), and those without delirium had a median stay of 3 (2-31) days. The length of stay for the group with delirium was significantly longer than those who did not develop delirium (P < 0.001).

Multivariable analysis: In multivariable logistic regression, we noted that there was a significant association between delirium and age [odds ratio (OR) = 0.91 for every month increase in age, P = 0.016], weight (OR = 1.34 for every kg increase in weight, P = 0.039), and sex (OR = 0.30 in boys vs. girls, P = 0.022). Duration of ventilation and stay in the ICU were not significantly associated with delirium in multivariable logistic regression (P = 0.461 and P = 0.374, respectively).

When looking at the weight of the patients, we observed that after adjusting for characteristics of the patients, weight had an opposite effect. For every kilogram increase in weight, the odds of delirium increased (OR = 1.34, P = 0.039). This shift from univariable to multivariable results potentially occurred because the multivariable analysis takes other factors into account (age, sex, etc.), which can change the direction of the relationship between weight and delirium. The details of the multivariable analysis are listed in table 2.

Discussion

We demonstrated that delirium in pediatric patients following heart surgery in OH-ICU, who were extubated and were not receiving sedatives, was associated with younger age, female sex, and increasing weight.

Delirium is a syndrome of acute brain dysfunction and it is a culmination of several pathways leading to the disruption in brain homeostasis.[18] It has vast consequences on patients' outcomes, mortality, morbidity, and healthcare-related costs. Sohrabi et al. estimated the prevalence of delirium to be 28.5% among adults undergoing cardiac surgery.[19] We can observe, based on our results, that the prevalence of delirium among children seems to be higher (37%) indicating a need for more attention to this phenomenon in children. There are also many studies on pediatric populations, pointing to a prevalence ranging from 20% to 60%,[9-12,15] which is well in concordance with our study, further highlighting the importance of our study.

Patel et al. also noted that the prevalence of delirium was higher among children up to 2 years old versus those above 2 years old to 21 years old, and reached an overall of 49%.[11] We have also observed that age had a significant association with delirium and younger children were more at risk of delirium, particularly those under 2 years of age.

Schieveld et al. observed in their study that the development of complications among the pediatric population was more pronounced in boys compared to girls.[20] In several other studies, they also observed no significant associations between sex and acute events of delirium.[21] However, in our study, we observed that those with delirium were more likely to be of the female sex versus male.

Traube et al. in their study also noted that the prevalence of delirium was higher with increasing length of stay. They noted a 38% prevalence of delirium in children whose stay surpassed 6 days. They also noted an association with mechanical ventilation.[22] Patel et al. also described delirium as a predictor of lengthier hospital stays. They also observed that pediatric patients who developed delirium had a 60% longer stay in the ICU.[11] Another more recent study into this event by Staveski et al., similar to our study, pointed out that pediatric patients with delirium were more likely to have a longer duration of mechanical ventilation (13 vs. 5 days), received vasopressors, and had higher number of invasive catheters.[21] In our study, since all of the patients were intubated at one point during their stay, we had to investigate the correlation between the period of mechanical ventilation and delirium, which was not statistically significant in our sample.

Table 2. Multivariable binary logistic regression investigating the associations between delirium and age, weight, sex, duration of mechanical ventilation, and stay

	OR (95% CI)	P
Model		< 0.001
Age (1-year increase)	0.910 (0.843-0.982)	0.016
Sex (boys vs. girls)	0.305 (0.111-0.839)	0.022
Weight (1-kilogram increase)	1.339 (1.015-1.765)	0.039
Duration of mechanical ventilation (1-hour increase)	1.004 (0.993-1.016)	0.461
Duration of stay in hospital (1-day increase)	1.049 (0.944-1.164)	0.374

OR: Odds ratio; CI: Confidence interval

We noted a median of 7 hours on mechanical ventilation for those without delirium and a median of 14.5 hours for those who had developed delirium. While this association was significant in univariable analysis, we did not find a significant trend in multivariable analysis, observing an adjusted OR (AOR) of 1.004 for every 1-hour increase in the duration of mechanical ventilation. Moreover, in our study, the median stay among those with delirium was 6 days, and among those without delirium was 3 days. We also observed the same trend as the previous studies; however, we could not establish this association in multivariable analysis of the results.

These results, in conjunction with the trend observed in our study, demonstrate a reciprocal relationship, showing that longer stays could lead to more events of delirium, and considering that those patients with more severe diseases are more likely to have lengthier stays, we believe this would be an important area for future studies, to better assess this relationship and better distinguish patients at higher risk of complications and events.

One of the strengths of our study was that this study was conducted in a referral center, and we observed cases with different backgrounds; however, this single-center setting will also limit our ability to generalize the data to all settings. Besides, another limitation we can mention is that some of the confidence intervals (CIs) in our study were wide, which could be attributed to lower sample size in some categories of comparison, and by increasing the sample size in future studies, we can increase precision and reduce the variability among subjects. We also only focused on patients who were extubated and did not examine this association during their intubation. For future studies, we also plan on investigating the effects of different medications on the risk of these events, as some studies indicated the association between opioid use and delirium.[11] We also suggest further prospective studies into the long-term outcomes of children who develop delirium during their ICU stay.

Conclusion

In this cross-sectional study, we observed that the patients who were admitted to the PICU after open heart surgery and developed delirium were more likely to be significantly younger, of female sex, and to have higher weight.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

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