Published in final edited form as:

Clin Pediatr (Phila). 2018 July ; 57(8): 913–919. doi:10.1177/0009922817737080.

Neurodevelopmental Disorders in the PICU Population

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Abstract

Attention deficit hyperactivity disorder (ADHD), affecting 11% of children and adolescents, increases risk for injury and may predispose children to illness. However, the prevalence of ADHD and other developmental disorders in the pediatric intensive care unit (PICU) has not been previously studied. We performed a single-center, prospective cohort study of children aged 6 to 12 years who were hospitalized in the PICU from May through August 2016. Parents described their child's educational and neurodevelopmental history, and completed ADHD and emotional/behavioral disorder screening on enrollment and 1 month after discharge. Twenty-four children were enrolled. Ten patients (42%) had a prior neurodevelopmental diagnosis, and 7 (29%) met study criteria for ADHD. Children hospitalized for critical illness have a high prevalence of neurodevelopmental disabilities and are more susceptible to the impact of critical illness on development and behavior. More research is needed to better understand how to support this vulnerable population after critical illness.

Keywords

pediatric critical illness; ADHD; developmental disorders; behavioral disorders; PICU follow-up

Introduction

Children who are developmentally delayed, disabled, or at high risk of disability are disproportionately hospitalized for long periods of time. Among hospitalized children younger than 3 years, more than half of patients hospitalized for at least 1 month were eligible for Early Intervention (EI) services, which provide support and education to children aged 0 to 3 years with developmental delays.¹ Similarly, the prevalence of neurodevelopmental and behavioral disorders among hospitalized children between the ages of 6 months to 17 years was more than twice as high as the prevalence among children in the community (33.5% vs 15%, respectively).^{2,3}

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Author Contributions

SAS and NPP conceptualized the study design. SP enrolled patients and completed preliminary analyses and an initial manuscript draft. SAS and NPP completed the final analyses and interpreted results. SAS wrote the final manuscript, and SAS, SP, and NPP approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Attention deficit hyperactivity disorder (ADHD) is the most common neurodevelopmental and behavioral disorder experienced by children, affecting an estimated 11% of school-aged children in the United States.⁴ Children with ADHD are more prone to severe trauma and injuries,^{5–9} and more likely to be hospitalized for nonfatal injuries and burns compared to those without ADHD.^{7,10,11} Whether ADHD is more frequently associated with other conditions (e.g., asthma, diabetes, infection, etc.) which result in hospital admission or severe illness leading to admission to the pediatric intensive care unit (PICU) has not been well studied.

ADHD is characterized by forgetfulness, inability to pay attention to details, and difficulty organizing tasks.¹² These symptoms, which tend to cluster in families,¹³ may plausibly increase the likelihood that children and families with ADHD fail to adhere to health recommendations, such as remembering controller asthma medication, properly monitoring glucose in diabetes, and taking prescribed medications for infection. As a result, children with ADHD may be at risk for complications from illness and chronic disease, resulting in increased rates of admission to the hospital and to the PICU.

To our knowledge, there are no published studies characterizing the prevalence of ADHD and other pediatric neurodevelopmental and behavioral disorders in the PICU population, nor are there studies quantifying ADHD symptomatology after discharge. We hypothesized that the prevalence of ADHD among school-aged patients in the PICU is high, and ADHD symptoms may likely worsen after discharge because of the stress and trauma of critical illness. Additionally, we expected that children with any neurodevelopmental disability would be overrepresented among children with critical illness.

Methods

Study Design

We conducted a prospective cohort study of PICU children who were hospitalized between May and August 2016 in our urban, academic, tertiary care PICU in Chicago which admits both medical and surgical patients. Parents/guardians of children who screened positive for ADHD, but who were not already under the care of a specialist for ADHD management, were offered an appointment in the Developmental and Behavioral Pediatrics (DBP) Outpatient Clinic 1 month after hospital discharge. Parents/guardians of children who did not screen positive for ADHD or who were already seeing a subspecialist for their ADHD management were contacted one month after PICU discharge for a telephone interview.

Subject Recruitment

We recruited all children admitted to the PICU who were school-aged (6–12 years), attending school, or anticipated to be re-enrolled in school if school was not in session during the PICU admission. Children who were in the legal custody of the state or who were not from English-speaking families were excluded. After receiving approval from the medical team, parents were approached for informed consent. This study was approved by the institutional review board at The University of Chicago.

Measures

Baseline information was collected during admission. Parents were asked to complete questionnaires, which included standardized testing instruments and were also interviewed regarding school supports and neurodevelopmental history. All follow-up questionnaires were completed by telephone or in the DBP Outpatient Clinic.

Demographic and Medical Information—Age, sex, and insurance status were collected from the medical record. For enrolled subjects, parents provided information on their child's race and ethnicity. Admission and discharge dates, mode of transport to the PICU, primary reason for admission (categorized into medical, surgical, or trauma), duration of mechanical ventilation, requirement for cardiopulmonary resuscitation, and use of invasive devices were determined from the medical record.

Educational History—Parents were asked questions about their child's current grade in school, participation in a Special Education Programs, Individualized Education Programs (IEP), and EI therapies.

Neurodevelopmental History—Parents were asked questions about their child's emotional/behavioral disorders, history of neurodevelopmental or psychiatric care (child neurologist, child psychiatrist, or DBP pediatrician), current therapies, and medications for behavior, attention, or mood problems.

ADHD Screening—We used the Vanderbilt Attention Deficit Hyperactivity Disorder Parent Rating Scale (Vanderbilt) to screen patients for ADHD. The Vanderbilt is a reliable and cost-effective tool for diagnosing ADHD in a community sample, and has been shown to be consistent with the diagnostic criteria for ADHD for predominantly inattentive, predominantly hyperactive/impulsive, or combined inattention/hyperactivity subtypes.¹⁴ The Vanderbilt questionnaire was administered at enrollment and again at follow-up 1 month after discharge. A diagnosis of ADHD (inattentive, hyperactive, or combined subtypes) requires a score of 2 or 3 on 6 or more subtype specific items and a problematic score on any of the performance measures. For the purposes of our study, parent responses to the Vanderbilt and reported prior diagnoses and medications were reviewed by a DBP pediatrician and the subject was classified as either having or not having ADHD.

Emotional/Behavioral Disorder Screening—The Strengths and Difficulties Questionnaire (SDQ) was administered at enrollment and follow-up. The SDQ is an effective screening tool for a number of child psychiatric disorders that has been validated in a community sample.^{15,16} The questionnaire generates scores for total difficulties, emotional problems, conduct problems, hyperactivity, peer problems, and prosocial behavior, and combines responses to generate diagnostic predictions (low, medium, and high risk) of an emotional disorder, a behavioral disorder, a hyperactivity or concentration disorder, or any disorder. Medium- and high-risk categories were combined for the analysis.

Statistical Methods

Study data were collected and managed using REDCap electronic data capture tools.¹⁷ Characteristics of those who enrolled were compared to those who did not using Student's 2-sample *t* tests or Wilcoxon rank-sum tests for continuous variables, and chi-square tests or Fisher's exact tests for categorical variables. Assessment of changes in outcomes over time was performed using mixed-effects or generalized estimating equation (GEE) linear or logistic regression models that account for the correlation between multiple observations per patient. Statistical analyses were completed using Stata/SE 14 (Stata Corp, College Station, TX). Statistical significance was defined as a 2-tailed *p* value less than .05.

Results

We screened 253 children in the PICU. Fifty-two children were eligible, and 33 (63%) of the eligible children were approached. (Figure 1) Regarding those not approached, study staff were not available for 9 patients, parents were not available for 8 patients, and the medical team declined study inclusion due to severity of illness or injury for 2 patients. Of the 33 families approached, 24 (73%) consented to participate in the study. Seventeen of the 24 families (71%) completed follow-up, 16 by phone and 1 during a follow-up appointment in the DBP Outpatient Clinic. One additional patient met criteria for a follow-up appointment, but was unable to attend secondary to insurance reasons. Follow-up was completed an average of 40.1 days (SD = 7.6 days) after hospital discharge.

At recruitment, the mean age of those enrolled was 9.3 ± 2.1 years and 14 (58%) were male. (Table 1) Forty-two percent of enrolled patients were non-Hispanic African American, 25% were non-Hispanic white, 17% were Hispanic, and 17% reported mixed or other race. Half of the participants had public insurance, 46% had private insurance, and 1 participant (4%) had both public and private insurance. Thirteen patients (54%) were admitted for medical reasons such as diabetic ketoacidosis, asthma exacerbation, or infection. A quarter of patients were admitted for a surgical intervention and 5 patients (20%) were admitted for traumatic injury. Length of stay in the hospital ranged from 2 to 12 days, with an average stay of 5.4 ± 2.8 days. The study cohort did not differ significantly from eligible nonparticipants with regard to age, gender, race/ethnicity, insurance status, or reason for admission.

Nine participants (38%) had an IEP, and 6 (25%) were enrolled in special education (Table 2). Ten children (42%) had a prior neurodevelopmental diagnosis, with most reporting multiple diagnoses ($n = 6$). The most common conditions reported were ADHD ($n = 6$), epilepsy ($n = 6$), and developmental delay ($n = 3$). Twelve participants (50%) had seen a child neurologist, psychiatrist, or DBP pediatrician in the past, and 9 (38%) were currently seeing at least 1 such specialist. Five patients (22%) were receiving a medication for a behavior, attention, or mood disorder.

Nearly a third of the enrolled patients ($n = 7$) were determined to have ADHD. Of these, 6 had been previously diagnosed with ADHD; 1 did not report a previous diagnosis, but was receiving stimulant treatment. Five of these patients had ADHD-range symptoms on the Vanderbilt screen at the time of enrollment (Table 3). Of those who met Vanderbilt criteria, 2

were identified as having ADHD–Inattentive subtype, 1 as having ADHD–Hyperactive subtype, and 2 as having ADHD–Combined Inattention/Hyperactivity. Six of the children with ADHD were receiving some form of treatment; 4 were taking medication and seeing a neurodevelopmental specialist (child neurologist 2, DBP 1, and both a child neurologist and DBP 1), 1 was taking medication only, and 1 was seeing a child neurologist only.

At follow-up, there were no significant differences found between inattention symptoms or the overall number of children who met ADHD criteria (Table 3), though there was a trend toward increased hyperactivity symptoms ($p = .09$). Twenty-six percent of subjects were found to be at medium or high risk for having any hyperactive, concentration, emotional, or behavioral disorder on the baseline SDQ versus 29% at follow-up ($p > .05$).

Discussion

We observed high levels of children with ADHD in the PICU population (29%), nearly triple the population rate of 11%⁴ and high rates of children screened at risk for any behavioral, emotional, or hyperactive/inattentive disorder (26%). Furthermore, 42% of our subjects had a neurodevelopmental diagnosis. These results suggest that children who have critical illness have high levels of premorbid neurodevelopmental needs as compared with the general population.

The high burden of both premorbid and post-PICU neurodevelopmental issues suggests a potential need for in-PICU screening for children's educational and behavioral competencies, as well as developing follow-up programs implemented by multidisciplinary teams, which may include partnerships between critical care and neurodevelopmental specialists, such as developmental and behavioral pediatricians, child psychiatrists, child neurologists, pediatric mental health providers, physiatrists, and educational advocates. Further studies are needed to clarify the prevalence of neurodevelopmental disabilities in the PICU, the post-PICU outcomes in children with neurodevelopmental disability, and what specific outpatient supports are needed.

We observed a trend toward significantly increased hyperactive symptoms in follow-up, which is consistent with our hypothesis that stress and trauma may manifest with attention and behavioral symptoms in children. This observation was not significant; our pilot study did not have sufficient power to detect this change because of a small sample size and incomplete follow-up. Larger studies are needed to investigate the effects of critical illness and a PICU hospitalization on children's behavior and emotions after discharge, both in the general PICU population and in children with preexisting neurodevelopmental comorbidities.

We recruited exclusively from a single urban, academic, tertiary care, children's hospital. Other clinical contexts, for example, community hospitals, may have distinct admission patterns with a different prevalence of neurodevelopmental disorders. We note that the majority of children in our study had previously been cared for by a neurodevelopmental specialist and nearly half had at least one neurodevelopmental diagnosis. Nearly a third of children were receiving therapy of some kind, a third had received EI services, and one fifth

were receiving pharmacotherapy to address behavior, attention, or mood. We recognize the potential selection bias for subspecialty access and service utilization which may have resulted from recruiting at a single pediatric center. The relative abundance of available subspecialists may not be universal.

In summary, our data suggest children admitted for critical illness have a high prevalence of neurodevelopmental disabilities. The Vanderbilt ADHD screen and Strengths and Difficulties Questionnaire may be useful tools to identify children who struggle with daily behavioral health at home and school. Future investigation should focus on understanding needs of this population in the setting of critical illness, incorporating a patient-centered approach, and ultimately developing PICU follow-up programs to support these vulnerable children.

Acknowledgments

We would like to acknowledge the PICU parents who participated in this study in spite of the tremendous demands of their time during their child's critical illness. We also wish to acknowledge Kristin Wroblewski, MS, for her consultation on statistical analysis.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Sarah A. Sobotka received support from The University of Chicago Patient Centered Outcomes Research K12 Training Program (5K12HS023007) and the T73 Leadership Education in Neurodevelopmental and Related Disorders Training Program (LEND).

Sarah Peters was supported by The University of Chicago Pritzker School of Medicine Summer Research Program.

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Figure 1.
Study design and enrollment.

Table 1Baseline Characteristics of Study Population.^a

	Enrolled (n = 24)	Not Enrolled ^b (n = 28)	P
Mean age, years (SD)	9.3 (2.1)	9.4 (2.3) (n = 25)	.92
Sex			
Male	14 (58.3)	14 (51.9)	.64
Female	10 (41.7)	13 (48.1)	
Race/Ethnicity ^c			.06 ^d
Non-Hispanic black/African American	10 (41.7)	19 (79.2)	
Non-Hispanic white/Caucasian	6 (25.0)	3 (12.5)	
Hispanic	4 (16.7)	1 (4.2)	
Other	4 (16.7)	1 (4.2)	
Insurance status			.06 ^d
Public insurance only	12 (50.0)	21 (77.8)	
Private insurance only	11 (45.8)	6 (22.2)	
Both	1 (4.2)	0 (0)	
Reason for admission			
Medical	13 (54.2)	19 (70.4)	.53 ^d
Surgical	6 (25.0)	4 (14.8)	
Trauma	5 (20.8)	4 (14.8)	
Median length of stay, days (IQR)	5 (4–8)	4 (3–13)	.47 ^e
Mode of transport to PICU			
From floor	10 (41.7)	7 (25.9)	.34
From ED	7 (29.2)	13 (48.2)	
Transfer from other hospital	7 (29.2)	7 (25.9)	
Cardiopulmonary resuscitation	1 (4.2)	1 (3.7)	1.00 ^d
Surgical procedure	16 (66.7)	9 (33.3)	.02
Intubated and mechanically ventilated in PICU	5 (20.8)	4 (14.8)	.72 ^e
Median ventilator days (IQR)	1 (1–5)	7 (2.5–13.5)	.14 ^e
Tracheostomy and mechanically ventilated	1 (4.2)	4/27 (14.8)	.35 ^d
Presence of invasive device(s)			
Endotracheal tube	15 (62.5)	9/27 (33.3)	.04
Arterial line	12 (50.0)	10/27 (37.0)	.35
Foley catheter	12 (50.0)	10/27 (37.0)	.35
NG tube/sump	5 (20.8)	6/27 (22.2)	.90
PICC/central line	5 (20.8)	7/27 (25.9)	.67
Chest tube	0 (0)	1/27 (3.7)	1.00 ^c
External ventricular drain	0 (0)	1/27 (3.7)	1.00 ^d
Other	4 (16.7)	0/27 (0)	.04 ^d

Abbreviations: PICU, pediatric intensive care unit; ED, emergency department; NG, nasogastric; PICC, peripherally inserted central catheter; IQR, interquartile range.

^aValues in table are n (%) unless otherwise noted and *P* values are from 2-sample *t* tests for continuous variables and chi-square tests for categorical variables unless otherwise noted.

^bAge was not collected for 3 nonenrolled participants, n = 25. For length of stay and other critical care variables, medical chart extraction was not completed for 1 nonenrolled participant, n = 27.

^cRace/Ethnicity reported by parent for enrolled group, taken from medical chart for those not enrolled.

^dFisher's exact test.

^eWilcoxon rank-sum test.

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Table 2

School, Therapy, and Neurodevelopmental Characteristics of Study Population (n = 24).

Characteristic	n (%)
Grade in school	
Kindergarten	4 (17)
1st	3 (13)
2nd	3 (13)
3rd	2 (8)
4th	4 (17)
5th	5 (21)
6th	2 (8)
7th	1 (4)
Special education	6 (25)
Individual Education Program (IEP)	9 (38)
Previous neurodevelopmental diagnoses	
Any diagnosis	10 (42)
Attention deficit hyperactivity disorder (ADHD)	6 (25)
Epilepsy	6 (25)
Developmental delay	3 (13)
Autism (or spectrum disorder)	1 (4)
Behavioral or conduct problems	1 (4)
Learning disorder	1 (4)
Other	1 (4)
Early Intervention	
Any Early Intervention services	7 (29)
Speech therapy	6 (25)
Physical therapy	5 (21)
Occupational therapy	5 (21)
Developmental therapy	3 (13)
Feeding therapy	3 (13)
Nutritional therapy	1 (4)
Social work	1 (4)
Current therapy	
Any therapy	7 (29)
Occupational therapy	6 (25)
Speech therapy	4 (17)
Physical therapy	3 (13)
Behavior therapy	1 (4)
Psychotherapy	1 (4)
Past neurodevelopmental specialists	
Any specialist	12 (50)
Child neurologist	10 (42)

Characteristic	n (%)
Developmental and behavioral pediatrician	6 (25)
Child psychiatrist	5 (21)
Other	1 (4)
Current neurodevelopmental specialists	
Any specialist	9 (38)
Child neurologist	8 (33)
Developmental and behavioral pediatrician	3 (13)
Child psychiatrist	0 (0)
Medication for behavior, attention, or mood	5 (22)

Table 3

Comparison of Parent-Rated Vanderbilt and Strengths and Difficulties Questionnaire Scores at Enrollment and Follow-up.^a

	PICU (n = 24)	Follow-up (n = 17)	<i>P</i> ^b
ADHD/Vanderbilt Assessment Scale			
Inattention, n (%)			.61
0 items	15 (62.5)	11 (64.7)	
1–5 items	5 (20.8)	4 (23.5)	
6 items	4 (16.7)	2 (11.8)	
Hyperactivity, n (%)			.09
0 items	13 (54.2)	6 (35.3)	
1–5 items	8 (33.3)	7 (41.2)	
6 items	3 (12.5)	4 (23.5)	
Met Vanderbilt ADHD criteria, n (%)	5 (20.8)	4 (23.5)	.93
Total symptom score, median (IQR)	8.5 (4.0–18.0)	11.0 (5.0–19.0)	.71
Strengths and Difficulties Questionnaire ^c			
Hyperactivity or concentration disorder	n=23	n=17	.51
Low risk	18 (78.3)	12 (70.6)	
Medium/High risk	5 (21.7)	5 (29.4)	
Emotional disorder	n=23	n=16	.15
Low risk	22 (95.7)	13 (81.3)	
Medium/High risk	1 (4.4)	3 (17.6)	
Behavioral disorder	n = 22	n = 16	—
Low risk	22 (100)	16 (100)	
Medium/High risk	0	0	
Any disorder	n = 23	n = 17	.92
Low risk	17 (73.9)	12 (70.6)	
Medium/High risk	6 (26.1)	4 (29.4)	

Abbreviations: PICU, pediatric intensive care unit; ADHD, attention deficit hyperactivity disorder; IQR, interquartile range.

^a A sensitivity analysis was completed comparing participants who completed follow-up versus those lost to follow-up; no significant differences were found; all enrolled participants were included in the analysis.

^b *P* values for inattention, hyperactivity, and total symptom scores generated using mixed model on square root transformed scores. *P* value for ADHD criteria generated using generalized estimating equation (GEE) logistic model. *P* value for hyperactivity or concentration disorder generated by mixed-effects logistic model. *P* value for emotional and any disorder generated by GEE logistic model.

^c For analysis purposes, the medium- and high-risk categories were combined because of small numbers.