Pediatric Oncology and Bone Marrow Transplant ICU Patients in Children's and General Hospitals

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Abstract

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Pediatric oncology and hematopoietic stem cell (HCT) care in the US is increasingly provided at children's hospitals (CH), but many children still receive care at general hospitals (GH). Little is known about the characteristics of pediatric oncology and HCT patients treated in intensive care units (ICUs) at these institutions, or how outcomes differ for patients treated in CH and GH. Using data from ICU admissions of pediatric oncology and HCT patients in the U.S. during 2001-2019, we examined possible differences between patients treated at CH versus GH with regard to characteristics that could bear on illness outcomes. Specifically, we used the Healthcare Cost and Utilization Project's State Inpatient Databases from a total of 21 U.S. states for 2001, 2004, 2010, 2016, and 2019. We used ICD-9 and 10 codes to identify diagnoses, chronic comorbidities and American Hospital Association linkage files to identify hospital type. Also, we

evaluated changes over time in the proportions of American pediatric ICU patients seen at CH versus GH. During the five years for which data were examined, there were 9,306 oncologic admissions and 1,497 HCT admissions to CH ICUs; over the same time period, there were 2,038 oncologic admissions and 238 HCT admissions to GH ICUs. There was little difference in the demographic characteristics of patients seen in the two ICU locations. The presence of chronic co-morbidities was somewhat greater in CH than GH patients (61.7% vs. 50.0%). The results of this study suggest that comparisons of illness outcomes for pediatric ICU patients with malignancies or HCT between CH and GH will not be appreciably confounded by differences in demographic characteristics. Subsequent studies that are able to assess illness severity at the time of admission will be needed to gauge the potential for confounding from this source.

INTRODUCTION

In 2024, there were approximately 15,000 new pediatric cancer cases in the United States.[1] It is expected that nearly half of these patients will have an intensive care unit (ICU) admission at some point during the course of their cancer treatment.[2-4] Among pediatric patients who have undergone a hematopoietic stem cell transplant (HCT), up to 39% will have an ICU admission following transplant.[5-8] In the US, ICUs are located in both specialized children's hospitals (CH) [9,10] and in general, non-children's hospitals (GH).[11-13] Given the high prevalence of ICU admission during oncologic and HCT treatment, the critical care capabilities of the location where patients receive hospital care may play a role in patient outcomes. For certain pediatric conditions, such as trauma, children have improved health outcomes on average when treated at a children's hospital compared to a general hospital.[14-16] There is a suggestion that the same is true among children hospitalized for cancer [13,17,18] or for centers that have higher volumes of pediatric oncology cases.[19] Specifically with regard to children with a hematologic malignancy or who have undergone HCT being treated in an ICU, the validity of studies that seek to compare health outcomes according to the location of the ICU will be enhanced by being able to control for patient characteristics that bear on the occurrence of these outcomes. In order to identify differences in these characteristics of pediatric ICU patients with malignancies or following HCT in relation to location of the ICU (CH versus GH), we analyzed data obtained from ICUs in 21 states in five separate years during 2001-2019.

Previous studies have demonstrated an increase in the risk of pediatric intensive care unit (PICU) admission over time both in general hospitalized pediatric populations and in oncologic populations.[5,10,20] Temporally, the risk of being admitted to a CH ICU decreased over time while the risk of being admitted to a GH ICU increased over time for patients who underwent HCT.

These trends may reflect multiple contributing factors, including hospital proximity and severity of illness at presentation; are children who seek care at GH more chronically ill at baseline or do they have a higher acute illness severity? Understanding historical trends in CH vs GH ICU admission for these patients can help detect the impact of broader changes, such as shifts in healthcare access sites or policy changes. Similarly, knowing the trends over time can guide interventions or support resource allocation decisions.

METHODS & MATERIALS

Study Design

We used the Healthcare Cost and Utilization Project's (HCUP) State Inpatient Databases (SIDs) from 21 geographically dispersed U.S. states in 2001, 2004, 2010, 2016, and 2019. We only included states that submitted SIDs to HCUP with revenue codes, which permitted identification of ICU care. These SIDs include inpatient records for all discharges from non-federal acute care hospitals in each state. We followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.[21] The study was exempt from human subject review as determined by the Seattle Children's Hospital Institutional Review Board.

Participants

We included all children aged 0-17 years with an oncologic or HCT diagnosis, as identified using *International Classification of Diseases, Ninth and Tenth Revision* (ICD-9 and ICD-10) codes, who were admitted to any non-neonatal ICU. We excluded those admitted to rehabilitation and psychiatric hospitals. Hospital type was categorized via the American Hospital Association's (AHA) designation for each included institution as a CH or GH. Patient characteristics including age, sex, race, ethnicity, and insurance status were included in the SIDs as reported by individual hospitals. We used ArcGIS to calculate the distance between the centroids of patients' home zip codes, their admitting hospital, and the closest children's hospital. We used ICD-9 and ICD-10 codes to identify diagnoses and comorbid conditions and classified the presence of chronic comorbidities using the Pediatric Complex Chronic Conditions classification system,[22] excluding codes for hematologic or oncologic conditions. Patients were diagnosed with MODS if they had two or more dysfunctional organ systems. We stratified

patients as having hematologic malignancies, solid malignancies, and HCT admissions, and then further tallied specific oncologic diagnoses.

Statistical Analysis

We summarized categorical variables using percentages and continuous variables using medians and interquartile ranges (IQR). We used generalized linear Poisson regression to estimate the relative risk (RR) of each categorical variable in each year relative to 2001. We calculated a ratio of CH to GH counts for each year to assess proportional change over time. We conducted all analyses using Stata version 17 (StataCorp LLC, College Station, TX).

RESULTS

Cohort Description

There were 82,988 total hospitalizations among oncologic patients and 7,381 total hospitalizations among patients with HCT across the five sample years. Of those hospitalizations, there were 9,306 oncologic admissions and 1,497 HCT admissions in CH ICUs (Table 1). Over the same time period, there were 2,038 oncologic admissions and 238 HCT admissions in GH ICUs. The two groups of pediatric ICU patients differed little with regard to age, gender, and race/ethnicity. Patients admitted to CH ICUs more commonly had public insurance than patients admitted to GH ICUs (38.0% vs 26.5%) and had a higher prevalence of one or more chronic comorbidities (61.7% vs 50.0%). The proportion of admitted patients living >50 miles from the admitting hospital were similar in both CH and GH ICUs (35.2% vs 32.6%, respectively).

ICU Admission Trends

Among children with an oncology or HCT diagnosis admitted to a CH, the proportion admitted to the ICU during their hospitalization decreased from 14.5% in 2001 to 13.6% in 2019. The corresponding proportions for GH were 13.6% in 2001 and 14.9% in 2019 (Table 2). From 2001 to 2019, the proportion of oncology and HCT patients admitted to ICUs identifying as Hispanic increased from 10.6% to 15.4% in CH (RR 1.45, 95% CI 1.14-1.86) and increased from 8.3% to 17.8% in GH (2.14, 95% CI 1.27-3.58). Among Hispanic patients admitted to ICUs, the proportion in a CH (as opposed to a GH) increased from 70.3% to 93.0% over the same timeframe. In both CH and GH ICUs, the proportion of patients who had public insurance rose during 2001-2019: from 24.1% to 44.4% in CH and from 20.7% to 44.4% in GH. Among children with cancer or who were undergoing HCT who were admitted to an ICU, the proportion

who had one or more chronic comorbidities increased during 2001 to 2019, both in CH (45.3% to 71.7%; RR 1.58, 95% CI 1.47-1.71) and GH (43.2% to 64.8%; RR 1.50, 95% CI 1.29-1.74). In these children with chronic comorbidities who were admitted to an ICU, the proportion treated at a CH (as opposed to a GH) increased from 64.1% to 93.5%. Illness severity, measured by proportion of ICU admissions with MODS, increased over time across all groups, with a greater absolute rise in CH than in GH from 2001 to 2019. The absolute peaks were also higher in CH compared to GH for children with oncology (34.6% vs 20.4%) and HCT diagnoses (40.8% vs 28.6%).

Trends in ICU Admission by Oncology and HCT Diagnosis

For children with each specific oncology and HCT diagnoses examined, the proportion admitted to an ICU in a CH increased between 2001 to 2019 (Table 3). Across all oncologic diagnoses, the proportion admitted to CH ICUs increased from approximately 60% in 2001 to over 90% in 2019, with the biggest absolute difference occurring in lymphoma and the smallest absolute difference occurring in patients with Acute Lymphoblastic Leukemia (ALL). The proportion of patients with HCT due to oncologic conditions admitted to ICUs in a CH also increased, but to a somewhat lesser extent.

DISCUSSION

In this large, national dataset, we investigated admission patterns and ICU admission prevalence in pediatric oncology and HCT patients within CHs and GHs. We discovered that the proportion of patients admitted to CH ICUs relative to GH ICUs increased from 2001 to 2019. In such patients receiving ICU care in CH and GH, there were no appreciable demographic differences, and the hospital distance from a child's home was similar in both CH and GH. Those admitted to a CH ICU in recent years had a higher prevalence of chronic illness compared to those admitted to a GH ICU.

Few prior studies have taken a comprehensive, systems-level approach to examining how geographic and sociodemographic factors may shape where children with cancer or undergoing HCT receive care. One study in Japan noted that the travel burden was higher for children who required specialized oncologic care yet resided in rural areas.[23] This was consistent in both adult and pediatric oncologic populations in the US.[24,25] Some families opt to relocate from rural settings to be closer to specialized pediatric cancer centers to continue receiving care.[26] Our findings build on the notion that the location of a child's home plays a role in where patients seek care. We found that children and families traveled similar distances to both CH and GH for care, yet nearly one-third of patients traveled >50 miles in either case. We also expand on earlier studies by including children who underwent HCT in our analysis. Given that a significant number of patients traveled substantial distances, access and urgency may have influenced their choice to receive care at GHs.

Beyond geographic proximity, differences in chronic health burden may influence whether children with cancer or those undergoing HCT receive care at a CH or GH ICU. Our findings suggest that in recent years CH ICUs more commonly care for children with chronic

illness compared go GH ICUs. We found a higher prevalence of chronic comorbidities and a greater proportion of patients with MODS among those admitted to CH ICUs compared to GH ICUs. However, because our data do not capture the timing of MODS onset, we cannot exclude the possibility that patients presenting to GHs were more acutely ill at the time of admission, which may have driven ICU admission at those sites. The research on pediatric illness severity at presentation to non-CH ICUs remains limited. One study from 2015 found that GHs were less likely than CHs to perform invasive procedures for critically ill pediatric patients.[27] This pattern appears to be evolving for the pediatric oncologic population, where the likelihood of receiving interventions in PICUs has increased in recent years relative to previous years.[20] GHs may function as access points to stabilize children, which may be necessary in an ICU, before potentially transferring to a CH ICU for more advanced and prolonged care.

Our study had several limitations. Our administrative dataset is based principally on billing codes and lacks granular clinical detail. In particular, we were unable to determine timing of events, such as the development of organ failure or MODS, and therefore cannot determine if patients were admitted with certain conditions or developed them afterwards. This is important in analyzing differences in populations as the increased risk over time of GH ICU admission for HCT patients previously described[5] may be due to hospital capabilities or comfort as opposed to patient clinical characteristics. There also may be some changes in prevalence of diagnoses as coding transitioned from ICD-9 to ICD-10 during the years of our study. This could alter sensitivity and specificity of diagnoses. While we categorized hospital type through AHA designation at the level of the hospital, there remains potential for misclassification error. Some GHs may see more pediatric patients than other centers designated as CHs, or some GHs may have pediatric floors but are still classified as GHs. Such variability in hospital function

146 challenges the binary classification of hospital type and could obscure meaningful differences in
147 care delivery and outcomes. Several studies have recognized this labeling challenge and utilized
148 alternative strategies to categorize hospitals, including combining datasets,[27] number of pediatric
149 admissions,[28] hospital pediatric bed capacity,[29] or proportion of patients seen under age 18.[30]
150 Ultimately, these methods seeks to better capture the functional role of CH or GH in pediatric
151 critical care, though each has its own advantages and disadvantages to consider.

CONCLUSION

We found that over time in the US, CH have an increasingly larger proportion of ICU admissions for oncology and HCT patients, though GH ICUs continue to care for many of these patients. Those admitted to CH ICUs have higher prevalence of chronic illness and higher prevalence of MODS during hospitalization. Our findings suggest that demographic differences are unlikely to substantially confound comparisons of outcomes between CH and GH ICUs for children with malignancies or those undergoing HCT. Future research incorporating measures of illness severity at the time of ICU admission will be essential to fully assess potential residual confounding when comparing outcomes of pediatric ICU patients in relation to the location of the ICU.

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Table 1: Patient Characteristics of ICU Patients from 2001 to 2019

	Oncology and HCT, 2001-2019	
Characteristic	CH	GH
ICU Admissions, No. (% of hospitalizations)		
Oncology	9,306 (13.8)	2,038 (14.0)
HCT	1,497 (25.1)	238 (17.5)
Female, No. (% of ICU admits)	4,455 (44.3)	967 (45.2)
Age, median (IQR)	7 (3-13)	8 (3-13)
Ethnicity, No. (% of ICU admits)		
Another	717 (8.8)	95 (6.4)
Asian or Pacific Islander	371 (4.5)	64 (4.3)
Black, non-Hispanic	1,063 (13.0)	184 (12.4)
Hispanic	1,074 (13.1)	194 (13.1)
White, non-Hispanic	4,978 (60.7)	942 (63.7)
Insurance, No. (% of ICU admits)		
Public	3,817 (38.0)	566 (26.5)
Private	5,643 (56.2)	1,442 (67.5)
Other	585 (5.8)	128 (6.0)
Distance to Hospital (miles), No. (% of ICU admits)		
<15	2,611 (32.6)	591 (36.6)
15-50	2,576 (32.2)	498 (30.8)
50-100	1,235 (15.4)	218 (13.5)
>100	1,584 (19.8)	308 (19.1)
Chronic comorbidities, No. (% of ICU admits)	6,211 (61.7)	1,069 (50.0)

CH = Children's Hospitals, GH = General Hospitals, ICU = Intensive Care Unit, No = Number

Table 2: Patient Characteristics for Oncology & HCT Over Time Admitted to ICUs

	Year				
	2001	**2004**	**2010**	**2016**	**2019**
ICU Admissions, No. (% of Hospitalizations)					
CH	923 (14.5)	1,342 (15.1)	2,696 (15.1)	2,984 (13.9)	2,120 (13.6)
RR (95% CI)	Reference	1.04 (0.96-1.12)	1.04 (0.97-1.12)	0.96 (0.90-1.03)	0.94 (0.87-1.01)
GH	542 (13.6)	450 (12.9)	578 (14.7)	406 (15.4)	162 (14.9)
RR (95% CI)	Reference	0.95 (0.85-1.07)	1.08 (0.97-1.20)	1.13 (1-1.27)	1.10 (0.93-1.29)
CH:GH (%)	63.0	74.9	82.3	88.0	81.4
Female, No. (% of ICU admits)					
CH	437 (47.4)	592 (44.1)	1,214 (45.0)	1,265 (42.4)	947 (44.7)
RR (95% CI)	Reference	0.93 (0.85-1.02)	0.95 (0.88-1.03)	0.90 (0.83-0.97)	0.94 (0.87-1.03)
GH	239 (44.1)	205 (45.6)	260 (45.0)	187 (46.1)	76 (46.9)
RR (95% CI)	Reference	1.03 (0.90-1.19)	1.02 (0.89-1.16)	1.04 (0.91-1.20)	1.06 (0.88-1.29)
CH:GH (%)	64.6	74.3	82.4	87.1	92.6
Hispanic, No. (% of ICU admits)					
CH	71 (10.6)	108 (11.4)	283 (11.4)	334 (14.5)	277 (15.4)
RR (95% CI)	Reference	1.08 (0.81-1.43)	1.08 (0.84-1.37)	1.37 (1.08-1.74)	1.45 (1.14-1.86)
GH	30 (8.3)	30 (10.5)	67 (19.3)	46 (12.6)	21 (17.8)
RR (95% CI)	Reference	1.25 (0.77-2.03)	2.31 (1.5-3.46)	1.51 (0.97-2.33)	2.14 (1.27-3.58)
CH:GH (%)	70.3	78.3	80.9	87.9	93
Public Insurance, No. (% of ICU admits)					
CH	222 (24.1)	419 (31.2)	995 (36.9)	1,252 (42.1)	937 (44.4)
RR (95% CI)	Reference	1.30 (1.13-1.49)	1.54 (1.36-1.74)	1.75 (1.55-1.97)	1.85 (1.63-2.09)
GH	112 (20.7)	115 (25.6)	162 (28.1)	106 (26.1)	72 (44.4)
RR (95% CI)	Reference	1.24 (0.98-1.55)	1.36 (1.10-1.68)	1.26 (1.00-1.59)	2.15 (1.69-2.73)
CH:GH (%)	66.5	78.5	86.0	92.2	92.9
Chronic comorbidities, No. (% of ICU admits)					
CH	418 (45.3)	660 (49.2)	1,583 (58.7)	2,031 (68.1)	1,519 (71.7)
RR (95% CI)	Reference	1.09 (0.99-1.19)	1.30 (1.19-1.40)	1.50 (1.39-1.62)	1.58 (1.47-1.71)
GH	234 (43.2)	218 (48.4)	276 (47.8)	236 (58.1)	105 (64.8)
RR (95% CI)	Reference	1.12 (0.98-1.29)	1.11 (0.97-1.26)	1.35 (1.19-1.53)	1.50 (1.29-1.74)
CH:GH (%)	64.1	75.2	85.1	89.6	93.5
MODS, No. (% of ICU admits)					
Oncology					
CH	61 (11.7)	116 (13.5)	418 (25.1)	713 (30.3)	568 (34.6)
GH	40 (9.3)	35 (9.9)	88 (17.1)	115 (37.1)	20 (20.4)
HCT					
CH	6 (17.1)	33 (23.1)	110 (35.5)	94 (28.7)	86 (40.8)
GH	7 (17.1)	10 (24.4)	11 (20.4)	12 (30.0)	6 (28.6)

CH = Children's Hospital, GH = General Hospital, ICU = Intensive Care Unit, MODS = Multiple Organ Dysfunction Syndrome, No = Number, RR = Relative Risk

Table 3: ICU Admission Proportion by Immunocompromise Diagnosis Over Time

	Year				
Diagnosis	2001	2004	2010	2016	2019
Hematologic Malignancy					
ALL, No. (%)					
CH	175 (66.8)	242 (71.6)	511 (82.2)	590 (90.2)	477 (90.7)
GH	87 (33.2)	96 (28.4)	111 (17.9)	64 (9.8)	49 (9.3)
AML, No. (%)					
CH	80 (65.0)	128 (81.5)	246 (86.9)	185 (86.0)	122 (95.3)
GH	43 (35.0)	29 (18.5)	37 (13.1)	30 (14.0)	6 (4.7)
Lymphoma, No. (%)					
CH	29 (56.9)	66 (71.7)	83 (79.8)	177 (83.9)	148 (93.7)
GH	22 (43.1)	26 (28.3)	21 (20.2)	34 (16.1)	10 (6.3)
Solid Malignancy					
Brain, No. (%)					
CH	300 (63.0)	447 (79.5)	861 (86.7)	950 (91.7)	611 (93.6)
GH	176 (37.0)	115 (20.5)	132 (13.3)	86 (8.3)	42 (6.4)
NBL, No. (%)					
CH	127 (58.0)	138 (65.7)	250 (65.8)	267 (82.9)	160 (91.9)
GH	92 (42.0)	72 (34.3)	130 (34.2)	55 (17.1)	14 (8.1)
HCT					
Oncology, No. (%)					
CH	75 (68.2)	123 (83.7)	224 (86.2)	201 (90.1)	115 (84.6)
GH	35 (31.8)	24 (16.3)	36 (13.9)	22 (9.9)	21 (15.4)

ALL = Acute Lymphoblastic Leukemia, AML = Acute Myeloid Leukemia, CH = Children's Hospital, GH = General Hospital, HCT = Hematopoietic Stem Cell Transplant, NBL = Neuroblastoma, No = Numbe